Acute Kidney Injury and Exposure to Pesticides among Chilean Agricultural Workers in the Maule Cohort (MAUCO) Study

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BACKGROUND

Agricultural workers frequently face occupational exposure to pesticides.

Previous studies suggest that pesticide exposures may be associated with acute kidney injury (AKI), which can lead to chronic kidney disease (CKD).

Still, there are limited studies that have evaluated the relationship between pesticide exposures and acute kidney injury, particularly in Latin America.

OBJECTIVE

To examine associations between occupational exposure to pesticides and acute kidney injury among agricultural workers in Chile.

METHODS

Study Population: We recruited 43 male agricultural workers from the Maule Cohort (MAUCO) in Chile. Each participant responded to a questionnaire, wore a silicone wristband for 7-10 days, and provided samples of blood and urine.

Exposure Assessment: We quantified urinary levels of 10 pesticide biomarkers and corrected for specific gravity. We measured concentrations of 20 pesticides in passive samplers (silicone wristbands).

Outcome Assessment: Urinary concentrations of five biomarkers of acute kidney injury were measured and adjusted for specific gravity. Serum creatinine was used to calculate estimated glomerular filtration rate (eGFR), the standard measure of kidney function, using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Statistical Analysis: We calculated summary statistics for each participant's demographic information, urinary and wristband levels of pesticide exposures, and kidney health parameters.

We modeled associations between pesticide exposures and levels of AKI biomarkers using covariate-adjusted linear regression.

Table 1. Participant demographic characteristics stratified by agricultural work category.

	Overall (n = 43)	Administrative/ Supervisor (Control) (n = 11)	Agricultural Worker Non-Pesticide Applicator (n = 17)	Agricultural Worker Pesticide Applicator (n = 15)
Age, mean (SD)	53.2 (5.7)	52.5 (5)	51.8 (6.1)	55.3 (5.0)
Ethnicity, n (%)				
Chilean	41 (95)	11 (100)	17 (100)	13 (87)
Mapuche	2 (5)	-	-	2 (13)
Education Level, n (%)				
<8 years	22 (51)	-	11 (65)	11 (73)
>=8 years	21 (49)	11 (100)	6 (35)	4 (27)
Years Worked, mean (SD)	24.3 (13.4)	14.6 (10.6)	24.7 (13.6)	30.8 (11.2)
Days Worked (Past 7 Days), mean (SD)	5.0 (1.3)	5.2 (1.8)	4.9 (0.7)	4.9 (1.4)
Hours Worked (Past 7 Days), mean (SD)	38.7 (13.8)	43.5 (16.2)	37.3 (12.5)	36.8 (13.5)
Work Responsibilities				
Apply Pesticides	20 (47)	1 (9)	5 (29)	14 (93)
Apply Pesticides (Past 7 Days)	5 (12)	-	-	5 (33)

RESULTS

Table 2. Summary statistics for specific-gravity corrected **urinary concentrations (pg/mL) of acute kidney injury biomarkers** (n=43).

Acronym	Biomarker Name	LOD	%>LLOD	Mean (SD)	GM (GSD)	Min	Median (p25, p75)	Max
IL-18	Interleukin 18	4.6	97	37.1 (35.7)	26.9 (2.2)	<LLOD	26.8 (17.7, 40.7)	171.1
KIM-1	Kidney Injury Molecule-1	4.6	100	959.1 (1174.0)	622.3 (2.7)	33.5	689.4 (416.7, 1191.8)	7439.4
MCP-1	Monocyte Chemoattractant Protein-1	1.7	100	159.4 (190.3)	116.6 (2.1)	17.2	115.4 (75.1, 182.7)	1265.9
YKL-40	Chitinase-3-Like Protein 1	34.1	72	181.3 (337.8)	75.5 (3.7)	<LLOD	78.5 (29.6, 146.1)	1951.6
NGAL	Neutrophil Gelatinase-Associated Lipocalin	35.8	100	15,929.4 (31,396.2)	8,068.1 (2.9)	1,305.50	8,252.9 (4,631.6, 12,450.2)	197,654.0
eGFR	estimated Glomerular Filtration Rate	-	-	94.6 (14.2)	93.5 (1.18)	53.4	99.5 (86.5, 104.3)	113.7

Note: Summary statistics calculated using instrumental read values or LOD/√2 when missing.

Table 3. Summary statistics for specific-gravity corrected **urinary concentrations (ng/mL) of pesticide biomarkers** (n=43).

Pesticide Class	Parent Compound(s)	Biomarker Name	Acronym	LOD	%>LOD	Mean (SD)	GM (GSD)	Min	Median (p25, p75)	Max
Organophosphorus Insecticides	Diazinon	2-isopropyl-4-methyl-pyrimidinol	IMPY	0.1	40	0.54 (1.23)	0.18 (3.65)	<LOD	<LOD (<LOD, 0.33)	6.96
	Malathion	2-[(dimethoxyphosphoro-thioyl) sulfanyl] succinic acid	MDA	1.0	0	<LOD	<LOD	<LOD	<LOD	<LOD
	Parathion, Methyl parathion	4- nitrophenol	PNP	0.1	100	1.70 (3.66)	0.97 (2.35)	0.32	0.78 (0.56, 1.48)	24.24
	Chlorpyrifos	3,5,6-trichloro-2-pyridinol	TCPY	0.1	100	3.73 (8.00)	1.74 (2.76)	0.44	1.41 (0.82, 3.06)	43.49
Pyrethroid Insecticides	Cyfluthrin, Permethrin, others	3-phenoxybenzoic acid	3-PBA	0.1	100	1.19 (0.81)	0.99 (1.82)	0.3	0.95 (0.65, 1.49)	4.51
	Cyfluthrin	4-fluoro-3-phenoxybenzoic acid	4F-3PBA	0.1	5	<LOD	<LOD	<LOD	<LOD	0.16
Chlorophenoxy Herbicides	2,4-D	2,4- dicholorphenoxyacetic acid	2,4-D	0.25	30	0.29 (0.26)	0.23 (1.87)	<LOD	<LOD (<LOD, 0.30)	1.37
	2,4,5-T	2,4,5-tricholorphenoxyacetic acid	2,4,5-T	0.1	0	<LOD	<LOD	<LOD	<LOD	<LOD
Organophosphorus Herbicides	Glyphosate	Aminomethylphosphonic acid	AMPA	0.2	84	0.54 (0.60)	0.38 (2.15)	<LOD	0.33 (0.23, 0.49)	3.39
	Glyphosate	Glyphosate	GPS	0.2	93	0.73 (1.00)	0.51 (2.07)	<LOD	0.50 (0.30, 0.70)	6.45

Note: Summary statistics calculated using instrumental read values or LOD/√2 when missing.

Table 4. Summary statistics for **average weekly (7-day) wristband pesticide concentrations (ng/g)** among 40 METALES participants.

Pesticide Class	Pesticide Name	Acronym	LOD	%>LOD	Mean (SD)	GM (GSD)	Min	Median (p25, p75)	Max
Insect Repellent	N,N-diethyl-meta-toluamide	DEET	2.89	80.0	90.5 (210.4)	18.3 (6.09)	1.27	19.1 (6.27, 55.4)	1050.9
Organochlorine Insecticide	1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene	p,p'-DDE	0.04	82.5	1.04 (1.30)	0.38 (5.55)	0.02	0.48 (0.14, 1.58)	5.22
Organophosphorus Insecticide	Chlorpyrifos	CPF	0.38	97.5	528.7 (2356.0)	24.1 (9.51)	0.19	19.0 (5.01, 100.5)	14,672.0
Pyrethroid insecticide	cis-Permethrin	cisPer	1.00	93.0	22.8 (32.8)	10.3 (3.95)	0.44	12.2 (4.45, 25.3)	145.3
	trans-Permethrin	transPer	0.88	100.0	34.4 (44.2)	19.0 (3.03)	1.95	17.1 (9.97, 38.0)	183.7
	Cypermethrin	cyPer	6.43	60.0	52.3 (106.2)	16.6 (4.60)	2.82	19.3 (3.55, 42.2)	637.0
Herbicide	Oxyfluorfen	OXYF	0.26	45.0	130.9 (426.6)	1.35 (22.3)	0.11	0.15 (0.14, 8.55)	2312.4
Fungicide	Cyprodinil	CYPR	0.04	50.0	2.87 (9.15)	0.16 (10.7)	0.02	0.10 (0.02, 0.76)	48.7

a. Summary statistics calculated after replacing values <LOD with the LOD/√2.

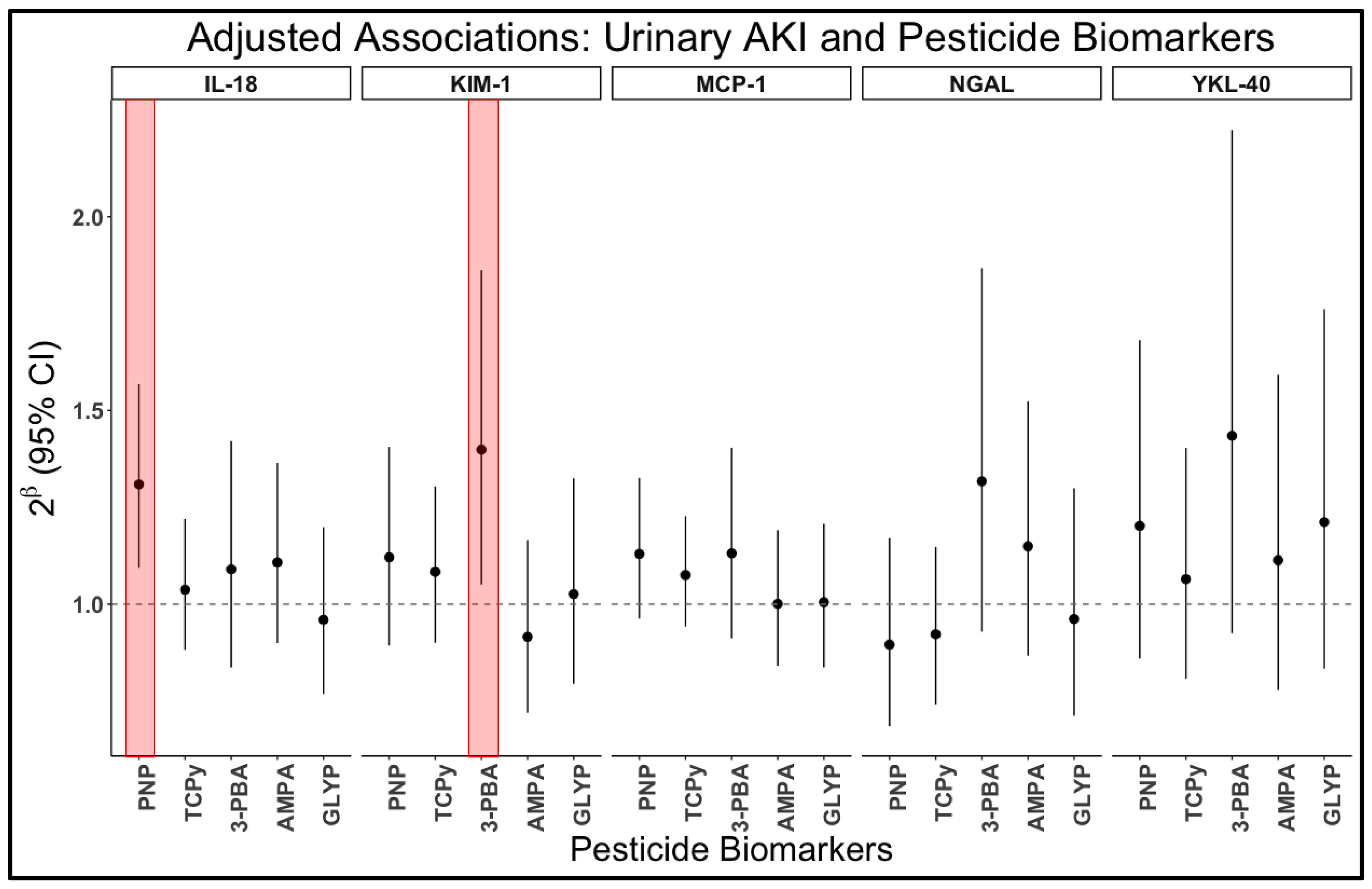

Figure 1. Adjusted associations of urinary acute kidney injury biomarkers with urinary levels of pesticide biomarkers, adjusted for age, education, and agricultural work group.

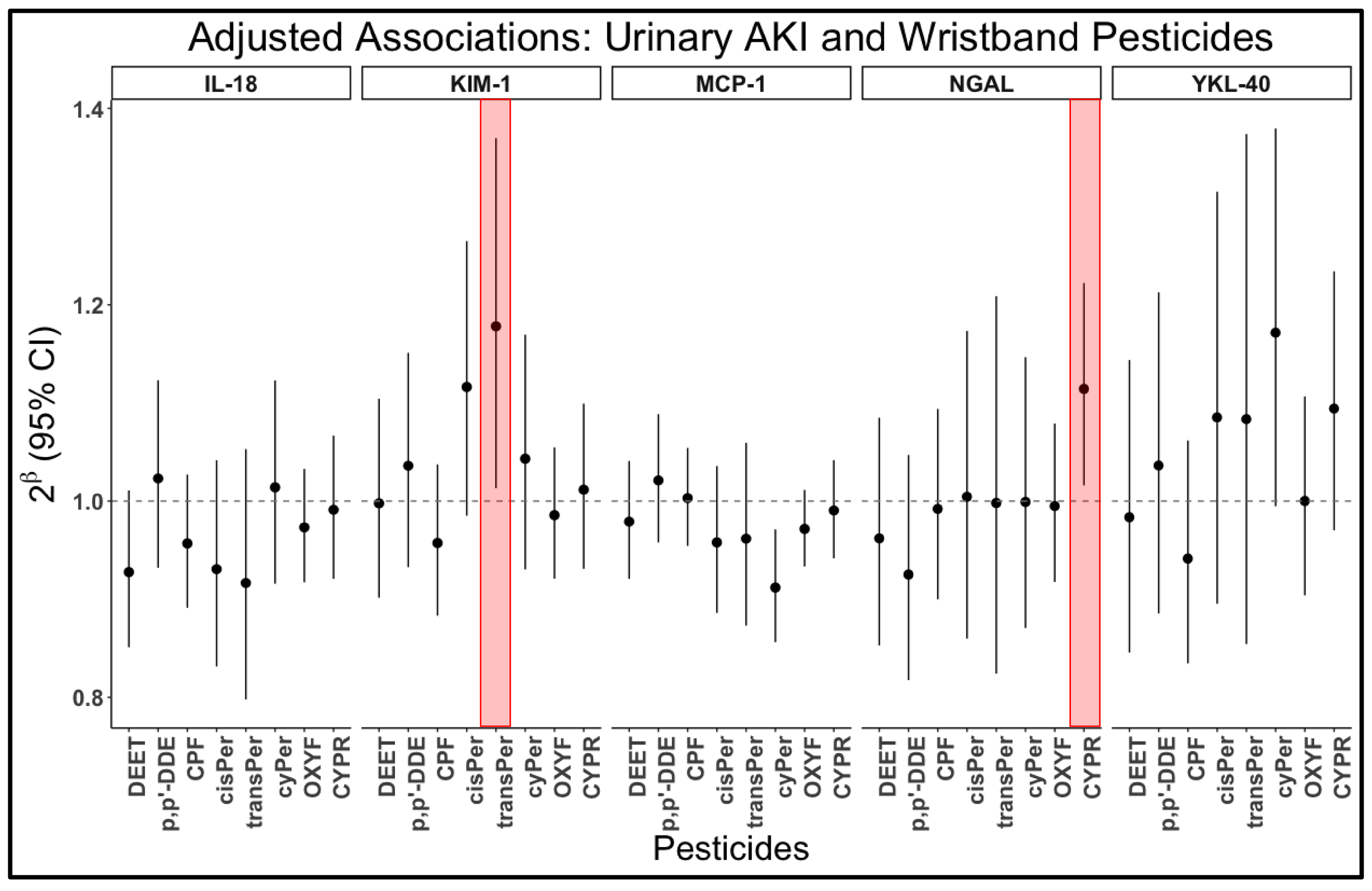

Figure 2. Adjusted associations of urinary acute kidney injury biomarkers with 7-day average wristband levels of pesticides, adjusted for age, education, and agricultural work group.

Table 5. Spearman correlation matrix for specific gravity-corrected urinary acute kidney injury biomarker concentrations (n = 43).

	eGFR	IL-18	KIM-1	MCP-1	YKL-40	NGAL
eGFR	1.00	0.22	0.16	0.10	0.22	0.00
IL-18		1.00	**0.36***	**0.42****	**0.60****	0.29
KIM-1			1.00	**0.44****	**0.51****	0.22
MCP-1				1.00	0.27	0.20
YKL-40					1.00	**0.35***
NGAL						1.00

Abbreviations: eGFR: estimated glomerular filtration rate; IL-18: Interleukin 18; KIM-1: Kidney Injury Molecule-1; MCP-1: Monocyte Chemoattractant Protein-1; YKL-40: Chitinase-3-Like Protein 1; NGAL: Neutrophil Gelatinase-Associated Lipocalin.*Significant at p ≤ 0.05. **Significant at p ≤ 0.01.

CONCLUSIONS

- Among our study sample, all five urinary AKI biomarkers and estimated glomerular filtration rate were positively correlated.
- Five pesticide biomarkers and eight pesticides were frequently detected (DF≥45%) in urine samples and wristbands, respectively.
- Increased exposure to select pesticides, including pyrethroid insecticides, was associated with increased urinary concentrations of acute kidney injury (AKI) biomarkers.
- This is the first study to simultaneously examine both acute kidney injury and pesticide exposures through objective matrices.
- Small sample size limits the generalizability of study findings.
- Findings provide evidence of how pesticide exposures may contribute to the development of kidney disease through acute injury and will inform future investigations of CKD among agricultural workers.

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