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Microbiome alterations associated with phthalate exposures in a US-based sample of Latino workers

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ABSTRACT

Low-wage service sector jobs are largely occupied by racial/ethnic minority workers who often experience an increased risk of elevated chemical exposures, including chemicals like phthalates, compared to the general public. Phthalates have been linked with adverse health effects, including increased risk of atopy and asthma. An important etiological component in respiratory disease, including asthma, is the role of the upper respiratory microbiota in atopic disease development. However, it is unclear how the upper respiratory microbiome is affected by chemical exposures, and how this may impact respiratory outcomes. As Latino workers are often disproportionately exposed to increased concentrations of chemicals and Hispanics have higher rates of adverse respiratory health conditions such as asthma, the aim of this pilot study was to evaluate the effects of 10 unique phthalate urinary biomarkers on the 16S rRNA nasal microbiome. Nasal and urinary samples were collected from 20 facility workers (plumbers, landscapers, electricians) and 20 custodial workers. Our analysis revealed altered microbial composition and diversity according to phthalate urinary biomarker concentration within the two worker groups. Higher urinary biomarker concentrations of select phthalates (MBP, MBIP, and ∑DEHP) were associated with increased *Moraxella* relative abundance, which has been positively associated with asthma. Within-sample alpha diversity levels were decreased in facility workers and were generally inversely associated with most phthalate urinary biomarker concentrations. Our research suggests that exposure to chemicals in this vulnerable worker group may impact the respiratory microbiome, which may increase risk of development of adverse health conditions. Further research is warranted to refine the mechanistic pathways that underpin the relationships between phthalate exposures and respiratory microbial communities to provide key insights on respiratory pathologies and, most importantly, to identify modifiable risk factors that can be used to direct mitigation efforts aimed at ameliorating the harmful effects of chemical exposures in this understudied occupational population.

1. Introduction

Environmental health disparities in the U.S. are prevalent among low-income populations of racial and ethnic minorities, including Latinos (Frumkin et al., 1999). One cause of this is that these populations are often overrepresented in higher risk lower-wage service sector jobs (Frumkin et al., 1999; U.S. Bureau of Labor Statistics, 2020a; 2020b), exposing them to many chemicals of concern (e.g. phthalates, solvents, pesticides, disinfectants, volatile organic compounds, VOCs) (Burstyn and Kromhout, 2000; Castillo et al., 2021; Jaakkola Jouni J.K. and Knight Trudy L., 2008; Janasik et al., 2010; Jang et al., 2007; Nguyen et al., 2020; Quiros-Alcala et al., 2019). Analyses in the U.S. representative National Health and Nutrition Examination Survey (NHANES) indicate that Latinos are disproportionately exposed to several chemicals, including phthalates (Mitro et al., 2019; Silva et al., 2004; Varshavsky et al., 2016). Elevated occupational exposures to phthalates has been reported to occur among select worker populations including those working in low-wage jobs (Petrovičová et al., 2016). Exposure to phthalates is essential to characterize as increased exposure has been linked to various adverse health conditions (Benjamin et al., 2017). Specifically, increasing epidemiologic evidence supports the potential for phthalates to be associated with development and exacerbation of allergic conditions and asthma (Benjamin et al., 2017; Fandiño-Del-Rio et al., 2022; North et al., 2014; Robinson and Miller, 2015; Wang et al., 2019). Asthma disparities are reported among Hispanics when compared to non-Hispanic whites (Attina et al., 2019; Louisias and Phipatanakul, 2017; Rosser et al., 2014), as well as in low-wage occupations compared to the general public (Kobrosly et al., 2012; Mitro

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et al., 2019). However, studies on occupational exposures among minority and immigrant workers and the resulting health disparities, including respiratory conditions, are limited (Moyce and Schenker, 2017; Quiros-Alcala et al., 2019).

An important component to consider is the well-established connection between respiratory outcomes, particularly atopic conditions like asthma, and respiratory microbial communities, including those that colonize the nose and upper respiratory tract. Modifications and disturbances to those communities, both microbial populations generally and respiratory pathogens specifically, are involved in the pathogenesis of respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), and bronchitis (Dickson et al., 2016; Marsland et al., 2013). More recently, evidence suggests that chemical exposure interactions with the microbiome may lead to altered health statuses. Chemical exposures, including to phthalates, have been shown in preliminary animal models to disrupt the microbiome, resulting in dysbiosis that could impact host health (Rosenfeld, 2017; Yang et al., 2019). Microbial dysbiosis can also result in altered levels of microbial enzymes and subsequent metabolism of chemicals to their active forms, thus modifying their potential toxic effects (Rosenfeld, 2017). This link between chemical exposures, the microbiome, and adverse health outcomes is especially important to evaluate in the occupational context where low-wage workers are exposed to chemicals as a part of their job function, frequently at rates higher than the general public, potentially leading to disparate microbial disturbances and consequential health outcomes, yet there is sparse research examining this link.

Given continual exposures to potentially harmful chemicals among low-wage Latino workers, specifically to phthalates, and the documented increased risk for adverse respiratory conditions in this population, there is a need to characterize the potential role of the nasal microbiome in the relationship of occupational phthalate exposure and adverse respiratory conditions. In the present pilot study, we investigated the effects of 10 unique phthalate urinary biomarkers on the nasal microbiome in Latino service sector workers who may be exposed to chemicals as part of their routine work functions. We focused on workers in facility and custodial roles due to their frequent use of chemical products that may contain phthalates and because this vulnerable population has been understudied in previous research and faces multiple health challenges (Allotey et al., 2021; Velasco-Mondragon et al., 2016; Zock, 2005). In addition, previous work in this cohort has found positive associations between cleaning products, such as bleach, and phthalate biomarker concentrations (Allotey et al., 2021), which highlights the importance to recognize subsequent pathophysiological disruptions from increased chemical exposures.

2. Methods

2.1. Study design and participant recruitment

Data for the present study was obtained from a subset of samples from participants in a cross-sectional study comprised of 156 predominantly female Latino adults in Maryland that aimed to assess workplace exposures and health behaviors among a Latino service sector worker population. Participant recruitment was conducted between November 2017 and March 2018. Eligibility criteria for study participants included being >18 years of age, working in a service-based industry at the time of enrollment, and willing to provide biospecimens and complete an interviewer-administered questionnaire. For the present pilot study, we used data and samples collected from a subset of 40 workers. Data on phthalate metabolites were available on 94 individuals. We performed a stratified randomized selection, based on phthalate biomarker concentrations and work group, to select the 40 participants in the present study, to strengthen the similarity to the larger parent cohort (Allotey et al., 2021). Participants were grouped into two service-based industries: facilities management (e.g., plumbers, landscapers, electricians), termed "facility workers," and custodial services in residential facilities, termed "custodial workers." Participation in the study was voluntary for all study participants and study protocols were reviewed and approved by the University of Maryland's Institutional Review Board (IRB). Written informed consent was obtained from all workers prior to study enrollment.

2.2. Data and biospecimen collection

An initial baseline questionnaire administered by trained bilingual/bicultural study interviewers elicited information on participant demographics, health-related information (e.g., respiratory and reproductive health), and lifestyle and workplace behaviors (e.g., smoking status, alcohol consumption, use of personal protective equipment (PPE), cleaning products at home and work, etc.). To assess phthalate exposure, we collected a spot urine sample from each study participant. Spot urine samples were collected in phthalate-free polypropylene urine collection containers, aliquoted into cryovials, and stored at −80 °C until laboratory analysis. Prior to storage, we measured specific gravity in each sample with a digital ATAGO refractometer (Atago USA, Inc.) to account for urine dilution in our analysis. Nasal swabs for microbiome were collected from the anterior nares of each participant at the time of urine collection using sterile flocked swabs (Puritan, Guilford, ME, USA), as previously described (Dalton et al., 2021) and stored at −80 °C until laboratory analysis.

2.3. Phthalate urinary biomarkers laboratory analysis

Details on sample processing have been described in detail elsewhere (Allotey et al., 2021). Briefly, we quantified concentrations of 9 phthalate metabolites, representing exposure to 6 parent phthalate compounds in each urine sample at the University of Maryland Exposome Small Molecule Core Facility (College Park, Maryland): monoethyl phthalate (MEP, a metabolite of diethyl phthalate, DEP); mono-n-butyl phthalate (MBP, a metabolite of di-n- butyl phthalate, DBP); mono-isobutyl phthalate (MiBP, a metabolite of di-isobutyl phthalate (DiBP)); monobenzyl phthalate (MBzP, a metabo-lite of benzylbutyl phthalate, BBzP); four metabolites of di-2-ethylhexyl phthalate, $\sum$DEHP [mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl- 5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECCP)]; and mono(3-carboxypropyl) phthalate (MCPP, a non-specific metabolite of several phthalates including di-n-butyl phthalate, DBP and di-n-octyl phthalate, DOP). We evaluated individual DEHP biomarkers (MEHP, MEHHP, MEOHP, MECPP) as the concentrations of individual phthalate biomarkers as well as their combined molar sum (ΣDEHP) as follows: $\Sigma\text{DEHP}\ (\mu\text{mol/L}) = C_{MEHP}\ (\text{ng/mL}) * (1/MW_{MEHP}) + C_{MEHHP}\ (\text{ng/mL}) * (1/MW_{MEHHP}) + C_{MEOHP}\ (\text{ng/mL}) * (1/MW_{MEOHP}) + C_{MECPP}\ (\text{ng/mL}) * (1/MW_{MECPP})$; where C_{MEHP} (ng/mL), for example, is the individual's urinary concentration of MEHP in ng/mL, MW_{MEHP} is the molecular weight of MEHP in g/mol. Metabolite concentrations were corrected for dilution using the following formula: $Csg = C \times [(SGm - 1)/(SG - 1)]$, where Csg is the specific gravity-corrected phthalate metabolite concentration (in μg/L), C is the observed phthalate metabolite concentration (in μg/L), SGm is the mean specific gravity value in our study population, and SG is the specific gravity of the urine sample (Silva et al., 2007; Xia et al., 2014). Concentrations below the limit of detection were assigned the instrumental reading values when available or replaced with a value of $LOD/\sqrt{2}$ if the instrumental reading value was not available (Lubin Jay H. et al., 2004).

2.4. 16S rRNA sequencing and Bioinformatics for microbiome

Sample nasal swabs were thawed prior to DNA extraction. DNA sequencing was performed as previously described (Dalton et al., 2021; Misic et al., 2015). For each set of extractions, one blank swab exposed to laboratory air was processed as a negative laboratory control. The

V1-3 region of the 16S rRNA gene was amplified using barcoded primers (27F, 534R) for the Illumina platform as previously described (Fadrosh et al., 2014) via the MiSeq instrument (Illumina, San Diego, CA) using 300 base paired-end chemistry at the University of Pennsylvania Next Generation Sequencing Core. QIIMEv2.7 was used for paired-end read assembly and quality filtering for the sequences from all samples (Bolyen et al., 2019). The DADA2 plug-in for QIIME2.7 was used to remove chimeric sequences and sequences greater than 300bp in length, and cluster sequences into amplicon sequence variants (ASVs) (Callahan et al., 2016), and matched to taxonomy with Greengenes13.8 99% OTU match (McDonald et al., 2012). Overall read counts for samples ranged from 1 to 102,343, with a mean of 28,638 reads and a median of 29,656 reads. Sampling depth was rarified to 10,347 read counts for downstream analysis to maximize sample retention.

2.5. Statistical analysis

Statistical analysis was performed in RStudio v1.1.423 (R Development Core Team, 2010). We analyzed taxa tables, and matching phylogeny and taxonomy, using the phyloseq pipeline to calculate alpha and beta diversity metrics (McMurdie and Holmes, 2013). The primary analysis was the change in microbial composition by personal phthalate urinary biomarker concentrations, stratified by worker group. Differential abundance of specific taxa between groups were analyzed using DESeq2 (Love et al., 2014), as well as Spearman correlations with phthalate biomarker concentration and abundance of top taxa. Within-sample alpha diversity was measured with the Shannon index, which accounts for species richness and evenness. We used the Kruskal-Wallis nonparametric one-way analysis of variance test to examine differential alpha diversity across all groups, and the Wilcoxon rank-sum test for pair-wise comparisons within groups; both tests were adjusted for multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) correction. We conducted linear regression models to examine associations between each phthalate biomarker and alpha diversity, both unadjusted and controlling for work group. We assessed beta diversity using the unweighted UniFrac metric (Lozupone and Knight, 2005) principal coordinate analysis (accounts for phylogenetic distance between sets of taxa), and the non-parametric permutational multivariate analysis of variance (PERMANOVA) model to examine which factors were most important in determining microbial composition (Anderson, 2017).

3. Results

3.1. Study population and phthalate exposures

Table 1 shows the characteristics and concentrations of phthalate urinary biomarkers (specific gravity corrected) for the 40 participants. In general, there were no significant differences in demographic characteristics between our two worker groups, except for body mass index (BMI; facility workers generally had a higher BMI, p = 0.03 compared to custodial workers), and MBZP phthalate urinary biomarker concentrations (mean 0.34 ± 0.35 for facility workers versus mean 0.12 ± 0.47 for custodial workers, p = 0.09). There was no significant difference between our 40-participant subset and the original 156-parent cohort in terms of participant characteristics and median phthalate biomarker concentrations.

Table 1
Demographic study population characteristics and summary statistics on specific gravity corrected phthalate biomarker concentrations.

	Characteristics	Facilities Management (N = 20)	Residential Facilities (N = 20)	P-value for Group Difference
Gender, N (%)	Female	17 (85)	18 (90)	P = 1.00
	Male	3 (15)	2 (10)	
Age, N (%)	18–39	1 (5)	2 (10)	P = 0.55
	40–49	11 (55)	7 (35)	
	50–59	6 (30)	10 (50)	
	60+	2 (10)	1 (5)	
BMI, N (%)	Normal weight	0 (0)	3 (15)	**P = 0.03*
	Overweight	6 (30)	6 (30)	
	Class I Obesity	7 (35)	10 (50)	
	Class II Obesity	6 (30)	0 (0)	
	Class III Obesity	1 (5)	1 (5)	
Education, N (%)	Junior high or less	8 (40)	7 (35)	P = 0.72
	High school/vocation school	6 (30)	9 (45)	
	College or more	6 (30)	4 (20)	
Income, N (%)	<29,999	7 (35)	7 (37)	P = 1.00
	30,000–59,999	7 (35)	6 (32)	
	>60,000	6 (30)	6 (32)	
Nationality, N (%)	Central America	18 (90)	17 (85)	P = 1.00
	Mexico	0 (0)	1 (5)	
	Caribbean	1 (5)	0 (0)	
	South America	1 (5)	2 (10)	
Time in US, N (%)	<20 years	5 (25)	7 (35)	P = 0.85
	20–29 years	9 (45)	8 (40)	
	>30 years	6 (30)	5 (25)	
Phthalate biomarker concentrations (ng/mL), Median ± SD	MEP	184.80 ± 252.56	118.29 ± 235.45	P = 0.39
	MBP	8.07 ± 5.79	5.91 ± 5.24	P = 0.22
	MBIP	6.45 ± 15.02	3.00 ± 3.10	P = 0.32
	MEHP	0.81 ± 2.66	0.67 ± 1.13	P = 0.82
	MEHHP	7.30 ± 12.22	8.78 ± 17.07	P = 0.76
	MEOHP	3.87 ± 6.89	4.25 ± 8.57	P = 0.88
	MECPP	9.48 ± 21.07	8.60 ± 19.38	P = 0.89
	MBZP	2.96 ± 2.45	2.26 ± 2.54	P = 0.38
	MCPP	0.44 ± 0.51	1.04 ± 2.03	P = 0.21
	∑DEHP*	0.07 ± 0.14	0.07 ± 0.15	P = 0.95

*∑DEHP was estimated as the molar sum of DEHP-devolving biomarkers.

3.2. Abundance of top genera

There was similar composition of the most abundant genera when comparing between the two worker groups (Kruskal-Wallis $p > 0.07$ for all seven top genera), as shown in Fig. 1A. Across all samples, *Corynebacterium* had the highest relative abundance across samples (0.332 ± 0.252), followed by *Propionibacterium* (0.309 ± 0.256), then *Staphylococcus* (0.085 ± 0.149). When considering trends in the top seven genera by phthalate urinary biomarker concentrations in Fig. 1B, there was a significant positive correlation in relative abundance of *Moraxella* taxa with concentrations of MBP, MBIP, MEHHP, MEOHP, and ∑DEHP within custodial workers (correlations [p-values] −0.716 [<0.001], −0.38 [0.099], −0.401 [0.08], −0.451 [0.046], −0.384 [0.095], respectively), but not within facility workers.

3.3. Alpha diversity levels

Custodial workers had statistically higher within-sample (nasal microbial community) Shannon alpha diversity levels compared to facility workers (custodial 2.14 median vs. facility 1.84 median, Wilcoxon rank-sum test p-value $p = 0.068$), as displayed in Fig. 1C. Although no phthalate biomarkers were significantly associated with alpha diversity levels in the unadjusted models and models adjusted by worker group (p-values < 0.28), we observed an overall inverse trend with higher phthalate urinary biomarker concentrations associated with decreased alpha diversity (8 out of 10 phthalate biomarkers had negative coefficients in unadjusted and adjusted models). MEHP and MCPP were the only two phthalate biomarkers that were positively associated with alpha diversity. The difference in alpha diversity levels by worker group when adjusting by the different phthalate biomarkers did not greatly change compared to the overall alpha diversity difference in the unadjusted model (difference in Shannon alpha diversity by work group, controlling for phthalate biomarker concentration, ranged from 0.233 to 0.254, p-values from 0.05 to 0.08). The addition of other covariates listed in Table 1 did not drastically change the model estimates. Shannon diversity levels by phthalate urinary biomarker concentrations within the two worker groups are available in the Supplemental Section, Figure S1.

3.3.1. Beta diversity levels

Fig. 1Dshows the overall distribution of samples in principal coordinate analysis plots for unweighted UniFrac beta diversity metric by worker group. Overall, the axes accounted for a maximum of 6.1% variation, and there was no obvious clustering by worker group (PERMANOVA by worker group R2 0.021, F p-value 0.971). No phthalate biomarker was significantly associated with beta diversity distribution in both the unadjusted PERMANOVA model and a model adjusted for worker group.

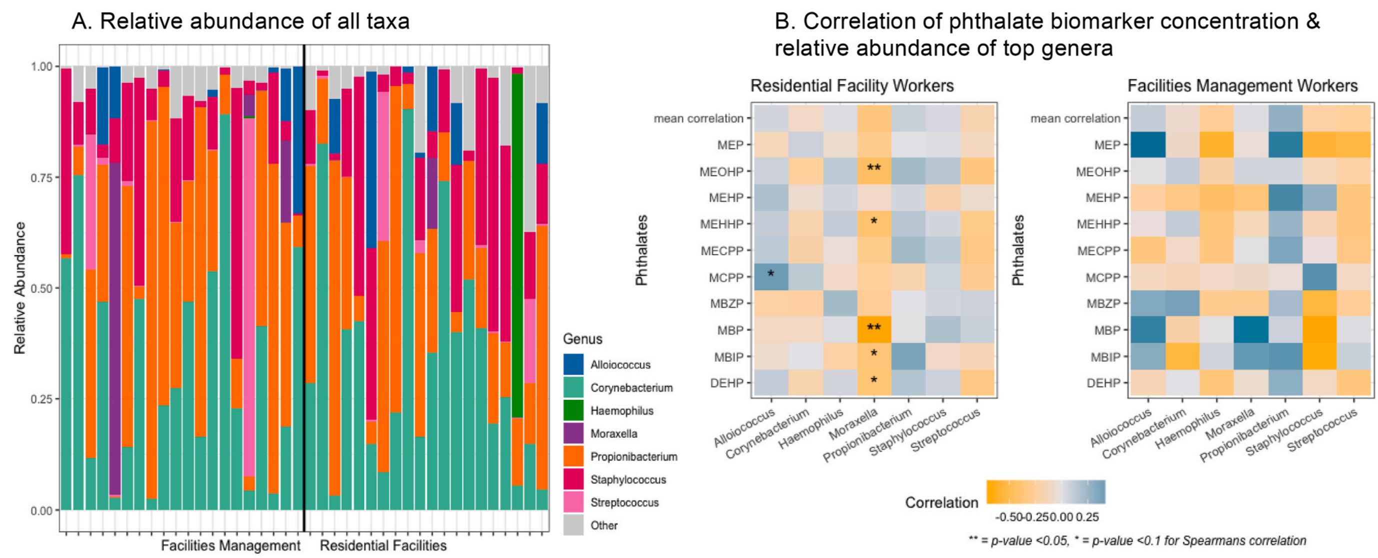
4. Discussion

This study is a novel contribution to the literature in assessment of the association between phthalate urinary biomarker concentrations and nasal microbiome composition and diversity among an understudied population of US-based Latinos in low-wage jobs (custodial and facility workers), who are exposed to chemicals as part their job. Our analysis revealed significant differences in microbial diversity by worker group; chiefly higher levels of within-worker group alpha diversity in custodial workers compared to facility workers. Most notably, we observed a significant association between phthalate urinary biomarker concentration and microbial composition, in that *Moraxella* levels were generally increased with higher phthalate urinary biomarker concentrations among custodial workers for MBP, MBIP, MEHHP, MEOHP, and ∑DEHP. We also observed that within-sample alpha diversity levels tended to be decreased with higher phthalate urinary biomarker concentrations, regardless of worker group. Notably, we were able to observe these associations despite that overall phthalate concentrations were generally lower in this worker population compared to the general population in the U.S. (Allotey et al., 2021). Altogether, this supports the potential for exposures to chemicals like phthalates to impact the upper respiratory microbiome in this vulnerable worker group.

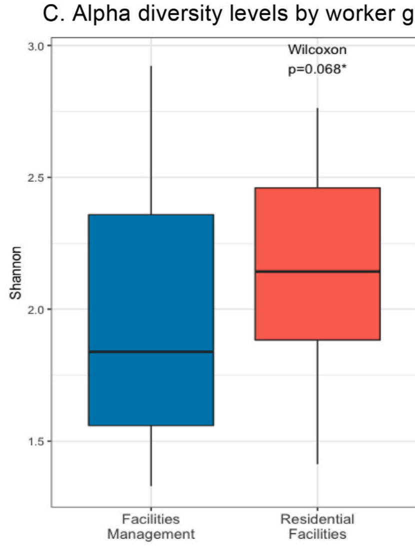
It is unclear why we observed lower concentrations in this worker population compared to those reported in the U.S. general population. Differences in biomarker concentrations across populations and across other studies could reflect differences in cultural norms and behaviors that may impact exposure to phthalates, as well as differences in excretion patterns or differences in overall declining exposure trends based on the year in which samples were collected. It is also important to note that our study population consisted of mostly females, from Central America, who were also mostly overweight or obese, which could have limited our ability to assess differences in metabolite concentration in our study population. It has been posited that individuals with more adiposity may excrete lower levels of phthalates in urine because they are stored in the available adipose tissue. Therefore higher BMI might explain why our participants appear to have lower exposures (Ribeiro et al., 2019). We also observed higher MEP concentrations compared to other biomarkers in this predominantly female worker group. This finding is in line with what has been reported in prior studies and is likely due to higher personal care product use (i.e., cosmetics, hair and skin care products) as the parent compound for MEP, diethyl phthalate, is use in these products and use of said products is recognized to be higher among women (Parlett et al., 2013).

Our results show differences in the microbial composition based on phthalate urinary biomarker concentration. Overall, custodial and facility workers had similar microbial compositions, as demonstrated by the similar relative abundance of top taxa. However, considering only custodial workers, there was an overall positive correlation between phthalate concentrations and abundance of *Moraxella* genus. Higher levels of *Moraxella* have been shown in previous microbiome studies to be associated with adverse respiratory health outcomes, particularly asthma, and this genus includes *Moraxella catarrhalis*, an important respiratory pathogen (Bisgaard et al., 2007; Richardson et al., 2019; Teo et al., 2015). This relationship was significant for five phthalate biomarkers – MBP, MBIP, MEHHP, MEOHP, and ∑DEHP – all of which are reported to be associated with respiratory conditions (Benjamin et al., 2017; North et al., 2014; Robinson and Miller, 2015; Wang et al., 2019). ∑DEHP and its individual metabolites, the most commonly evaluated phthalate biomarkers in research studies, have been shown to be associated with disruptions in the gut microbiome in newborns (Yang et al., 2019) and in controlled laboratory animal studies (Fan et al., 2020; Hu et al., 2016; Lei et al., 2019). This study contributes novel information regarding ∑DEHP and nine other unique phthalate biomarkers in the context of the nasal microbiome.

In addition to alterations in specific bacterial taxa, phthalate urinary biomarker exposures were found to be associated with altered within-worker group alpha diversity levels. Custodial workers had significantly higher alpha diversity levels compared to facility workers. While we may be underpowered to identify statistically significant findings, it is important to note trends and we found that, in general, increased concentrations for the majority of phthalate biomarkers were associated with decreased alpha diversity, regardless of occupational group (MEHP and MCPP had a slight positive association). It was shown that in our study population, the two worker groups had similar concentrations of phthalate urinary biomarkers (Allotey et al., 2021). This suggests that while phthalate exposure may partially contribute to altered microbial diversity levels observed, other exposures, whether occupational or personal, could be responsible for the decrease in microbial diversity seen in facility workers, such as other chemicals used at the workplace. Custodial and facility workers are exposed to different chemicals as part of their routine job functions, which could potentially account for differential phthalate exposure as well as the differential microbial diversity levels observed. Cleaning agents, including those that may be



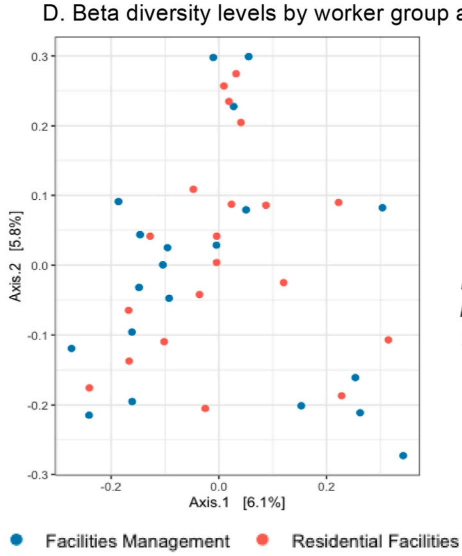
C. Alpha diversity levels by worker group and phthalate biomarker concentration



Linear Regression Models,
coefficient (p-value)

	Unadjusted	Adjusted by Work Group
MEP	-0.079 (0.438)	-0.072 (0.467)
MBP	-0.163 (0.284)	-0.12 (0.423)
MBIP	-0.119 (0.396)	-0.081 (0.559)
MEHP	0.082 (0.549)	0.055 (0.683)
MEHHP	-0.054 (0.749)	-0.059 (0.719)
MEOHP	-0.038 (0.784)	-0.028 (0.833)
MECPP	-0.033 (0.826)	-0.019 (0.894)
MBZP	-0.142 (0.394)	-0.068 (0.689)
MCPP	0.127 (0.387)	0.094 (0.515)
DEHP	-0.048 (0.767)	-0.046 (0.772)

D. Beta diversity levels by worker group and phthalate biomarker concentration



PERMANOVA Regression Models,
R2 (F p-value)

	Unadjusted	Adjusted by Work Group
MEP	0.0233 (0.83)	0.0233 (0.826)
MBP	0.0242 (0.695)	0.0242 (0.72)
MBIP	0.0236 (0.79)	0.0236 (0.804)
MEHP	0.028 (0.169)	0.028 (0.182)
MEHHP	0.027 (0.279)	0.027 (0.302)
MEOHP	0.0239 (0.744)	0.0239 (0.759)
MECPP	0.0252 (0.558)	0.0252 (0.568)
MBZP	0.0276 (0.211)	0.0276 (0.223)
MCPP	0.0227 (0.884)	0.0227 (0.891)
DEHP	0.0264 (0.342)	0.0264 (0.369)

Fig. 1. Microbial composition and diversity by phthalate biomarker concentration and worker group.

used by custodial staff, have previously been shown to influence environmental pathogens (Shahbazian et al., 2017); these products may not be used as frequently by facility workers.

Microbial diversity levels are important to evaluate as dysbiosis and decreased diversity levels have been associated with various negative health outcomes, including respiratory outcomes with nasal dysbiosis (Mahdavinia et al., 2016; Ooi et al., 2020; Ta et al., 2018). In our pilot study, we focused on a novel outcome, in a vulnerable and historically understudied population of Latino workers that continues to grow in the US (U.S. Bureau of Labor Statistics, 2020a). To our knowledge, this is the first study to explore the association between a suite of phthalate biomarkers and the nasal microbiome in a worker group. However, our study has several limitations, most notably our small sample size. Limited resources prevented us from characterizing phthalate exposures in a more racially/ethnically diverse sample of workers and restricted our ability to collect more than one urine and nasal sample per participant. Therefore, it was not possible to assess phthalate exposure and microbial composition variability and temporality, which may vary within and between individuals due to episodic exposures and variations in bioavailability. These factors may have contributed to the low variability observed in our beta diversity principal coordinate analysis plot (maximum of 6.1% variation accounted). We additionally only collected microbiome samples from host nasal cavity; however the nasal microbiome has been shown previously to be susceptible to environmental exposures, is linked to both lower respiratory microbiota and respiratory diseases, and can influence microbial composition at other body sites (Man et al., 2017). Because we wanted to facilitate sample collection logistics for our participants, we also did not account for time of urine collection in our analysis and exposure concentrations might vary with time of day. The primary objective of this research was to collect pilot data to assess the feasibility for future research efforts to test our central hypothesis that phthalate urinary biomarker concentrations would be associated with differential composition and diversity in the nasal microbiome, rather than to investigate causal relationships. Future studies should aim to collect samples from workers at relevant temporal intervals, as well as additional potential confounders such as home chemical use, to better characterize occupational phthalate exposures and nasal microbiota in and improve generalizability to this population and others.

In summary, our findings suggest that phthalate exposures can alter host nasal microbiota at concentrations lower than other adult populations (Allotey et al., 2021). This may have important implications to respiratory health and other adverse health outcomes, as microbial dysbiosis could be a mediator and/or modifier in the relationship between occupational chemical exposure and health outcomes. These findings add to the evidence on the link between environmental chemical exposure and the microbiome, specifically in Latino populations exposed to a myriad of chemicals that may pose unique health risks (Allotey et al., 2021; Davis et al., 2019). Our preliminary findings support the need for more research in this field to better depict the complex relationships between chemical exposures, the microbiome, and various health outcomes among this understudied population, and is critical to the larger goal of reducing exposures in worker and community populations. Future environmental health studies should consider evaluating microbial composition when researching how chemical and adverse occupational exposures alter health outcomes. Our work can be used to inform and design future studies in larger and more racially/ethnically diverse population of workers in order to characterize potential health disparities. These studies could also help to identify modifiable exposure factors and inform mitigation strategies and regulations of potentially harmful chemicals that are particularly disruptive to the microbiome. Overall our study represents an important first step toward understanding exposure pathways among understudied and underrepresented occupational groups.

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Declaration of competing interest

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.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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