

Exposure Status Of Children To Chemical Pesticides In Food: Systematic Review

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Abstract

Pesticides are toxic for humans. Most children are susceptible, and once they are exposed to chemicals, they may develop a wide range of adverse health outcomes. Children are exposed to chemical pesticides through inhalation, oral ingestion, and dermal uptake. Oral dietary ingestion is a significant pathway for children's exposure to pesticide residue found in crops, fruits, and vegetables, which are among the primary sources of pesticide exposure through the diet. The main objective of this study was to review the exposure status of children to chemical pesticides in food in different research articles. Children's exposure status to different pesticide was identified (reviewed) through literature searches in "PubMed, Science Direct, Web of Science and Springer Link" by using different search items and search criteria. A total of 1192 out of 1301 research articles and review articles were screened after excluding duplicate articles. After the literature review, only 89

articles met the eligibility criteria in which 21 randomly selected articles were included in this review. The result of residue estimation from the review of dietary supply of different research articles has summarized pesticide residue for 21 commodities. Among the fruit samples, Avocado and strawberries were found to contain less pesticide residue. Similarly, vegetable cabbage contains fewer pesticides. Organophosphate pesticides are used in an excessive amount in developed countries and produce di-alkyl phosphate metabolites including diethyl phosphate, diethyl di-thiophosphate, dimethyl phosphate, dimethyl triphosphate, and dimethyl dithiophosphate. Therefore, pesticides harm children as the concentration of these metabolites in the blood level determines the health status of children. safer or less toxic pesticides should be used and it should be determined whether the pesticide use on food is safe for children and includes an additional safety factor.

Keywords: children, exposure, pesticide, metabolites, diet, food

INTRODUCTION

Pesticide is a chemical that is used to prevent, kill, repel or mitigate pests (Ding and Bao, 2014). Pesticides are classified into three groups based on their molecular structure: carbamates, organophosphates, and organ chlorinated pesticides. These pesticides are commonly employed on fruits and vegetable yields across the world, whereas herbicides are largely employed on maize in industrialized nations (Hu et al., 2016). Worldwide, Pesticides are ubiquitous in the environment. Children are particularly considered to be more susceptible to the hazards associated with the toxic effects of pesticides mainly (Organophosphate) than adults.

Children's can be exposed to pesticides through various routes including air (inhalation), food (ingestion), dust (dermal absorption), from mother to child in utero and during breastfeeding (like DDT), and in rural areas children can be exposed to pesticide when they play in the nearby pesticide-treated fields and residues brought to the home by farmworkers (Ding and Bao, 2014, Mekonen et al., 2015 and Vidi et al., 2017). It is expected that the major route for pesticide exposure through consumption of contaminated food is to be five times greater in contrast to exposure from the air or drinking water. Young children consuming an organic diet containing pesticides were significantly reduced in excretion concentration of pesticide metabolites through urinary discharge due to the bioaccumulation nature of pesticides (Bradman et al., 2015 and Mekonen et al., 2017). Various agricultural practices accounted for 71% of all child labor in 2016, exposing 108 million girls and boys to regularly dangerous working circumstances, particularly direct exposure to pesticides, as a result of variables such as extreme poverty (UNICEF, 2018). Children involved in the cocoa industry, in 2002, were 284,000 children and 153,000 of them sprayed pesticides without any protective equipment (UNICEF, 2018).

The major route of pesticide exposure to children is pesticide intake which may significantly contribute to children's total daily pesticide dose and low dose exposure may cause chronic disease (Freeman et al., 2016, Wason et al., 2013 and Akoto et al., 2015). The main reasons for pesticides' effects on children are as follows: their brain does not develop until the age of twelve; physiological differences (heartbeat rate, immature metabolism, breath more air); behavioral factors (size, enzyme differences, crawling on the ground, hand-to-mouth behavior) and consume more food and beverage relative to their body mass than adults (Butler-dawson et al., 2016, Garry, 2004, Lozowicka, 2015, Mekonen et al., 2015 and Wason et al., 2013). Pesticides exposure could be harmful to children than adults because they are associated with many health problems including delayed neurodevelopment and neuro-compatibility (impact central nervous system development), an increased risk for reporting problems, poorer intelligence, changed growth, reduced lung function, childhood cancer, and others (Hyland and Laribi, 2017).

The consumption of a diet that contains a large number of pesticide residues such as fruits, vegetables, grain, and milk has been studied as a major source of pesticide exposure among children in the United States of America (USA) (Holme et al., 2016 and Hyland and Larbi, 2017). Lu et al., (2010) have reported that 11 organophosphate and 3 pyrethroid insecticides in children's food samples have been detected in the USA with levels ranging from 1 to 387 ng/g for Organophosphate and 2 to 1.13 ng/g for pyrethroid insecticides. Intakes of glyphosate via food and water by children 1 to 2 years old, accounted for 13% of the chronic endpoint of 1.75 mg/kg BW/day (EPA, 2006).

Significance of the review: Now a day, chemical pesticides are used highly in agricultural areas in the world for Crops, vegetables, and fruit production and cultivation. Even though, a significant amount of chemicals is retained on the edible parts of food. This review research articles are conducted on chemical pesticides in food of humans experimentally and collected as one paper. This is significantly important to address the exposure status of children and concentration of chemical pesticides presented in different food kinds, and this gives crucial information to the reader, scientific researcher, and policymaker to intervene on the solution on the malpractice of chemical pesticide application on the food of human.

Objectives

General Objective: To review the exposure status of children to chemical pesticides in food from different research articles from 2006-2018 worldwide.

Specific Objective: To review pesticide concentration on different dietary foods in different countries and to review the Exposure level of children with chemical pesticides on different dietary components.

RESEARCH METHODOLOGY

Study design and period: This systematic review was done with reference reporting items using PRISM-P statements. The articles, which published from 2006-2018 on chemical pesticides were included as the primary data source for this review.

Eligibility criteria: Inclusion criteria were following.

1. Dietary exposure assessment of pesticides in children.
2. Exposure comparison of pesticide to children and adults; and studies published from 2006 to 2018.
3. Quantitative presentation of laboratory results of chemical pesticides in dietary food items.
4. Presented the exposure level of children with expressed as mean daily intake g/kg/day of organophosphate concentration in food dietary.

Following were the exclusion criteria for the current research.

1. The language of the research is written other than English.
2. Non-laboratory-based research.
3. Qualitative study design.
4. Research results are not relevant to the reviewed objective.

Information source and Search strategy: Epidemiological studies, which included Organophosphate, pyrethroids, herbicidal, and pesticide exposure assessment, are the primary objective source of information from reviewed articles. Those articles contain all dietary items and are analyzed experimentally and frequently eaten by children and exposed daily, and the results presented as ADI g/kg/day of concentration of chemical pesticide through food were the source of information taken from the articles. The relevant pieces of literature with the topic were drawn from different searches engines such as PubMed, Science Direct, Web of Science, EBSCO, and Springer Link using key terms such as Organophosphate, Pyrethroids, Insecticide, Carbamate, Pesticides, and children due to daily dietary exposure on children through consumption of common food items with pesticide chemical residue in cereals, vegetables, and fruit.

Selection process: The articles were selected using key terms such as children, exposure, and pesticide, metabolites, diet, and food items. The research is exploratory, because no substantial study on the same subject may be contained in the literature. Required data was also collected from the research and review articles published in reputable journals from 2006-2018. For each study author's name, place, and year of publication.

Data collection and technique: A total of 1301 research articles and review works of literature were collected using search terms. After deletion of duplicate articles, 1192 were screened in which only 142 articles met the inclusion criteria and finally 21 articles were included to review (Fig 1).

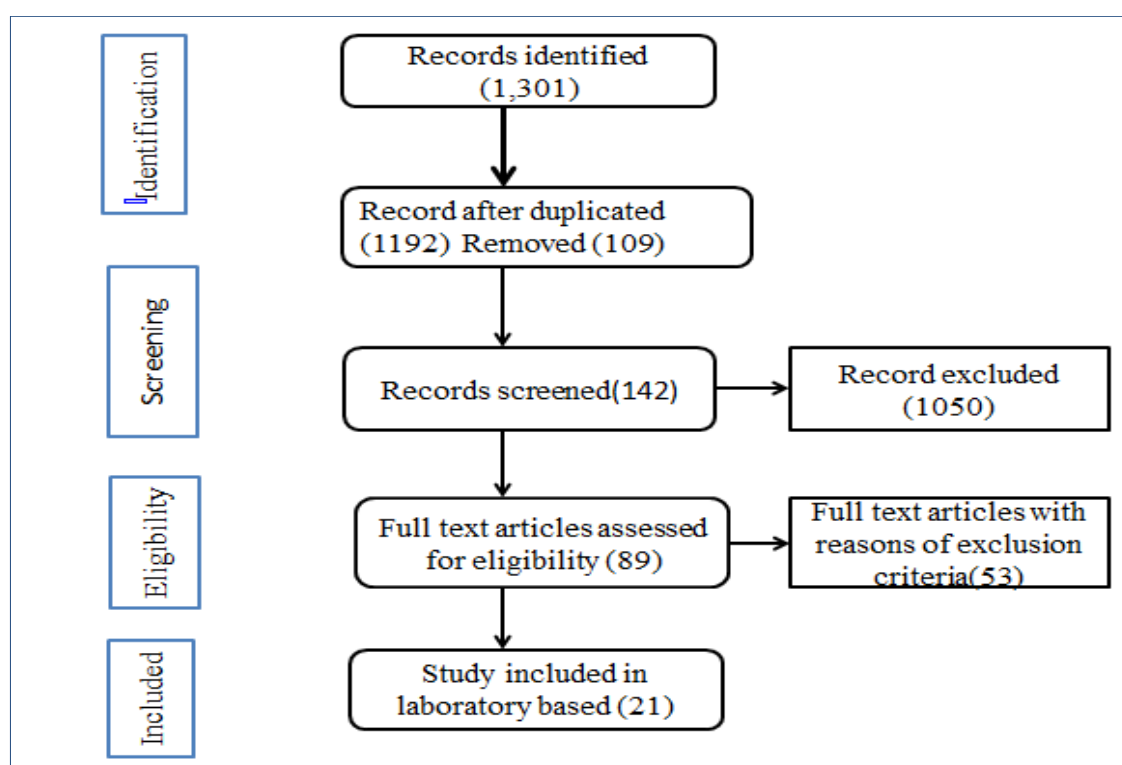


Figure 1.Flow diagram of included relevance studies identified through systematic searching strategy by using keywords human, children, chemical pesticides, fruit, vegetable, and cereals, etc.

Effect measures: It is expected that chemical pesticides present with disrespected to low concentration on daily exposure through food dietary results chronic and acute human health effect.

Data synthesis:Data were described narratively as chemical pesticide type, concentration, and human characteristics such as male and female and adult and children. The presence of chemical pesticide concentration and human daily consumption of different food items with mean daily intake as g/kg/day were extracted from each eligible article.

RESULTS AND DISCUSSION

The results of residue estimation from the review of dietary supply of different research articles are presented in table 1. The three studies in table 1 have summarized pesticide residue for 21 commodities with 1) for Mean (g/kg BW/day) in Spain; 2) Mean (g/kg BW/day) in Denmark survey done from 2011-2013 and 3) Mean (g/kg BW/day) in Denmark survey done from 2003-2008. Morgan and Jones, (2013) have reported that foods such as fruits and vegetables that are usually consumed by children may be a cause of their exposures to dietary pesticides. Among the fruit samples that were eaten by children in different areas, the least pesticide residues were found in Strawberry (0.02g/kg BW/day), Avocado (0.017g/kg BW/day), and Strawberry (0.17) with study area in Spain and Denmark (between 2011-2013 and 2013-2014) respectively.

According to the report of EPA, (2006), the “dirty dozen” list of the fruits and vegetables are categorized into highest levels and little or no pesticide residues. These are: With highest pesticide residue: Apples, Celery, Strawberries, Peaches, Spinach, imported nectarines, Imported grapes, Sweet bell peppers, Potatoes, Domestic blueberries, Lettuce and Kale/collard greens with little or no pesticide residue: Onions, Avocados, Sweet corn, Pineapples, Mango, Sweet peas, Asparagus, Kiwi fruit, Cabbage, Eggplant, Cantaloupe, Watermelon, Grapefruit, Sweet potatoes, and sweet onions. The result in Denmark (between 2011-2013) and the report by EPA, (2006) is similar because Avocado is found in lower pesticide residue concentrations. But the result in Spain and Denmark (between 2013-2014) is in contrast to the report of EPA, (2006) because strawberry is found to have lower pesticide concentration in the EPA report and higher pesticide residue values in the current study.

Among the vegetable samples that were eaten by children in different areas, the least pesticide residue was found in Cabbage in all study areas with a concentration of 0.05, 0.098, and 0.04 in Spain and Denmark between 2011-2013 and 2013-2014) respectively. This result shows similarity with the report of EPA, (2006) which states that cabbage has the least pesticide residue concentration than the other vegetables. The presence of Chlorpyrifos is not allowable for use in the US on tomatoes and apples due to their role in exposure to susceptible groups such as infants and children, but it is still registered in Israel for these uses (Berman et al., 2013).

Table 1. Mean value of ADI (g/kg BW/day) data from a dietary supply of crop, vegetable and fruit containing organophosphate, carbamate, and pyrethroid pesticide in Spain (Quijano et al., 2016), Denmark survey done 2011–2013 (Larsson et al., 2018) and in Denmark for the years 2013 and 2014 (Larsson et al., 2017).

Crop/ Commodity	Quijano et al. (2016) in Spain		Larsson et al. (2018) in Denmark						Larsson et al., (2017) in Denmark			
	Adult	<u>Child</u>	<u>Adult</u>	<u>Male</u>	<u>Female</u>	<u>Child</u>	<u>Male</u>	<u>Female</u>	<u>Adult</u>	<u>Male</u>	<u>Female</u>	
											<u>Child</u>	<u>Child</u>
Citric fruit	0.69	0.84	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Cabbage	0.04	0.05	0.084	0.075	0.091	0.098	0.089	0.135	0.03	0.03	0.04	0.04
Strawberry	0.01	0.02	0.071	0.040	0.096	0.137	0.095	0.199	0.09	0.05	0.12	0.17
Pea	0.03	0.04	0.119	0.106	0.131	0.135	0.185	0.191	0.03	0.03	0.03	0.03
Bean	0.11	0.13	0.018	0.016	0.020	0.032	0.028	0.031	NA	NA	NA	NA
Apple	0.40	0.41	1.280	1.040	1.480	3.300	2.623	2.694	2.77	2.25	3.20	7.13
Potato	0.16	0.49	1.270	1.490	1.090	2.270	1.510	1.040	0.32	0.38	0.28	0.58
Cucumbers	0.09	0.06	0.222	0.162	0.271	1.350	0.324	0.406	0.04	0.03	0.05	0.23
Pepper	0.13	0.07	0.100	0.074	0.120	0.248	0.122	0.190	NA	NA	NA	NA
Banana	0.34	0.95	0.454	0.347	0.541	1.270	0.690	0.883	NA	NA	NA	NA
Tomato	0.87	1.09	0.518	0.464	0.563	0.971	0.740	0.756	0.19	0.19	0.21	0.36
Grabs	0.06	0.06	0.173	0.100	0.234	0.372	0.269	0.401	NA	NA	NA	NA
Carrot	0.19	0.33	0.498	0.349	0.620	1.480	0.558	1.040	0.23	0.16	0.29	0.69
Citrus juice	0.28	0.42	0.790	0.667	0.891	1.982	1.240	1.248	NA	NA	NA	NA
Avocado	NA	NA	0.030	0.014	0.043	0.017	0.035	0.064	NA	NA	NA	NA
Tea	NA	NA	0.022	0.014	0.029	0.003	0.024	0.034	NA	NA	NA	NA
Rice	NA	NA	0.082	0.083	0.081	0.162	0.111	0.093	NA	NA	NA	NA
Wheat	NA	NA	1.120	1.130	1.110	3.120	1.110	1.060	0.64	0.64	0.63	1.78
Sugar beat	NA	NA	0.687	0.710	0.656	2.110	0.699	0.648	0.21	0.22	0.20	0.65
Corn	NA	NA	0.005	0.003	0.007	0.043	0.002	0.009	0.004	0.003	0.005	0.030
Onion	<u>NA</u>	<u>NA</u>	<u>0.149</u>	<u>0.156</u>	<u>0.144</u>	<u>0.210</u>	<u>0.184</u>	<u>0.176</u>	<u>0.41</u>	<u>0.43</u>	<u>0.39</u>	<u>0.57</u>

bw= body weight, NA= Not available

These vegetables and fruits that contain pesticide residue are changed into their metabolites. Nowadays Organo phosphates pesticides are used in an excessive amount in developed countries and produce dialkyl phosphate metabolites even if organochlorine pesticides are used in developing countries. Tables 2 summarizes the mean concentrations of six dialkyl phosphates with standard deviations, range, and exposure variable for each measured metabolite including diethyl phosphate, diethyl dithiophosphate (o,o-diethyl thiophosphate), dimethyl phosphate, dimethyl trio phosphate (o,o-dimethyl thiophosphate), and dimethyl dithiophosphate (O, O-dimethyl dithiophosphate) for

review literature. The detection ranges of organophosphate metabolites in children's urine varied in each reviewing literature and practice the different patterns of the mean concentrations were observed.

The result of the current study shows that, the range (min and max value) of dimethyl phosphate metabolite concentration represented in $\mu\text{g/L}$ in Spain (3.5-115.8 in December 2011 and 3.5-72.6 in May 2011), China ($<\text{LOD}$ -408.09 for infant and $<\text{LOD}$ -185.74 for children) and Norway (1.1-900). On the other hand, Heudorf et al. (2006) proposed reference ranges for the German population as follows: dimethyl phosphate 135 $\mu\text{g/L}$, dimethyl trio phosphate 160 $\mu\text{g/L}$, and diethyl phosphate 16 $\mu\text{g/L}$. Accordingly, the range of the result in Spain is less than the reference value given by Heudorf et al., (2006) and vice versa for the research done in China and Norway.

Children with levels of urinary dimethyl phosphate above the median had double the odds of being diagnosed with ADHD than those with non-detectable levels of urinary dimethyl phosphates (Roca et al., 2014). According to Curl et al., (2003) mean concentration of organic diet in μg /diethyl phosphate, diethyl dithiophosphate, dimethyl phosphate, dimethyl trio phosphate, and dimethyl dithiophosphate metabolites are 1.0, 2.7, 1.1, 4.3, and 0.8 with a standard deviation of 0.7, 2.7, 1.0, 4.3 and 0.5 $\mu\text{g/L}$ respectively. However, in the current study, the mean (SD) value of diethyl phosphate metabolite in Chili (December 2010 and May 2011) and Norway varies from 9.1 (1.1), 8.7 (1.09), and 5.3 respectively which shows great variation with the report of Curl et al., (2003). The greater mean value of diethyl dithiophosphate was recorded in Australia and chili, dimethyl phosphate, dimethyl trio phosphate, and dimethyl dithiophosphate in the current study is recorded as 8.3 (23.5) in Australia.

Table 2. Dialkyl Phosphate in the urine of children relative to vegetable & fruit intake from Dec 2010 and May 2011 in Chili (Muñoz-Quezada et al., 2012), in Australia (Babina et al., 2012), China (Wang et al., 2017), Taiwan (Chang et al., 2018) and Norway (Cequier et al., 2007).

Reference/Authors		Metabolites	Diethyl Phosphate		Diethyl Dithio Phosphate		DMP		DMTP		DMDTP	
			Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
(Muñoz-quezada et al., 2012)	Dec, 2010	µg/L	9.1 (1.1)	3.5417.1	8.3	3.5-691.4	5.2	3.5115.8	5.5	3.594.6)	8.9	7.1146.
	Chili	µg/g	8.7 (1.09)	3.5268	(1.09)	3.5-843	(1.06)	3.5146	(1.06)	3.5121	(1.04)	4)
	May, 2011	nm/L	59.3	22.92708.4	7.7	20.84067.1	5.1	28.1919.1	5.3	24.9666.2	8.7	7.1126
(Babina et al., 2012)	Urban	µg/g	19.5		48.9	3.5-24	41.3	3.574.0	38.8	3.5120	56.1	-
	Peri-urban	nm/L	(1.09)		(1.09)	0-147.6	(1.06)	0576.2	(1.06)	0980.3	(1.04)	926. 6
	Rural	µg/g	18.6	3.5383.8	3.7		4.5	NA	4.5	<LOD	7.1	7.1-
		µg/g	126.4		(1.01)		(1.05)	NA	(1.05)	-346.5	(1)	7.1
			7.4 (9.5)		3.7		4.4		4.4	<LOD	7.1	7.1-
		µg/g	84.1	3.5237	21.8		36.0	NA	32	-1615	44.75	7.1
			(175.3)	0-2492			NA		20.2	<LOD	12.4	044.8
			79.2	<LOD	8.3	<LOD-	NA		(48.2)	-981.3	(14.9)	<LO
			(151.8)	55.7	(23.5)	195.1			135.9		15.7	D-
				<LOD-	24.7	<LOD-	NA		(259.		(21.2)	75.5
(Wang et al., 2017) China	Infant(12 month)	µg/g	NA	<LOD-	NA	<LOD-	NA	<LOD	NA	>LOD	NA	NA
		µg/g	NA	269.24	NA	116.59		-		-	NA	NA
		µg/L		<LOD-		<LOD-		744.5		381.7		
				49.72		21.77		8		5		
							NA	<LOD	NA	<LOD		
								-		-65.43		

							408.0					
							9					
	Child	µg/g	NA	<LOD-	NA	<LOD159.	NA	<LOD	NA	<LOD	NA	NA
	(24			259.45		99		-		-		
	month)							2084.		123.1		
								09		8		
		µg/L	NA	<LOD-	NA	<LOD-	NA	<LOD	NA	<LOD	NA	NA
				105.02		77.06		-		-32.80		
								185.7				
							4					
Chang et al., 2018	Childre	nm/g	72.11	1.86–	102.9	0.81–	271.5	3.25–	189.4	1.66–	24.93	0.65 –
Taiwan	n (4–		(13.57)	2316.8	5	1163.61	9	2306.	6	1885.	(2.18)	201.
	15)			9	(11.6		(17.3	18	(19.1	63		29
					4)		9)		9)			
	Child	µg/L	5.3	0.36-	1.6	0.31-12	28	1.1-	12	0.19-	1.2	0.6-
(Cequier et al.,	(6 to			20				900		212		25
2017)	12											
Norway	years)											

Diethyl Phosphate= diethylphosphate; DETP= diethylthiophosphate; DMP= dimethylphosphate; DMTP= dimethylthiophosphate; DMDTP= dimethyldithiophosphate; NA=Not available, nm=Nano mole

According to the report of Roca et al., (2014) and Teresa et al., (2013) the major metabolic precursor of each dialkyl phosphate are listed as follows.

- Dimethyl phosphate (DMP): Azinphos-methyl, dichlorvos, Chlorpyrifos, dicotophos
- Dimethyl thiophosphate (DMTP): dimethoate, fenitrothion, fenthion, malathion, Chlorpyrifos
- Dimethyl dithiophosphate (DMDTP): methylparathion, trichlorfon, chlorpyrifos-methyl, primiphos-methyl, tetrachlorvinphos
- Diethyl phosphate (DEP): Chlorethoxyphos, chlorpyrifos, coumaphos
- Diethyl thiophosphate (DETP): diazinonc, disulfotonc, ethionc, parathionc, phoratec

From the major metabolic precursor of dialkyl phosphate, the level of chlorpyrifos(3,5,6-trichloro-2-pyridinyl [TCP]), which is metabolized to diethyl dialkyl phosphate levels, is associated with child neurodevelopment, an increase in the occurrence of atopic conditions, the occurrence of childhood

asthma, loss of muscle strength, modification in vision and smell sense and structural brain anomalies at school age including disruption of normal sexual dimorphisms in brain structure (Eskenazi, et al., 1999, Ding and Bao, 2014, Andersen et al., 2015 and Asghar et al., 2016). For chlorpyrifos, it is quickly metabolized into diethyl phosphate and diethyl thiophosphate, and these metabolites are primarily excreted in urine (Morgan and Jones, 2013). According to the report of Gad Alla et al., (2015), the acceptable daily intake (ADI) value of Chlorpyrifos was analyzed from Cucumber, Lettuce, Water Cress, Pepper, Lettuce, and Tomato samples of Egypt was 0.01 mg⁻¹ kg⁻¹ BW pesticide residues. Detection of short-lived urinary metabolites in a significant proportion of urine samples from a large group of subjects in a cross-sectional study would be indicative of ongoing (chronic) exposure in the population (Babina et al., 2012). Urinary dimethyl and diethyl dialkyl phosphate (dialkyl phosphate) levels were significantly higher during spray months compared to non-spray months.

Conclusion: Vegetables, fruits, and cereals are a good source of food but most children are exposed to the pesticide through ingestion of different dietary supplements. Pesticide exposure can be more harmful to children as compared to adults by causing a variety of disorders. From fruits, the pesticide exposure of strawberries is less than the report by the EPA, and in Avocado is greater than the report of EPA. On the other hand, the pesticide exposure to children through vegetation is lesser through the cabbage. The pesticide residue mostly organophosphate that enters the body of children is changed to its metabolites (dialkyl phosphate) including diethyl phosphate, diethyl dithiophosphate, dimethyl phosphate, dimethyl trio phosphate, and dimethyl dithiophosphate. The concentration of this metabolite in the blood level determines the health status of children. Urinary dimethyl and diethyl dialkyl phosphate levels were significantly higher during spray months compared to non-spray months. Therefore, safer or less toxic pesticides should be used and it should be determined whether the pesticide use on food is safe for children and includes an additional safety factor.

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