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Original Article

Associations Between Volatile Organic Compounds and Respiratory Health: Insights from NHANES 2013–2018

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) and asthma significantly impact public health. Using NHANES 2013–2018 data, this study examined associations between volatile organic compounds (VOCs) and these conditions. Weighted logistic regression models revealed significant disparities in COPD prevalence across demographic groups, including higher rates among non-Hispanic whites, low-income individuals, and older adults. Adjusted models identified CYHA, HEM, HPM, MB3, and PMM as significantly associated with COPD (ORs: 1.57–1.98). For asthma, 2MH (OR = 1.12, p = 0.0022) and PMM (OR = 1.14, p = 0.0071) were significant after adjustment. These results highlight the role of VOCs in respiratory health and inform efforts to mitigate environmental risk factors.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) and asthma stand as two significant respiratory conditions imposing a substantial burden on public health and the economy worldwide. Asthma is a major noncommunicable disease(NCD) that causes the airway to swell and narrow and may produce extra mucus. This can lead to various major and minor influences including cough, wheezing, shortness of breath, and chest tightness, affecting patients' daily activities[2][3]. COPD is another Chronic pulmonary disease after exposure to irritating gasses or particulate matter. COPD also causes lung inflammation, obstructing airflow.[4] Both diseases, characterized by airflow limitation and respiratory symptoms, affect millions of individuals globally, leading to impaired quality of life, increased healthcare utilization, and significant economic costs. Moreover, COPD and asthma often coexist with other health conditions, exacerbating their impact on affected individuals.

Numerous studies have examined the risk factors associated with COPD and asthma, shedding light on various environmental factors such as smoking and exposure to air

pollutants and genetic contributors such as AAT deficiency caused by mutation and family history. Among the environmental factors, volatile organic compounds (VOCs) have garnered attention due to their ubiquitous presence in both occupational and residential settings [7]. VOCs encompass a diverse array of chemical compounds emitted from various sources such as building materials, household products, and industrial activities. These compounds have been implicated in respiratory health outcomes, including exacerbation of COPD and asthma symptoms, yet comprehensive research examining their association with these conditions remains limited.

The study aims to assess the effects of VOCs on COPD and asthma using large nationally representative data. We hypothesized that VOCs, at least some forms of VOCs, have a positive correlation with the prevalence of COPD and asthma among U.S. adults. Weighted logistic regression models are the major methodology we used to assess VOCs that have such an impact on outcomes. The study provides important information for Healthcare providers and policymakers to reduce the negative impact of environmental VOCs.

Methods

Sample and database

We extracted data from the National Health and Nutritional Examination Survey (NHANES) from 2013 to 2018 spanning three cycles of surveys [1]. NHANES is a population-based, nationally representative study that collected health and nutritional data from non-institutionalized U.S. citizens using a multi-stage sampling strategy. It continuously conducts surveys created by the National Center of Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) to keep track of the diverse health statuses of the non-institutionalized civilian population in the USA. The NHANES program began to collect data on diverse health issues from different demographic groups in the early 1960s.

Dependent variables

The dependent variables in this study are two prevalent respiratory conditions: Chronic Obstructive Pulmonary Disease (COPD) and asthma. These conditions are assessed through a structured medical condition questionnaire in NHANES surveys. The questionnaire was administered as ‘Has COPD?’ (yes, no) and ‘Has asthma?’ (yes, no). The respondents provided self-reported information about their COPD and asthma status.

Independent variables

The Independent variable of interest for this study is volatile organic compounds

(VOC) detected in participants' urine samples, which is log-transformed to determine the association between VOC and dependent variables COPD and asthma. VOC encompasses a series of chemical compounds, including 2MH,34M, AAM, AMC, ATC, BMA, BPM, CEM, CYHA, CYM, DHB, GAM, HEM, HP2, HPM, IPM3, MAD, MB3, PHE, PHG, PMM, and TTC. The VOC was measured using capillary gas chromatography (GC) and mass spectrometry (MS) with selected-ion monitoring (SIM) detection and isotope dilution [2].

Statistical analysis

To describe the disparities of demographic groups by COPD and asthma, we conducted descriptive analysis for gender, age, income, and race using sample size (n = 1420) and weighted proportions percentages (%). The associations between individual demographic variables and dependent variables were evaluated by Chi-squared tests. The central tendency of VOCs was described as the mean of log-transformed values as well as standard errors. To assess the influence of VOCs on COPD and asthma, we conducted univariate logistic regression models using log-transformed VOCs as independent variables, and COPD or asthma as dependent variables. To adjust the potential confounding effects, we also conducted multiple logistic regression models adjusting for COPD. All logistic regression models included sample weights to reduce the bias of the sampling collection process. A p-value less than .05 is considered statistical significance. All analyses were conducted using R software version [6]

Results

Table 1 shows the sample characteristics of COPD and Asthma. Compared to non-COPD, the COPD population has a significantly higher percentage of non-Hispanic whites (82.2% in COPD vs. 62.3% in non-COPD, p-value = 0.006). Compared to the non-COPD group, there is a large percentage of the population having lower income (PIR <=130%) among participants with COPD (39.7% for COPD vs 20.3% for non-COPD). Compared to the non-COPD group, there is a large percentage (90%) of the population that is middle-aged or elderly(50-older) among participants with COPD. The mean and standard error of all VOCs were described in supplemental table S1

Table 2 shows the univariate and multiple logistic regression models between VOC and COPD. Among all 20 VOCs, VOCs such as 2MH, 34M, AMC, CEM, CYM, IPM3, MAD, and PHE were significantly associated with a higher likelihood of having COPD in the crude model without adjusting for other covariates. However, in the adjusted model (multiple logistic regression), those VOCs were no longer significantly associated with COPD, indicating that adjusting for covariates may attenuate the effects of these VOCs on COPD. VOCs such as CYHA, HEM, HPM, MB3, and PMM were statistically significantly associated with higher prevalence in COPD in both crude and adjusted models after adjusting for age, gender, poverty

income ratio, and age. The odds ratios and 95% CI for CYHA, HEM, HPM, MB3, and PMM were 1.61 [1.22, 2.12], 1.98[1.35, 2.88], 1.57 [1.23, 2], 1.65 [1.18, 2.29], 1.69 [1.16, 2.45] respectively.

Table 3 shows the univariate and multiple logistic regression models between VOC and asthma. The model does not show a significant association between Asthma and VOCs in the univariate logistic regression model. However, in the multiple logistic regression model, 2MH was significantly associated with a higher likelihood of having asthma (OR = 1.12 CL = [0.59], p-value = 0.0022) PMM also exhibited a significant influence on the probability of having asthma, with an OR = 1.14, CL = 0.605, p-value = 0.0071. These significant effects of 2MH and PMM in the adjusted model but not the crude model may indicate the existence of suppressors in covariates.

Discussion

This study investigated the effects of volatile organic compounds (VOCs) on two prevalent respiratory diseases: asthma and Chronic Obstructive Pulmonary Disease (COPD). Our findings indicate that certain VOCs, such as N-Acetyl-S-(1-cyano-2-hydroxyethyl)-L-cysteine (CYHA), N-acetyl-S-(2-hydroxyethyl)-L-cysteine, and N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine, were significantly associated with an increased likelihood of COPD, suggesting that exposure to VOCs may contribute to the development of this disease. Additionally, compounds like 2-methylhippuric acid and N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine showed associations with asthma, pointing to distinct molecular mechanisms through which VOCs influence respiratory diseases.

Our findings align with those of [8], who also observed a positive correlation between VOC exposure and COPD, supporting the notion that VOCs may be key contributors to the morbidity associated with COPD. However, our study differs in its methodological approach; while [9] focused on blood concentrations of benzene and o-xylene, we measured VOC concentrations in urine samples. This difference in the biological matrix examined could help explain the consistency of our results with previous studies.

This study also extends the work of [10] by exploring the association between VOCs and asthma, offering a more comprehensive understanding of the impact of VOCs on respiratory health.

Strengths and Limitations

A key strength of this study lies in the use of NHANES data, which offers a nationally representative sample of the U.S. population. The large, diverse dataset provides reliable, real-world evidence of the association between VOC exposure and respiratory diseases, making the results broadly applicable. NHANES' accuracy in capturing health data makes it a valuable resource for epidemiological research.

However, the study is not without limitations. First, the cross-sectional design limits our ability to draw causal inferences. While an association between VOCs and respiratory diseases is evident, the temporal relationship between exposure and disease onset remains unclear. Additionally, the reliance on self-reported data for COPD and asthma diagnoses may introduce reporting bias, as individuals may fail to recognize or report early symptoms of these conditions, potentially

underestimating the association between VOC exposure and respiratory health.

Conclusion

Our research provides valuable insights into the relationship between VOC exposure and respiratory diseases, specifically asthma and COPD. We found that VOCs, including N-Acetyl-S-(1-cyano-2-hydroxyethyl)-L-cysteine and N-acetyl-S-(2-hydroxyethyl)-L-cysteine, are positively correlated with COPD, while VOCs such as 2-methyl hippuric acid and N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine are linked to asthma. These differential effects suggest that VOCs may influence respiratory health through distinct molecular pathways.

Future studies should investigate potential moderators of the VOC-respiratory disease relationship, particularly among vulnerable populations, such as minorities or those with low income. Identifying these at-risk groups could inform targeted interventions to mitigate the impact of VOC exposure on respiratory health.

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Table 1.

Variable	Total	Non-COPD	COPD	p value	Non-Asthma	Asthma	p value
	n(%)	n(%)	n(%)				
Gender							
Male	700(48.6)	659(58.3)	41(41.7)	0.341	586(49.1)	134(64.0)	0.0061
Female	720(51.4)	678(51.1)	42(58.3)		609(50.9)	91(36.0)	
Race							
Mexican American	187(9.2)	185(9.6)	2(0.9)		169(9.9)	18(5.2)	
Non-Hispanic Black	322(10.9)	311(11.1)	11(6.0)	0.006	260(10.4)	62(13.4)	0.2171
Non-Hispanic White	507(63.3)	449(62.3)	58(82.2)		424(63.2)	83(63.4)	
Other	404(16.7)	392(16.9)	12(10.9)		342(16.5)	62(17.8)	
PIR							
≤130%	421(21.2)	379(20.3)	42(39.7)		343(20.4)	78(25.6)	
131–350%	566(34.9)	535(34.8)	31(36.0)	0.017	485(35.1)	81(33.7)	0.4846
≥350%	433(43.9)	423(44.9)	10(24.4)		367(44.5)	66(40.7)	
Age group							
20-35	277(23.6)	276(24.6)	1(2.6)		225(23.0)	52(26.8)	
35-49	332(26.2)	326(27.1)	6(7.5)	<	283(26.2)	49(26.2)	0.4976
50-65	432(30.9)	402(30.0)	30(49.7)	0.001	358(30.6)	74(32.2)	
65 and older	379(19.4)	333(18.4)	46(40.3)		329(20.2)	50(14.8)	

Note: % is weighted proportions; PIR, poverty income ratio.

Table 2.

	Univariate				Multiple logistic regression			
Variables	OR	LCL	UCL	P value	OR	LCL	UCL	P value
2MH	1.41	1.03	1.93	0.0488	1.38	0.97	1.94	0.1293
34M	1.5	1.1	2.04	0.0216	1.45	1.01	2.1	0.1034
AAM	1.09	0.81	1.46	0.5934	1.12	0.73	1.71	0.6384
AMC	1.54	1.14	2.1	0.0146	1.42	1.03	1.96	0.084
ATC	1.19	0.87	1.61	0.2983	1.24	0.83	1.84	0.3409
BMA	1.01	0.75	1.36	0.9536	1.01	0.74	1.37	0.9686
BPM	0.95	0.8	1.13	0.5946	1.15	0.94	1.4	0.2234
CEM	1.4	1.07	1.82	0.0256	1.34	1	1.8	0.1095
CYHA	1.54	1.25	1.9	0.0012	1.61	1.22	2.12	0.0205
CYM	1.24	1.08	1.42	0.0087	1.26	1.04	1.54	0.0682
DHB	1.42	0.97	2.08	0.0903	1.33	0.87	2.02	0.2446
GAM	1.36	0.78	2.37	0.2914	1.37	0.7	2.69	0.405
HEM	1.51	1.09	2.09	0.0266	1.98	1.35	2.88	0.0166
HP2	1.23	1.01	1.51	0.0628	1.33	1.02	1.73	0.0867
HPM	1.5	1.2	1.87	0.003	1.57	1.23	2	0.0151
IPM3	1.48	1.17	1.88	0.0056	1.5	1.08	2.08	0.0617
MAD	1.41	1.07	1.85	0.0266	1.41	1.03	1.93	0.0883
MB3	1.61	1.25	2.07	0.0024	1.65	1.18	2.29	0.0317
PHE	1.6	1.13	2.26	0.0181	1.55	0.99	2.43	0.112
PHG	1.41	0.95	2.07	0.1082	1.33	0.9	1.97	0.2121
PMM	1.72	1.28	2.31	0.003	1.69	1.16	2.45	0.0409
TTC	1.13	0.96	1.32	0.1558	1.14	0.99	1.32	0.1277

Note: OR, odds ratio;
CI, confidence interval.

Table 3.

	Univariate				Multiple logistic regression			
Variables	OR	LCL	UCL	P value	OR	LCL	UCL	P value
2MH	1.11	0.91	1.34	0.3191	1.12	0.94	0.24	0.0022
34M	1.14	0.92	1.41	0.255	1.14	0.96	1.36	0.2068
AAM	1.13	0.89	1.44	0.3329	1.15	0.94	1.4	0.2378
AMC	1.17	1.01	1.34	0.052	1.17	1.01	1.35	0.0915
ATC	1.03	0.8	1.31	0.8292	0.92	0.73	1.16	0.514
BMA	0.97	0.81	1.15	0.737	0.95	0.81	1.11	0.5593
BPM	0.96	0.84	1.1	0.6064	0.99	0.87	1.13	0.8945
CEM	0.97	0.77	1.21	0.7762	0.99	0.8	1.22	0.9192
CYHA	1.14	0.97	1.33	0.1232	1.1	0.97	1.24	0.213
CYM	1.04	0.93	1.16	0.4812	1.02	0.93	1.13	0.6606
DHB	1.11	0.84	1.46	0.4928	1.17	0.9	1.51	0.287
GAM	1.26	0.93	1.71	0.1623	1.22	0.94	1.59	0.2013
HEM	1.15	0.9	1.46	0.2891	1.05	0.85	1.3	0.6403
HP2	0.97	0.79	1.2	0.797	0.99	0.81	1.2	0.9076
HPM	1.05	0.9	1.22	0.5683	1.06	0.93	1.22	0.4225
IPM3	1.09	0.91	1.3	0.3574	1.08	0.93	1.25	0.3705
MAD	1.08	0.84	1.38	0.5606	1.08	0.88	1.33	0.5092
MB3	1.04	0.82	1.31	0.7512	1.03	0.85	1.25	0.774
PHE	1.12	0.82	1.52	0.4926	1.1	0.85	1.42	0.4967
PHG	1.08	0.78	1.51	0.6387	1.09	0.82	1.45	0.5886
PMM	1.12	0.91	1.39	0.2932	1.14	0.96	0.25	0.0071
TTC	1.23	0.91	1.67	0.2002	1.27	0.93	1.74	0.1987

Supplemental table

VOC			Non-COPD		COPD		Non-Asthma		Asthma	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
2MH	70.43	18.96	68.82	19.74	104.11	27.96	73.33	22.72	54.65	5.16
34M	333.87	71.81	323.65	74.76	547.15	156.01	343.12	86.37	283.55	30.45
AAM	88.60	4.23	87.84	4.17	104.44	24.42	86.31	5.11	101.08	9.11
AMC	261.75	18.96	250.80	18.24	490.03	130.20	262.59	21.66	257.18	26.32
ATC	163.10	3.97	160.07	4.10	226.23	37.72	160.34	5.10	178.11	17.14

BMA	11.35	0.92	11.38	0.92	10.80	2.09	11.63	1.13	9.83	0.99
BPM	13.67	1.46	13.91	1.52	8.54	1.33	14.23	1.59	10.60	1.73
CEM	151.95	8.28	148.16	8.21	230.99	52.95	153.66	9.52	142.61	10.20
CYHA	9.12	1.11	8.10	0.86	30.40	13.08	8.57	1.14	12.14	2.09
CYM	39.63	4.35	36.18	3.37	111.56	43.35	37.86	4.68	49.30	7.71
DHB	402.53	14.72	399.33	14.81	469.30	29.93	400.62	16.29	412.91	26.17
GAM	12.66	0.57	12.42	0.51	17.61	4.89	12.41	0.63	14.02	1.09
HEM	1.52	0.12	1.46	0.11	2.87	1.08	1.48	0.14	1.78	0.38
HP2	67.52	5.98	66.82	6.16	82.09	22.85	69.11	6.75	58.86	9.02
HPM	541.97	42.51	507.67	30.28	1257.49	473.75	538.76	46.09	559.45	68.02
IPM3	15.88	1.88	13.88	1.01	57.63	28.29	15.53	2.04	17.76	2.82
MAD	193.71	8.47	191.32	8.22	243.66	40.33	191.80	9.16	204.10	19.74
MB3	11.95	1.12	10.82	0.70	35.53	14.87	11.86	1.26	12.42	1.81
PHE	1.31	0.06	1.28	0.04	1.97	0.48	1.29	0.04	1.40	0.16
PHG	278.83	10.39	275.09	10.11	357.00	47.27	277.54	11.62	285.87	23.02
PMM	466.46	36.61	429.59	27.06	1235.43	417.88	456.81	39.72	518.94	59.57
TTC	26.04	1.42	25.92	1.58	28.48	6.46	24.79	1.93	32.86	5.85