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The Relationship between Organophosphate Pesticide Exposure and Anthropometric Outcomes among a Cohort of Children from Four Informal Settlements in the Western Cape

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Abstract: There is limited data on the association between pesticide exposure in children and anthropometric outcomes, particularly in non-agricultural communities and developing countries. This study investigated the association between organophosphate pesticide (OPP) exposure and anthropometric outcomes in primary schoolchildren from four informal settlements in Western Cape Province in South Africa. Using a repeated cross-sectional design of 600 schoolchildren over a 12-month period, urinary dialkyl phosphate (DAP) metabolites, diethylphosphate (DEP), dimethylphosphate (DMP), and dimethylthiophosphate (DMTP) were measured at baseline with DEP and DMP measured at follow-up. Anthropometric measurements height, weight, and Body Mass Index (BMI) were collected at both time points. The mean age for all participants at baseline was 9.93 ± 0.90 years and mean ΣDAP at baseline was 41.78 ± 33.80 ng/mL. Mean changes in weight, height, and BMI from baseline to follow-up for all participants were 6.04 ± 5.29 kg, 6.83 ± 4.00 cm, and 1.05 ± 2.01 kg/m^2, respectively. Eighty percent of participants measured below the 50th percentile in height-for-age at baseline, and 76.8% at follow-up. No consistent associations were found between DAPs and anthropometric outcomes. Urinary OPP metabolite measurements and the prevalence of short stature among children in the study were high compared to other settings. The study did not find evidence of an association between OPP exposure and child anthropometric outcomes. Large longitudinal studies with follow-up periods exceeding two years and incorporating pesticide biomonitoring at multiple time-points are recommended.

Keywords: organophosphate pesticides; anthropometric outcomes; children; non-agricultural settings; informal settlements

1. Introduction

Organophosphate pesticides (OPPs) are the most commonly used insecticides globally, with South Africa being the top importer of pesticides in sub-Saharan Africa [1,2]. OPPs have been found to be endocrine disruptors and in animal studies to impact brain development [3]. With specific regions of the brain responsible for growth and development, alterations to the hormone and enzymatic mechanisms in those regions may contribute to adverse

growth outcomes [4]. Foetuses and young children have been shown to have lower levels than adults of the enzymes paraoxonase and chlorpyrifos-oxonase which are responsible for inactivating organophosphates [5]. Exposure to OPPs prenatally and postnatally may therefore pose a greater health risk to infants and children [6]. Some preclinical studies suggest OPPs may act as obesogens due to changes in the infant's glucose metabolism [7].

There is limited research on the association between non-occupational exposure to OPPs and anthropometric outcomes, especially among children [6–10]. Furthermore, data in Africa is limited. Modes of non-occupational pesticide exposure in non-agricultural settings among children include residential exposures, residues in food and water, non-residential environmental exposures from non-agricultural pesticide spraying, and agricultural spray-drift [11,12]. Spray drift, which is inhaled via air-borne droplets, has been found in areas several kilometers away from the target site [13]. Pest infestation is a particular challenge in South Africa's low-income urban communities due in large part to inadequate housing construction, emblematic of informal settlements. Controlling pests such as cockroaches, mosquitoes, and rats cheaply and effectively is often accomplished using illegally sold pesticides not registered for domestic purposes that include OPPs [14]. OPPs are also commonly used in South African agriculture.

In an Indonesian study, stunting in children aged 8–12 years from a district marked by high onion farming was four times higher than in the non-farm district [15]. Similarly, school-age boys living on farms in South Africa's Western Cape Province exposed to pesticides were found to have lower anthropometric measurements compared to boys who did not live on farms [16]. This study investigated the association between OP pesticide exposure and anthropometric outcomes among children living in informal settlements in non-agricultural settings in the Western Cape, South Africa.

2. Materials and Methods

2.1. Study Design

This analysis investigated the longitudinal and repeated cross-sectional associations between exposure to organophosphate pesticides and child anthropometric outcomes among children residing in informal settlements in the Western Cape over a 12-month period. This investigation is a sub-study using data collected from a prospective cohort study (hereafter referred to as the "parent study") on the association between ambient air pollution and asthma-related outcomes [17].

Boys and girls residing in informal settlements located within one of four identified study areas in the Western Cape were recruited to participate in the parent study. The study areas shared similar socio-economic conditions but differed in the degree of industrialization. The locations were settlements in an urban industrialized area of Cape Town (Milnerton), a peri-urban informal settlement just outside Cape Town (Khayelitsha), and a rural town approximately 400 km from Cape Town (Oudtshoorn). The fourth location, and a low-industrialised urban settlement approximately 36 km from Cape Town (Masiphumulele), was selected in the parent study for its minimal levels of ambient air pollutants to maximize an air pollution exposure contrast [17]. Data were collected during a six-month period in 2015, considered baseline assessments, and once more 12 months later.

Full details of the sampling and the protocol are provided elsewhere [17]. Briefly, 600 schoolchildren were recruited from one or two primary schools per study area. If the consented number of students exceeded the target goal, random sampling was used to determine the final list of students included. The selected schools were chosen for their relatively easy access, governing board's approval to participate in the study, and closest proximity to the City of Cape Town's metro air quality monitoring stations. Grade 4 learners were recruited because they would remain in primary school for the duration of the data collection phase, thus reducing loss to follow from graduating to secondary school. Additionally, Grade 4 learners are on average 10-years-old and capable of completing the study assessments. The investigators received a list of the Grade 4 students from each school's principal including the home address. Trained field staff visited the home of each student to obtain consent from the parent/guardian and assent from the student, a process conducted in the participants' preferred language.

2.2. Study Instruments

2.2.1. Questionnaire

A questionnaire was administered to caregivers and child participants at their homes by trained interviewers in the former's preferred language. The questionnaire incorporated the standardised and validated International Study of Asthma and Allergies in Childhood (ISAAC) and included items on the child's demographic characteristics (age, sex, study area), prenatal maternal smoking, birth weight, and indoor exposures at home (pesticide use, cigarette smoking, pet ownership and fuel use for cooking and heating) [17]. The interviewers administered and captured the questionnaire using mobile technology. It was translated and back-translated.

2.2.2. Pesticide Biomonitoring

Urine samples were collected from each participant at school into a colourless pre-labelled, 50 mL plastic sterile cup with a screw-top lid. Each participant provided a mid-stream, non-first morning void urine sample at baseline, and once again at the 12-month follow-up period. The urine sample collections were performed in the privacy of a toilet after being clearly informed. The urine samples were transported on dry ice to the Clinical Pharmacology Laboratory at UCT at the end of each data collection day and stored at −20 °C until analysis.

The samples were analysed for three OPP metabolites using high-resolution nuclear magnetic resonance (NMR) and a validated liquid chromatography tandem mass spectrometry assay developed by the Division of Clinical Pharmacology Laboratory at the University of Cape Town. Three dialkyl phosphate (DAP) metabolites were measured at baseline, Diethyl phosphate (DEP), Dimethyl thiophosphate (DMTP), and Dimethyl phosphate (DMP), with only Diethyl phosphate (DEP) and Dimethyl phosphate (DMP) measured at follow-up. The samples were subsequently processed with a protein precipitation extraction method using isoniazed-d4 and acetyl isoniazid-d4 as internal standards, followed by liquid chromatography with MS/MS detection using a SCIEX API 3000 instrument. We are aware that DAP urinary excretion would require creatinine adjustment to account for variations in concentration. However, we could not correct our results for creatinine due to a lack of funding to conduct the analyses

2.2.3. Anthropometric Measurements

Participants' heights were measured by qualified nurses using a calibrated wall-mounted tape measure.

The weight measurements were done using a calibrated scale. Body Mass Index (BMI) was calculated using the equation $BMI = \frac{\text{weight (kg)}}{\text{height } (m)^2}$. The WHO growth tables—derived outcome measures from the WHO Multicentre Growth Reference Study [18], were used as the reference data during the analysis phase. Each participant's measures were calculated against the corresponding WHO growth table indicator-for-age to determine if the participant fell below the 25th percentile, 50th percentile, and/or more than two standard deviations above or below the mean, thereby determining the proportion of participants falling outside the normal distribution of the international physiological growth curve standard.

2.3. Data Analysis

Regression analyses were conducted to assess each covariate at baseline and follow-up with the anthropometric outcomes of interest observed over the two timepoints.

In addition to covariates identified apriori, statistically significant covariates ($p < 0.1$) identified in the bivariate analyses were used to conduct multivariate linear and logistic regression models, both cross-sectional and across the two time points, to assess the associations between the anthropometric outcomes and each pesticide exposure. The covariates used were age, sex, study area, pesticide use in the home, pet ownership, and type of cooking fuel used. The linear regression models adjusted for these covariates when analysing the change in weight, change in height, and change in BMI over the follow-up period with the average sum of metabolites measured at baseline and follow-up (i.e., ΣDAP = DEP + DMP). The logistic regression models investigated the association between measurements of more than two Standard Deviations above and below the mean for BMI at baseline and follow-up, and more than two Standard Deviations below the mean for height at baseline and follow-up using the World Health Organization's reference population data (19), with each individual metabolite available for each timepoint as well as the sum of the metabolites. Age of participants were converted from whole years to corresponding months at year + 6 months. Weight-for-age reference data is not available for ages over 10 years + 0 months, therefore, weight data were only included in analyses involving change in weight from baseline to follow-up.

Statistical analyses were conducted using Python version 3.12.1 and statsmodels (version 0.14.2) and scipy statistical packages (version 1.13.1). All continuous data were summarised using the mean and standard deviation. Categorical data were summarised using frequency distributions. The measurements for ∑DAP were log-transformed using the natural log prior to the analysis.

2.4. Ethics Approval

Ethics approval was granted for the main study (HREC Ref: 697/2014) and for this sub-study (HREC Ref: 667/2024) by the Health Sciences Research Committee of the University of Cape Town. South Africa's Department of Education granted approval to conduct research at the selected primary schools. Informed consent was obtained from parents or legal guardians, and informed assent was obtained from the participating children prior to the commencement of any study procedures.

3. Results

3.1. Descriptive Demographics

A summary of demographic, host characteristics, household and outdoor exposures among the 600 participating schoolchildren is presented in Table 1. The mean age for boys at baseline was 10.1 years, and 9.7 years for girls. Reported household pesticide use increased from 9.0% at baseline to 15.5% at follow-up. DMP concentration levels were significantly more prevalent than DEP concentration levels. DMTP concentration level data were only available at baseline and measured similarly to DMP levels. The average (DEP + DMP) during the baseline and follow-up was higher among girls (mean 67.95 ± 55.11 ng/m) compared to boys (mean 49.02 ± 39.79 ng/mL).

Table 1. Demographic factors and pesticide exposures of children living in informal settlements of the Western Cape Province stratified by sex.

Variable	Boys (*n* = 297)		Girls (*n* = 303)		All (*n* = 600)	
	Baseline	Follow-Up	Baseline	Follow-Up	Baseline	Follow-Up
Demographic variables						
Age (yrs)	10.17 ± 0.90	11.17 ± 0.90	9.70 ± 0.84	10.69 ± 0.84	9.93 ± 0.90	10.93 ± 0.90
Low Birthweight (<2.5 kg)	24 (8.2)	-	22 (7.3)	-	46 (7.7)	-
Prenatal maternal smoking	49 (16.8)	-	59 (19.7)	-	108 (18.3)	-
Pesticide use in home	29 (10.0)	55 (18.5)	24 (8.0)	38 (12.5)	53 (9.0)	93 (15.5)
Cigarette smoking in the home	8 (3.7)	42 (15.9)	81 (27.0)	54 (19.9)	164 (27.8)	96 (17.9)
Pet ownership	65 (22.5)	19 (7.1)	52 (17.3)	22 (8.1)	117 (19.9)	41 (7.6)
Cooking fuel *	171 (59.3)	178 (67.4)	182 (60.8)	196 (72.3)	353 (60.1)	374 (69.9)
Area						
Khayelitsha peri-urban	75 (25.2)	59 (22.3)	88 (29.0)	72 (26.5)	163 (27.1)	131 (24.4)
Oudtshoorn rural	78 (26.7)	73 (27.6)	92 (30.3)	86 (31.7)	170 (28.3)	159 (29.7)
Milnerton urban industrialised	76 (25.5)	69 (26.1)	74 (24.4)	67 (24.7)	150 (25.9)	136 (25.4)
Masiphumulele urban low-industrialised	68 (22.8)	63 (23.8)	49 (16.1)	46 (16.9)	117 (19.5)	109 (20.3)
Pesticide metabolites (ng/mL)						
DEP	4.39 ± 11.64	4.28 ± 4.57	3.47 ± 3.57	3.84 ± 4.90	3.93 ± 8.60	4.04 ± 4.72
DMP	19.53 ± 20.06	26.51± 34.32	18.69 ± 21.27	22.08 ± 23.82	19.14 ± 20.69	24.20 ± 29.36
DMTP	20.44 ± 19.26	N/A	17.06 ± 16.12	N/A	18.73 ± 23.24	N/A

Continuous data presented as mean ± SD; categorical data as number (%). * Cooking fuel: electricity, used as a proxy for socioeconomic status; N/A: Not available; DEP: diethyl phosphate; DMP: dimethyl phosphate; DMTP: dimethyl thiophosphate.

3.2. Anthropometric Outcomes

The anthropometric measures among schoolchildren residing in the selected informal settlements at baseline, follow-up, and calculated change between the two timepoints stratified by sex are presented in Table 2. The largest observed change between baseline and follow-up was height, with girls experiencing a greater change compared to boys (5.64% vs. 4.53%). Girls experienced a greater mean change compared to boys from baseline to follow-up for weight and BMI (weight: 6.07kg vs. 4.76kg, BMI: 1.10 kg/m^2 vs. 0.87 kg/m^2).

3.3. Percentage of Anthropometric Outcomes by WHO Reference Population Percentiles

The anthropometric outcomes among schoolchildren living in the four informal settlements were compared to standard growth percentiles using the World Health Organization's reference population data [19] to determine if the schoolchildren were underweight, overweight, stunted, or tall. The results are summarised in Table 3. Nearly half the participants (48.6%) were below the 50th percentile for BMI-for-age at baseline, with a similar proportion at follow-up (42.1%). Height-for-age measurements deviated more significantly than BMI-for-age from the standard reference data, with 80.0% of participants below the 50th percentile at baseline and 76.8% below the 50th percentile at follow-up. Just over fifteen percent of participants were more than two standard deviations below the mean in height-for-age at baseline and 14.4% at follow-up. The proportion of boys was greater than girls in this category at both timepoints (18.4% vs. 12.7% at baseline and 17.4% vs. 11.5% at follow-up). The results were negligible for study participants' height-for-age, measuring more than two standard deviations above the mean (0.1% at baseline and 0.5% at follow-up), compared to BMI-for-age, which found 7.8% of participants were more than two standard deviations above the mean at baseline and 10.1% at follow-up.

Table 2. Anthropometric outcomes of children living in informal settlements of the Western Cape Province stratified by sex.

Variable	Boys			Girls			All		
	Baseline	Follow-Up	Change from Baseline to Follow-Up	Baseline	Follow-Up	Change from Baseline to Follow-Up	Baseline	Follow-Up	Change from Baseline to Follow-Up
	(*n* = 292)	(*n* = 263)	(*n* = 258)	(*n* = 296)	(*n* = 269)	(*n* = 262)	(*n* = 588)	(*n* = 532)	(*n* = 520)
Weight (kg)	32.18 ± 7.37	36.87 ± 9.33	4.76 ± 3.20	32.15 ± 8.11	38.32 ± 10.23	6.07 ± 3.27	32.17 ± 7.75	37.60 ± 9.82	5.42 ± 3.30
	(*n* = 254)	(*n* = 254)	(*n* = 254)	(*n* = 258)	(*n* = 258)	(*n* = 258)	(*n* = 512)	(*n* = 512)	(*n* = 512)
Height (cm)	134.92 ± 7.56	141.03 ± 7.35	6.10 ± 3.93	133.77 ± 7.84	141.32 ± 7.32	7.55 ± 3.95	134.34 ± 7.72	141.17 ± 7.33	6.83 ± 4.00
						(*n* = 256)			(*n* = 510)
BMI (kg/m^2)	17.63 ± 3.32	18.48 ± 3.72	0.87 ± 1.82	17.82 ± 4.07	19.07 ± 3.95	1.10 ± 1.88	17.73 ± 3.72	18.77 ± 3.85	0.98 ± 1.86

Continuous data presented as mean ± SD.

Table 3. Percentage of anthropometric outcomes of children living in informal settlements of the Western Cape Province by WHO Reference Population Percentiles.

	Boys								Girls								All							
Outcome	Baseline				Follow-Up				Baseline				Follow-Up				Baseline				Follow-Up			
	SD2neg	P(25)	P(50)	SD2pos	SD2neg	P(25)	P(50)	SD2pos	SD2neg	P(25)	P(50)	SD2pos	SD2neg	P(25)	P(50)	SD2pos	SD2neg	P(25)	P(50)	SD2pos	SD2neg	P(25)	P(50)	SD2pos
Weight (kg)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Height in [cm (%)]	54 (18.4)	164 (56.1)	239 (81.8)	1 (0.3)	46 (17.4)	150 (57.0)	210 (79.8)	1 (0.3)	38 (12.7)	182 (61.0)	233 (78.1)	0 (0.0)	31 (11.5)	208 (77.3)	199 (73.9)	2 (0.7)	92 (15.5)	346 (58.6)	472 (80.0)	1 (0.1)	77 (14.4)	358 (67.2)	409 (76.8)	3 (0.5)
BMI in [kg/m^2(%)]	9 (3.0)	82 (28.0)	151 (51.7)	22 (7.5)	7 (2.6)	63 (23.9)	125 (47.5)	28 (10.6)	14 (4.7)	76 (25.6)	135 (45.6)	24 (8.1)	5 (1.8)	54 (20.0)	99 (36.8)	26 (9.6)	23 (3.9)	158 (26.8)	286 (48.6)	46 (7.8)	12 (2.2)	117 (21.9)	224 (42.1)	54 (10.1)

Categorical data presented as number (%). Number in brackets indicate % of participants with metrics below the reference population thresholds although for P(25) and P(50) it indicates the percentile; SD2neg is the measurement of more than 2 Standard Deviations below the mean; SD2pos is the measurement of more than 2 Standard Deviations above the mean. Reference thresholds obtained from WHO's growth tables [19]. N/A: not applicable as WHO weight-for-age data is not available for ages ≥10 yrs.

3.4. Association between Anthropometric Outcomes and OP Pesticides

The covariates found to be statistically significant (p-value < 0.1) in the bivariate analysis at baseline were: pesticide use in the home, pet ownership, study area, and fuel for cooking (Table S5). The associations between each anthropometric outcome and each OP pesticide at baseline and follow-up using multivariable linear regression models adjusting for covariates are summarised in Table 4. None of the urinary individual and sum of DAPs metabolites were statistically significantly associated with weight, height, or BMI (p-value > 0.05). There were also no statistically significant associations between the change in anthropometric outcomes over the 12-month follow-up period and the average sum of the OP pesticides measured at follow-up adjusting for covariates (Figure 1).

The associations between the study population's height-for-age and BMI-for-age more than two standard deviations above and below the mean measured against the WHO reference data [19], and urinary OP pesticide metabolites at baseline and follow-up are summarised in Table 5. Because tallness does not indicate a metabolic imbalance, we chose to examine only two standard deviations below the mean for height (SD2neg). All the models adjusted for the same set of covariates as above. Although none reached statistical significance, besides the association of the sum of DAP at follow-up (adjusted OR: 2.23, 95% CI: 1.09–4.57), all the other urinary DAP measures were positively associated with low BMI-for-age (i.e., BMI values more than two standard deviations below the WHO growth chart reference).

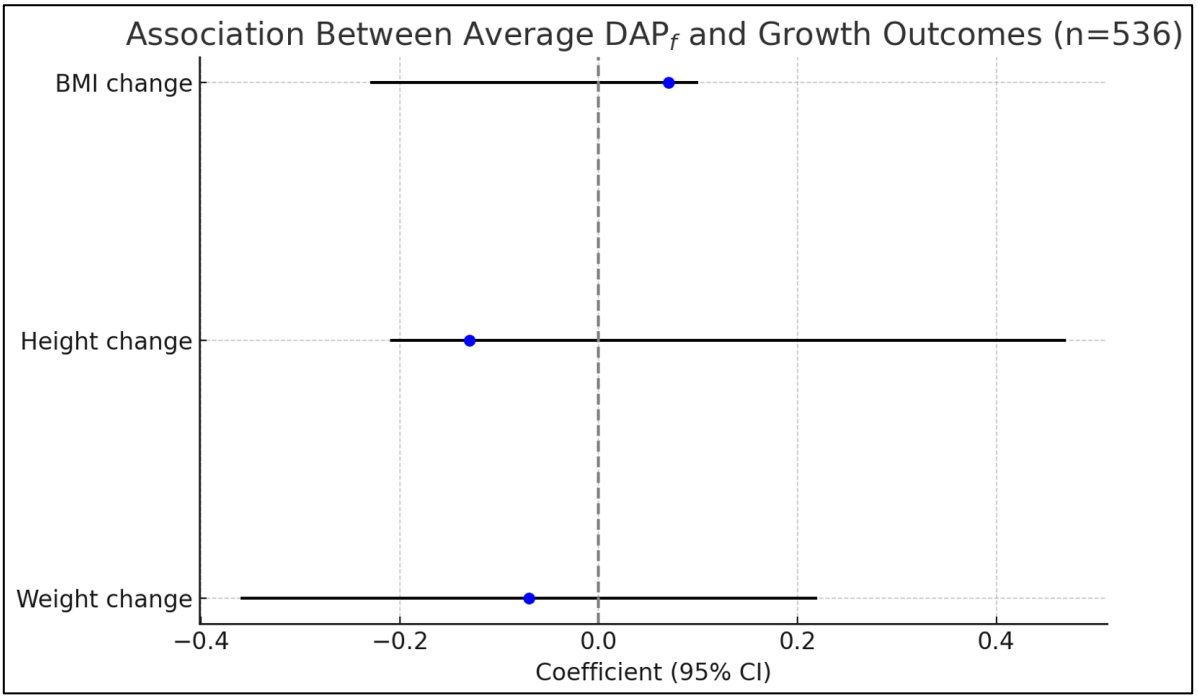

Figure 1. Association between change in anthropometric outcomes and urinary levels of OP pesticides over the 12-month follow-up period using multiple linear regression models. Average DAP_f = [(baseline DEP + baseline DMP) + (follow-up DEP + follow-up DMP)]/2. Covariates used in analysis: age, sex, study area, pet ownership, pesticide use in home, fuel for cooking. Statistical significance adjusted $p < 0.05$.

Table 4. Association between anthropometric outcomes and urinary levels of OP pesticides at baseline and follow-up using multiple linear regression models.

	Baseline [*n* = 589]				**Follow-Up [*n* = 536]**		
	DEP	**DMP**	**DMTP**	**$\sum DAP_b$**	**DEP**	**DMP**	**$\sum DAP_f$**
Outcome	Coefficient (95% CI)						
Weight (kg)	−0.18 (−0.79–0.43)	0.23 (−0.35–0.81)	0.01 (−0.57–0.59)	0.12 (−0.46–0.69)	−0.43 (−1.27–0.42)	−0.50 (−1.36–0.35)	−0.42 (−1.27–0.43)
Height (cm)	−0.48 (−1.13–0.17)	0.12 (−0.49–0.73)	0.06 (−0.56–0.68)	0.05 (−0.56–0.67)	−0.12 (−0.75–0.53)	0.05 (−0.60–0.69)	0.09 (−0.56–0.73)
BMI (kg/m^2)	−0.08 (−0.42–0.25)	0.05 (−0.26–0.36)	−0.07 (−0.38–0.25)	0.01 (−0.33–0.30)	−0.14 (−0.47–0.19)	−0.20 (−0.53–0.13)	−0.17 (−0.50–0.16)

DEP: diethyl phosphate, DMP: dimethyl phosphate, DMTP: dimethyl thiophosphate, $\sum DAP_b$ = sum DAP at baseline (DEP + DMP + DMTP) and $\sum DAP_f$ = sum DAP at follow-up (DEP + DMP). Covariates used in baseline analysis: age, sex, study area, DEP; covariates used in follow-up analysis: age, sex, study area. Statistical significance $p < 0.05$.

Table 5. Association between anthropometric outcomes relative to WHO reference values and urinary levels of OP pesticides at baseline and follow-up using multiple logistic regression models.

	Baseline [*n* = 589]				**Follow-Up [*n* = 536]**					
	DEP	**DMP**	**DMTP**	**$\sum DAP_b$**	**DEP**	**DMP**	**$\sum DAP_f$**	**Average DEP**	**Average DMP**	**Average DAP_f**
Outcomes	aOR (95% CI)									
SD2neg height	1.17 (0.89–1.53)	0.92 (0.72–1.19)	0.92 (0.71–1.18)	0.94 (0.73–1.21)	1.05 (0.80–1.37)	1.00 (0.75–1.33)	1.02 (0.77–1.36)	1.40 (0.72–2.73)	1.61 (0.83–3.15)	1.72 (0.89–3.32)
SD2neg BMI	1.05 (0.60–1.86)	1.45 (0.80–2.64)	1.55 (0.86–2.77)	1.55 (0.86–2.80)	1.79 (0.95–3.39)	1.93 (0.92–4.05)	**2.23 (1.09–4.57)**	1.40 (0.72–2.73)	1.61 (0.83–3.15)	1.72 (0.89–3.32)
SD2pos BMI	1.14 (0.79–1.65)	0.95 (0.69–1.31)	0.91 (0.65–1.26)	0.92 (0.66–1.28)	1.01 (0.73–1.39)	1.07 (0.67–1.50)	1.08 (0.77–1.52)	0.84 (0.59–1.19)	0.93 (0.67–1.30)	0.91 (0.65–1.26)

Bold: indicates a statistically significant association. SD2neg: >2 standard deviations below the mean using WHO reference data, SD2pos: >2 standard deviations above the mean using WHO reference data [19]. $\sum DAP_b$ = sum DAP at baseline (DEP + DMP + DMTP); $\sum DAP_f$ = sum DAP at follow-up (DEP + DMP); Average DEP: (baseline DEP + follow-up DEP)/2; Average DMP: (baseline DMP + follow-up DMP)/2; Average DAP_f: [(baseline DEP + baseline DMP) + (follow-up DEP + follow-up DMP)]/2. Covariates: sex, study area, pesticide use in home, pet ownership, fuel for cooking. Statistical significance adjusted $p < 0.05$.

4. Discussion

This study investigated the association between environmental exposure to organophosphate pesticides and children's growth and development, particularly in resource limited settings, which were four informal settlements in the Western Cape province of South Africa. No consistent associations were found between DAP metabolites and any of the anthropometric outcomes. Before discussing the findings of the association observed in this study, it is important to highlight some nuances underpinning the findings in the current study.

First, concentrations of each OP metabolite were similar at baseline and follow-up among the children, indicating consistency in type and quantity of exposure over the previous year. Second, the mean urinary concentration level of DAP metabolites at baseline and follow-up in the current study was higher than the levels measured in children residing in non-agricultural and agricultural settings elsewhere. For example, in Turkey [20], a study assessing exposure levels to organophosphate and pyrethroid pesticides in children ages three to six years living in an industrial region and an agricultural region found the mean urinary concentration of OP metabolites DEP, DMP, and DMTP were all below the limit of detection (LOD: 0.025, 0.005, and 0.05, respectively). Similarly, measured OP levels in our current study were higher than the levels of DEP, DMP, and DMTP observed among children ages three to eleven years residing in agricultural and urban settings in Spain [21] where all were below the limit of detection (0.1 ng/mL). A study in Queensland [22], Australia, comprising both urban and rural areas, that measured OP metabolites in children ages zero to five years, were lower than those in this study for DEP, DMP, and DMTP.

Furthermore, a previous study [23] among schoolchildren of similar age in these study areas found 77% of boy participants from the rural Western Cape fell below the 50th percentile and 57% below the 25th percentile of height-for-age using the CDC's and WHO's reference data that is consistent with the results of the current study (80.0% at baseline and 76.8% at follow-up in the study were below the 50th percentile height-for-age of the WHO reference data) and therefore indicates that boys and girls from low income rural settings of the Western Cape have shorter stature compared to international reference data standards.

Factors that could have contributed to the lack of associations found between urinary DAP metabolites and anthropometric outcomes in the study include a short follow-up period, insufficient power to detect any subtle association, including increased variability [36% power using a sample size of 600 and binary outcome of low BMI to detect 0.2 SD change in BMI]. With regard to the latter, the spot non-first morning void urine sample and lack of adjusting for hydration status (the procedure was not set-up in the laboratory) may likely have resulted in increased statistical variability and non-differential higher random errors and non-significant findings [17].

A similar study among 269 boys in rural Western Cape previously reported significant associations between the pesticide exposure (as assessed through a proximity index, which measured the lifetime average distance from pesticide spraying) and shorter stature (a factor of −1.7cm in height), and lower weight (i.e., −1.24 kg) [23]. Our results are not comparable with the few studies conducted so far in other settings on the association between pesticide exposure and anthropometric outcomes in children due to differences in the pesticides investigated and/or exposure settings (rural, urban) and/or exposure window (pre-/postnatal). A 2022 study conducted in an agricultural setting in China found a negative association between pre-and post-natal urinary levels of the carbamate, carbofuranphenol, and height, weight, chest circumference, and waist circumference in children at age three [24]. Another study among participants of two provinces of South Korea found post-natal urinary concentrations of the pyrethroid, 3-phenoxybenzoic acid, to be positively associated with weight and BMI z-scores of girls at age four, but no associations with height [25]. No associations were found in a U.S. based study between serum DDT levels and anthropometric measures among adolescent boys [26]. Another U.S. study based in New York also found no association between prenatal urinary levels of OP metabolites of mothers and postnatal child anthropometric measurements [7]. This underscores the inconclusive state of evidence on the association between pesticide exposure and anthropometric outcomes.

It is biologically plausible for organophosphate pesticides to affect growth and development in children due to the potentially endocrine-disrupting nature of OPPs. Endocrine-disrupting chemicals have been shown to interfere with hormone mechanisms responsible for growth and development, and there is experimental evidence that exposure to these chemicals can result in decreased anthropometric growth [27]. Exposure can be especially harmful during critical windows of development, such as the fetal stage and in early childhood.

There are additional study limitations to those mentioned above. Inconsistent measurements and lack of data collected at one or both time points led to a smaller sample size for analysis. Only three of the six known OP metabolites were measured at baseline, and two of the six were measured at follow-up. The metabolites measured are, however, by-products of most of the OP active ingredients that break down into DAPs [28]. The measurement of one urine spot sample at each time point might not reflect 24-h OP exposure and chronic exposure [28].

However, although OP metabolites vary during a day, urinary elimination of DAPs may reach a steady state that reflects average exposure over time with chronic OP exposure [29,30].

Although DAP results were not adjusted for creatinine because of a lack of funding, urine spot samples were collected under the same circumstances and at approximately the same time of the day at baseline and follow-up measurements. Analyzing the urine samples for other co-exposures to environmental pollutants such as heavy metals—which research suggests may have a negative association with childhood growth and development [31]—were not investigated. Finally, the lack of detailed information about the participants' diets limited our consideration of an important confounder. Nutrition during early life stages—beginning in utero and extending through infancy, childhood, and adolescence—impacts bone growth. Many studies show dietary intake of key micro and macro nutrients, including calcium, vitamin D, phosphorous, and protein, are crucial to avoid certain skeletal development deficiencies such as stunting and rickets [32].

Despite the limitations, this study has several strengths. The study participants were recruited from four heterogeneously non-agricultural informal settlements within the Western Cape. This allowed the investigation of non-agricultural-related pesticide exposure that might have resulted from household sources. Additionally, the repeated cross-sectional study design allowed for the collection of the exposure, outcomes, and covariates at these two time points, despite it not being long enough to assess an extended longitudinal effect. However, it allowed for an insight into the prevalence of these metabolites at two cross-sectional time point. Lastly, the study employed OP biomonitoring, which allowed an objective means to assess exposures to pesticides.

5. Conclusions

This study found relatively high concentrations of DAP metabolites in comparisons to other settings among children living in four non-agricultural, informal settlements in the Western Cape of South Africa. Most of the participating children exhibited short stature when compared to the WHO reference range. No evidence of an association between urinary DAP metabolites and child anthropometric outcomes were found. These findings highlight the need to address environmental health risks in non-agricultural, low-income communities that may nonetheless experience higher than average pesticide exposure. Considering the study's limitations, future research should employ large-scale longitudinal designs with follow-up periods exceeding two years, incorporate repeated pesticide biomonitoring at multiple time-points, and collect detailed dietary intake data from participants. These enhancements would improve the accuracy of OP exposure measurements and allow for an adequate consideration of nutritional intake as a potential confounding factor.

Supplementary Materials

The additional data and information can be downloaded at: https://media.sciltp.com/articles/others/25122513 42043632/WAH-25110084-Supplementary-Materials.pdf.

Author Contributions

H.W.: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing—original draft, Writing—review & editing; M.A.D.: Conceptualization, Funding acquisition, Methodology, Project Administration, Formal analysis, Investigation, Resources, Validation, Visualization Supervision, Writing—review & editing; T.O.: Methodology, Project Administration, Formal analysis, Investigation, Validation, Visualization Supervision, Writing—review & editing; L.W.: Methodology, Writing—review & editing; W.B.: Data curation, Writing—review & editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki. Ethics approval was granted for the main study (HREC Ref: 697/2014) and for this sub-study (HREC Ref: 667/2024) by the Health Sciences Research Committee of the University of Cape Town. South Africa's Department of Education granted approval to conduct research at the selected primary schools.

Informed Consent Statement

Informed consent was obtained from parents or legal guardians, and informed assent obtained from the participating children prior to the commencement of any study procedures.

Data Availability Statement

The raw data of this study is available upon request.

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Conflicts of Interest

The authors declare no conflict of interest. DEA&DP (Western Cape governmental department), the major funder, project managed the parent study on air pollution and asthma from which data was used for this sub-study. Given the role as the Editorial Board Member, Mohamed Aqiel Dalvie had no involvement in the peer review of this paper and had no access to information regarding its peer-review process. Full responsibility for the editorial process of this paper was delegated to another editor of the journal.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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