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Associations between Urinary Concentrations of Polycyclic Aromatic Hydrocarbons and Overactive Bladder in US Adults: Data from the National Health and Nutrition Examination Survey 2005–2016

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Polycyclic aromatic hydrocarbons · Overactive bladder · NHANES · Reproduction toxicity

Abstract
Introduction: Polycyclic aromatic hydrocarbons (PAHs) are a group of chemicals that can induce oxidative stress and related cytotoxicity. Whether urinary concentrations of PAHs have effects on overactive bladder (OAB) in the general population is still unclear. This study investigated the associations between urinary PAHs and OAB. ***Methods:*** 7,146 adults aged over 20 who participated in the US National Health and Nutrition Examination Survey 2005–2016 were studied. The impact of the six PAHs on OAB was evaluated by multivariate logistic regression, and percent changes related to different quartiles of those six PAH levels were calculated. Confounders including age, logarithmic urinary creatinine, gender, race, body mass index, educational level, marriage, poverty income ratio, diabetes, hypertension, and metabolic syndrome were controlled. ***Results:*** There is a significant positive correlation between urinary concentrations of the six PAHs we include in the study and the occurrence of OAB. Furthermore, individuals with higher PAH levels also reported a more severe OAB symptom score (OABSS). ***Conclusions:*** Our findings revealed that adult men in the USA with higher urinary PAHs had a higher risk of OAB incidence. These findings suggest the importance of strong environmental regulation of PAHs to protect population health. However, the underlying mechanisms still need further exploration.

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are a ubiquitous group of chemicals found in the environment. These compounds are present in various sources, such as vehicle exhausts, asphalt, wildfires, coal tar, charbroiled foods, agricultural burning, and tobacco smoke, which can expose people to mixtures of PAHs [1].

Overactive bladder (OAB) is a medical condition characterized by a frequent and urgent need to urinate, which can significantly affect an individual's quality of life [2]. While OAB is not life-threatening, it can persist for years, impacting an individual's overall wellbeing. Notably,

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OAB is responsible for 40–70% of urinary incontinence cases [3]. Literature reports suggest that OAB and its associated symptoms can contribute to a higher prevalence of depression, particularly among females [4]. This clearly demonstrates that OAB and its associated symptoms greatly affect individuals' daily lives and social interactions.

To the best of our knowledge, there has been limited research investigating the potential relationship between urinary concentrations of PAHs and the development of OAB. Therefore, our study aimed to assess the impact of six types of urinary PAHs on the development of OAB, utilizing data from the US National Health and Nutrition Examination Survey (NHANES). Our study focused on adults over the age of 20.

Materials and Methods

Data Source and Participants

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey series that assesses the health and nutritional status of the US population. NHANES uses a complex, multistage, probability sampling methodology to obtain data that accurately reflect the civilian, non-institutionalized US population [5, 6]. Further details can be found on the NHANES website (NHANES – National Health and Nutrition Examination Survey Homepage (cdc.gov)). The NHANES research has been approved by the NCHS Institutional Review Board, and all participants provided written informed consent.

This study utilized NHANES website data from 2005 to 2016 (n = 60,936) to examine the relationship between urinary PAHs and the prevalence and severity of OAB. Our sample was restricted to participants aged 20 years and older who completed the Kidney Conditions questionnaire and consented to the urinary BPA measurements. We excluded participants who were younger than 20 years (n = 26,756), lacked urinary PAH data (n = 24,098), lacked an OAB assessment (n = 953), or were missing data on urine creatinine, body mass index (BMI), education, marital status, and family income (n = 1,983). Ultimately, our sample consisted of 7,146 participants.

Assessment of OAB Symptom

The NHANES Kidney Conditions-Urology questionnaire was investigated to get data on OAB symptoms including urge urinary incontinence (UUI) and nocturia. The following two questions were used to assess the severity of urge incontinence: "During the past 12 months, have you leaked or lost control of even a small amount of urine with an urge or pressure to urinate and you couldn't get to the toilet fast enough?" and "How frequently does this occur?". Severity of nocturia was assessed based on another question: "During the past 30 days, how many times per night did you most typically get up to urinate, from the time you went to bed at night until the time you got up in the morning?".

We further quantified OAB symptoms with the aid of a well-established OAB questionnaire (overactive bladder symptom score, OABSS). Finally, the OABSS for each subject in the NHANES was obtained by adding the nocturia score and the UUI score. Nocturia frequency was divided into one, two, three, four, and five times a night, and the corresponding nocturia score of each level was defined as 0, 1, 2, 3, 3, 3. UUI frequency was defined as never, less than once a month, a few times a month, a few times a week, and every day and/or night, and the corresponding scores for each level are 0, 1, 1, 2, 3. Individuals with a total score ≥3 were considered to have a diagnosis of OAB disorder.

Concentrations of Urinary PAHs

The concentrations of urinary PAHs were designed as the exposure variable. PAH metabolites were measured in spot urine samples from participants. Measurement of urinary metabolites indicates exposure to the parent PAHs. Urine specimens were processed, stored, and shipped to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for analysis. Urinary PAHs were analyzed by the following procedure: enzymatic hydrolysis of urine, solid-phase extraction, derivation, and analyzed by GC/HRMS. The urinary creatinine was measured using Beckman Synchron CX3 Clinical Analyzer at the University of Minnesota [7]. Finally, the following six analytes were included in this study: 1-Hydroxynapthalene (1-Naphthol), 2-Hydroxynapthalene (2-Naphthol), 3-Hydroxyfluorene, 2-Hydroxyfluorene, 1-Hydroxyphenanthrene, and 1-Hydroxypyrene.

Other Covariates

Demographic Variables

Individuals' self-reported age, gender (categorized as male; female), race (categorized as Mexican American; other Hispanic; non-Hispanic White; non-Hispanic Black; or other race), education level (categorized as less than high school graduate; high school graduate; more than high school graduate), marital status at interview (categorized as married; widowed; divorced; separated; never married; living with partner), and poverty income ratio (<1; 1–3; ≥3) were obtained from the NHANES demographic files.

Body Mass Index

BMI data of study subjects were recorded in NHANES body measurements, which were collected by trained health technicians in a mobile examination center (MEC).

Urinary Creatinine

Urinary creatinine was naturally log-transformed (because the distribution of urinary creatinine is lognormal).

Diabetes Mellitus

A subject meeting any of the following criteria will be diagnosed with diabetes:

1. doctor told you that you have diabetes;
2. glycohemoglobin HbA1c (%) >6.5;
3. fasting glucose (mmol/L) ≥7.0;
4. random blood glucose (mmol/l) ≥11.1;
5. two-hour oral glucose tolerance test blood glucose (mmol/L) ≥11.1; and
6. use of antidiabetic agents.

Hypertension

Hypertension in NHANES was defined as participant self-reported hypertension (answer yes to the question, "Have you ever been told by a doctor or other health professional that you had

hypertension, also called high blood pressure?" or elevated blood pressure during physical examination (mean systolic blood pressure ≥140, or mean diastolic blood pressure ≥90).

Metabolic Syndrome

Metabolic syndrome is diagnosed when a person has at least 3 out of 5 specific health issues: high blood pressure, high triglyceride levels, low HDL cholesterol levels, abdominal obesity, or high fasting blood sugar. The specific values used to define these issues are:

1. high blood pressure;
2. triglyceride levels of 150 mg/dL or medication for high triglycerides;
3. HDL cholesterol levels of 50 mg/dL for women and 40 mg/dL for men, or medication for low HDL;
4. waist circumference of 88 cm in women and 102 cm in men; and
5. fasting blood sugar of 100 mg/dL or medication for hyperglycemia.

Data Analysis

Subsample B weights in a 12-year data circle and complex, multistage, probability sampling design were taken into consideration when we were conducting data analyses. Urinary creatinine is needed to form natural log-transformed lognormal distribution. Arithmetic means and standard deviations (SDs) were provided for normally distributed continuous data, whereas for lognormally distributed continuous data, geometric means (GMs) and 95% confidence intervals (95% CIs) were supplied [8]. In addition, categorical variables were expressed as proportions. Differences between OAB positive group and OAB negative group were calculated by analysis of variance or χ^2 test.

Multivariate logistic regression was used to assess the association of urinary concentrations of PAHs and other covariates with onset of OAB [9]. Furthermore, we constructed an ordinal logistic regression model to evaluate the relationship between each PAH and the severity of OAB, including nocturia score, urge incontinence score, and OABSS [10].

The odds ratios (ORs) and 95% CIs from logistic regressions were provided, so were the β and 95% CIs from ordinal logistic regression. P for trend values was estimated to explore dose-response trends. Subgroup analyses with full adjustment model were designed to explore the stratified relationships between PAHs and risk factors (age, logarithmic urinary creatinine, gender, race, BMI, educational level, marriage, poverty income ratio, diabetes, hypertension, and metabolic syndrome), after testing the heterogeneity of relationships between the subgroups of interests by *p* for interaction.

Result

Population Characteristics

The characteristics of the study participants were presented in Table 1 and sorted by whether they suffered from OAB. A total of 7,146 people were included in the study, and the average (standard error) age of participants was 48.81 years (17.60 years), with males representing 50.38%. About 1,425 of 7,146 were assessed positive for OAB. After analysis of variance, there was no significant statistical difference in the logarithmic treatment of urinary creatinine levels between the two groups. However, there were significant differences in other continuous variables after analysis of variance, and there are significant differences in categorical variables after χ^2 test.

It could be seen that if the 7,146 participants were classified according to the nocturia score, those who scored 0, 1, 2, and 3 points accounted for 32.36%, 37.00%, 17.60%, and 13.04%, respectively. If classified according to UUI score, the proportion of those with scores of 0, 1, 2, and 3 is 79.20%, 15.53%, 3.19%, and 2.08%. If classified according to OABSS level, the proportion of those with a score of 0, 1–2 (mild), 3–4 (moderate), and 5–6 (severe) is 28.88%, 51.18%, 17.38%, and 2.56%, and the proportion of those who were identified as suffering from OAB is 19.94%.

Multivariate Regression Analysis

The main multivariate regression results are shown in Table 2 below. When considering the six PAHs directly as continuous variables, *p* values of 1-Hydroxynaphthalene (OR = 1.14 95% CI: 1.08, 1.22), 2-Hydroxynaphthalene (OR = 1.20 95% CI: 1.09, 1.33), 2-Hydroxyfluorene (OR = 1.14 95% CI: 1.05, 1.26) and 1-Hydroxypyrene (OR = 1.17 95% CI: 1.05, 1.31) are less than 0.01, while *p* values of 3-Hydroxyfluorene (OR = 1.11 95% CI: 1.02, 1.20) and 1-Hydroxyphenanthrene (OR = 1.12 95% CI: 1.004, 1.26) are all less than 0.05, which means that the six substances we included in the regression were all significantly associated with the occurrence of OAB.

Table 2 shows the regression results of PAHs grouped by quartiles after full adjustment. We can find that compared with Q1, Q4 (OR = 1.74 95% CI: 1.30, 2.32) of 1-Hydroxynaphthalene, Q3 (OR = 1.43 95% CI: 1.10, 1.85) and Q4 (OR = 1.73 95% CI: 1.28, 2.34) of 2-Hydroxynaphthalene, Q4 (OR = 1.43 95% CI: 1.05, 1.95) of 3-Hydroxyfluorene, Q4 (OR = 1.41 95% CI: 1.00, 1.99) of 2-Hydroxyfluorene, Q3 (OR = 1.36 95% CI: 1.00, 1.85) of 1-Hydroxyphenanthrene, Q3 (OR = 1.47 95% CI: 1.11, 1.94), and Q4 (OR = 1.39 95% CI: 1.02, 1.91) of 1-Hydroxypyrene all had a significantly high risk leading to OAB. Apart from 1-Hydroxyphenanthrene, other PAHs all had a significant linear trend (*p* for trend of the five PAHs were 0.001, 0.001, 0.036, 0.026, and 0.018). Moreover, we also can find in Table 2 that, apart from 3-Hydroxyfluorene, the trend test of other 5 urinary PAHs are all statistically significant, which means people with a higher urinary concentration of PAHs are at higher risk for more severe OAB disorder.

Table 1. Weighted characteristics stratified by overactive bladder (OAB), NHANES 2005–2016

	OAB−	OAB+	*p* value	Total
Patients, *n*	5,721	1,425		7,146
Age, years	46.26±17.10	59.08±15.77	0.001##	48.81±17.60
Logarithmic creatinine, urine	4.55±0.75	4.54±0.68	0.760	4.55±0.74
Gender, %				
Male	52.67	41.19		50.38
Female	47.33	58.81	0.00##	49.62
Race, %				
Mexican American	14.77	14.60		14.74
Non-Hispanic White	44.73	40.35		43.86
Non-Hispanic Black	18.60	27.79		20.43
Other Hispanic	10.16	10.74		10.27
Other race – including multi-racial	11.74	6.53	0.001##	10.70
BMI, %				
<25	31.34	20.49		29.18
25–30	33.68	30.45		33.04
>30	34.98	49.06	0.001##	37.78
Education, %				
<High school	21.22	33.89		23.75
High school	22.30	24.21		22.68
>High school	56.48	41.90	0.001##	53.57
Marriage, %				
Married	52.04	48.07		51.24
Widowed	5.51	14.52		7.31
Divorced	9.84	15.23		10.92
Separated	2.85	3.65		3.01
Never married	20.84	12.70		19.21
Living with partner	8.92	5.83	0.001##	8.31
Poority, %				
<1	20.24	27.79		21.74
1–3	40.64	45.82		41.67
>3	39.12	26.39	0.001##	36.59
Diabetes, %				
No	85.04	67.93		81.63
Yes	14.96	32.07	0.001##	18.37
Hypertension, %				
No	62.40	35.95		57.14
Yes	37.59	64.05	0.001##	42.86
Metabolic syndrome, %				
No	79.16	64.28		76.20
Yes	20.84	35.72	0.001##	23.80

For continuous variables, arithmetical means (standard errors) were reported and statistic differences in different quintiles were compared by analysis of variance. OAB+, participants had overactive bladders; OAB−, participants did not have overactive bladders; CI, confidence interval. #$p < 0.05$. ##$p < 0.01$.

Subgroup Analysis

Table 3 presents the results of subgroup analyses that were conducted to investigate the association between PAHs and OAB. The subgroups were categorized based on gender (male and female), age (20–40 including 20, 40–60 including 40, and ≥60), and BMI (<25, 25–30 including 25, and ≥30). The analysis was adjusted for age, logarithmic urinary, gender, race, BMI, educational level, marriage, poverty income ratio, diabetes, hypertension, and metabolic syndrome.

The influence of gender, age, and BMI on the association between urinary concentrations of PAHs and OAB was examined in this study. After adjusting for confounding factors, the effects of 1-Hydroxyphenanthrene and 1-Hydroxypyrene on OAB were significantly influenced by gender, with a higher impact on women than men. However, no significant gender differences were found for the other four PAHs. When grouping by age, no statistically significant interaction was found.

Table 2. The adjusted ORs (95% CIs) for the association between the quartiles of urinary PAHs and OAB, NHANES 2005–2016

	Nocturia score	Urgenturia score	OBASS LEVEL	OAB+
1-Hydroxynaphthalene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.11 (0.91, 1.35)	1.30 (1.04, 1.63)#	1.17 (0.97, 1.43)	1.22 (0.92, 1.65)
Q3	1.09 (0.92, 1.31)	1.36 (1.02, 1.80)#	1.18 (0.80, 1.45)	1.22 (0.89, 1.68)
Q4	1.22 (1.01, 1.46)#	1.93 (1.47, 2.51)##	1.34 (1.09, 1.65)##	1.74 (1.30, 2.32)##
p for trend	0.041#	0.001##	0.007##	0.001##
2-Hydroxynaphthalene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.12 (0.94, 1.31)	1.22 (0.95, 1.55)	1.15 (1.01, 1.34)	1.21 (0.94, 1.55)
Q3	1.16 (0.98, 1.38)	1.25 (0.95, 1.65)	1.20 (1.01, 1.43)#	1.43 (1.10, 1.85)##
Q4	1.39 (1.13, 1.70)##	1.57 (1.16, 2.14)##	1.40 (1.14, 1.73)##	1.73 (1.28, 2.34)##
p for trend	0.003##	0.008##	0.003##	0.001##
3-Hydroxyfluorene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.01 (0.84, 1.22)	1.02 (0.79, 1.32)	1.08 (0.89, 1.32)	0.93 (0.71, 1.22)
Q3	0.90 (0.74, 1.08)	1.05 (0.82, 1.35)	0.99 (0.82, 1.19)	0.83 (0.64, 1.08)
Q4	1.08 (0.89, 1.31)	1.62 (0.81, 2.12)##	1.21 (0.99, 1.49)	1.43 (1.05, 1.95)#
p for trend	0.722	0.001##	0.129	0.036#
2-Hydroxyfluorene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.14 (0.95, 1.36)	1.18 (0.91, 1.54)	1.22 (1.00, 1.48)#	1.02 (0.75, 1.40)
Q3	1.22 (0.98, 1.48)#	1.11 (0.85, 1.42)	1.27 (1.04, 1.55)#	1.17 (0.88, 1.54)
Q4	1.28 (1.05, 1.55)#	1.70 (1.27, 2.27)##	1.42 (1.19, 1.75)##	1.41 (1.00, 1.99)#
p for trend	0.011#	0.001##	0.002##	0.026#
1-Hydroxyphenanthrene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.15 (0.97, 1.35)	1.07 (0.85, 1.36)	1.21 (1.01, 1.43)#	1.12 (0.84, 1.49)
Q3	1.27 (1.05, 1.54)#	1.28 (0.99, 1.67)	1.34 (1.09, 1.63)##	1.36 (1.00, 1.85)#
Q4	1.23 (1.04, 1.46)#	1.34 (1.03, 1.72)#	1.32 (1.13, 1.57)##	1.30 (0.96, 1.76)
p for trend	0.022##	0.021#	0.002##	0.053
1-Hydroxypyrene, ng/L				
Q1	Reference	Reference	Reference	Reference
Q2	1.09 (0.91, 1.31)	1.16 (0.90, 1.51)	1.20 (0.99, 1.43)	1.21 (0.91, 1.62)
Q3	1.20 (1.02, 1.39)#	1.45 (1.13, 1.86)##	1.34 (1.15, 1.58)##	1.47 (1.11, 1.94)##
Q4	1.19 (1.02, 1.38)##	1.63 (1.23, 2.14)##	1.31 (1.13, 1.52)##	1.39 (1.02, 1.91)#
p for trend	0.003#	0.001##	0.001##	0.018#

ORs were adjusted for all covariates including age, logarithmic urinary (mg/dL), gender, race, body mass index (BMI), educational level, marriage, poverty income ratio, diabetes, hypertension, and metabolic syndrome. OAB+, participants had overactive bladder; CI, confidence interval. #$p < 0.05$. ##$p < 0.01$.

For the six PAHs, the influence of urinary PAHs on OAB did not differ across age groups. For BMI, all but 1-Hydroxynaphthalene had a significant interaction with OAB. Notably, lower BMI groups were found to have a higher risk of developing OAB, particularly for 2-Hydroxynaphthalene, 3-Hydroxyfluorene, 2-Hydroxyfluorene, 1-Hydroxyphenanthrene, and 1-Hydroxypyrene.

Discussion

We conducted a large-scale correlation study in American adults using the NHANES database to investigate the association between six types of PAHs found in urine and the prevalence of OAB. When conducting stratified analysis, multiple layers of the six PAHs showed significant correlation with OAB.

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Table 3. Subgroup analysis of association between urinary PAHs and OAB, NHANES 2005–2016

	Male	Female	*p* for interaction	<40	40–60	>60	*p* for Interaction	<25	25–30	>30	*p* for Interaction
1-Hydroxynaphthalene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	0.96 (0.51, 1.79)	1.40 (1.01, 1.95)#		1.54 (0.85, 2.80)	1.01 (0.61, 1.65)	1.30 (0.91, 1.86)		1.11 (0.64, 1.91)	1.68 (1.05, 2.67)#	1.07 (0.69, 1.66)	
Q3	1.30 (0.75, 2.26)	1.14 (0.77, 1.67)		1.48 (0.70, 3.11)	1.17 (0.71, 1.92)	1.15 (0.80, 1.66)		1.36 (0.73, 2.55)	1.37 (0.89, 2.12)	1.09 (0.69, 1.73)	
Q4	1.81 (1.05, 3.09)#	1.67 (1.24, 2.27)##		2.25 (1.04, 4.86)#	1.93 (1.19, 3.12)##	1.32 (0.92, 1.89)		1.97 (1.15, 3.37)#	2.13 (1.30, 3.49)##	1.44 (0.92, 2.26)	
p for trend	0.005##	0.008##	0.298	0.071	0.004#	0.245	0.295	0.012#	0.10#	0.103	0.114
2-Hydroxynaphthalene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	1.22 (0.86, 1.73)	1.17 (0.84, 1.64)		2.08 (1.07, 4.06)#	1.19 (0.74, 1.91)	1.03 (0.75, 1.39)		1.97 (1.18, 3.30)#	0.82 (0.53, 1.26)	1.26 (0.81, 1.97)	
Q3	1.38 (0.93, 2.04)	1.46 (1.04, 2.05)#		2.29 (1.19, 4.44)#	1.35 (0.84, 2.18)	1.34 (0.96, 1.88)		2.07 (1.20, 3.58)##	1.17 (0.70, 1.95)	1.38 (0.90, 2.12)	
Q4	1.59 (1.02, 2.48)#	1.80 (1.25, 2.59)##		2.85 (1.30, 6.22)##	1.92 (1.10, 3.34)#	1.30 (0.92, 1.84)		3.06 (1.82, 5.17)##	1.58 (0.92, 2.71)	1.42 (0.88, 2.31)	
p for trend	0.035#	0.001##	0.134	0.009##	0.015#	0.040#	0.553	0.001##	0.081	0.163	0.048#
3-Hydroxyfluorene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	0.84 (0.56, 1.26)	0.97 (0.72, 1.30)		2.16 (1.15, 4.05)#	0.84 (0.54, 1.29)	0.73 (0.48, 1.12)		1.53 (0.92, 2.55)	1.05 (0.60, 1.85)	0.68 (0.46, 0.99)#	
Q3	0.75 (0.49, 1.16)	0.87 (0.62, 1.21)		1.40 (0.71, 2.76)	0.51 (0.31, 0.84)##	0.98 (0.68, 1.43)		1.38 (0.77, 2.45)	1.10 (0.70, 1.73)	0.54 (0.34, 0.85)##	
Q4	1.34 (0.79, 2.28)	1.45 (1.02, 2.04)		2.60 (1.42, 4.77)##	1.28 (0.73, 2.24)	1.14 (0.71, 1.82)		2.12 (1.26, 3.60)##	1.89 (1.07, 3.36)#	0.98 (0.62, 1.54)	
p for trend	0.217	0.073	0.479	0.030#	0.346	0.403	0.631	0.017#	0.032#	0.964	0.024#
2-Hydroxyfluorene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	0.90 (0.57, 1.45)	1.06 (0.73, 1.53)		1.68 (0.90, 3.14)	0.95 (0.57, 1.58)	0.89 (0.57, 1.38)		1.54 (0.96, 2.46)#	1.13 (0.65, 1.96)	0.77 (0.52, 1.15)	
Q3	1.07 (0.66, 1.75)	1.19 (0.83, 1.70)		2.55 (1.34, 4.86)##	0.88 (0.50, 1.57)	1.06 (0.75, 1.49)		1.90 (1.13, 3.19)#	1.54 (0.89, 2.67)	0.75 (0.49, 1.15)	
Q4	1.23 (0.69, 2.21)	1.46 (0.98, 2.17)		3.08 (1.53, 6.19)##	1.32 (0.70, 2.51)	0.97 (0.62, 1.52)		2.22 (1.40, 3.51)##	1.84 (0.99, 3.43)	0.91 (0.55, 1.50)	
p for trend	0.311	0.041#	0.255	0.001##	0.315	0.858	0.185	0.002##	0.037#	0.898	0.007##
1-Hydroxyphenanthrene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	1.13 (0.75, 1.70)	1.09 (0.76, 1.54)		1.32 (0.77, 2.26)	0.93 (0.56, 1.57)	1.14 (0.79, 1.65)		0.99 (0.58, 1.72)	1.40 (0.87, 2.27)	1.03 (0.67, 1.58)	
Q3	1.27 (0.80, 2.02)	1.40 (0.91, 2.14)		1.68 (0.93, 3.01)	1.14 (0.67, 1.93)	1.31 (0.87, 1.98)		1.21 (0.67, 2.17)	2.12 (1.21, 3.70)##	1.04 (0.67, 1.61)	
Q4	0.93 (0.58, 1.48)	1.62 (1.08, 2.44)#		1.93 (1.00, 3.70)#	1.06 (0.61, 1.85)	1.20 (0.80, 1.81)		1.84 (1.01, 3.39)#	1.63 (0.92, 2.88)	0.97 (0.61, 1.53)	
p for trend	0.72	0.010##	0.009##	0.057	0.656	0.295	0.803	0.036#	0.050#	0.864	0.022#

Table 3 (continued)

	Male	Female	*p* for interaction	<40	40–60	>60	*p* for Interaction	<25	25–30	>30	*p* for Interaction
1-Hydroxypyrene											
Q1	Reference	Reference		Reference	Reference	Reference		Reference	Reference	Reference	
Q2	1.00 (0.68, 1.46)	1.35 (0.92, 1.96)		0.89 (0.50, 1.57)	1.82 (1.06, 3.11)[#]	0.98 (0.73, 1.32)		1.49 (0.82, 2.70)	1.96 (1.25, 3.10)[##]	0.78 (0.53, 1.15)	
Q3	1.29 (0.84, 1.97)	1.56 (1.08, 2.24)[#]		1.74 (0.92, 3.27)	1.55 (0.89, 2.76)	1.40 (0.96, 2.05)		1.36 (0.74, 2.49)	2.56 (1.60, 3.12)[##]	1.01 (0.67, 1.55)	
Q4	1.07 (0.69, 1.67)	1.64 (1.09, 2.47)[#]		2.65 (0.80, 3.40)	1.79 (1.02, 3.12)[#]	0.92 (0.58, 1.47)		2.17 (1.29, 3.63)[##]	2.08 (1.20, 3.59)[##]	0.84 (0.49, 1.43)	
p for trend	0.498	0.014[#]	0.011[#]	0.091	0.161	0.475	0.83	0.005[##]	0.005[##]	0.817	0.019[#]

Subgroup analysis were adjusted for all covariates including age, logarithmic urinary creatinine, gender, race, body mass index (BMI), educational level, marriage, poverty income ratio, diabetes, hypertension, and metabolic syndrome. CI, confidence interval. [#]$p < 0.05$. [##]$p < 0.01$.

Among them, two out of the four quantiles of 2-Hydroxynaphthalene and 1-Hydroxypyrene have a statistically significant positive correlation with OAB, which indicates that they have a high correlation with OAB. As OABSS level, three out of the four quantiles of 2-Hydroxyfluorene and 1-Hydroxyphenanthrene have a statistically significant positive correlation with OABSS, indicating that they may cause more severe OAB symptoms.

In the subgroup analysis of our study, we found significant inter-group differences for 2-Hydroxynaphthalene, 3-Hydroxyfluorene, 2-Hydroxyfluorene, 1-Hydroxyphenanthrene, and 1-Hydroxypyrene when conducting subgroup analysis based on BMI grouping. Interestingly, we also observed that participants with media or lower BMI were at higher risk of OAB when exposed to these PAH compounds, contrary to the commonly held belief that higher BMI is associated with higher risk. When grouping by gender, 1-Hydroxyphenanthrene and 1-Hydroxypyrene showed significant gender differences, with women being significantly more susceptible to OAB than men, which is consistent with existing research results [11]. However, no statistically significant differences were observed among the other four PAHs among different genders. And when grouping and analyzing by age, no significant intergroup differences were observed among the six PAHs. The traditional view suggests that the risk of OAB increases with age [12], but it was not observed in our study.

Histological investigations of the bladder urothelium and suburothelium have shown that chronic inflammation is present in 60% of baseline biopsies of patients with OAB [13]. The inflammatory responses triggered by the activation of primary sensory neurons also induce overexpression of transient receptor potential vanilloid receptor subfamily type 1 (TRPV1) in the suburothelium as well as c-fos protein in the dorsal root ganglia, which have been demonstrated in rat models of OAB and in human bladder biopsies [14, 15]. In another natural experiment among travelers, the researchers have found that PAH exposure accompanied with increased C-reactive protein, fibrinogen, IL-8, and IL-10 and decreased MCP-1, sCD40L, and sCD62P levels in the blood [16]. Hence, it is plausible to speculate that PAHs induce the production of inflammatory factors in the body, leading to the subsequent onset of OAB and its associated symptoms. PAHs are able to span the cells' membrane due to their lipophilic characteristics and can also act as PAH saryl hydrocarbon receptor (AhR) ligands. After a ligand is bound, the AhR translocates into the nucleus, and it

binds to ARNT (a member of the bHLH-PAS family) to form an active heterodimer, which modulates the expression of targets by binding to xenobiotic responsive elements and coregulators [17]. Activation of AhR upregulates cytochrome P450 (CYP) metabolizing enzymes that can transform PAHs into quinones, which can be further metabolized into semiquinones [18]. In this pathway, PAHs can induce reactive oxygen species formation through the AhR-CYP1A1 pathway and cause lipid peroxidation and DNA damage [19, 20]. In addition, PAHs can also generate strong pro-inflammatory responses; exposure to PAHs in the air can cause macrophages to release pro-inflammatory cytokines, leading to chronic airway inflammation such as asthma [21]. Moreover, it has been shown that the activation of AhR can influence mitochondrial membrane potential and apoptosis [22, 23], while reactive oxygen species overproduction induces oxidative damage and activates the Nrf2 signaling pathways, finally inducing reduced mitochondrial membrane potentials and reduced mtDNAcns [24, 25]. In a study on Polish workers exposed to PAHs, workers with PAH exposure showed higher mtDNAcn compared with controls [26]. Similarly, shNrf2 cells exposed to the organic extracts showed lower mitochondrial membrane potential and lower mtDNA copy number [24]. Recent investigation of urinary chemokines in OAB patients also showed increases in monocyte chemotactic protein-1 (MCP-1) and some pro-inflammatory cytokines; the mean urine cytokine/chemokine levels were higher in OAB-wet than OAB-dry, suggesting a linear relationship between symptom severity and cytokine levels [27, 28], which is consistent with the conclusions drawn in our study.

Although our research contains several innovative and unique aspects, it also has several limitations that merit attention. The primary limitation is the cross-sectional nature of NHANES, which precludes the drawing of temporal or causal inferences regarding the association of PAHs and OAB. Second, due to the lack of OAB-related treatment data in the NHANES database, we cannot exclude patients who receive OAB-related treatment. However, these biases are likely to be non-differential, minimizing any observed association. More in-depth clinical and translational research is needed, including research on potential mechanisms. Notwithstanding these limitations, the study's findings are interesting, as they include a relatively large nationally representative multiethnic sample, standardized data collection approaches in NHANES, and the ability to adjust for potential confounders.

Conclusion

Our study revealed that adult men in the USA with elevated levels of six urinary PAHs had a greater risk of OAB. Furthermore, individuals with higher PAH levels also reported a more severe OABSS, indicating more pronounced symptoms of nocturia and urinary incontinence.

Statement of Ethics

Ethical approval and consent were not required as this study was based on publicly available data. This study did not require Institutional Review Board approval of the First Affiliated Hospital of Nanjing Medical University.

Conflict of Interest Statement

The authors declare that they have no real or potential competing interests.

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Author Contributions

Shihang Pu: data collection or management and data analysis. Qi Li and Zhijun Tao: manuscript writing/editing and data analysis. Songbo Wang and Xiangyu Meng: manuscript editing. Shangqian Wang: data collection or management. Zengjun Wang: protocol/project development. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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