Original Article

Association between Organochlorine Exposures and Lung Functions Modified by Thyroid Hormones and Mediated by Inflammatory Factors among Healthy Older Adults

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Abstract

Objective To examine the mechanistic of organochlorine-associated changes in lung function.

Methods This study investigated 76 healthy older adults in Jinan, Shandong Province, over a five-month period. Personal exposure to organochlorines was quantified using wearable passive samplers, while inflammatory factors and thyroid hormones were analyzed from blood samples. Participants' lung function was evaluated. After stratifying participants according to their thyroid hormone levels, we analyzed the differential effects of organochlorine exposure on lung function and inflammatory factors across the low and high thyroid hormone groups. Mediation analysis was further conducted to elucidate the relationships among organochlorine exposures, inflammatory factors, and lung function.

Results Bis (2-chloro-1-methylethyl) ether (BCIE), was negatively associated with forced vital capacity (FVC, –2.05%, 95% *CI*: –3.11% to –0.97%), and associated with changes in inflammatory factors such as interleukin (IL)-2, IL-7, IL-8, and IL-13 in the low thyroid hormone group. The mediation analysis indicated a mediating effect of IL-2 (15.63%, 95% *CI*: 0.91% to 44.64%) and IL-13 (13.94%, 95% *CI*: 0.52% to 41.07%) in the association between BCIE exposure and FVC.

Conclusion Lung function and inflammatory factors exhibited an increased sensitivity to organochlorine exposure at lower thyroid hormone levels, with inflammatory factors potentially mediating the adverse effects of organochlorines on lung function.

Key words: Healthy older adults; Inflammatory factors; Lung function; Organochlorines; Thyroid hormones

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INTRODUCTION

In contemporary society, organochlorines are extensively utilized across agricultural, industrial, and household applications, including pesticides and plastics, due to their advantageous chemical properties[1,2]. During the latter half of the 20th century, global consumption of organochlorine pesticides reached a staggering 2 million tons[3]. As one of the world's leading agricultural nations, China plays a crucial and undeniable role in both the production and consumption of organochlorines[4,5]. Despite the evident benefits these compounds offer, their potential for causing environmental contamination and ecological disruption has led to the prohibition of many organochlorines under the Stockholm Convention[6]. However, the legacy of their extensive use has left a lasting imprint on the environment, presenting ongoing challenges for environmental management and posing a significant threat to human health[7-9]. In regions such as the Yangtze River Delta of China, atmospheric concentrations of organochlorines range from 17.9 to 168 pg/m^3[10], while areas more dramatically affected, such as the pesticide-contaminated southwestern regions of China, concentrations can reach as high as 195 ng/m^3[11]. These persistent environmental pollutants elevate the likelihood that these harmful substances will enter the human body, amplifying concerns regarding their health implications[12].

Extensive research has demonstrated a link between exposure to organochlorines and risks of developing chronic diseases[13,14]. The elderly population, given their physiological decline and cumulative environmental exposures, manifests heightened vulnerability to the detrimental effects of these pollutants[15,16]. The respiratory system, particularly the lungs, serve as the primary interface for interaction with airborne pollutants, rendering it especially susceptible to the detrimental effects of these compounds[17,18]. The negative impact of lung impairment on the general health and overall quality of life of the elderly cannot be ignored. While existing studies on effects of organochlorines on the lung function have predominantly concentrated on pediatric and adult populations[19,20], the relationship between these compounds and lung function in the elderly remains relatively underexplored. This knowledge gap underscores the critical need for targeted research on the impact of organochlorines on lung health, especially in the context of a rapidly aging global population.

The weakening of lung function generally involves multiple biological processes, with inflammatory responses playing a pivotal role[21,22]. The degeneration of lung tissue is frequently accompanied by the onset of inflammation, which tends to intensify when triggered by external stimuli[23,24]. This amplified inflammatory response is particularly concerning in the context of environmental pollutant exposures. In addition, thyroid hormones, recognized as crucial endocrine regulators, not only modulate metabolic processes but also significantly influence lung development and function[25,26]. However, the specific role of thyroid hormones on the association between organochlorine exposure and lung function remains largely unknown. Our prior research has identified the detrimental effects of organochlorines on lung function among 26 airborne organic pollutants[27]. Building upon these findings, this study aimed to investigate the complex interplay among organochlorine exposure, inflammatory factors, and thyroid hormone levels in relation to lung function, and to offer new insights into the mechanisms through which organochlorines affected lung health in the elderly.

MATERIALS AND METHODS

Study Design

This research constitutes a segment of the China Biomarkers of Air Pollutant Exposure (BAPE) Study, involving the recruitment of 76 healthy older adults (50% male), with ages from 60 to 69, from Jinan, Shandong Province[28]. The enrollment flowchart and the specific times of exposure measurements for the study participants have been thoroughly documented in our prior publications[28]. The initial assessment was performed at Ankang Community Hospital in September 2018, with subsequent five monthly follow-ups until January 2019. Data regarding sociodemographic factors were collected by face-to-face interviews through electronic questionnaires. In parallel, physical examinations were conducted to obtain critical metrics such as participants' height and weight. Fasting venous blood samples were also collected for subsequent analysis. It is essential to highlight that during each follow-up, participants' information underwent a comprehensive re-collection, which encompassed the measurement of exposure levels, physical examinations, and sample collection. Consequently, each participant contributed multiple data

measurements for every variable assessed throughout the study. This research was approved by the Ethics Review Committee of the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (NIEH, China CDC, No. 201816), and informed consent was obtained from all participants. Detailed research protocols have been documented in prior literature[28-30].

Exposure Assessment

Personal exposure to organochlorines was monitored using a Fresh Air wristband[31]. At each stage of the survey, participants wore these wristbands continuously for three days continuously, only removing them when showering. At the end of the exposure period, we extracted the polydimethylsiloxane sorbent bars from each wristband and transported them to the Yale School of Public Health with cold chain preservation for chemical analysis[31,32]. In this study, five specific organochlorines, namely bis (2-chloro-1-methylethyl) ether (BCIE), hexachlorobutadiene (HCBD), 4-chloroaniline, 1,3-dichlorobenzene, and 1,4-dichlorobenzene were evaluated.

Lung Function Assessment

Lung function of all participants was assessed by trained medical personnel using a spirometer (SP10BT, Oranger Technology Co. Ltd., Tianjin, China). To warrant the reliability of the results, multiple measurements were obtained for each participant, using the quality control standards outlined by the ATS/ERS guidelines[33]. This rigorous process continued until we obtained three measurements that met the predefined criteria. Subsequently, the best value was selected as the definitive result for the lung function assessment among these measurements. We evaluated four pulmonary function indicators, namely forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), the ratio of FEV_1 to FVC (FEV_1/FVC), and peak expiratory flow (PEF)[34].

Measurement of Inflammatory Factors

The serum concentrations of inflammatory factors were determined using the Luminex MagPix system with a Milliplex Mitogen-Activated Protein (MAP) High-sensitivity Human Cytokine Panel (HSCYTO-60, Millipore Corp.), adhering to the protocol of the manufacturer[30]. The concentrations of the following 13 inflammatory factors were assessed, including interleukin (IL)-1β, IL-2, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-21, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ.

Measurement of Thyroid Hormones

The serum concentrations of thyroid-stimulating hormone (TSH), triiodothyronine (T_3), and thyroxin (T_4) were quantified using fluorescence detection system (Magpix®, Luminex Corporation, Austin, TX, USA)[35]. This assay employed carboxyl-modified microspheres as reaction carrier, coupled with fluorescence-based quantification, to facilitate the simultaneous analysis of multiple analytes.

Covariate Measurement

Information on covariates such as age (years), gender (male, female), income (10,000 yuan/year), and educational attainment (below primary school, primary, junior and senior high school, and university and above) was gathered through face-to-face follow-up assessments. Body mass index (BMI, kg/m^2) was calculated using participants' height and weight measured during physical examinations, employing the formula where weight is divided by height squared. Additionally, blood samples were analyzed to determine cotinine levels (ng/mL) as an indicator of passive tobacco exposure using Hypersil GOLD C18 Selectivity HPLC Columns (ThermoFisher Scientific) interfaced with an LC-Q-Exactive Orbitrap Mass Spectrometer (ThermoFisher Scientific)[29].

Statistical Analysis

Preceding the analysis, the concentrations of organochlorines were Log_2-transformed to improve the normality of the data. For continuous variables, the mean and standard deviation (SD) were used for description, and categorical variables were characterized by percentages. And organochlorines' distribution characteristics were described employing the median and interquartile range (IQR). The inter-correlations among the 5 organochlorines were evaluated using Spearman's correlation analysis. We employed the latent profile analysis (LPA) to partition the study samples into distinct subgroups based on TSH, T_3, and T_4 levels. LPA is a robust statistical technique grounded in a mixed distribution model, aiming to discern latent, unobserved subgroups within the data[36,37]. LPA posits that the sample data originates from a mixture of distributions corresponding to distinct potential groups, each characterized by its own unique mean and variance. Specifically, LPA leveraged Bayes' theorem to assign each sample to the thyroid hormone spectrum most likely to be a

member based on the relative similarity of participants' thyroid hormone characteristics. Our analysis ultimately identified two distinct categories. One group was characterized by elevated levels of TSH, T_3, and T_4 compared to the other, leading us to designate it as the "high" group, with the other group being labeled as the "low" group. This classification was determined by comparing the relative characteristics of the thyroid hormone profiles across two groups. Subsequent analyses, including association and mediation analyses, were conducted within these two groups, both derived through the LPA method, to probe the intricate relationship between organochlorines exposure and various physiological indicators. We selected several covariates for inclusion in our analysis, specifically age, gender, income, educational attainment, BMI, and serum cotinine. The rationale for considering these covariates is multifaceted. Firstly, age and gender are fundamental demographic variables known to significantly influence both thyroid function and lung health[38-40]. Socioeconomic factors such as income and educational attainment are critical as they affect healthcare access, lifestyle choices, and exposure to environmental pollutants[41-43]. Furthermore, BMI serves as an important health indicator, closely associated with respiratory function and overall health status[44]. To control for the effect of passive smoking on the results, serum cotinine was also included as a covariate. Subsequent analyses were conducted in three stages. First, a linear mixed-effect model (LMM) was employed to examine the relationship between 5 organochlorines and 4 pulmonary function indicators, after taking into account covariates such as age, gender, income, educational attainment, BMI, and serum cotinine. Participants' ID was incorporated as a random intercept term to account for individual variations, with a false discovery rate (FDR) less than 0.05 determined statistically significant. Second, a similar approach investigated associations between 5 organochlorines and 13 inflammatory factors. Finally, mediation analyses were performed to evaluate the mediating impact of inflammatory factors on the relationship between exposure to organochlorines and lung function. Specifically, the assessment of mediating effects was based on the construction of the following two models: 1) the mediation model, which utilized a LMM to investigate the association between organochlorine exposure and inflammatory factors; 2) the outcome model, which also based on a LMM to assess the effects of both organochlorine exposure and inflammatory factors on lung function. Both models incorporated previously identified covariates. The mediation proportion was calculated using nonparametric bootstrapping (500 resampling). All data analyses were conducted using R (version 4.2.3).

RESULTS

Description of the Study Population and Characteristics of Organochlorine Exposure

After excluding missing values, we integrated 290 measurements from 75 healthy older adults into the analysis. The participants, with an average age of 65.0 ± 2.8 years, consisted of 37 males (49.3%). Table 1 presents the participant characteristics, including lung function, thyroid hormone levels, inflammatory factor concentrations, and other relevant variables. The detailed results of the five measurements of physiological indicators are provided in Supplementary Table S1. Furthermore, Supplementary Table S2 presents the organochlorine exposure levels of the participants. Consistent with previous studies[27,31], among the five organochlorines examined, 1,3-dichlorobenzene displayed the highest concentration, with a median value of 2.36 ng/m^3, while 4-chloroaniline exhibited the lowest concentration at 0.43 ng/m^3. Generally, there were positive inter-correlations among the 5 organochlorines assessed (Supplementary Table S3).

Associations between Organochlorine Exposure and Lung Function

Figure 1 illustrates the associations between personal exposure to 5 organochlorines and lung function by two groups with different levels of thyroid hormones. The results indicate that only one organochlorine, BCIE, was significantly associated with a pulmonary function indicator of FVC. This result aligns consistently with previously findings[27]. However, this association was only observed in the low thyroid hormone group. Specifically, an increase of one IQR in BCIE concentration was associated with a decrease of 2.05% (95% *CI*: –3.11%, –0.97%) in FVC.

Associations between Organochlorine Exposure and Inflammatory Factors

Figure 2 and Supplementary Table S4 show the associations between personal exposure to various organochlorines and inflammatory factors, stratified by thyroid hormone levels. Our findings reveal that

Table 1. Descriptive statistics of the study population (*n* = 75 with 290 measurements)

Variables	Mean ± SD or Number (%)	Ranges
Age (years)	65.0 ± 2.8	60.0–70.0
Gender		
Male	37 (49.3)	
Female	38 (50.7)	
Income (10,000 yuan/year)	10.0 ± 6.8	0–24.0
BMI (kg/m^2)	25.1 ± 2.3	17.9–28.2
Cotinine (ng/mL)	1.2 ± 6.3	0.01–84.4
Educational attainment		
Below primary school	5 (6.7)	
Primary school	3 (4.0)	
Junior high school	21 (28.0)	
Senior high school	32 (42.7)	
University and above	14 (18.6)	
FVC (L)	3.2 ± 0.7	1.9–6.1
FEV_1 (L)	2.4 ± 0.6	1.3–4.1
FEV_1/FVC (%)	76.0 ± 6.5	21.7–86.5
PEF (L/s)	5.9 ± 1.8	1.7–10.3
IL-1β (pg/mL)	0.8 ± 1.9	0.2–8.3
IL-2 (pg/mL)	2.2 ± 2.3	0.1–20.8
IL-5 (pg/mL)	1.4 ± 1.6	0.1–22.5
IL-6 (pg/mL)	1.5 ± 3.2	0.04–30.7
IL-7 (pg/mL)	9.0 ± 3.8	0.9–25.4
IL-8 (pg/mL)	5.7 ± 5.0	0.9–67.0
IL-10 (pg/mL)	7.9 ± 40.9	0.4–482.6
IL-12 (pg/mL)	1.8 ± 1.7	0.1–11.5
IL-13 (pg/mL)	4.2 ± 3.5	0.1–16.1
IL-17A (pg/mL)	4.1 ± 2.9	0.2–21.3
IL-21 (pg/mL)	1.3 ± 2.1	0.1–20.6
TNF-α (pg/mL)	3.8 ± 1.4	1.1–8.9
IFN-γ (pg/mL)	5.8 ± 4.3	0.2–26.7
TSH (mIU/L)	5.1 ± 4.3	0.7–30.3
T_3 (nmol/L)	1.5 ± 1.1	0.1–15.5
T_4 (nmol/L)	44.5 ± 13.1	0.2–101.1

Note. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FEV_1/FVC, the ratio of FEV_1 to FVC; PEF, peak expiratory flow; IL, interleukin; TNF, tumor necrosis factor; IFN, interferon; TSH, thyroid-stimulating hormone; T_3, triiodothyronine; T_4, thyroxin.

1,3-dichlorobenzene, 4-chloroaniline, BCIE, and HCBD induced alterations in the levels of several inflammatory factors. Particularly, the low thyroid hormone group exhibited greater sensitivity to the inflammatory factors induced by organochlorine exposure. Specifically, BCIE was associated with significant changes in the levels of IL-2, IL-7, IL-8, and IL-13 within the low thyroid hormone group. Contrastingly, no significant association between BCIE and inflammatory factors was observed in the high thyroid hormone group.

Mediation Effects of Inflammatory Factors in the Relationship between BCIE and FVC

Based on the mediation analysis, we found that IL-2 and IL-13 significantly mediated the relationship between BCIE exposure and FVC, with 15.63% (95% *CI*: 0.91%, 44.64%) and 13.94% (95% *CI*: 0.52%, 41.07%) of mediating effects, respectively (Figure 3 and Supplementary Table S5).

DISCUSSION

As far as we know, this is the first study to explore the complex interplay among organochlorines exposure, inflammatory factors, and alterations in lung function, after taking into account the modulatory role of thyroid hormone levels. Our findings suggest that organochlorine exposure led to a decline of lung function by the induction of inflammatory factors. Importantly, low thyroid hormone levels may amplify this adverse effect, suggesting an increased vulnerability to the impacts of organochlorine exposure under hypothyroid conditions.

Inflammation is a fundamental immune response triggered by various stimuli, including exposure to environmental pollutants[45]. Numerous studies have demonstrated that organochlorines can induce inflammatory disorders within the body[46-48]. For instance, a cross-sectional study conducted in Portugal revealed a positive correlation between blood concentrations of hexachlorocyclohexane and levels of IL-10 among women aged 22 to 59 years[46]. Similarly, *in vitro* experiments performed by Thota et al. indicated that pentachlorophenol exposure resulted in elevated levels of inflammatory mediators, including IL-1β, IL-6, TNF-α, and IL-8[48]. Research by Jang et al. on Sprague-Dawley rats identified a positive correlation between endosulfan exposure with increased TNF-α and IL-1β levels[47]. Aligning with these previous reports, our study uncovered a significant association between

organochlorine exposure and altered inflammatory profiles, highlighting that inflammation may play a key role in lung function impairment associated with organochlorine exposure. It is widely acknowledged that the dysregulation of inflammatory factors contributes to the impairment of lung function[49,50]. Specifically, Lee et al. and Kubysheva et al. proposed that IL-2, IL-13, IL-18, and TNF-α may be associated with the decline in lung function[51,52]. While this study identified only two significant inflammatory mediators, IL-2 and IL-13, it is important to recognize the importance of the overall inflammatory environment, which encompasses additional inflammatory factors, even though they were not statistically significant in our analysis. The inflammatory process is pervasive within lung

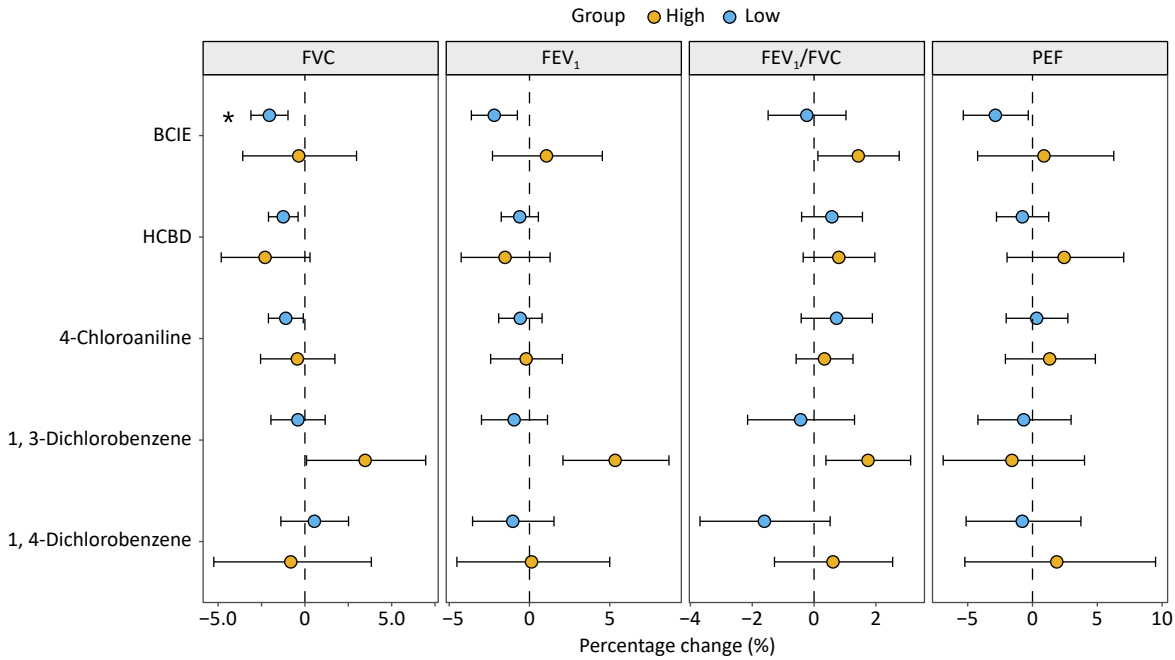

Figure 1. Associations between personal exposure to organochlorines and changes in lung function by different groups of thyroid hormones. *represents FDR < 0.05. BCIE, Bis (2-chloro-1-methylethyl) ether; HCBD, Hexachlorobutadiene; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FEV_1/FVC, the ratio of FEV_1 to FVC; PEF, peak expiratory flow.

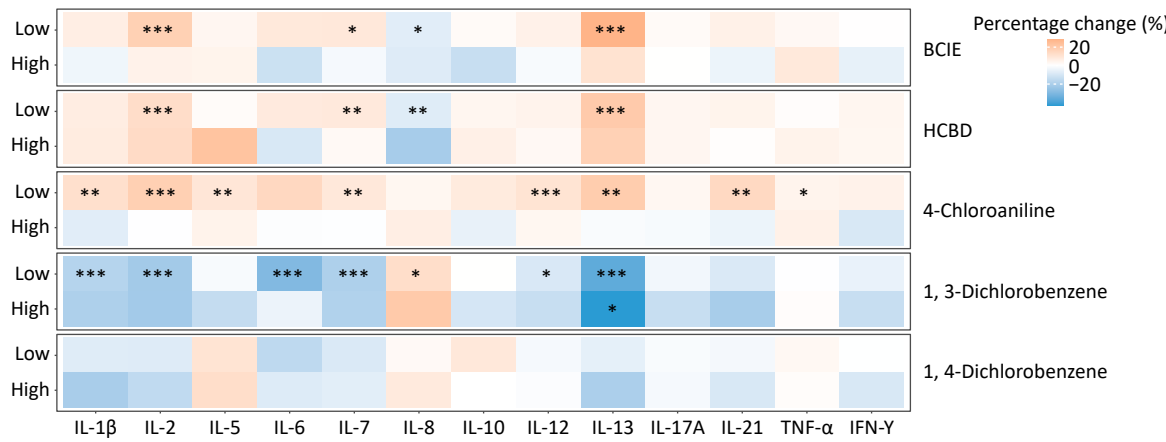

Figure 2. Associations between organochlorines and changes in inflammatory factors by different groups of thyroid hormones. *, **, and *** represents FDR < 0.05, 0.01 and 0.001, respectively. BCIE, Bis (2-chloro-1-methylethyl) ether; HCBD, Hexachlorobutadiene; IL, interleukin; TNF, tumor necrosis factor; IFN, interferon.

tissues, and immune cells like macrophages and lymphocytes are abundant throughout the lung parenchyma[53]. When pollutants infiltrate the lungs, inflammatory homeostasis can be disrupted, leading to the secretion of a plethora of inflammatory factors[54]. Persistent inflammation can result in the degradation of elastin and the destruction of alveolar cells, leading to a decline in lung function[55,56]. While research specifically examining inflammation-mediated organochlorine damage to lung function remains limited, existing studies have substantiated the critical role of inflammatory factors in the impairment of lung function caused by other environmental pollutants. For instance, Xiao et al. utilized data from the National Health and Nutrition Examination Survey (NHANES) to investigate the mechanisms linking polycyclic aromatic hydrocarbons (PAHs) to chronic obstructive pulmonary disease (COPD)[57]. Their findings revealed that PAHs increased the risk of COPD by influencing systemic inflammation. Similarly, Zheng et al. demonstrated that systemic inflammation mediated the relationship between dust exposure and the decline in FEV_1[58]. Furthermore, immune cells closely associated with inflammatory responses, such as lymphocytes and white blood cells, were also found to be vital mediators of lung diseases induced by air pollution[59]. These findings support our observations and underscore the underlying mechanism for the intricate relationship between inflammatory responses and respiratory health. Collectively, our study offers novel insights into the complex interplay among organochlorine exposure, inflammatory responses and lung function impairment, and emphasizes the importance of sustaining pulmonary inflammatory homeostasis for maintaining respiratory health in the elderly population.

Furthermore, we employed LPA to categorize samples according to thyroid hormone concentrations. This grouping methodology has been widely utilized in various researches, which substantiates its reliability and effectiveness[60-62]. For instance, Qin et al. successfully applied LPA to delineate distinct estrogen spectra, demonstrating its ability to identify meaningful differences in hormonal profiles[60]. Similarly, Lin et al. leveraged LPA to classify individuals into various subgroups based on diverse characteristics of the built environment, further illustrating the robustness of this analytical approach[61]. By comparing the effects of organochlorines across different groups, this study further explored whether thyroid hormones modified the relationship between organochlorine exposure and lung function. Thyroid hormones are essential for the regulation of metabolism, energy production, and the proper functioning of tissues, including the lungs[25]. During lung development, thyroid hormones activate relevant gene expression, promoting the formation of alveoli and vascular structures, thereby facilitating lung maturation[63,64]. They also play a role in the synthesis of surfactant substances within the alveoli, which are essential for reducing surface tension and stabilizing the alveoli[65]. Furthermore, thyroid hormones contribute to the maintenance of respiratory muscle endurance and strength, and influence the elasticity and compliance of lung tissue, thereby facilitating proper respiratory movements[66,67]. Reduced sensitivity to thyroid hormones correlates with impaired lung function, while a clear link exists between hypothyroidism and decreased respiratory capacity[68,69]. Bassi et al. revealed that thyroid hormone supplementation positively impacts lung function[70]. Consistent with these findings, our study identified the adverse effects of low thyroid hormone levels on lung function in the elderly. Moreover, our study revealed that low levels of thyroid hormone increased the sensitivity of

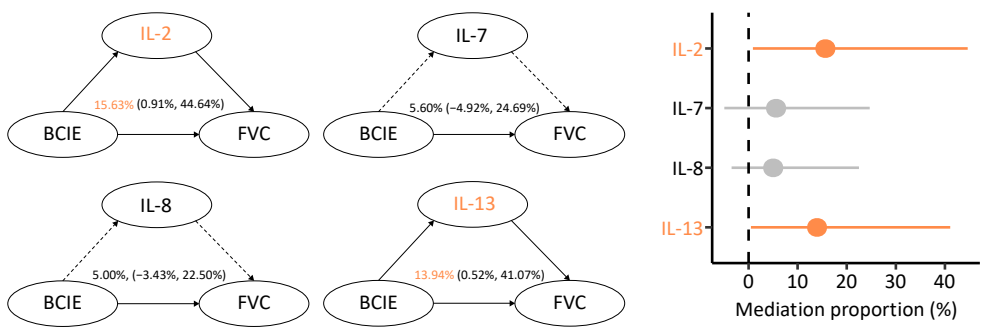

Figure 3. The mediation effect of inflammatory factors on the association between BCIE and FVC among healthy older adults. BCIE, Bis (2-chloro-1-methylethyl) ether; FVC, forced vital capacity; IL, interleukin.

inflammatory factors to organochlorine exposure, likely due to the immunomodulatory role of thyroid hormones in immune cell function[71]. Evidence suggests that hypothyroidism can induce a systemic inflammatory response, affecting various cytokines and adversely impacting overall health[72]. Perrotta et al. have shown that T_3 can mitigate inflammation by modulating the proliferation and differentiation of macrophages[73]. These findings provide further support for our results that thyroid hormone deficiencies elevated inflammatory sensitivity, thus exacerbating the adverse effects of organochlorine exposure on lung function. And findings may provide a foundation for targeted interventions to mitigate lung function impairments caused by environmental exposures through enhancing inflammatory homeostasis and maintaining normal thyroid hormone levels, ultimately safeguarding respiratory health among the elderly.

This study has several strengths. Firstly, it employed a panel design with multiple repeated measurements, enhancing accuracy and reliability. Secondly, the utilization of Fresh Air wristband to measure individual organochlorine exposure concentrations might offer a more accurate representation of real exposure levels. Finally, our research considered the roles of both thyroid hormones and inflammatory factors in the relationship between organochlorine exposure and lung function, adding valuable insights to the existing literature. However, there are also limitations in this research. Firstly, the study population was confined to healthy older individuals, which might limit the generalization of our results to the overall population. Secondly, the investigation only focused on short-term measurements taken over a five-month period, limiting our capacity to assess long-term effects of organochlorine exposure. Lastly, the sample size was relatively modest, requiring further large-scale epidemiological or experimental research to validate and expand our understanding of these relationships.

CONCLUSION

This study investigated the intricate interplay among organochlorine exposure, inflammatory factors, thyroid hormones, and lung function. Our findings elucidate that inflammatory factors might play a mediating role in the detrimental effects of organochlorine exposure on lung function. Furthermore, low thyroid hormone levels significantly enhanced the body's sensitivity to organochlorine exposure, leading to the development of inflammatory disorders and compromised lung function. Our findings may improve our understanding of the biological mechanisms underpinning respiratory injuries associated with organochlorine exposure. Furthermore, we recommend that elderly individuals adopt certain measures, including adequate sleep, a balanced diet, and moderate exercise, to maintain stable levels of thyroid hormones and inflammatory factors which contribute to promoting respiratory health and mitigate risks associated with environmental exposures.

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Competing Interests The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics This research was approved by the Ethics Review Committee of the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (NIEH, China CDC, No. 201816), and informed consent was obtained from all participants.

Authors' Contributions Writing - original draft, Visualization, Software, Methodology, Conceptualization: Xiaojie Guo; Validation, Methodology: Huimin Ren; Validation, Methodology: Jiran Zhang; Validation, Methodology: Xiao Ma; Writing-review & editing, Validation: Shilu Tong; Writing-review & editing, Methodology, Investigation, Data curation, Conceptualization: Song Tang; Writing-review & editing, Validation, Methodology: Chen Mao; Supervision, Project administration, Funding acquisition, Data curation, Conceptualization: Xiaoming Shi.

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REFERENCES

1. Ensley SM. Organochlorines. In: Gupta RC. Veterinary Toxicology. 3rd ed. Elsevier. 2018, 509-13.
2. Carolin C F, Kamalesh T, Senthil Kumar P, et al. An insights of organochlorine pesticides categories, properties, eco-toxicity and new developments in bioremediation process. Environ Pollut, 2023; 333, 122114.
3. Ali U, Syed JH, Malik RN, et al. Organochlorine pesticides (OCPs) in South Asian region: a review. Sci Total Environ, 2014; 476-477, 705-17.
4. Hu JX, Zhu T, Li QL. Organochlorine pesticides in China. Dev Environ Sci, 2007; 7, 159−211.
5. Zhang Y, Qi SH, Xing XL, et al. Legacies of organochlorine pesticides (OCPs) in soil of China—a review, and cases in southwest and Southeast China. In: De Vivo B, Belkin HE, Lima A. Environmental Geochemistry. 3rd ed. Elsevier. 2024, 519-47.
6. Sheriff I, Debela SA, Mans-Davies A. The listing of new persistent organic pollutants in the Stockholm convention: its burden on developing countries. Environ Sci Policy, 2022; 130, 9−15.
7. Lu Y, Zhou SB, Li BX. Exposure to environmental hexachlorocyclohexane (HCH) and dichlorodiphenyltrichloroethane (DDT) among rural children in north Eastern China. Biomed Environ Sci, 2010; 23, 230−3.
8. Olisah C, Okoh OO, Okoh AI. Occurrence of organochlorine pesticide residues in biological and environmental matrices in Africa: a two-decade review. Heliyon, 2020; 6, e03518.
9. Pattnaik M, Pany BK, Jena D, et al. Effect of organochlorine pesticides on living organisms and environment. Chem Sci Rev Lett, 2020; 9, 682−6.
10. Zhang LF, Dong L, Yang WL, et al. Passive air sampling of organochlorine pesticides and polychlorinated biphenyls in the Yangtze River Delta, China: concentrations, distributions, and cancer risk assessment. Environ Pollut, 2013; 181, 159−66.
11. Fang YY, Nie ZQ, Die Q, et al. Organochlorine pesticides in soil, air, and vegetation at and around a contaminated site in Southwestern China: concentration, transmission, and risk evaluation. Chemosphere, 2017; 178, 340−9.
12. Taiwo AM. A review of environmental and health effects of organochlorine pesticide residues in Africa. Chemosphere, 2019; 220, 1126−40.
13. Rea WJ, Patel KD. Pesticides and chronic diseases. In: Rea WJ, Patel KD. Reversibility of Chronic Disease and Hypersensitivity, Volume 4. CRC Press. 2017, 649-904.
14. Mohammadkhani MA, Shahrzad S, Haghighi M, et al. Insights into organochlorine pesticides exposure in the development of cardiovascular diseases: a systematic review. Arch Iran Med, 2023; 26, 592−9.
15. Mata TM, Felgueiras F, Martins AA, et al. Indoor air quality in elderly centers: pollutants emission and health effects. Environments, 2022; 9, 86.
16. Chen YY, Klein SL, Garibaldi BT, et al. Aging in COVID-19: vulnerability, immunity and intervention. Ageing Res Rev, 2021; 65, 101205.
17. de Paula Santos U, Arbex MA, Braga ALF, et al. Environmental air pollution: respiratory effects. J Bras Pneumol, 2021; 47, e20200267.
18. Zhu YB, Liang RZ, Pu LN, et al. Relevance of household chemical usage to respiratory diseases in older adults in China. Biomed Environ Sci, 2024; 37, 1373−84.
19. Ye M, Beach J, Martin JW, et al. Association between lung function in adults and plasma DDT and DDE levels: results from the Canadian health measures survey. Environ Health Perspect, 2015; 123, 422−7.
20. Balte PP, Kühr J, Kruse H, et al. Body burden of dichlorodiphenyl dichloroethene (DDE) and childhood pulmonary function. Int J Environ Res Public Health, 2017; 14, 1376.
21. Lugg ST, Scott A, Parekh D, et al. Cigarette smoke exposure and alveolar macrophages: mechanisms for lung disease. Thorax, 2022; 77, 94−101.
22. Brandenberger C, Mühlfeld C. Mechanisms of lung aging. Cell Tissue Res, 2017; 367, 469−80.
23. Bezerra FS, Lanzetti M, Nesi RT, et al. Oxidative stress and inflammation in acute and chronic lung injuries. Antioxidants (Basel), 2023; 12, 548.
24. Wang GF, Zhang YZ, Yang HY, et al. Impact of air pollutants on lung function and inflammatory response in asthma in Shanghai. Biomed Environ Sci, 2024; 37, 811−22.
25. Liu YY, Milanesi A, Brent GA. Thyroid hormones. In: Litwack G. Hormonal Signaling in Biology and Medicine. Elsevier. 2020, 487-506.
26. Flory CM, Norris BJ, Larson NA, et al. A preclinical safety study of thyroid hormone instilled into the lungs of healthy rats-an investigational therapy for ARDS. J Pharmacol Exp Ther, 2021; 376, 74−83.
27. Guo XJ, Ren HM, Sun PJ, et al. Personal exposure to airborne organic pollutants and lung function changes among healthy older adults. Environ Res, 2024; 258, 119411.
28. Tang S, Li TT, Fang JL, et al. The exposome in practice: an exploratory panel study of biomarkers of air pollutant exposure in Chinese people aged 60-69 years (China BAPE study). Environ Int, 2021; 157, 106866.
29. Ding EM, Deng FC, Fang JL, et al. Association between organophosphate ester exposure and insulin resistance with glycometabolic disorders among older Chinese adults 60-69 years of age: evidence from the China BAPE study. Environ Health Perspect, 2023; 131, 047009.
30. Ding EM, Deng FC, Fang JL, et al. Exposome-wide ranking to uncover environmental chemicals associated with dyslipidemia: a panel study in healthy older Chinese adults from the BAPE study. Environ Health Perspect, 2024; 132, 097005.
31. Guo PF, Lin EZ, Koelmel JP, et al. Exploring personal chemical exposures in China with wearable air pollutant monitors: a repeated-measure study in healthy older adults in Jinan, China. Environ Int, 2021; 156, 106709.
32. Koelmel JP, Lin EZ, Guo PF, et al. Exploring the external exposome using wearable passive samplers - the China BAPE study. Environ Pollut, 2021; 270, 116228.
33. Brusasco V, Crapo R, Viegi G. Coming together: the ATS/ERS consensus on clinical pulmonary function testing. Eur Respir J, 2005; 26, 1−2.
34. Fang JL, Gao Y, Zhang MY, et al. Personal $PM_{2.5}$ elemental components, decline of lung function, and the role of DNA methylation on inflammation-related genes in older adults: results and implications of the BAPE study. Environ Sci Technol, 2022; 56, 15990−6000.
35. Shi WY, Fang JL, Ren HM, et al. Association between exposure to chemical mixtures and epigenetic ageing biomarkers: modifying effects of thyroid hormones and physical activity. J Hazard Mater, 2024; 469, 134009.
36. Williams GA, Kibowski F. Latent class analysis and latent profile analysis. In: Jason LA, Glenwick DS. Handbook of Methodological Approaches to Community-Based Research: Qualitative, Quantitative, and Mixed Methods. Oxford University Press. 2016, 143-51.
37. He J, Fan X. Latent profile analysis. In: Zeigler-Hill V, Shackelford TK. Encyclopedia of Personality and Individual

Differences. Springer. 2020, 1-4.
38. Barroso AT, Martín EM, Romero LMR, et al. Factors affecting lung function: a review of the literature. Archivos Bronconeumol, 2018; 54, 327–32.
39. Salisbury ML, Xia M, Zhou YR, et al. Idiopathic pulmonary fibrosis: gender-age-physiology index stage for predicting future lung function decline. Chest, 2016; 149, 491–8.
40. Chen XX, Zheng XL, Ding ZJ, et al. Relationship of gender and age on thyroid hormone parameters in a large Chinese population. Arch Endocrinol Metab, 2019; 64, 52–8.
41. Fang WB, Cao YW, Chen YY, et al. Associations of family income and healthy lifestyle with all-cause mortality. J Glob Health, 2023; 13, 04150.
42. Dieteren C, Bonfrer I. Socioeconomic inequalities in lifestyle risk factors across low-and middle-income countries. BMC Public Health, 2021; 21, 951.
43. Low BS, Selvaraja KG, Ong TH, et al. Education background and monthly household income are factors affecting the knowledge, awareness and practice on haze pollution among Malaysians. Environ Sci Pollut Res Int, 2020; 27, 30419–25.
44. The GBD 2015 Obesity Collaborators. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med, 2017; 377, 13–27.
45. Suzuki T, Hidaka T, Kumagai Y, et al. Environmental pollutants and the immune response. Nat Immunol, 2020; 21, 1486–95.
46. Ferro A, Teixeira D, Pestana D, et al. POPs' effect on cardiometabolic and inflammatory profile in a sample of women with obesity and hypertension. Arch Environ Occup Health, 2019; 74, 310–21.
47. Jang TC, Jang JH, Lee KW. Mechanism of acute endosulfan intoxication-induced neurotoxicity in Sprague-Dawley rats. Arh Hig Rada Toksikol, 2016; 67, 9–17.
48. Thota S, Begum R, Kaur G, et al. Pentachlorophenol mediated regulation of DAMPs and inflammation: in vitro study. Toxicol In Vitro, 2022; 83, 105378.
49. Moldoveanu B, Otmishi P, Jani P, et al. Inflammatory mechanisms in the lung. J Inflamm Res, 2008; 2, 1–11.
50. Kallapur SG, Jobe AH. Contribution of inflammation to lung injury and development. Arch Dis Child Fetal Neonatal Ed, 2006; 91, F132–5.
51. Lee JS, Rosengart MR, Kondragunta V, et al. Inverse association of plasma IL-13 and inflammatory chemokines with lung function impairment in stable COPD: a cross-sectional cohort study. Respir Res, 2007; 8, 64.
52. Kubysheva N, Boldina M, Eliseeva T, et al. Relationship of serum levels of IL-17, IL-18, TNF-α, and lung function parameters in patients with COPD, asthma-COPD overlap, and bronchial asthma. Mediators Inflamm, 2020; 2020, 4652898.
53. Keskinidou C, Vassiliou AG, Dimopoulou I, et al. Mechanistic understanding of lung inflammation: recent advances and emerging techniques. J Inflamm Res, 2022; 15, 3501–46.
54. Arias-Pérez RD, Taborda NA, Gómez DM, et al. Inflammatory effects of particulate matter air pollution. Environ Sci Pollut Res Int, 2020; 27, 42390–404.
55. Benjamin JT, Plosa EJ, Sucre JMS, et al. Neutrophilic inflammation during lung development disrupts elastin assembly and predisposes adult mice to COPD. J Clin Invest, 2021; 131, e139481.
56. He F, Liao BL, Pu JD, et al. Exposure to ambient particulate matter induced COPD in a rat model and a description of the underlying mechanism. Sci Rep, 2017; 7, 45666.
57. Xiao YQ, Zhang L, Liu H, et al. Systemic inflammation mediates environmental polycyclic aromatic hydrocarbons to increase chronic obstructive pulmonary disease risk in United States adults: a cross-sectional NHANES study. Front Public Health, 2023; 11, 1248812.
58. Zheng YZ, Hu JQ, Chen JQ, et al. Association between dust exposure and lung function levels in steelworkers: mediation analysis of inflammatory biomarkers. Int Arch Occup Environ Health, 2024; 97, 971–980.
59. Wang YC, Yu YQ, Zhang XX, et al. Combined association of urinary volatile organic compounds with chronic bronchitis and emphysema among adults in NHANES 2011-2014: the mediating role of inflammation. Chemosphere, 2024; 361, 141485.
60. Qin XD, Zhou Y, Bloom MS, et al. Prenatal exposure to PFAS, associations with preterm birth and modification by maternal estrogen levels: the Maoming birth study. Environ Health Perspect, 2023; 131, 117006.
61. Lin JS, Leung J, Yu B, et al. Socioeconomic status as an effect modifier of the association between built environment and mortality in elderly Hong Kong Chinese: a latent profile analysis. Environ Res, 2021; 195, 110830.
62. Yonkman AM, Alampi JD, Kaida A, et al. Using latent profile analysis to identify associations between gestational chemical mixtures and child neurodevelopment. Epidemiology, 2023; 34, 45–55.
63. Ogilvy-Stuart AL. Thyroid hormones and lung development. J Pediatr Endocrinol Metab, 2007; 20(S), 115-8.
64. Pelizzo G, Calcaterra V, Baldassarre P, et al. The impact of hormones on lung development and function: an overlooked aspect to consider from early childhood. Front Endocrinol, 2024; 15, 1425149.
65. Dev N, Sankar J, Vinay MV. Functions of thyroid hormones. In: Imam SK, Ahmad SI. Thyroid Disorders: Basic Science and Clinical Practice. Springer. 2016, 11-25.
66. Owji MS, Varedi M, Naghibalhossaini F, et al. Thyroid function modulates lung fluid and alveolar viscoelasticity in mechanically ventilated rat. J Surg Res, 2020; 253, 272–9.
67. Schlenker EH. Effects of hypothyroidism on the respiratory system and control of breathing: human studies and animal models. Respir Physiol Neurobiol, 2012; 181, 123–31.
68. Wang ZX, Lu B, Wu MH, et al. Reduced sensitivity to thyroid hormones is associated with lung function in euthyroid individuals. Heliyon, 2024; 10, e30309.
69. Akter P, Begum S, Ali T, et al. FVC, FEV_1 and FEV_1/FVC% in hypothyroid female and their relationships with thyroid hormones. J Bangladesh Soc Physiol, 2011; 6, 45–51.
70. Bassi R, Dhillon SV, Sharma S, et al. Effect of thyroid hormone replacement on respiratory function tests in hypothyroid women. Pak J Physiol, 2012; 8, 20–3.
71. Jara EL, Muñoz-Durango N, Llanos C, et al. Modulating the function of the immune system by thyroid hormones and thyrotropin. Immunol Lett, 2017; 184, 76–83.
72. Lai R, Yin BZ, Feng ZY, et al. The causal relationship between 41 inflammatory cytokines and hypothyroidism: bidirectional two-sample Mendelian randomization study. Front Endocrinol (Lausanne), 2023; 14, 1332383.
73. Perrotta C, Buldorini M, Assi E, et al. The thyroid hormone triiodothyronine controls macrophage maturation and functions: protective role during inflammation. Am J Pathol, 2014; 184, 230–47.