Association Between Polycyclic Aromatic Hydrocarbons and Urinary Incontinence in U.S. Adult: NHANES 2007-2016

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Research

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Abstract

Background: It has been reported that polycyclic aromatic hydrocarbons (PAHs) were associated with a variety of diseases, but it is still unclear whether PAHs are associated with urinary incontinence (UI). This study aims to assess the association between PAHs and UI.

Methods: Data were collected from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2016. 10 PAHs were detected totally. UI was diagnosed and distinguished into stress UI (SUI), urgency UI (UUI), and mixed UI (MUI) by answers of self-reported questions. Multivariate logistic regression analyses categorizing PAHs as quartiles were performed to detect the correlation between urinary PAHs and all three UI subtypes. Models were adjusted for common epidemiological factors including demographic and living habits factors.

Results: A total of 12,393 participants of NHANES with available urine PAHs and UI data were eligible. No significant differences were observed between characteristics of participants with and without UI. Increasing prevalence of UUI was associated with the highest quartiles of 1-hydroxynaphthalene (OR=1.208, 95%CI=1.026-1.422, p for trend=0.036), 1-hydroxyphenanthrene (OR=1.203, 95%CI=1.017-1.423, p for trend=0.004), and 1-hydroxypyrene (OR=1.251, 95%CI=1.062-1.475, p for trend=0.013) compared with the lowest quartiles. Increasing rate of SUI was observed in participants with higher exposure of all 9 PAHs (p for trend<0.025) except 3-hydroxyfluorene (OR=1.115, 95%CI=0.929-1.338, p for trend=0.241). Compared with the lowest quartiles, association between MUI and the highest quartiles of 1-hydroxyphenanthrene (OR=1.554, 95%CI=1.244-1.942, p for trend<0.001) and 1-hydroxypyrene (OR=1.307, 95%CI=1.047-1.630, p for trend=0.018) was observed.

Conclusion: Our study suggested a positive relationship between U-PAHs and the prevalence of all three types of UI. Almost all PAHs are positively correlated with SUI.

Introduction

Polycyclic Aromatic Hydrocarbons (PAHs) are organic substances distributed in air, soil, water and even food. They are composed of aromatic rings and consist of carbon as well as hydrogen atoms (1; 2). PAHs are mainly generated by the incomplete combustion of organic matters (3). Automobile exhaust, fossil fuels using, tobacco smoking, asphalt production, and agricultural burning are the main ways of human exposure to PAHs (4). There have been studies assessing relationships between PAHs exposure and health problems, and some of them showed that PAHs may have carcinogenesis, teratogenesis, genotoxicity, immune abnormality and other adverse effects on human body (5–8).

Urine incontinence (UI) is described as an involuntary loss of urine, which often increases with age (9). According to the publications, the involuntary urine loss can occur in up to 69% women as well as 39% men, which stands as an important factor in the overall health and quality of life (10–13). As the population ages, the medical costs associated with UI are placing a huge burden on society (14). Thus, there has been a flurry of research in recent years focusing on the factors associated with UI. UI is commonly categorized into stress UI (SUI), urgency UI (UUI), and mixed UI (MUI).

UI has been revealed with a strong relation with sex hormones by a number of previous studies. (15; 16) Meanwhile, a recent evidence suggested that PAHs were also associated with sex hormones. (17) To the best of my knowledge, few results on the relationship between PAH exposure and UI have been reported. The present study assessed the relationship between urinary PAHs and UI in the United States general population.

Methods

Study Design and Population

The present study used data from five cycles (2007–2016) of National Health and Nutrition Examination Survey (NHANES) (<http://www.cdc.gov/nchs/nhanes.htm>). NHANES collects demographic, behavioral, clinical, social, dietary, and laboratory data from non-institutional people in the United States, which is a cross-sectional survey of a representative population of the nation

with purpose of making assessment of the health and nutrition condition of adults and minors across the country. The survey is programmed of National Center for Health Statistics (NCHS). Detailed information on participants' demographics, dietary factors, socioeconomic status, and medical status was collected in-home by professional interviewers. Standardized medical physical examinations as well as the biospecimen collection were performed by experienced medical personnel in mobile examination centers (MECs). Patients without laboratory data of urinary PAHs metabolites and without UI questionnaire information were excluded. The study was approved by Ethics Review Board of NCHS, and all participants had been required to sign an informed consent form before the study began.

Polycyclic Aromatic Hydrocarbons

Through the survey, urine samples were collected by professionally trained technicians and then frozen in -20 ° C environment according to Laboratory/Medical Procedures pending further analysis. PAHs in urine samples were tested using capillary gas chromatography combined with high resolution mass spectrometry (GC-HRMS), isotope dilution gas chromatography/tandem mass spectrometry (GC-MS/MS), and isotope dilution online solid phase extraction high performance liquid chromatography/tandem mass spectrometry (online SPE-HPLC-MS/MS). The specific test method varied with the year. (<http://www.cdc.gov/nchs/nhanes.htm>). Ten hydroxylated urinary PAH, namely, 1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-chydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxypyrene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, and 4-hydroxyphenanthrene were observed.

Outcome Information

UI was determined and classified by following questionnaires among all participants over the age of 20. Participants with positive answer to "Have you leaked or lost control of even a small amount of urine with activity like coughing, lifting, or exercise during the past 12 months?" were categorized as SUI. UUI was diagnosed as answering yes to "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 during the past 12 months?" People with answer YES to both UUI and SUI questions were diagnosed with MUI. The above questions were asked at MECs by trained interviews, using the Computer-Assisted Personal Interview system.

Covariates Measurement

The covariates adjusting association between urinary PAHs and UI include age, race (Mexican Hispanic, other Hispanic, non-Hispanic white, non-Hispanic black, and others), body mass index (BMI), ratio of family income-poverty, marital status (living alone and married or living with partner and married or living with partner), educational level (under high school, high school or general educational development, and above high school), physical activity level (under moderate, moderate, and vigorous), Charlson comorbidity index, smoking status (never, former, and current), and alcohol drinking level (none, moderate, heavy). Smoking level was classified as never smoking (< 100 cigarettes during the life), former smoking ($\geq$ 100 cigarettes during the life, currently not smoking) and current smoking ($\geq$ 100 cigarettes during the life, currently smoking). The alcohol consumption categories were defined as none (0 g per day), moderate (0.1–27.9 g per day for men and 0.1–13.9 g per day for women), and heavy (no less than 28.0 g per day for men and no less than 14.0 g per day for women). All information is available on NHANES website (<http://www.cdc.gov/nchs/nhanes.htm>).

Statistical Analysis

The characteristics of participants were presented in the form of numbers (percentage) for categorical variables and mean $\pm$ standard deviation (SD) for continuous variables. Differences between base line characteristics of people with UI and without UI were calculated using either Kruskal Wallis H test on continuous variables or a weighted chi-square test on categorical variables.

Since the concentrations of PAHs were diluted by urine, we adjusted it and used the creatinine corrected PAHs concentrations instead of the original concentrations for analysis. Because the urine PAHs showed a highly skew distribution, log transformation was performed then. Due to the same reason, PAHs levels were presented as geometric mean (GM), median,

upper and lower quartiles. When the urine PAHs concentrations is lower than the lower limit of detection (LLOD), it is replaced by the square root of 2. The continuous variables of urine PAHs concentrations were separated into four ranges by the median, upper and lower quartiles, and were transformed into categorical variables. Multivariable logistic regression models were used and the relationships between urinary PAHs and three UI subtypes were estimated with odds ratios (ORs) and corresponding 95% confidence intervals (95%CI). Three models were established: a non-adjusted model (Model I), a partially adjusted model (Model II) with age, race, and BMI adjusted, and a fully adjusted model (Model III) with age, race, BMI, ratio of family income-poverty, educational level, marital status, physical activity, Chalon comorbidity index, smoking status, and alcohol drinking adjusted.

Missing values were entered by the median of existing continuous variables or by mode of existing categorical variables. All statistical analyses were performed with R ([http:// www.R-project.org](http://www.R-project.org), The R Foundation) and Empower (www.empowerstats.com). Considering the complex sampling design of NHANES, weighted analyses were conducted. The p-values of multiple testing were all adjusted and statistically significant were defined as two-tailed $p < 0.05$.

Results

In the NHANES database from 2007 to 2016, a total of 50,588 participants aged over 20 were enrolled in the survey, among which 13,085 participants with detectable level of urinary PHAs metabolites were included. 692 participants were excluded due to lack of UI information. Finally, a total of 12,393 adults over 20 years of age were analyzed. Figure 1 showed the flowchart of participants selection.

Table 1 presented the basic characteristics of all participants in groups with UI and without UI. Significant differences in age, gender, race, ration of family income-poverty, educational level, marital, BMI, Charlson comorbidity index, and alcohol drinking were observed between participants with and without UI. Table 2 presented the distribution of detectable urinary PAHs, including GM, median and quartiles (Q1, Q2) for each .

Table 1
Basic characteristics of participants in the US adults, NHANES 2007 ~ 2016

Characteristics (n = 12,393)	UI (n = 4,229)	Without UI (n = 8,164)	P value ^a
Age, mean ± SD (years)	55.62 ± 16.88	45.99 ± 17.86	< 0.001
Gender, n (%)			< 0.001
Male	1051 (24.85%)	5104 (62.52%)	
Female	3178 (75.15%)	3060 (37.48%)	
Race, n (%)			< 0.001
Mexican American	739 (17.47%)	1369 (16.77%)	
Other Hispanic	313 (7.40%)	692 (8.48%)	
Non-Hispanic White	2061 (48.73%)	3678 (45.05%)	
Non-Hispanic Black	861 (20.36%)	1661 (20.35%)	
Other Race	255 (6.03%)	764 (9.36%)	
Ratio of Family Income to Poverty, n (%)			0.024
< 1.3	1227 (29.01%)	2286 (28.00%)	
1.3 ~ 3.5	1804 (42.66%)	3372 (41.30%)	
> 3.5	1198 (28.33%)	2506 (30.70%)	
Education Level, n (%)			< 0.001
Less than High School	1198 (28.33%)	2036 (24.94%)	
High School/GED	994 (23.50%)	1864 (22.83%)	
Above High School	2037 (48.17%)	4264 (52.23%)	
Marital, n (%)			0.001
Married or Living with Partner	2479 (58.62%)	5030 (61.61%)	
Living Alone	1750 (41.38%)	3134 (38.39%)	
BMI, n (%)			< 0.001
≤ 25	1031 (24.38%)	2659 (32.57%)	
25 ~ 30	1297 (30.67%)	2843 (34.82%)	
> 30	1901 (44.95%)	2662 (32.61%)	
Charlson Comorbidity Index, n (%)			< 0.001
0	1951 (46.13%)	5323 (65.20%)	
1	1560 (36.89%)	2199 (26.94%)	
2, 3, 4, and 5	718 (16.98%)	642 (7.86%)	
Smoking, n (%)			0.241

abbr. UI, urinary incontinence; GED, general educational development; BMI, body mass index; SD, standard deviation; n, number of subjects; %, weighted percentage

^a Difference in characteristics between participants with and without UI

Characteristics (n = 12,393)	UI (n = 4,229)	Without UI (n = 8,164)	P value ^a
Never	2233 (52.80%)	4398 (53.87%)	
Former	1272 (30.08%)	2337 (28.63%)	
Current	724 (17.12%)	1429 (17.50%)	
Alcohol Drinking, n (%)			< 0.001
None	3441 (81.37%)	6024 (73.79%)	
Moderate	262 (6.20%)	793 (9.71%)	
Heavy	526 (12.44%)	1347 (16.50%)	
abbr. UI, urinary incontinence; GED, general educational development; BMI, body mass index; SD, standard deviation; n, number of subjects; %, weighted percentage			
^a Difference in characteristics between participants with and without UI			

Table 2
Distribution of urinary PAH levels (ng/L) in US adults, NHANES 2007 ~ 2016

U-PAHs	GM	Q1	Median	Q3
1-Hydroxynapthalene	31032.023	787.00	1890.00	6470.00
2-Hydroxynapthalene	8434.22	1730.78	4090.00	9846.27
3-Hydroxyfluorene	320.18	41.00	85.50	260.00
2-Hydroxyfluorene	628.55	114.73	237.00	596.00
3-Hydroxyphenanthrene	211.30	43.00	86.60	178.72
1-Hydroxyphenanthrene	214.97	68.40	130.00	242.00
2-Hydroxyphenanthrene	113.08	33.73	65.20	126.00
1-Hydroxypyrene	198.17	49.50	94.00	199.00
9-Hydroxyfluorene	602.18	144.00	299.65	625.47
4-Hydroxyphenanthrene	44.23	12.00	25.00	50.08
abbr. GM, geometric mean; Q1, quartile 1; Q3, quartile 3.				

Table 3 showed the association between 10 PAHs and UI and the results of trend test. Significantly increasing UI prevalence was associated with the highest quantiles compared with the lowest quantiles of 1-hydroxynapthalene (OR = 1.208, 95%CI = 1.026–1.422, p for trend = 0.036), 1-hydroxyphenanthrene (OR = 1.203, 95%CI = 1.017–1.423, p for trend = 0.004), and 1-hydroxypyrene (OR = 1.215, 95%CI = 1.062–1.475, p for trend = 0.013) in Model III. The association between PAHs and SUI and trend test were presented in Table 4. In Model III, significantly increases of SUI odds were observed in all PAHs (p for trend all lower than 0.025) except 3-hydroxyfluorene (OR = 1.115, 95%CI = 0.020–1.338, p for trend = 0.241). Table 5 showed the results of analysis of association between PAHs categorized as quartiles and MUI. Compared with the lowest quantile, positive association between the highest quantile of 1-hydroxyphenanthrene (OR = 1.554, 95%CI = 1.244–1.942, p for trend < 0.001) and 1-hydroxypyrene (OR = 1.307, 95%CI = 1.047–1.630, p for trend = 0.018) and MUI was observed in the fully adjusted model.

Table 3
Association between urinary PAHs and UUI among US adults, NHANES 2007 ~ 2016

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
1-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	1.025(0.904,1.162)	0.701	1.076(0.938,1.235)	0.297	1.061(0.924,1.219)	0.403
quantile 3	1.110(0.981,1.256)	0.098	1.141(0.995,1.309)	0.059	1.100(0.955,1.266)	0.187
quantile 4	1.174(1.038,1.328)	0.011	1.394(1.209,1.607)	< 0.001	1.208(1.026,1.422)	0.023
p for trend		0.010		< 0.001		0.036
2-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.877(0.777,0.991)	0.035	1.021(0.893,1.168)	0.758	0.967(0.843,1.108)	0.628
quantile 3	0.909(0.805,1.025)	0.120	1.237(1.075,1.422)	0.003	1.108(0.958,1.281)	0.168
quantile 4	0.853(0.755,0.964)	0.011	1.325(1.140,1.540)	< 0.001	1.063(0.893,1.264)	0.492
p for trend		0.054		< 0.001		0.416
3-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.852(0.756,0.960)	0.008	0.981(0.856,1.123)	0.776	0.953(0.831,1.092)	0.487
quantile 3	0.733(0.649,0.829)	< 0.001	0.974(0.843,1.126)	0.725	0.911(0.785,1.057)	0.217
quantile 4	0.788(0.698,0.889)	< 0.001	1.204(1.038,1.396)	0.014	0.940(0.777,1.137)	0.521
p for trend		0.020		< 0.001		0.896
2-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.919(0.815,1.035)	0.164	1.086(0.947,1.246)	0.236	1.032(0.898,1.186)	0.654

abbr. PAH, polycyclic aromatic hydrocarbons; UUI, urgency urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 3	0.779(0.690,0.881)	< 0.001	1.045(0.902,1.210)	0.562	0.953(0.818,1.110)	0.535
quantile 4	0.835(0.740,0.943)	0.004	1.294(1.111,1.507)	< 0.001	1.005(0.832,1.215)	0.957
p for trend		0.030		< 0.001		0.937
3-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.861(0.749,0.989)	0.035	1.017(0.870,1.189)	0.832	0.963(0.822,1.129)	0.645
quantile 3	0.696(0.602,0.804)	< 0.001	0.931(0.784,1.104)	0.409	0.839(0.703,1.000)	0.051
quantile 4	0.823(0.715,0.948)	0.007	1.238(1.034,1.483)	0.020	1.016(0.833,1.240)	0.875
p for trend		0.044		0.003		0.408
1-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.865(0.766,0.976)	0.019	0.999(0.870,1.146)	0.984	0.964(0.839,1.108)	0.605
quantile 3	0.857(0.759,0.968)	0.013	1.149(0.989,1.335)	0.069	1.083(0.930,1.262)	0.304
quantile 4	0.880(0.780,0.993)	0.038	1.333(1.134,1.566)	< 0.001	1.203(1.017,1.423)	0.031
p for trend		0.162		< 0.001		0.004
2-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.907(0.788,1.045)	0.176	1.137(0.970,1.333)	0.113	1.079(0.918,1.269)	0.354
quantile 3	0.867(0.752,0.999)	0.049	1.241(1.043,1.476)	0.015	1.131(0.946,1.352)	0.177
quantile 4	0.815(0.707,0.941)	0.005	1.291(1.071,1.556)	0.007	1.090(0.892,1.332)	0.400
p for trend		0.009		0.025		0.704

abbr. PAH, polycyclic aromatic hydrocarbons; UUI, urgency urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
1-hydroxypyrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.884(0.784,0.996)	0.043	1.091(0.959,1.241)	0.185	1.066(0.935,1.214)	0.339
quantile 3	0.816(0.721,0.923)	0.001	1.262(1.097,1.452)	0.001	1.181(1.022,1.365)	0.024
quantile 4	0.758(0.669,0.858)	< 0.001	1.446(1.243,1.681)	< 0.001	1.251(1.062,1.475)	0.008
p for trend		< 0.001		< 0.001		0.013
9-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.884(0.759,1.030)	0.114	0.988(0.834,1.171)	0.892	0.938(0.789,1.114)	0.463
quantile 3	0.847(0.726,0.988)	0.035	1.047(0.873,1.255)	0.624	0.941(0.780,1.135)	0.524
quantile 4	0.869(0.746,1.013)	0.073	1.149(0.948,1.394)	0.158	0.915(0.737,1.136)	0.423
p for trend		0.192		0.077		0.575
4-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.949(0.769,1.171)	0.626	1.054(0.835,1.330)	0.660	1.046(0.826,1.325)	0.709
quantile 3	0.893(0.721,1.105)	0.296	1.095(0.853, 1.405)	0.477	1.072(0.829,1.387)	0.596
quantile 4	0.843(0.679,1.045)	0.119	1.181(0.901,1.548)	0.228	1.090(0.812,1.463)	0.566
p for trend		0.121		0.231		0.645
abbr. PAH, polycyclic aromatic hydrocarbons; UUI, urgency urinary incontinence; OR, odds ratio; CI, confidence interval						
^a . Model I: unadjusted model						
^b . Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).						
^c . Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).						

Table 4
Association between urinary PAHs and SUI among US adults, NHANES 2007 ~ 2016

Exposure	Model Ia		Model IIb		Model IIIc	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
1-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.867(0.771,0.975)	0.017	1.102(0.971,1.251)	0.132	1.122(0.987,1.275)	0.079
quantile 3	0.774(0.687,0.872)	< 0.001	0.993(0.873,1.130)	0.914	1.043(0.912,1.193)	0.538
quantile 4	0.811(0.721, 0.913)	< 0.001	1.204(1.053,1.377)	0.007	1.266(1.082,1.481)	0.003
p for trend		0.025		0.008		0.006
2-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.782(0.695,0.879)	< 0.001	1.037(0.913,1.178)	0.575	1.051(0.923,1.197)	0.455
quantile 3	0.835(0.743,0.938)	0.002	1.248(1.093,1.424)	0.001	1.281(1.115,1.472)	< 0.001
quantile 4	0.764(0.679,0.860)	< 0.001	1.376(1.194,1.587)	< 0.001	1.454(1.233,1.714)	< 0.001
p for trend		0.001		< 0.001		< 0.001
3-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.733(0.654,0.823)	< 0.001	0.989(0.870,1.123)	0.860	1.001(0.879,1.139)	0.992
quantile 3	0.624(0.554,0.702)	< 0.001	0.993(0.867,1.138)	0.921	1.020(0.886,1.174)	0.781
quantile 4	0.622(0.553,0.700)	< 0.001	1.051(0.914,1.209)	0.483	1.115(0.929,1.338)	0.241
p for trend		< 0.001		0.314		0.177
2-hydroxyfluorene						

abbr. PAH, polycyclic aromatic hydrocarbons; SUI, stress urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model Ia		Model IIb		Model IIIc	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.765(0.682,0.859)	< 0.001	1.059(0.930,1.205)	0.387	1.075(0.942,1.227)	0.285
quantile 3	0.679(0.604,0.763)	< 0.001	1.081(0.941,1.241)	0.271	1.129(0.976,1.305)	0.102
quantile 4	0.669(0.595,0.753)	< 0.001	1.198(1.037,1.384)	0.014	1.322(1.103,1.585)	0.003
p for trend		< 0.001		0.015		0.003
3-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.855(0.748,0.977)	0.021	1.193(1.029,1.383)	0.019	1.201(1.034,1.397)	0.017
quantile 3	0.722(0.630,0.829)	< 0.001	1.201(1.022,1.410)	0.026	1.229(1.039,1.453)	0.016
quantile 4	0.654(0.568,0.752)	< 0.001	1.278(1.074, 1.520)	0.006	1.346(1.111,1.631)	0.002
p for trend		< 0.001		0.044		0.020
1-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.772(0.686,0.869)	< 0.001	1.123(0.984,1.282)	0.084	1.144(1.001,1.308)	0.048
quantile 3	0.804(0.716,0.904)	< 0.001	1.437(1.245,1.659)	< 0.001	1.497(1.292,1.734)	< 0.001
quantile 4	0.805(0.716,0.904)	< 0.001	1.718(1.470,2.009)	< 0.001	1.816(1.543,2.137)	< 0.001
p for trend		0.017		< 0.001		< 0.001
2-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
abbr. PAH, polycyclic aromatic hydrocarbons; SUI, stress urinary incontinence; OR, odds ratio; CI, confidence interval						
^a . Model I: unadjusted model						
^b . Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).						
^c . Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).						

Exposure	Model Ia		Model IIb		Model IIIc	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 2	0.768(0.671,0.879)	< 0.001	1.049(0.903,1.218)	0.532	1.056(0.907,1.230)	0.484
quantile 3	0.700(0.611,0.803)	< 0.001	1.124(0.954,1.325)	0.161	1.141(0.963,1.353)	0.127
quantile 4	0.694(0.605,0.796)	< 0.001	1.274(1.068,1.520)	0.007	1.307(1.081,1.581)	0.006
p for trend		< 0.001		0.004		0.003
1-hydroxypyrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.869(0.775,0.976)	0.018	1.022(0.905,1.154)	0.730	1.023(0.904,1.157)	0.719
quantile 3	0.751(0.666,0.847)	< 0.001	1.125(0.985,1.286)	0.083	1.147(0.999,1.317)	0.051
quantile 4	0.687(0.608,0.776)	< 0.001	1.247(1.080,1.439)	0.003	1.286(1.099,1.505)	0.002
p for trend		< 0.001		0.001		< 0.001
9-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.801(0.692,0.928)	0.003	1.051(0.895,1.234)	0.546	1.074(0.911,1.266)	0.394
quantile 3	0.735(0.633,0.853)	< 0.001	1.137(0.956,1.352)	0.147	1.171(0.977,1.404)	0.087
quantile 4	0.685(0.589,0.797)	< 0.001	1.208(1.003,1.454)	0.047	1.268(1.030,1.562)	0.025
p for trend		< 0.001		0.049		0.033
4-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.932(0.758,1.145)	0.501	1.273(1.015,1.597)	0.037	1.320(1.048,1.662)	0.019
quantile 3	0.824(0.668,1.018)	0.072	1.279(1.002,1.632)	0.048	1.369(1.063,1.763)	0.015

abbr. PAH, polycyclic aromatic hydrocarbons; SUI, stress urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model Ia		Model IIb		Model IIIc	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 4	0.883(0.716,1.088)	0.242	1.664(1.281,2.162)	< 0.001	1.849(1.390,2.459)	< 0.001
p for trend		0.322		< 0.001		< 0.001
abbr. PAH, polycyclic aromatic hydrocarbons; SUI, stress urinary incontinence; OR, odds ratio; CI, confidence interval						
a. Model I: unadjusted model						
b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), and BMI (≤ 25, 25 ~ 30, > 30).						
c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other races), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).						

Table 5
Association between urinary PAHs and MUI among US adults, NHANES 2007 ~ 2016

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
1-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.941(0.797,1.111)	0.472	1.101(0.921,1.315)	0.291	1.098(0.917,1.314)	0.311
quantile 3	0.940(0.796,1.110)	0.464	1.097(0.917,1.312)	0.311	1.075(0.893,1.294)	0.444
quantile 4	0.927(0.785,1.095)	0.371	1.263(1.048,1.523)	0.014	1.099(0.884,1.365)	0.397
p for trend		0.547		0.021		0.681
2-hydroxynapthalene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.858(0.728,1.012)	0.069	1.115(0.934,1.331)	0.228	1.063(0.888,1.274)	0.505
quantile 3	0.898(0.763,1.057)	0.196	1.359(1.131,1.632)	0.001	1.235(1.019,1.498)	0.032
quantile 4	0.806(0.683,0.952)	0.011	1.470(1.204,1.795)	< 0.001	1.230(0.976,1.551)	0.080
p for trend		0.040		< 0.001		0.134
3-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.802(0.685,0.939)	0.006	1.028(0.863,1.225)	0.754	1.014(0.849,1.211)	0.879
quantile 3	0.599(0.505,0.709)	< 0.001	0.920(0.759,1.115)	0.395	0.875(0.718,1.068)	0.190
quantile 4	0.710(0.604,0.835)	< 0.001	1.227(1.013,1.487)	0.037	1.045(0.810,1.348)	0.735
p for trend		0.015		0.006		0.452
2-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.833(0.710,0.977)	0.025	1.101(0.921,1.316)	0.292	1.057(0.881,1.268)	0.551
quantile 3	0.686(0.581,0.810)	< 0.001	1.059(0.873,1.285)	0.560	0.993(0.811,1.215)	0.942

abbr. PAH, polycyclic aromatic hydrocarbons; MUI, mixed urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other race), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 4	0.754(0.641,0.888)	< 0.001	1.359(1.115,1.658)	0.002	1.165(0.906,1.499)	0.234
p for trend		0.020		0.001		0.198
3-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.859(0.713,1.034)	0.108	1.152(0.940,1.412)	0.172	1.103(0.897,1.357)	0.354
quantile 3	0.686(0.564,0.834)	< 0.001	1.101(0.879,1.379)	0.403	1.029(0.814,1.301)	0.812
quantile 4	0.737(0.608,0.894)	0.002	1.388(1.094,1.760)	0.007	1.227(0.943,1.597)	0.127
p for trend		0.006		0.010		0.143
1-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.777(0.658,0.917)	0.003	1.042(0.868,1.252)	0.660	1.018(0.846,1.226)	0.848
quantile 3	0.841(0.715,0.990)	0.037	1.379(1.132,1.680)	0.001	1.331(1.088,1.629)	0.005
quantile 4	0.856(0.728,1.006)	0.059	1.649(1.332,2.041)	< 0.001	1.554(1.244,1.942)	< 0.001

abbr. PAH, polycyclic aromatic hydrocarbons; MUI, mixed urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other race), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
p for trend		0.350		< 0.001		< 0.001
2-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.927(0.768,1.120)	0.433	1.295(1.052,1.595)	0.015	1.246(1.008,1.541)	0.042
quantile 3	0.823(0.678,0.998)	0.048	1.391(1.104,1.752)	0.005	1.308(1.030,1.661)	0.028
quantile 4	0.798(0.657,0.969)	0.023	1.557(1.215,1.995)	< 0.001	1.387(1.062,1.812)	0.017
p for trend		0.024		0.004		0.081
1-hydroxypyrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.920(0.784,1.080)	0.308	1.124(0.950,1.329)	0.172	1.103(0.930,1.308)	0.262
quantile 3	0.802(0.678,0.949)	0.010	1.280(1.063,1.542)	0.009	1.210(0.998,1.467)	0.052
quantile 4	0.734(0.618,0.871)	< 0.001	1.476(1.207,1.805)	< 0.001	1.307(1.047,1.630)	0.018
p for trend		< 0.001		< 0.001		0.035
9-hydroxyfluorene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.781(0.636,0.958)	0.018	0.993(0.795,1.239)	0.947	0.952(0.760,1.194)	0.671
quantile 3	0.768(0.625,0.943)	0.012	1.146(0.903,1.452)	0.262	1.059(0.826,1.358)	0.649
quantile 4	0.690(0.559,0.852)	< 0.001	1.167(0.902,1.509)	0.240	0.981(0.733,1.313)	0.898
p for trend		0.004		0.189		0.949
4-hydroxyphenanthrene						
quantile 1	1.000	-	1.000	-	1.000	-
quantile 2	0.866(0.653,1.149)	0.319	1.110(0.816,1.509)	0.508	1.138(0.832,1.558)	0.419

abbr. PAH, polycyclic aromatic hydrocarbons; MUI, mixed urinary incontinence; OR, odds ratio; CI, confidence interval

^a. Model I: unadjusted model

^b. Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other races), and BMI (≤ 25, 25 ~ 30, > 30).

^c. Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other race), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).

Exposure	Model I ^a		Model II ^b		Model III ^c	
	OR (95%CI)	p value	OR (95%CI)	p value	OR (95%CI)	p value
quantile 3	0.886(0.668,1.176)	0.403	1.313(0.948,1.819)	0.102	1.400(0.996,1.968)	0.053
quantile 4	0.749(0.558,1.004)	0.053	1.326(0.924,1.902)	0.126	1.392(0.937,2.066)	0.101
p for trend		0.077		0.167		0.167
abbr. PAH, polycyclic aromatic hydrocarbons; MUI, mixed urinary incontinence; OR, odds ratio; CI, confidence interval						
^a . Model I: unadjusted model						
^b . Model II: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, and other races), and BMI (≤ 25, 25 ~ 30, > 30).						
^c . Model III: adjusted for age (< 60, ≥60), race (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other race), BMI (≤ 25, 25 ~ 30, > 30), ratio of family income to poverty (< 1.3, 1.3 ~ 3.5, > 3.5), education level (less than high school, high school or general educational development), marital status (married or living with partner, living alone), Charlson comorbidity index (0, 1, 2, 3, 4, 5), physical activity (less than moderate, moderate, vigorous), smoking status (never, former, current), alcohol drinking (none, moderate, heavy).						

Discussion

In present study, we provide a new evidence for the association between PAHs and UI using the NHANES database from 2007 to 2016. This study suggested that increasing urine PAHs were possibly associated with the increasing prevalence of all three subtypes of UI.

The biological mechanism of the association between PAHs and UI is still unclear. Thus, we can only propose a hypothesis for the underlying mechanism based on the available research evidence. Studies have shown that exposure to PAHs has certain effects on reproductive function and serum sex hormones levels (18–21). Associations between sex hormones and all three subtypes of UI were reported in other studies (15; 22; 23). Thus, PAHs may potentially affect UI prevalence by changing levels of several sex hormones.

The significant association between almost all urine PAHs and SUI were described in the present study. The previous study of Augoulea et. al revealed the association between the reduction of serum estradiol (E2) and Δ4-Androstendione (Δ4A) levels and SUI (24). The decreasing level E2 was also observed in participants with increasing exposure of PAHs by Yang et. al (25). Ahn et al. reported that E2 and follicle-stimulating hormone (FSH) were related to urodynamics in female patients with SUI (23), which called for studies between PAHs exposure and urodynamic parameters in SUI patients.

This study has the following strengths. First, this study had a large sample size, including a total of 12,393 participants from 2007 to 2016. Second, the sample selection in this study was relatively random, and the selected sample population was national representative. Thirdly, the data collection standards of this study were relatively uniform, and all the data related to this study were collected in accordance with the NHANES survey collection standards.

However, several limitations of this study also need to be acknowledged. First, this study was a cross-sectional study, which caused that it cannot be determined whether the causal relationship between PAHs and UI existed. Second, UI diagnosis was based on self-reported questionnaires, which may generate measurement bias. Thirdly, a single sample can only show the PAHs levels at a specific time, and the short half-lives of PAHs make it unable to account for persistent exposure and individual differences. Further cohort studies and experimental studies need to be conducted to verify the result of the present study.

Conclusion

Our study found a positive association between U-PAHs and all three subtypes of UI risk. Almost all PAHs have positive relations with SUI. The results of this study need to be verified by further cohort studies and experimental studies.

Abbreviations

PAHs, polycyclic aromatic hydrocarbons; UI, urinary incontinence; SUI, stress urinary incontinence; UUI, urgency urinary incontinence; GC-HRMS, capillary gas chromatography combined with high resolution mass spectrometry; GC-MS/MS, isotope dilution gas chromatography/tandem mass spectrometry; online SPE-HPLC-MS/MS, isotope dilution online solid phase extraction high performance liquid chromatography/tandem mass spectrometry; MUI, mixed urinary incontinence; OR, odds ratio; 95%CI, 95% confidence intervals; NHANES, National Health and Nutrition Examination Survey; NCHS, National Center for Health Statistics; MECs, mobile examination centers; BMI, body mass index; SD, standard deviation; GM, geometric mean; LLOD, lower limit of detection; E2, estradiol; Δ 4A, Δ 4-Androstendione; FSH, follicle-stimulating hormone.

Declarations

Ethics Approval and Consent to Participate

The study was approved by Ethics Review Board of NCHS, and all participants had been required to sign an informed consent form before the study began.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets generated and/or analysed during the current study are available in the National Health and Nutrition Examination Survey repository, [<http://www.cdc.gov/nchs/nhanes.htm>].

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.

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Author's Contributions

Zilong Zhang: Data collection; Methodology; Writing - original draft; Kun Jin: Methodology; Formal analysis; Writing - original draft; Shi Qiu: Methodology; Data curation; Writing - original draft; Xinyi Huang: Data collection, Table and figure preparation; Dan Hu: Data collection; Zhongyuan Jiang: Validation and Editing; Mingda Wang: Validation and Editing; Lu Yang: Methodology; Formal analysis; Tianhai Lin: Data collection; Supervision; Xianghong Zhou: Data collection; Di Jin: Data

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Figures

Figure 1

In the NHANES database from 2007 to 2016, a total of 50,588 participants aged over 20 were enrolled in the survey, among which 13,085 participants with detectable level of urinary PHAs metabolites were included. 692 participants were excluded due to lack of UI information. Finally, a total of 12,393 adults over 20 years of age were analyzed. Figure 1 showed the flowchart of participants selection.

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