Organophosphate Pesticide Urinary Metabolites Among Latino Immigrants

North Carolina Farmworkers and Non-farmworkers Compared

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Background: This analysis documents detections and concentrations of the six dialkylphosphate (DAP) urinary metabolite of organophosphorus (OP) pesticides among North Carolina Latino migrant farmworkers, with comparison to non-farmworker Latino immigrants. **Methods:** Participants provided up to four urine samples during the 2012 and 2013 agricultural seasons. Composite urine samples for each year were analyzed. **Results:** DAP urinary metabolite detections were similar in farmworkers and non-farmworker; for example, for 2012, 75.4% of farmworkers and 67.4% of non-farmworkers and, for 2013, 89.3% of farmworkers and 89.7% of non-farmworkers had dimethylthiophosphate detections. DAP geometric mean concentrations were high; for example, dimethylphosphate concentrations among farmworkers were 11.39 μg/g creatinine for 2012 and 4.49 μg/g creatinine for 2013, while they were 10.49 μg/g creatinine for 2012 and 1.97 μg/g creatinine for 2013 for non-farmworkers **Conclusions:** Research to reduce pesticide exposure among Latino farmworkers and non-farmworkers is needed.

Learning Objectives

- Become familiar with previous data on agricultural exposure to organophosphate (OP) pesticides and their health effects, including available research in migrant and seasonal farmworkers.
- Summarize the new findings on OP pesticide exposure in Latino migrant farmworkers, compared to non-farmworker Latino immigrants.
- Discuss the implications for further research on pathways of OP pesticide exposure and for public occupational and environmental health policy.

All pesticides can affect human health.[1] One class of pesticides, organophosphorus (OP) insecticides, is a particular concern due to its extensive use and varied health effects. Thirty-three million pounds of OP pesticides were applied in the United States (US) in 2007, down from 88 million pounds applied in 2000.[2] OP pesticides are neurotoxicants that work by inhibiting cholinesterase and thereby disrupting the nervous system.[1] The immediate effects of small doses of OP pesticides include burning eyes, itch, rash, muscle ache, nausea, and fatigue.[1] The immediate effects of large doses of OP pesticides include coma and death.[1] The long-term effects of small and large doses of OP pesticides for adults are increased risks for respiratory and reproductive problems,[3–6] neurological problems, including dementia and parkinsonism,[7–10] and cancer.[11] For children, OP exposure has been related to developmental problems, in particular, decreased intelligence quotient.[12–14]

OP pesticides are a concern for all of those employed in agriculture. The Agricultural Health Study, a study of 80,000 ''licensed pesticide applicators'' and their family members (http://aghealth.nih.gov/about/advisory.html),[15] has documented the extent to which farmers are exposed to OP pesticides and the health consequences of this exposure. Less research has examined OP pesticide exposure and health effects of migrant and seasonal farmworkers. These farmworkers have low incomes with few health benefits, have limited formal education, are largely Latino immigrants with limited English language skills, often are undocumented, and are mobile.[16] They have limited access to health care, while experiencing high rates of occupational injury and illness.[17–19] They have little control over their exposure to pesticides in the workplace, receive little training about pesticide safety, and earn few rewards as a result of their exposure, making pesticide exposure in this vulnerable population an issue of occupational and environmental justice.[20]

Much of the research examining farmworker OP pesticide exposure is old, with data collection predating regulations in the early 2000s that restricted the use of some OP pesticides.[21–25] However, several recent analyses with farmworkers in Washington, Florida, and North Carolina document continuing substantial exposure to OP pesticides.[26–28] Research on OP exposure using the six dialkylphosphate (DAP) urinary metabolites of OP pesticides has been conducted in several non-US agricultural populations, including Mexico,[29] France,[12] Greece,[30] Japan,[31] and Thailand.[32,33] Results from these analyses show a great range in metabolite levels.

OP pesticide exposure is also a concern for nonagricultural populations in the US and elsewhere. Although most OP pesticides were withdrawn from residential use in the US in the early 2000s, data from the 2007 to 2008 National Health and Nutrition Examination Survey (NHANES) indicate that exposure remains common.[34,35] OP exposure pathways in the nonagricultural US population include OP pesticide residues on food,[36,37] environmental exposures to remaining residues from residential pesticide application,[38] and nonagricultural occupational exposures.[39] Assessments of OP pesticide exposure in nonagricultural US populations have focused on vulnerable

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communities and have been largely limited to analyses of prenatal and early life OP exposure and child development.[40–43]

Regulations surrounding pesticide use and safety continue to evolve. Several OP pesticides were either removed from all use (eg, diazinon) or from residential use (eg, chlorpyrifos) in the early 2000s. Safety regulations for agricultural pesticides have recently been revised (https://www.epa.gov/pesticide-worker-safety/revisions-worker-protection-standard). Research continues to document OP pesticide exposure, particularly for vulnerable populations. Research documenting pesticide exposure in this evolving environment for farmworker and for nonagricultural populations is needed to inform occupational and environmental safety policy. Focusing on the DAP urinary metabolites of OP insecticides, this analysis has two goals. First, it describes pesticide DAPs detections and concentrations in two populations of Latino immigrant men: migrant farmworkers and non-farmworker urban residents. Second, it determines how occupation is associated with DAP detections and concentrations among these immigrant Latino men.

METHODS

Data are from Preventing Agricultural Chemical Exposure 4 (PACE4), a community-based participatory research collaboration between the North Carolina (NC) Farmworkers Project (Benson, NC), El Buen Pastor Latino Community Services (Winston-Salem, NC), and the Center for Worker Health, Wake Forest School of Medicine (Winston-Salem, NC). Other collaborators include Toxic-Free NC (Raleigh, NC), and Student Action with Farmworkers (Durham, NC). PACE4 compares Latino migrant farmworkers with Latino immigrant non-farmworker in NC. Farmworkers were recruited from three agricultural counties in east central NC (Harnett, Johnston, Sampson), and non-farmworkers were recruited from an urban area in west central NC (Winston-Salem, Forsyth County). The research protocol was approved by the Wake Forest School of Medicine Institutional Review Board; all participants gave signed informed consent.

Participants

Participants were men, aged 30 to 70 years, who self-identified as Latino or Hispanic, and did not have a diagnosis of diabetes. Farmworkers had to be currently employed as farmworkers and to have worked in agriculture for at least 3 years; non-farmworkers could not have been employed for the past 3 years in jobs with known exposure to pesticides, including farm work, forestry, landscaping, grounds keeping, lawn maintenance, and pest control. The inclusion and exclusion criteria reflect the needs of the parent study, which examined subclinical cognitive and neurological outcomes of pesticide exposure.[44]

Community partners assisted with participant recruitment. NC Farmworkers Project staff approached farmworker camps, explained the project to the residents, including the inclusion and exclusion criteria, time commitments, and asked for volunteers, who were screened to ensure that they met the inclusion criteria. We could not calculate farmworker participation rates. Groups of farmworkers were asked to volunteer; only the number who agreed to volunteer is available (the denominator is not known). Generally, all of the farmworkers in a camp who met the inclusion criteria volunteered. Individual farmworkers who did not want to participate could have avoided contact with the project staff or may have indicated that they did not meet the inclusion criteria to avoid refusal.

Wake Forest School of Medicine staff worked with El Buen Pastor Latino Community Services and other community organizations to identify potential non-farmworker participants. Project staff contacted potential participants, explained the project, including the inclusion and exclusion criteria and time commitments, asked if they wanted to volunteer, and screened them to ensure that they met the inclusion criteria. Among the 400 non-farmworkers contacted by project staff, 101 individuals did not meet the inclusion criteria. Of 299 who met the inclusion criteria, 87 individuals refused to participate, for a participation rate of 70.9% (212/299). Reasons given for refusing included the time commitment and length of the study (51), blood draws (27), need to come to a clinic for data collection (31), and providing contact information (30) (individuals could give more than one reason for refusing).

Data Collection

Participants completed baseline interviews from May through August 2012. They completed up to four follow-up contacts at monthly intervals from June through October 2012, and up to an additional four follow-up contacts at monthly intervals from June through October 2013. The same individuals participated in 2012 and 2013. At each of the eight follow-up contacts in 2012 and 2013, participants completed an interview and provided a urine sample. Participants were given an incentive of \$20 or \$30 for completing each follow-up, with the amount dependent on data collected at that contact; the maximum incentive that a participant could receive over the 2-year period was \$150 if he completed all nine of the data collection contacts (baseline in 2012, four monthly follow-up contacts in 2012, and four monthly follow-up contacts in 2013). A total of 235 farmworkers and 212 non-farmworkers completed the baseline interviews in 2012; 203 farmworkers and 129 non-farmworkers completed at least two follow-ups in 2012, and 112 farmworkers and 78 non-farmworkers completed at least two follow-ups in 2013, and are included in this analysis.

Interviews contained items used to construct measures of personal characteristics, including occupation. The interview questionnaires were developed in English and translated into Spanish. The Spanish and English versions were checked for comparable meaning for each item, and item wording was adjusted as needed. The questionnaire was pre-tested with several native Spanish speakers, and final corrections were made. Interviewers were native Spanish speakers. They completed training that addressed questionnaire content and proper interview technique. Baseline interviews with farmworkers were conducted in their camps, and baseline interviews with non-farmworkers were conducted in their homes or in a neutral site, such as a church. Study data were managed using Research Electronic Data Capture (REDCap) hosted at Wake Forest School of Medicine.[45] REDCap is a secure, web-based application designed to support data capture for research studies.

Participants provided a spot urine sample at each of the follow-up contacts. The volume of each urine sample was recorded, a 10-mL aliquot was prepared, and the aliquot was frozen at -80°C until it could be delivered to the laboratory for analysis.

Laboratory Analysis

Frozen urine samples were delivered to the laboratory at Emory University, Atlanta, GA. The six urinary DAP metabolites of OP pesticides were measured in urine samples using the mass spectrometry (MS)-based method by Prapamontol et al[46]: dimethylphosphate (DMP), dimethylthiophosphate (DMTP), dimethyldithiophosphate (DMDTP), diethylphosphate (DEP), diethylthiophosphate (DETP), and diethyldithiophosphate (DEDTP). Urine samples were thawed to room temperature. A composite sample was prepared for each participant based upon overall volume such that the resulting composite sample would reflect the average measurement of individually tested samples across the data collection period. A 1-mL aliquot of each sample was fortified with isotopically labeled internal standards, and then mixed. The urine samples were extracted with acetonitrile and diethyl ether and the DAP metabolites were chemically derivatized to their respective pentafluorobenzyl phosphate esters. The reaction mixture was concentrated, and the phosphate esters were measured using gas chromatography-MS in the single ion monitoring mode. Unknown

TABLE 1. Baseline Participant Characteristics PACE4 Project, 2012

	Farmworkers $n = 203$		Non-Farmworkers $n = 129$		
Participant Characteristics	***n***	**%**	***n***	**%**	***P***
Age, years					0.042
30–34	72	35.5	33	25.6	
35–44	77	37.9	46	35.7	
45 and older	54	26.6	50	38.8	
Married/living as married	194	95.6	90	69.8	<0.0001
Education*					<0.0001
0–6 years	90	44.6	44	34.1	
7–11 years	95	47.0	44	34.1	
12 or more years	17	8.4	41	31.8	
Mexico—Country of Birth	203	100	85	65.9	Not applicable
H-2A or H-2B Visa	193	95.1	0	—	
Spanish—Dominant language	200	98.5	128	99.2	Not significant
Occupation					Not applicable
Farm work	203	100			
Construction or maintenance			65	50.4	
Manufacturing			24	18.6	
Other†			40	31.0	

*Missing observations.
†Other occupations include food preparation and restaurant, sales, truck driver, mechanic, and unemployed.

analyte concentrations were quantified using isotope dilution calibration with calibration plots generated with each sample run. Limits of quantification were 0.3 μg/L for DMP, 0.2 μg/L for DMTP, 0.1 μg/L for DMDTP, 0.2 μg/L for DEP, 0.1 μg/L for DETP, and 0.1 μg/L for DEDTP. To ensure quality data, additional quality control materials, fortified samples, and blank samples were analyzed in parallel with all unknown samples.

Measures

Outcome measures include the detections and concentrations for the six DAP urinary metabolites of OP pesticides: DMP, DMTP, DMDTP, DEP, DEPT, and DEDTP. Detection of a metabolite is defined as a concentration greater than or equal to the limit of quantification (LOQ). Concentrations of each metabolite are adjusted for creatinine and are reported as μg/g creatinine. Total DAP molar weight (ΣDAPs) is the sum of the molar weights for five of the individual DAP urinary metabolites (DMP, DMTP, DMDTP, DEP, DETP), calculated by multiplying the concentrations by the molar weights. The molar weight for DEDTP was not included for ΣDAPs due to its infrequent detection.

Occupation has two sets of values: (1) farmworker versus non-farmworker; and (2) farmworker, construction or maintenance worker, manufacturing worker, and other worker (includes sales, customer service, food preparation and restaurant, mechanic, transportation, and unemployed). Participant personal characteristics used to describe the sample include age, in the categories 30 to 34 years, 35 to 44 years, and 45 years and older; whether married/living as married; education, in the categories 0 to 6 years, 7 to 11 years, 12 or more years; Mexico is the country of origin; H-2A or H-2B visa; and Spanish is the dominant language.

Analysis

Baseline participant characteristics were compared between farmworkers and non-farmworkers using Chi-square tests. For each metabolite, we first used frequency counts and percentages to summarize the presence of detection in each year. The difference in detection between farmworkers and non-farmworkers within each year was compared using Chi-square tests or Fisher exact tests when appropriate. For both years 2012 and 2013, the majority of the participants had DEDTP values below the LOQ. Therefore, DEDTP was not considered in subsequent analyses. Next, for values above the LOQ, the creatinine-adjusted concentrations were summarized using geometric means and geometric standard deviations and compared between farmworkers and non-farmworkers using general linear models (GLMs). Log transformations were used to achieve better approximation of normality and to stabilize variance.

To evaluate the overall DAP exposures, we imputed values below the LOQ for DEP, DETP, DMP, DMTP, and DMDTP.[47] In 2013, only one participant had DEP value < LOQ and it was simply replaced by the DEP LOQ. The values < LOQ for DEP in 2012 were imputed using maximum likelihood estimates (MLEs) obtained from 10 different bootstrap samples based on univariate log-normal distributions. For the rest of the metabolites, the values < LOQ were imputed using MLEs obtained from 10 different bootstrap samples based on bivariate log-normal distributions. All imputations were performed separately for farmworkers and non-farmworkers. The untransformed concentration (μg/L) of each metabolite (including both imputed and observed values) was converted to its molar concentration (DMP = concentration/0.126 μg/nmol; DMTP = concentration/0.142 μg/nmol; DMDTP = concentration/0.158 μg/nmol; DEP = concentration/0.154 μg/nmol; DETP = concentration/0.170 μg/nmol). ΣDAPs for each participant were calculated by summing the five individual weights. General linear mixed effects models (LMMs) were then employed to evaluate the difference between farmworkers and non-farmworkers for the imputed metabolite concentrations and ΣDAPs on the log scale. The model included the main effects for farmworker status and year as well as their interaction. The total number of urinary samples and the creatinine measures at each year were included in the model as time-varying covariates. Parameter estimates from the 10 imputed datasets were combined using SAS proc mianalyze procedure (Cary, NC) to obtain valid statistical inferences. Least square means were reported. Results were back transformed to the original scale and the standard errors were computed using Delta's method. Similar analyses were conducted to compare presence of detection, impute metabolites concentrations, and ΣDAPs across different occupations. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). A P value of less than 0.05 was considered statistically significant.

TABLE 2. Dialkylphosphate Urinary Metabolite Detections for Farmworkers and Non-Farmworkers, 2012 and 2013

	Detections				
	Farmworkers		Non-Farmworkers		
	>LOQ		>LOQ		
Dialkylphosphate Urinary Metabolites	***n***	**%**	***n***	**%**	***P***
2012					
	N = 203		*N* = 129		
DMP	112	55.2	55	42.6	0.026
DMTP	153	75.4	87	67.4	0.12
DMDTP	51	25.1	29	22.5	0.58
DEP	136	67.0	59	45.7	0.0001
DETP	80	39.4	43	33.3	0.26
DEDTP	2	1.0	0	0.0	—
2013					
	N = 112		*N* = 78		
DMP	81	72.3	55	70.5	0.79
DMTP	100	89.3	70	89.7	0.92
DMDTP	31	27.7	18	23.1	0.86
DEP	112	100.0	77	98.7	—
DETP	49	43.8	24	30.8	0.07
DEDTP	3	2.7	5	6.4	—

DEDTP, diethyldithiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate.

RESULTS

Participants

For 2012, 203 farmworkers and 129 non-farmworkers, and for 2013, 112 farmworkers and 78 non-farmworkers provided a sufficient number of urine samples to be included in the analysis (Table 1). Farmworkers were younger than non-farmworkers, with 35.5% of farmworkers and 25.6% of non-farmworkers aged 30 to 34 years. More farmworkers (95.6%) than non-farmworkers (69.8%) were married or living as married. Farmworkers had less formal education than non-farmworkers, with 44.6% of farmworkers and 34.1% of non-farmworkers having 6 or fewer years of education. All farmworkers, but 65.9% of non-farmworkers, were from Mexico, and Spanish was the dominant language of all but a few participants. About half (50.4%) of non-farmworkers worked in construction or maintenance, 18.6% worked in manufacturing, and 31.0% worked in other occupations.

DAP Detections and Concentrations for Farmworkers and Non-Farmworkers Compared

Detections of most of the DAP urinary metabolites were common for farmworkers and non-farmworkers (Table 2). DMTP detections were extremely common: for 2012, 75.4% of farmworkers and 67.4% of non-farmworkers had DMTP detections, while for 2013, 89.3% of farmworkers and 89.7% of non-farmworkers had DMTP detections. For 2012, there were significantly higher detections of DEP ($P = 0.0001$) and DMP ($P = 0.026$) in farmworkers than in non-farmworkers. DEP and DMP detections increased in both populations with no significant group differences. DEDTP was the metabolite that was least often detected, with two farmworkers and no non-farmworkers having detections in 2012, and three farmworkers and five non-farmworkers having detections in 2013.

The geometric mean concentrations for DMP among farmworkers were 11.39 μg/g creatinine for 2012 and 4.49 μg/g creatinine for 2013, while they were 10.49 μg/g creatinine for 2012 and 1.97 μg/g creatinine for 2013 for non-farmworkers (Table 3). The 2013 difference was significant ($P = 0.0021$). The geometric mean concentrations for DEP among farmworkers were 5.37 μg/g creatinine for 2012 and 4.20 μg/g creatinine for 2013, while they were 3.88 μg/g creatinine for 2012 and 4.26 μg/g creatinine for 2013 for non-farmworkers. The 2012 difference between farmworkers and non-farmworkers in DEP geometric mean was significant ($P = 0.0001$). There were no differences in the geometric means for the other metabolites. Mean concentrations that include imputed values for those below the level of detection are presented in Table 4. The findings parallel those found for the geometric means values with DMP ($P = 0.0197$) and DEP ($P < .0001$) being significantly greater for farmworkers than non-farmworkers in 2012, and for DETP ($P = 0.0201$) in 2013. ΣDAPs were greater for farmworkers than for non-farmworkers ($P = 0.0003$) for 2012.

DAP Detections and Concentrations by Occupation

Farmworkers had a greater proportion of detections (55.2%) for DMP than did those employed in construction (49.2%), manufacturing (41.7%), or other industries (32.5%) ($P = 0.052$) (Table 5). Farmworkers had a significantly greater proportion of detections (67.0%) for DEP than did those employed in construction or maintenance (53.9%), manufacturing (29.2%), or other industries (42.5%) ($P = 0.0002$) for 2012. Otherwise, farmworkers did not differ significantly in the proportion of detections for the DAP metabolites from those employed in other industries.

The concentration for DMP was greater for farmworkers than for other workers ($P = 0.0399$) (Table 6). Concentrations for DEP were significantly greater for farmworkers than for construction or maintenance workers ($P < 0.0039$), manufacturing workers ($P = 0.0080$), and other workers ($P = 0.0008$). ΣDAPs were greater for farmworkers than for other workers ($P = 0.0088$).

DISCUSSION

A high proportion of the farmworker and non-farmworker Latino men who participated in this study had detections of most of the DAP urinary pesticide metabolites. The creatinine-adjusted

TABLE 3. Dialkylphosphate Urinary Metabolite Concentrations (μg/g creatinine) for Farmworkers and Non-Farmworkers, 2012 and 2013

	Concentrations				
	Farmworkers		Non-Farmworkers		
Dialkylphosphate Urinary Metabolites	Geometric Mean	SE	Geometric Mean	SE	*P*
2012					
	N = 203		*N* = 129		
DMP	11.39	2.59	10.49	3.55	0.64
DMTP	4.41	3.45	5.11	4.13	0.40
DMDTP	2.29	3.18	3.03	3.24	0.30
DEP	5.37	2.30	3.88	3.15	0.27
DETP	1.53	2.33	1.39	2.44	0.54
DEDTP	*	*	*	*	
2013					
	N = 112		*N* = 78		
DMP	4.49	3.88	1.97	5.48	0.002
DMTP	3.39	3.43	3.51	3.87	0.86
DMDTP	1.34	3.14	2.20	2.63	0.13
DEP	4.20	2.58	4.26	3.44	—
DETP	1.05	2.35	0.93	2.12	0.57
DEDTP	*	*	*	*	—

DEDTP, diethyldithiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate.

*Geometric means could not be calculated due to the small number of detections.

TABLE 4. Dialkylphosphate Urinary Metabolite Concentrations (μg/L) and Total Molar Concentrations (nmol/L) for Farmworkers and Non-Farmworkers, 2012 and 2013

	Farmworkers		Non-Farmworkers		Farmworkers Compared With Non-Farmworkers		
Dialkylphosphate Urinary Metabolites	Mean	SE	Mean	SE	Mean	SE	*P*
2012							
	N = 203		*N* = 129				
DMP	0.81	0.18	0.34	0.11	2.42	0.91	0.0197
DMTP	1.68	0.28	1.10	0.24	1.52	0.39	0.0998
DMDTP	0.0042	0.0027	0.0028	0.0019	1.48	1.46	0.6979
DEP	0.97	0.17	0.20	0.05	4.89	1.37	<0.0001
DETP	0.06	0.01	0.04	0.01	1.30	0.51	0.5072
ΣDAPs	71.97	7.79	40.87	5.41	1.76	0.28	0.0003
2013							
	N = 112		*N* = 78				
DMP	1.56	0.35	1.23	0.36	1.27	0.45	0.4970
DMTP	4.14	0.83	3.85	0.87	1.08	0.31	0.8007
DMDTP	0.01	0.01	0.01	0.01	1.49	1.35	0.6665
DEP	7.08	1.55	6.18	1.41	1.15	0.34	0.6447
DETP	0.08	0.02	0.03	0.01	2.82	1.22	0.0201
ΣDAPs	157.51	20.48	147.83	21.27	1.07	0.20	0.7318

The model included farmworker status, year, farmworker by year interaction, the total number of urinary samples, and urinary creatinine. All analyses were based on 10 multiply imputed datasets. All results were back transformed to the original scale.

DEDTP, diethyldithiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate.

TABLE 5. Dialkylphosphate (DAP) Urinary Metabolite Detections by Occupation, 2012 and 2013

	2012									2013								
	Farmworkers		Construction/ Maintenance Workers		Manufacturing Workers		Other Workers			Farmworkers		Construction/ Maintenance Workers		Manufacturing Workers		Other Workers		
DAPs	n > LOD	%	n > LOD	%	n > LOD	%	n > LOD	%	P	n > LOD	%	n > LOD	%	n > LOD	%	n > LOD	%	P
DMP	112	55.2	32	49.2	10	41.7	13	32.5	0.052	81	72.3	24	75.0	13	72.2	18	64.3	0.81
DMTP	153	75.4	45	69.2	17	70.8	25	62.5	0.36	100	89.3	29	90.6	17	94.4	24	85.7	0.82
DMDTP	51	25.1	18	27.7	3	12.5	8	20.0	0.44	31	27.7	8	25.0	4	22.2	6	21.4	0.89
DEP	136	67.0	35	53.9	7	29.2	17	42.5	0.0002	112	100.0	31	96.9	18	100.0	28	100.0	.
DETP	80	39.4	25	38.5	8	33.3	10	25.0	0.37	49	43.8	10	31.3	7	38.9	7	25.0	0.24

DEDTP, diethyldithiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate.

metabolite concentrations for these men were high; in every instance, the geometric means for farmworkers and non-farmworkers were greater than any reference group for any year for which NHANES data have been reported.[48] Jain's[34] analysis of the 2003 to 2008 NHANES data reports that geometric means for men 20 years or older were 0.33 μg/L for DMP, 1.66 μg/L for DMTP, 0.18 μg/L for DEP, and 0.28 μg/L for DEPT; these are levels far below those found for farmworker and non-farmworker participants in this analysis.

With few exceptions, the farmworkers and non-farmworkers had similar levels of detection and concentration for the DAP urinary metabolites. In those instances in which farmworker and non-farmworker participants differed significantly, farmworkers always had a higher proportion of DAP detections and greater concentrations. Male farmworkers and non-farmworkers in the present study had similar DAP metabolite levels to those reported by Runkle et al[28] for Florida female farmworkers and controls in 2011. The non-farmworkers in both studies had similar levels of detections for the DAP metabolites as their farmworker counterparts, and they had similar concentration levels. However, the NC participants had higher levels of the total DAP metabolite levels than did the Florida participants. NC participants also had more detections and higher concentrations of DEP and DMP and more detections of DMDTP than Florida participants. Florida participants had higher concentrations of DMTP and had more detections and higher concentrations of DEDTP than did the NC participants.

Farmworkers in the current study generally had lower DAP metabolite concentrations in comparison to agricultural workers in recent non-US studies.[29–33] For example, for samples collected from Mexican floriculture workers in the 2004 to 2005 rainy season, Lacasaña et al[29] found about the same percents of detection for each of the DAP metabolites compared with the NC farmworkers who participated in this study; percents of detection of the metabolites for samples collected by Lacasaña et al[29] during the dry season were substantially lower than those found for the NC farmworkers. However, Lacasaña et al[29] report greater geometric means for the DAP metabolites for the Mexican workers than those of the NC farmworkers. The geometric mean DMP concentration for the Mexican workers during the rainy season was 97.06 μg/g creatinine and during the dry season was 10.08 μg/g creatinine for DMP, compared with 11.39 μg/g creatinine (2012) and 4.49 μg/g creatinine (2013) for farmworkers in this study, while those for DEP were 21.57 μg/g creatinine and 6.16 μg/g creatinine, respectively, compared with 5.37 μg/g creatinine (2012) and 1.05 μg/g creatinine (2013) for this study. Detections of the DAP metabolites for Japanese apple farmers ranged from 98% for DMP during the winter, to 100% for the other DAP metabolites in the summer and winter.[31] Geometric mean DMP concentrations for these Japanese apple farmworkers were 33.1 μg/g creatinine in the summer and 10.8 μg/g creatinine in the winter, with DEP levels being 4.2 μg/g creatinine in the summer and 4.7 μg/g creatinine in the winter. On the contrary, Hanchenlaksh et al[33] found that the geometric mean for

TABLE 6. Association of Dialkylphosphate (DAP) Urinary Metabolite Molar Concentrations and ΣDAPs (nmol/L) with Occupation, Averaged across 2012 and 2013

	Farmworkers Compared With								
	Construction/Maintenance Workers			Manufacturing Workers			Other Workers		
DAPs	Estimate	Standard Error	P	Estimate	Standard Error	P	Estimate	Standard Error	P
DMP	0.26	0.47	0.5812	0.49	0.69	0.4761	1.12	0.54	0.0399
DMTP	0.15	0.30	0.6308	0.03	0.42	0.9403	0.53	0.36	0.1425
DMDTP	0.05	0.98	0.9608	1.22	1.27	0.3396	0.48	1.10	0.6648
DEP	0.75	0.26	0.0039	0.96	0.36	0.0080	1.02	0.30	0.0008
DETP	0.30	0.48	0.5386	0.64	0.67	0.3341	1.22	0.69	0.0836
ΣDAPs	0.17	0.19	0.3863	0.28	0.27	0.2987	0.58	0.22	0.0088

The model included farmworker status, year, farmworker by year interaction, the total number of urinary samples, and urinary creatinine. All analyses were based on 10 multiply imputed datasets. All results were on log scale.

DEDTP, diethyldithiophosphate; DEP, diethylphosphate; DETP, diethylthiophosphate; DMDTP, dimethyldithiophosphate; DMP, dimethylphosphate; DMTP, dimethylthiophosphate.

total urinary DAP concentrations of Thai vegetable farmers was 51.1 μg/g creatinine and 122.2 μg/g creatinine for fruit farmers, compared with 71.9 μg/g creatinine (2012) and 157.51 μg/g creatinine (2013) for US farmworkers in the current study.

Non-farmworkers in the current study generally had similar or higher DAP metabolite concentrations than non-agricultural comparison groups in studies conducted outside of the US.[30,31,49] For example, among Japanese food distribution workers included in the study by Ueyama et al,[31] DAP detections ranged from 87% to 100%; the geometric mean for DMP 7.0 μg/g creatinine in the summer and 3.8 μg/g creatinine in the winter, with DEP levels being 0.8 μg/g creatinine in the summer and 1.5 μg/g creatinine in the winter. In a study of Israel adults from the general population conducted in 2011, Berman et al[49] found that DMP was detected for 99% of participants, DMTP for 100%, DMDTP for 73%, DEP for 98%, DETP for 76%, and DEDTP was 44%; these detection levels are somewhat higher than those found for the NC non-farmworkers in this analysis. However, concentrations for several of the DAP metabolites for the Israel participants were lower than those for the NC non-farmworkers. Although the geometric mean concentrations for DMP (10.8 μg/g creatinine vs 10.49 μg/g creatinine for 2012) and DMTP (6.4 μg/g creatinine vs 5.11 μg/g creatinine for 2012) were similar, those for DMDTP (Israel 0.3 μg/g creatinine; NC non-farmworker 3.03 μg/g creatinine for 2012, 2.20 μg/g creatinine for 2013), DEP (Israel 1.5 μg/g creatinine; NC non-farmworker 3.88 μg/g creatinine for 2012, 4.26 μg/g creatinine for 2013), and DETP (Israel 0.4 μg/g creatinine; NC non-farmworker 1.39 μg/g creatinine for 2012, 0.93 μg/g creatinine for 2013) were higher among the NC non-farmworkers. Berman et al[49] conclude that the OP concentrations were high for the Israel participants compared with the general population in the US, Canada, and western European countries; if this is the case, then the concentrations NC Latino non-farmworkers are also relatively high in comparison to non-agricultural US, Canadian, and western European populations.

Farmworkers in NC continue to experience occupational exposure to OP pesticides. The frequency of this OP pesticide exposure, as indicated by the frequencies of detection for each of the six DAP metabolites, is similar to those found for farmworkers in 2007.[27] As important, Latino immigrants to NC, who are not employed in agriculture or other occupations in which pesticide exposure would be expected (eg, landscaping and lawn maintenance), experience exposure to OP pesticides at frequencies and concentrations comparable to Latino farmworkers. The sources of these non-agricultural exposures likely include residues on food, environmental exposure (eg, OP pesticides that remain from earlier residential pest control applications), and occupational exposure (eg, OP pesticides on vegetables used in commercial food preparation; OP pesticides used on construction sites).

The NC non-farmworkers and farmworkers do not differ significantly for several DAP metabolites. Therefore, they are experiencing similar exposure to general OP pesticides. Non-farmworkers and farmworkers differ most often for DEP and DMP metabolite detections and concentrations. DEP is a metabolite of chlorpyrifos and DMP is a metabolite of malathion[48]; this finding is reasonable given that both of these OP pesticides continue to be widely used in NC agriculture. Given that the non-farmworkers had relatively high levels of many DAPs with detections and concentrations comparable to the farmworkers, non-agricultural occupational exposure pathways need to be researched. We did not find exposure differences between the occupational categories of the non-farmworkers in this study.

What these occupational similarities and differences say about OP exposure for farmworkers and non-farmworkers is important. Ross and Ginevan[50] argue that DAPs are useful measures of OP exposure only for agricultural workers because the source and time of OP exposure for agricultural workers is known, allowing an unambiguous estimation of exposure levels. Past research in NC indicates that farmworkers are occupationally exposed to OP pesticides,[27,51] and the levels reported for farmworkers in this analysis are not substantially different from levels reported for 2007. Given the similarities between farmworkers and non-farmworkers DAP detections and concentrations, Ross and Ginevan's[50] assertion is called into question. If farmworker DAPs result largely from agricultural exposure pathways, as well as dietary exposure, then we should accept that the DAP results for non-farmworkers are resulting from occupational or environmental sources as well as dietary exposure. Latino non-farmworkers do not consume that much more nonorganic fruits and vegetables than do farmworkers. Therefore, for the non-farmworkers, these results indicate that Latino immigrants, whether farmworkers or not, have greater exposure to OP pesticides than does the general populations.

The results of this analysis should be interpreted in light of the study's limitations. Participants in this study were limited to men from restricted areas of a single state. Participants were not randomly selected. A substantial number of participants were lost over the 2 years of the study. Metabolite detections and concentrations are based on composite rather than individual urine samples. Detection of pesticide urinary metabolites is limited by the current state of laboratory procedures. The analysis focused on a small set of pesticide urinary metabolites, the DAPs, which reflect only a portion of the OP metabolites. However, the sample size for this analysis is relatively large, and the laboratory procedures that were used are the current state of the art.

CONCLUSIONS

Exposure to OP pesticides is common among Latino farmworkers and Latino non-farmworkers in NC. The farmworkers had higher exposure measures for metabolites for two common agricultural pesticides (chlorpyrifos and malathion). For all other DAPs, the farmworkers and non-farmworkers had comparable measures of exposure. Although agricultural application is the major farmworker exposure pathway to these OP insecticides, non-farmworker exposure pathways are unclear. All of the non-farmworker participants live in the same city; many live in the same neighborhoods. Further research is needed to determine pesticide exposure pathways among Latino non-farmworkers so that this disparity can be eliminated. In particular, this research should examine occupational exposure pathways in jobs not traditionally considered to be associated with pesticide exposure. Research on reducing pesticide exposure among farmworkers remains important, as these results do not indicate a reduction in exposure since data collected in 2007.[27] Public occupational and environmental health policy should be considered that reduces pesticide exposure. These policies should address occupational exposures and exposure in all vulnerable communities.

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