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HISTORY OF PESTICIDE EXPOSURE AS THE RISK FACTORS FOR STUNTING ON SCHOOL-AGED CHILDREN IN AGRICULTURAL AREAS: A STUDY IN BREBES DISTRICT INDONESIA

ABSTRACT

Stunting prevalence among school-aged children in Brebes District was the highest in Central Java (40.7%). Brebes District is an agricultural area with a very high intensity of pesticide use. The aim of the study was to prove pesticide exposure as the risk factor for stunting among children in agricultural areas. This case-control study had 160 children aged 8-12 years (48 cases and 112 controls) as the subjects. The history of pesticide exposure was measured based on the history of pesticide exposure since the fetus, infant, and child. Stunting was determined as height for age Z-scores (HAZ)<-2SD. Confounding variables measured were TSHs, IGF-1, haemoglobin, zinc, albumin, history of infection, low birth weight (LBW), and mother's height. Data were analyzed by mean difference, Chi-square tests, Odds Ratio (OR) calculation, and multivariate logistic regression. There was no difference in characteristics and confounding variables between the cases and controls ($p>0.05$), except for the mean IGF-1 level, which was lower in the cases (76.0 ± 35.98 ng/mL) compared to the controls (138.6 ± 86.69 ng/mL), with p-value of 0.0001. Children with a history of 'high' pesticides exposure had a risk of 3.2; 95% CI: 1.1-9.7 higher than the unexposed children. Two risk factors of stunting were 'high' pesticide exposure (adj-OR=4.5; 95% CI:1.4-15.1; p=0.013) and 'low' IGF-1 levels (adj-OR=5.8; 95% CI:2.7-12.5; p=0.0001). High pesticide exposure was the risk factors of stunting among children in agricultural areas.

Keywords: pesticide, stunting, school-aged children, agricultural area, Indonesia

INTRODUCTION

Stunting, or poor linear growth (low length- or height-for-age) in young children is the result of poor nutritional intake, in terms of both quality and quantity, high morbidity, or a combination of both. These conditions are often found in low and middle-income countries[1]. Low consumption of macronutrients and micronutrients, especially during the growth period, will disrupt the process, and result in stunting[2]. In addition to food consumption factors, stunting is also influenced by genetic factors[3,4], recurrent (chronic) infections, such as acute respiratory infections (ARI) and diarrhea[5].

The problem of stunting in children should be a concern because it is a reflection of the quality of human resources in the future. Some studies showed an association between stunting with impaired cognitive function[6,7] and the learning achievement of children of school age[8]. Impaired cognitive function in children with stunting, in the long term, will affect their economic potential. Stunting conditions in childhood generally continue into adulthood and will affect their work capacity and productivity[9].

Stunting prevalence in school-age children (5-12 years) in Indonesia reached 30.7%. The prevalence of stunting in children of the same age in Central Java was 28.6%, while in Brebes District reached 40.7%, the highest among the other districts in Central Java[10]. Brebes District is one of the districts in Central Java province that relies on agricultural sector as the source of local revenue, an especially onion that requires pesticides spraying 2-3 times per week, even everyday in the rainy season[11].

Toxic substances exposure from the environment might also interfere the synthesis of Insulin-like Growth Hormone 1 (IGF-1)[12]. Research in Spain showed that serum IGF-1 levels of boys aged 6-15 years exposed to organochlorine pesticides were significantly lower than the non exposed[13]. Low IGF-1 levels in serum were associated to growth disorders. The results of the study in preschool children in Senegal show that there was a relationship between IGF-1 levels and stunting[14].

A study in Brebes District showed that the history of organophosphate pesticide exposure was the risk factor for hypothyroidism in women at child-bearing age in agricultural areas[11]. Exposure to organophosphate pesticides might cause neurodevelopment disorders[15,16].

Pesticides exposure in children may occur directly, because of their involvement in agricultural activities, or indirectly through contact with the environment: water, soil, or food contaminated by pesticide residues. The study results in one of the primary schools in Brebes onion farming areas indicated that 81.3% of the students were involved in agricultural activities, such as finding pests, helping with the harvest, and removing onions from stalks[17].

METHODS

This study used a case-control design to show pesticide exposure as the risk factor for stunting in children in agricultural areas. The study was conducted in four primary schools in Bulakamba Sub-district as this area had high prevalence of stunting in school children and the onion farming area is quite wide. Bulakamba Sub-districts on 3 meters above sea level, which includes lowland areas.

The minimum sample size calculation used a formula for a case-control study with a significance level of 0.05 and the research power of 80%. Using the pesticide exposure proportion in the no stunting children of 22.9% and Odds Ratio (OR) of 3,26 [5], the minimum sample size were 43 for each group (case and control). The inclusion criteria for the subjects were 8-12 years old, no abnormalities of the spine (such as scoliosis), and had not menarche yet for the female subjects.

The measurement of child height for screening was conducted on 238 subjects (elementary students) consisted of 119 (50.0%) males and 119 (50.0%) females. Based on WHO growth standard (2006), 52 subjects (21.8%) were classified as stunting and 186 (78.2%) normal. Of 238 subjects who were measured, 51 subjects refused to had blood samples taken. Of the 187 subjects who had blood samples, 28 subjects had incomplete data on interviews and home observations. Thus, 48 cases and 112 controls have complete data and were analysed (Figure.1.)

Subjects and mothers/caregivers were interviewed in this study. Structured questionnaires were used to collect characteristics data (sex, age, parents' educational and occupational status), pesticide exposure, history of acute respiratory infections and diarrhea in the last month, and history of low birth weight/LBW (less than 2500 grams).

History of pesticide exposure is a composite variable of three sub-variables: 1) mother's involvement in agricultural activity during pregnancy; 2) subjects were brought to farm by the mother, at infant and /or toddler period; and 3) subjects' involvement in agricultural activities at school age period. In each of the three sub-variables, they were categorized into 1) 'high' exposure history, when they answered "Yes" in all the three time periods (exposed when pregnant women, infants/toddlers, and school age); 2) 'moderate' exposure history, when they answered "Yes" at two time periods; 3) 'low' exposure history, when they answered "Yes" at any one time period; 4) unexposed, when they answered none in the three time periods.

The age of the children was derived from the school register. Measurements of height were taken by two postgraduate nutrition students who were trained on the standard procedure of measuring height. The height was measured using a Seca® 213 stadiometer (to the nearest 0.1 centimeters). The measurements were done on the subject with the erect position, without shoes and with the eyes looking horizontally and the feet together on a horizontal level. Stunting was defined as HAZ below minus two standard deviation (-2 SD) , and normal was defined as HAZ equal to minus two (-2 SD) until two (2 SD) of WHO Child Growth Standards [18]. The mother's height was measured with a stadiometer in the same way as the measurements for the children.

Non-fasting peripheral venous blood samples were obtained from 160 students in the morning from 09.00 to 11.00. a.m. TSH levels were measured with a mini VIDAS® (bioMérieux S.A.), that is a compact automated immunoassay system based on the Enzyme Linked Fluorescent Assay (ELFA) principles. TSH levels greater than 4.5 mIU/mL was considered as hypothyroidism[19]. Serum concentration of IGF-1 was measured with the Quantikine® Human IGF-I ELISA kit (R&D Systems). Determination of cut-off point for the levels of IGF-1 using the Receiver Operating Characteristic (ROC). Based on the ROC curve coordinate table, the cut-off point for IGF-1 was 82.66 ng/mL (with a sensitivity of 72.3% and a specificity of 66.7%), and were categorized as 'Low' if the levels of IGF-1 less than 82.66 ng/mL. Hemoglobin was measured using the KX-21 automated hematology analyzer (Sysmex). Anemia was determined using cut-off point of hemoglobin less than 12 g/dL [20]. Zinc serum concentrations were measured using Shimadzu® Atomic Absorption Flame Emission Spectrophotometers (AAS) Model: AA-6401F. Zinc serum fewer than 70 µg/dL was categorized as low [21]. Serum albumin levels were measured using the Bromocresol green (BCG) method. Serum albumin concentration of less than 3.5 g/dL were considered as low [22].

Data were analyzed using SPSS for Windows software (version 18). For bivariate and multivariate analysis, descrete scale variables were transformed into categorical scales. The means and standard deviations of age, height, HAZ, TSHs, IGF-1, hemoglobin, Zinc level in the case and control groups were compared using the mean difference test (Mann-Whitney and Independent t-test). Proportions were calculated for categorical variables, and they were compared using the Chi-square tests. Potential risk factors associated with stunting were identified by the odds ratios (ORs) and their 95% confidence intervals (CI). A multivariate analysis to assess the risk of pesticide exposure for stunting were done by including some confounding variables in multivariate logistic regressions. Statistical significance was determined at 95% level of significance or p-value <0.05.

Ethics approval

Ethical approval and clearance were obtained from the Diponegoro University Medical Faculty Ethical Committee (No. 481/EC/FK-RSDK/2015). The teachers, subjects, and parents were well-informed of the purpose and benefits of this study, and parents signed the informed consent forms.

RESULTS

In the stunting and normal groups, the largest proportion of subjects was 10 years old, respectively 41.7%, 34.8%. The mean birth weight of the subjects in the stunting group was 3008 ± 539.6 grams while the normal group was 3174 ± 532.9 grams. There were 4 mothers in the stunting group and 10 mothers in the normal group who had no records and the mothers forgot the birth weight of the subjects. The mean mother's height of stunting and normal group is almost the same as 150.2 ± 5.96 cm and 150.2 ± 5.65 cm respectively. There were some mothers who were not measured their height at the time of the study because the mother worked outside the study area. The majority of father's and mother's had a low level of schooling. The highest proportion of mother's occupations were farmers, in both stunting and normal groups, 47.9% and 34.8% respectively. The highest proportion of father's occupations in the stunting group were farmers (43.8%), while in the normal group were merchants (46.4%) (Table 1).

There were no difference in the mean levels of TSHs between stunting (4.6 ± 3.28 mIU/mL) and normal group (4.3 ± 4.13 mIU/mL). The mean IGF-1 levels in the stunting group were lower (76.0 ± 35.98 ng/mL) than the normal group (138.6 ± 86.69 ng/mL). The proportion of low zinc levels in stunting group (9.7%) was not different than the normal group (9.4%). The proportion of anemia in the stunting group was higher (16.7%) than in the normal group (8.9%), but not statistically significant (p=0.252). All subjects, both stunting and normal groups had normal albumin levels. The majority of subjects in both groups did not have a history of chronic infection, 93.8% and 86.6% respectively , and low birth weight (LBW) (90.9% and 94.1% respectively) (Table 2).

The OR values of the children involvement in agricultural activities showed that this was the risk factor for stunting (OR = 2.0 and 95% CI = 1.0-4.2). Bivariate logistic regression results showed that children with high pesticide exposure had a risk of more than three times for stunting compared to the unexposed children (OR = 3.2 and 95% CI = 1.1-9.7), while for moderate exposure, the OR was 1.6 (95% CI = 0.6-4.3) and low exposure was 1.2 (95% CI = 0.4-3.2) (See Table 3).

The results of multivariate logistic regression using backward method, showed that there were two dominant risk factors for stunting: high pesticides exposure (adjusted-OR = 4.5 and 95% CI = 1.4-15.1; p = 0.013;) and low IGF-1 levels (adjusted-OR = 5.8 and 95% CI = 2.7-12.5; p = 0.0001) (See Table 4).

DISCUSSION

Stunting is a condition of linear growth disorder [23] and has been more often associated with poor nutritional intake [24]. Less intake of macronutrients, especially energy and protein, were the cause of growth disorders in children [25]. Amino acids present in the body as well as those derived from food, are essential ingredients in the formation of proteins as well as collagen. Food sources of energy (amino acids, carbohydrates, fats) support the growth process directly or indirectly through the provision of fuel for neutrophils, macrophages, lymphocytes, and other cells that function in cell or tissue regeneration [26]. The role of nutrition in linear growth occurs through various mechanisms. Experiments with animals showed that the restriction of energy and protein in the diet lowered the plasma concentration of Insulin-like Growth Factor-1 (IGF-1), a hormone that is needed in the process of linear growth [27] and will return to normal after energy and protein refeeding. The effect of intake restriction on IGF-1 levels, was more visible on protein restriction than on energy restriction. IGF-1 levels also decreased in patients with kwashiorkor (acute protein deficiency) and in children with protein-energy malnutrition (PEM) [26].

In addition to macronutrients, several micronutrients are also essential for growth, namely Zinc (Zn) [28], iron (Fe) and vitamin A [25]. Zn deficiency in rats decreased IGF-1 and growth hormone (GH) plasma concentrations [29]. Zn was associated to bone metabolism [30], played a role in the synthesis of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), and also interacts with important hormones involved in bone growth such as somatomedin-c, osteocalcin, testosterone, thyroid hormones, and insulin [31]. Other micronutrient deficiencies, such as iron (Fe) and magnesium (Mg), can cause anorexia, and result in impaired growth indirectly, due to reduced dietary intake including energy and protein. Zinc, iron, and selenium are also associated with immune function and disease risk, which can interfere with growth [32].

The results showed that there was no significant difference in the mean of albumin levels between the stunting (4.5±0.32 g/dL) and normal (4.6±0.30 g/dL) groups p=0.409. The results also showed that there was no significant difference in Zinc level mean between the stunting and normal group. Chi-square tests showed that there was no difference of anemia proportion between the stunting and normal groups (p=0.252). Thus, we can conclude that the potential confounding variables of nutrient intake, both macro and micro nutrients, in this study can be controlled.

Based on the causes, stunting can be divided into two categories, namely growth hormone deficiency and idiopathic [3,33]. Children borned and raised in agricultural areas have the potential to be exposed to pesticides since they were in the womb, making them at risk for various health problems including growth disorder. Growth disorders caused by the exposure of pesticides can work through several mechanisms, such as the disruption of the hormone system that plays a role in the growth process. Several types of pesticides, including organophosphates and carbamates that are widely used in agricultural activities, are classified as EDCs, chemicals in the environment that can interfere with synthesis, secretion, transport, metabolism, binding action, and elimination of hormones in the body that keep homeostasis, reproduction, and the process of growth and development [34]. Thyroid hormone and IGF-1 are the hormones that are necessary for the process of children growth. Several studies had shown that exposure to pesticides was the risk factor for hypothyroidism [11,35-37]. Thyroid hormone deficiency (hypothyroidism) will cause metabolic disorders in the cells so that the process of growth and development are also disrupted [38]. The thyroid dysfunction caused by pesticides exposure was work through some mechanisms, which disrupts the TSH receptor on the thyroid gland [39], the similarity of the pesticide chemical structure with thyroid hormone [39], lowering the D1 (deiodinase type 1) enzyme [40], and stimulate the D3 enzyme [39]. Exposure to pesticides, especially organochlorines groups, can also disrupt the IGF-1 function [12,13]. Research in Spain has shown that the mean IGF-1 levels in the women who had DDT metabolites detected were lower than those who were not detected [12]. Multivariate logistic regression analysis showed that the children with low levels of IGF-1 had 5.8 times higher risk for stunting compared to the normal IGF-1 levels. IGF-1 hormones play a role in growth through its role as a mitogen and cell proliferation stimulator and play an important role in tissue repair/regeneration [41]. IGF-1 also mediates protein anabolic processes and increases growth hormone (GH) activity for linear growth [27,42]. Some other chemicals such as lead [plumbum (Pb)] [33,43], phthalate [44] have been shown to disrupt the function of the IGF-1 hormone. Lead is a toxic substance that is widely available in the environment, among others in paint, toys, cookware, battery, electronic equipment, and others. Lead exposure in children can occur through several paths, i.e. oral (contaminated food/drink) and inhalation [45], phthalate is a chemical contained in plastic raw materials in toys and building materials, such as wall paint, which also potentially exposed to the children in their daily activities [46]. Other chemicals, dioxins and polychlorinated biphenyls (PCBs) have also been shown to interfere child growth [46].

The pesticide exposure measurements in this study was based on information from the interviews limited this study. For further studies, examination of pesticide metabolites in the urine can be done to ensure the pesticide exposures. In addition, there was no assessment of other toxic materials as confoundings, such as lead, phthalates, dioxins, and PCBs in this study.

CONCLUSION

The results showed that there were no differences in characteristics and most confounding variables on the stunting and normal group. Multivariate logistic regression analysis proved that high pesticides exposure and low IGF-1 levels were the risk factor for stunting.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1. Characteristics of the subjects

Variables	Stunting (*n*=48)	Normal (*n*=112)
	Mean ± SD	Mean ± SD
Age (years)	9.9±0.98	10.0±0.96
Height (cm)	123.8±4.81	134.9±6.22
HAZ (SD)	-2.5±0.48	-0.8±0.75
Birth weight [a] (g)	3008±539.59	3174±532.91
Mother's height [b] (cm)	150.2±5.96	150.2±5.65
	n (%)	n (%)
Sex		
Male	25 (52.1)	55 (49.1)
Female	23 (47.9)	57 (50.9)
Mother's Education level		
Illiterate	1 (2.1)	4 (3.6)
Middle school or below	45 (93.7)	104 (92,8)
High school	2 (4.2)	4 (3,6)
Father's Education level		
Illiterate	0 (0.0)	1 (0.9)
Middle school or below	46 (95.8)	101 (90.2)
High school	2 (4.2)	10 (8.9)
Mother's Occupations		
Unemployed	7 (14.6)	30 (26.8)
Farmers	23 (47.9)	39 (34.8)
Merchants	13 (27.1)	34 (30.4)
Others	5 (10.4)	9 (8.0)
Father's Occupations		
Farmers	21 (43,8)	46 (41,1)
Merchants	20 (41,7)	52 (46,4)
Government employees	0 (0,0)	1 (0,9)
Others	7 (14,6)	13 (11,6)

[a] Stunting=44, Normal=102; [b] Stunting=37, Normal=75

Table 2. Comparison of confounding variables between stunting and normal

Variable	Mean±SD		p
	Stunting ***n*=48**	**Normal** ***n*=112**	
TSHs (mIU/mL)	4.6 ± 3.28	4.3 ± 4.13	0.299 [b]
IGF-1 (ng/mL)	76.0 ± 35.98	138.6 ± 86.69	**0.000*** [b]
Zn[c] (μg/dL)	98.4 ± 24.26	107.7 ± 26.88	0.078 [a]
Hb (g/dL)	12.8 ± 0.87	13.1 ± 0.99	0.024 [a]
Albumin (g/dL)	4.5 ± 0.32	4.6 ± 0.30	0.409 [b]
	n (%)	n (%)	
TSHs:			
Hypotiroid	16 (33.3)	28 (25.0)	0.374
No hypotiroid	32 (66.7)	84 (75.0)	
IGF-1:			
Low	35 (72.9)	45 (40.2)	0.000*
Normal	13 (27,1)	67 (59.8)	
Zinc [c]:			
Low	3 (9.7)	9 (9.4)	1.000
Normal	28 (90.3)	87 (90.6)	
Hemoglobin:			
Anemia	8 (16.7)	10 (8.9)	0.252
Normal	40 (83.3)	102 (91.1)	
Albumin:			
Low	0 (0.0)	0 (0.0)	NA
Normal	48 (100.0)	112 (100.0)	
History of infections:			
Yes	3 (6.3)	15 (13.4)	0.300
No	45 (93.8)	97 (86.6)	
History of LBW[d] :			
Yes	4 (9.1)	6 (5,9)	0.728
No	40 (90.9)	96 (94.1)	

*Significant at p<0.001; [a]*Independent t-test;* [b]*Mann-Whitney*; [c] Stunting=31, Normal=96; [d] Stunting=44, Normal=102; NA=Not Analyzed

Table 3. Association between history of pesticide exposure and stunting

Variable	**Stunting** *n*=48	**Normal** *n*=112	**OR (95% CI)**	***p***
Mothers involvement in agricultural activity during pregnancy:				
Yes	26 (54.2)	50 (44.6)	1.5 (0.7-2.9)	0.351[a]
No	22 (45.8)	62 (55.4)		
Subjects at the time of infant/ toddler brought the mother to farm/stall:				
Yes	19 (39.6)	29 (25.9)	1.9 (0.9-3.8)	0.123[a]
No	29 (60.4)	83 (74.1)		
Involvement of subjects in agricultural activities at school age:				
Yes	35 (72.9)	64 (57.1)	2.0 (1.0-4.2)	0.088[a]
No	13 (27.1)	48 (42.9)		
History of pesticide exposure (composite variable) [b]:				
'High'	13 (27.1)	14 (12.5)	3.2 (1.1-9.7)	0.034*
'Moderate'	14 (29.2)	31 (27.7)	1.6 (0.6-4.3)	0.373
'Low'	13 (27.1)	39 (34.8)	1.2 (0.4-3.2)	0.764
'Unexposed' [(ref)]	8 (16.6)	28 (25.0)	-	-

*Significant at p<0.05; [a]Chi-square; [b]Logistic regression; [(ref)]reference category

Table 4. Multivariate logistic regression analysis of stunting risk factors

Variable	B	Se	Odds ratio	95% Confidence Intervals		p-value
				Lower	Upper	
History of pesticide exposure:						
'High'	1.515	0.612	4.548	1.370	15.100	0.013*
'Moderate'	0.714	0.556	2.041	0.686	6.072	0.200
'Low'	0.424	0.552	1.527	0.517	4.508	0.443
'Low' IGF-1	1.764	0.390	5.835	2.719	12.521	0.000**
Constant	-2.301	0.508	0.100			0.000

*Significant at p<0.05; **Significant at p<0.001

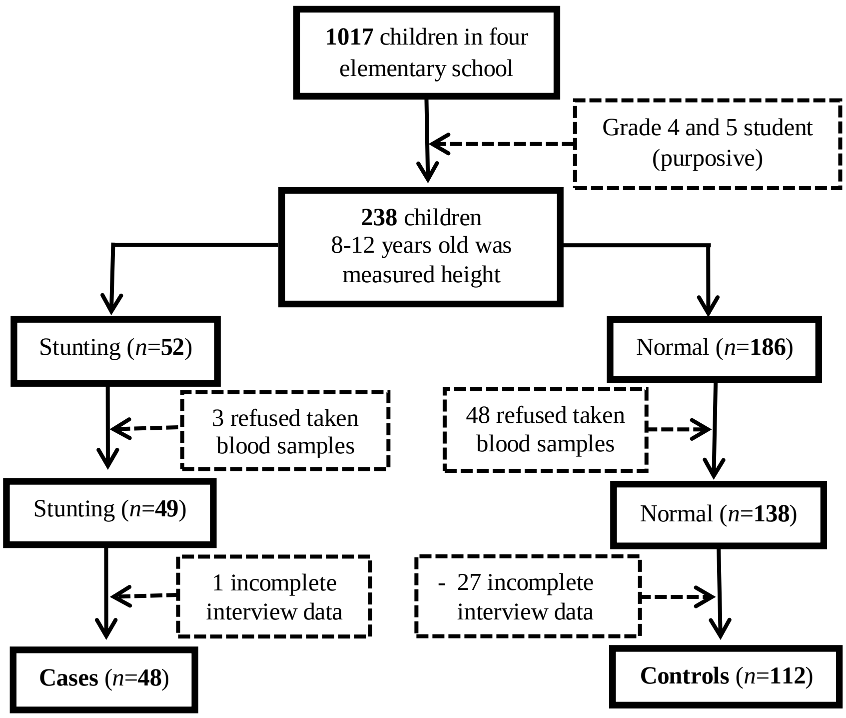

Figure.1. Subjects selection flow chart

2. *Reviewer's Comments*

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On Sat, Oct 14, 2017 at 10:31 AM, Dr R K Sharma <rksharma1@gmail.com> wrote:

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> Medico-legal Consultant
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Tanggal: Minggu, 19 November 2017 06.55 WIB

Dear Editor, IJPHRD,

I am here to resubmit our article entitled **GOITER AND HYPOTHYROIDISM AMONG ELEMENTARY SCHOOL CHILDREN IN LOWLAND AGRICULTURAL AREA, BREBES DISTRICT INDONESIA** which has been revised as per the editor's suggestion.

Thank you,

Suhartono

Environmental Health Department

Faculty of Public Health, Diponegoro University

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Make all tables properly closed.

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Add Source of Funding just before the references and resubmit.

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GOITER AND HYPOTHYROIDISM AMONG ELEMENTARY SCHOOL CHILDREN IN LOWLAND AGRICULTURAL AREA, BREBES DISTRICT INDONESIA

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ABSTRACT
The most common cause of goiter is the lack of iodine intake and usually occurs in many communities in upland areas. However, several studies indicate a number of people with goiter in lowland areas. Pesticides are widely used in the agricultural area, and it was probably the cause of goiter. This research is aimed to identify goiter and hypothyroidism among elementary school children in lowland agricultural areas. This cross-sectional study recruited sample of 100 children aged 9-12 years old from three elementary schools in Brebes District, Indonesia. Variables studied were characteristics measured with a structural questionnaire; goiter existence determined by palpation of a trained nutritionist; level of thyroid stimulating hormone (TSH) measured with mini vidas test kits for TSH levels; and Urinary Iodine Concentration (UIC) measured with acid digestion method with persulfate ammonium. Univariate and bivariate data analysis (Chi-square test and risk estimate) were applied. Proportion of goiter and hypothyroidism was 53.0% and 17.4% respectively. Median UIC was 346 µg/dL. Proportion of goiter in the children whose fathers were farmer and non-farmer was 80,8% and 43,2% respectively (p=0.002; Prevalence Ratio=1.9; 95% CI=1.3-2.6). The proportion of hypothyroidism in the children whose fathers were farmers (29.4%) tends to be higher than non-farmers (13.5%). However, there was no significance difference proportion of hypothyroidism in both group (p=0.255; Prevalence Ratio=2,2; 95% CI=0.8-6.0). The proportion of goiter and hypothyroidism among elementary school children in lowland agricultural area was high although the iodine intake was adequate.
Keywords: Goiter, Hypothyroidism, Children, Agricultural Area, Indonesia

INTRODUCTION

Goiter is an enlargement of thyroid gland located in the neck caused by malfunctioning or changing gland structures or its morphology. The enlargement of the thyroid gland can influence the positions of organs. The negative effects of goiter can be a cosmetic problem and difficulties in swallowing and breathing[1]. Thyroid gland has a function to produce thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Thyroid hormone plays an important role in a process of body growth, brain development, nervous system, and teeth and skeletal development[2]. The lack of thyroid hormone will increase a level of Thyroid Stimulating Hormone (TSH), a type of hormone that increases a synthesis of thyroid hormone and stimulates an enlargement of thyroid gland[3]. Goiter occurred on children is responsible for growth and development disruption such as stunting, low Intelligence Quotient, and mental disorders[4].

Goiter in an endemic area is mainly caused by the lack of iodine intakes as the critical raw material in the process of thyroid hormone synthesis. Endemic goiter, well-known as Iodine Deficiency Disorder (IDD)[5], is generally found in highland areas due to low iodine levels in soil, water, and agricultural products. Goiter rate in lowland areas is also quite high even though the content of iodine levels in soil, water, and agricultural commodities is sufficient[6]. Related to this phenomenon, some theories stated that thyroid dysfunctions occurred due to exposures of heavy metals in the environment such as lead, mercury, cadmium, polychlorinated biphenyl (PCB), and pesticide[7,8].

Bulakamba, one of the Subdistricts in Brebes District, is the area with high-intensity pesticide use and depends on agricultural products (paddy, shallots, corn, green bean, and chili). Meanhwile, Kluwut Public Health Center located in the Bulakamba Subdistrict was the highest total goiter rate (TGR) among elementary school students in Brebes District (38.5%). The result of the measurement of UIC demonstrated that median UIC ranged from 286-293µg/L (Brebes District Health Offices, unpublished data 2010). These values were not categorized as iodine deficiency[9].

MATERIAL AND METHODS

A cross-sectional study design was conducted in Brebes district, Central Java Indonesia in 2012. Minimum sample size were 97 students calculated using the formula for estimating the population proportion[10]. Notwithstanding, as many as 100 students aged 9-12 years old randomly selected from three elementary schools of Bulakparen 01, Dukuhlo 02 and MI Mujahidin Kluwut.

Variables of characteristics were collected using a structured questionnaire by a trained interviewer. Thyroid gland palpation undertaken by trained nutritionists worked at Brebes District Health Office determined the occurrence of goiter. The thyroid size was graded according to the joint criteria of WHO, UNICEF and ICCIDD (non-palpable goiter = grade 0, palpable but not visible goiter = grade 1 and palpable and visible goiter = grade 2)[9].

Thyroid stimulating hormone (TSH) levels collected from sub-samples of 69 subjects were measured with a mini VIDAS® (bioMérieux S.A.), a compact automated immunoassay system based on the Enzyme Linked Fluorescent Assay (ELFA) principles at an accredited clinic laboratory. Non-fasting peripheral venous blood samples were obtained in the morning from 09.00 to 11.00. Subjects were categorized suffering from hypothyroidism when the TSH levels were $\geq$ 4.5 µIU/L[2]. Meanwhile, UIC levels were measured using a method of acid digestion with persulfate ammonium. Spot urine samples were obtained from sub-samples of 66 subjects.

The results were presented in the form of tables and text. Univariate analysis was used to describe frequencies for categorical data, mean±standard deviation, and range for continuous data. Chi-square test was performed to analyze the association between two variables.

Ethics approval was obtained from the health ethics committee of Faculty of Public Health, Diponegoro University, Semarang, Indonesia. Written permission to conduct this study was obtained from the head of Education Office Brebes District and the head teachers and chiefs of the schools involved. Parents also signed an informed consent form.

FINDINGS

A proportion of female was higher than a proportion of male in three elementary schools. Fathers and mothers educational status were mostly middle or less, respectively 95% and 97%. Meanwhile, as many as 26% of fathers worked as a farmworker and mothers as a farmworker as many as 21%. (Table 1).

Table 1. Characteristics of Subjects

Characteristics	Frequency (%)
Age (years):	
9	6 (6.0)
10	17 (17.0)
11	52 (52.0)
12	25 (25.0)
Sex:	
Male	43 (43.0)
Female	57 (57.0)
Fathers educational status:	
Middle or less	95 (95.0)
High school	5 (5.0)

Fathers occupation: Farmworker Non-farmworker	 26 (26.0) 74 (74.0)
Mothers educational status: Middle or less High school	 97 (97.0) 3 (3.0)
Mother's occupation: Unemployement Farmworker Non-farmworker	 33 (33.0) 21 (21.0) 46 (46.0)

The overall prevalence of goiter was found to be 53.0%. Prevalence of Grade 1 goiter was 27.0% and that of grade 2 was 26.0%. The results of TSH level measurement on 69 samples demonstrated that as many as 17% of them were categorized suffering from hypothyroidism (TSH > 4.5 µIU/L). Meanwhile, the results of UIC level measurement showed that there was no subject suffering from iodine deficiency (> 100 (µg/L) (Table 2).

Table 2. The occurrence of goiter, hypothyroidism, and median UIC

Characteristics	Frequency (%)
The occurrence of goiter (*n*=100): 1. Yes 2. No	 53 (53.0) 47 (47.0)
Grade: 1. Grade 0 2. Grade 1 1. Grade 2	 47 (47.0) 27 (27.0) 26 (26.0)
Hypothyroidism (*n*=69): 1. Yes 2. No	 12 (17.4) 57 (82.6)
TSH (mean±SD, range)	3,1±1,87 (0,4-11,4)
UIC (median, range) (µg/L) (*n=66*)	346 (192-349)

A proportion of goiter among subjects who had fathers working as a farmworker was equal to 80.8%, two times higher than that of subjects who had fathers working as non-farmworker (43.2%) (Table 3).

Table 3. The occurrence of goiter based on fathers' occupation

Fathers' occupation	The occurrence of goiter		*P*	Prevalence Ratio (95% CI)
	Yes	No		
Farmworker Non-farmworker	21 (80.8) 32 (43.2)	5 (19.2) 42 (56.8)	0.002*	1.9 (1.3-2.6)

Significant <0.05

A proportion of hypothyroidism among subjects who had fathers working as a farmworker was equal to 29.4%, two times higher than that of subjects who had fathers working as non-farmworker (13.5%) (Table 4).

Table 4. The occurrence of hypothyroidism based on fathers' occupation

Fathers' occupation	The occurrence of hypothyroidism		*P*	Prevalence Ratio (95% CI)
	Yes	No		
Farmworker Non-farmworker	5 (29.4) 7 (13.5)	12 (70.6) 45 (86.5)	0.255	2.2 (0.8-6.0)

DISCUSSION

This study found as many as 53% of elementary school students located in lowland areas suffered from goiter. Brebes is an agricultural area producer of shallot in Central Java province, Indonesia. The farmers usually spray pesticides 2-3 times per week, even every day in the rainy season. The yield rate of shallot in Brebes in 2014 as much as 121.46 quintals/hectare[11].

Goiter, a manifestation of thyroid hyperplasia and increased thyroid vascularity, results from a compensatory increase in the release of thyroid-stimulating hormone (TSH) as a result of lower triiodothyronine (T_4) levels and is traditionally detected and evaluated using inspection and palpation[12]. We used palpation in our study because ultrasonography is cumbersome and costly to carry out[13], and palpation is regarded as an acceptable and simple alternative. Palpation of the thyroid is important in assessing goiter prevalence, which is relatively easy to conduct, and training of personnel to do it[14].

UIC levels greater than 100 μg/L (Table 2) mean that there was no case of iodine deficiency on all research participants. Iodine deficiency early in life impairs cognition and growth, but iodine status is also a key determinant of thyroid disorders in adults. Dietary iodine intake is required for the production of thyroid hormone. Consequences of iodine deficiency include goiter, intellectual impairments, growth retardation, neonatal hypothyroidism, and increased pregnancy loss and infant mortality[15,16]. A main cause of goiter commonly is due to lack of iodine intakes. Iodine is the critical raw material for a process of thyroid hormone biosynthesis. Iodine plays an important role in growth and development, and brain function[17].

There are several accepted methods for the monitoring of population iodine status[18]. Because 90% of ingested iodine is renal excreted, median spot urinary iodine concentrations (UIC) serve as a biomarker for recent dietary iodine intake. Population iodine sufficiency is defined by median UIC of 100–299 μg/L in school-aged children[9]. A source of iodine in the environment depends on a location/geographical factor. Generally, sufferers of goiter are commonly found in highland areas (mountainous regions) because there is a lack of iodine levels in water and soil, where iodine has been washed away by glaciation and flooding[15]. On the other hand, oceans are the world's main repositories of iodine and very little of earth iodine is actually found in the soil. The deposition of iodine in the soil occurs due to volatilization from ocean water, a process aided by ultraviolet radiation. The coastal regions of the world are much richer in iodine content than the soils further inland[19].

IDD has a strong relationship with a geographical factor because it is generally found in highland areas among school age children. This age group is very susceptible to iodine intakes obtained from the environment. School-age children are considered as an appropriate target group for determining iodine deficiency due to their susceptibility to iodine deficiency, easily accessibility as a study group and representativeness of their community society as a whole[20]. Some studies demonstrated that the occurrence of goiter was due to a lack of iodine intake and generally found in highland areas. A study conducted at Kayseri, Turkey, where the goiter is endemic, goiter prevalence was 54.8% and median urinary iodine level was 9.54 μg/dl indicating mild iodine deficiency[21]. The prevalence of goiter among children 6-12 years old in Lay Armachiho Northwest Ethiopia was found to be 37.6%, whereas 70,3% of the subjects had inadequate iodine content (<15 ppm)[20]. A study in high altitude areas of Saudi Arabia revealed the goiter prevalence was 7.4% and about 71% of the participants had UIC less than 100μg/L[22]. Other studies demonstrated that goiter cases were found in areas with sufficient iodine intakes (non-endemic areas) such as coastal or lowland areas. Study at adult more than 18 years old in an iodine-sufficient area in Chengdu China revealed prevalences of goiter was 8.8%[23]. A study by Suhartono in District of Brebes found pesticide exposure as a risk factor for hypothyroidism among women at childbearing age living in an agricultural area, Brebes District, Indonesia[24].

The proportion of goiter and hypothyroidism was higher among farmworkers' children than among non-farmworker's children (Table 4). However, Iodine intakes in all research participants were sufficient. Pesticides might be a risk factor for goiter. A pesticide is a chemical widely used to increase agricultural products and to decrease food-borne or vector-borne diseases[25]. The use of a synthetic pesticide can contaminate soil, water, grass, and other vegetation. In addition to killing the insects or weeds, pesticides can be toxic to a number of other organisms, including birds, fish, beneficial insects, and non-target plants. Insecticides are generally the most acute toxic class of pesticides, herbicides but can also pose a risk to non-target organisms[26]. Pesticide residues leftover from agriculture not only contaminated crops but also the environment, such as ambient air, surface water, and soil. These findings reinforce the concern about pollution by organophosphates in areas surrounding agriculture areas of pesticide use[27]. Ideally, toxic effects of pesticide are on target organisms (pests) but in fact, the toxicity of most of the active ingredients of pesticide is not specific. Therefore, it is very harmful to human health[28].

Pesticides are categorized as endocrine disrupting chemicals (EDCs)[29]. Exposure by EDCs can disrupt thyroid function that is well-known as thyroid disrupting chemicals (TDCs)[30]. Thyroid dysfunction has an impact on growth and development of children[2]. Pesticide use around the world in the field of agriculture continues to increase. In the European Union, approximately 320,000 tons of pesticide active substances are sold every year, which accounts for a quarter of the world market[31]. Humans and animals are continuously contaminated with numerous pesticides due to human work, through diet (food, water) and environmental exposure (surface water, groundwater, soil, air)[32,33]. EDCs can bind and activate a variety of hormone receptors and then mimics the action of natural hormones (agonist action). EDCs also can bind to the receptors without activating them. Antagonist action would block and inhibit the action of the receptors. In addition, EDCs also can interfere with the synthesis, transport, metabolism and elimination of hormones, thus reducing the concentrations of natural hormones[32].

To prove a role of pesticide as a risk factor for goiter among elementary school children, there needs to measure pesticide metabolites in urine to determine pesticide exposure inside a human body. In addition, there needs to conduct further research that investigates the influence of other toxic materials toward thyroid function; i.e. heavy metals[34], tobacco smoking[35], and PCB[36,37].

CONCLUSIONS

The proportion of goiter among children in lowland agriculture areas was high. The proportion of goiter and hypothyroidism among children was two times higher in subjects whose fathers as farmworkers than non-farmworkers although the iodine intake was adequate.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

SOURCE OF FUNDING

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To
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Dear author/s

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GOITER AND HYPOTHYROIDISM AMONG ELEMENTARY SCHOOL CHILDREN IN LOWLAND AGRICULTURAL AREA, BREBES DISTRICT INDONESIA

Apoina Kartini[1], Suhartono [2*], Dina R. Pangestuti[1], M. Sakundarno Adi[3], Suratman[4], and Rasipin[5]

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GOITER AND HYPOTHYROIDISM AMONG ELEMENTARY SCHOOL CHILDREN IN LOWLAND AGRICULTURAL AREA, BREBES DISTRICT INDONESIA

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ABSTRACT
The most common cause of goiter is the lack of iodine intake and usually occurs in many communities in upland areas. Pesticides are widely used in the agricultural area, and it was probably the cause of goiter. This research is aimed to identify goiter and hypothyroidism among elementary school children in lowland agricultural areas. Cross-sectional study recruited sample of 100 children aged 9-12 years old from three elementary schools in Brebes District, Indonesia. Goiter existence determined by palpation of a trained nutritionist; level of thyroid stimulating hormone (TSH) measured with mini vidas test kits; and Urinary Iodine Concentration (UIC) measured with acid digestion method. Univariate and bivariate data analysis (Chi-square test,risk estimate) were applied. Proportion of goiter and hypothyroidism was 53.0% and 17.4% respectively. Median UIC was 346 µg/dL. Proportion of goiter in the children whose fathers were farmer and non-farmer was 80,8% and 43,2% respectively (p=0.002; Prevalence Ratio=1.9; 95% CI=1.3-2.6). The proportion of hypothyroidism in the children whose fathers were farmers (29.4%) tends to be higher than non-farmers (13.5%). However, there was no significance difference proportion of hypothyroidism in both group (p=0.255; Prevalence Ratio=2,2; 95% CI=0.8-6.0).

Keywords: Goiter, Hypothyroidism, Children, Agricultural Area, Indonesia

INTRODUCTION

Goiter is an enlargement of thyroid gland located in the neck caused by malfunctioning or changing gland structures or its morphology. The enlargement of the thyroid gland can influence the positions of organs. The negative effects of goiter can be a cosmetic problem and difficulties in swallowing and breathing[1]. Thyroid gland has a function to produce thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Thyroid hormone plays an important role in a process of body growth, brain development, nervous system, and teeth and skeletal development[2]. The lack of thyroid hormone will increase a level of Thyroid Stimulating Hormone (TSH), a type of hormone that increases a synthesis of thyroid hormone and stimulates an enlargement of thyroid gland[3]. Goiter occurred on children is responsible for growth and development disruption such as stunting, low Intelligence Quotient, and mental disorders[4].

Goiter in an endemic area is mainly caused by the lack of iodine intakes as the critical raw material in the process of thyroid hormone synthesis. Endemic goiter, well-known as Iodine Deficiency Disorder (IDD)[5], is generally found in highland areas due to low iodine levels in soil, water, and agricultural products. Goiter rate in lowland areas is also quite high even though the content of iodine levels in soil, water, and agricultural commodities is sufficient[6]. Related to this phenomenon, some theories stated that thyroid dysfunctions occurred due to exposures of heavy metals in the environment such as lead, mercury, cadmium, polychlorinated biphenyl (PCB), and pesticide[7,8].

Bulakamba, one of the Subdistricts in Brebes District, is the area with high-intensity pesticide use and depends on agricultural products (paddy, shallots, corn, green bean, and chili). Meanhwile, Kluwut Public Health Center located in the Bulakamba Subdistrict was the highest total goiter rate (TGR) among elementary school students in Brebes District (38.5%). The result of the measurement of UIC demonstrated that median UIC ranged from 286-293µg/L (Brebes District Health Offices, unpublished data 2010). These values were not categorized as iodine deficiency[9].

MATERIAL AND METHODS

A cross-sectional study design was conducted in Brebes district, Central Java Indonesia in 2012. Minimum sample size were 97 students calculated using the formula for estimating the population proportion[10]. Notwithstanding, as many as 100 students aged 9-12 years old randomly selected from three elementary schools.

Variables of characteristics were collected using a structured questionnaire by a trained interviewer. Thyroid gland palpation undertaken by trained nutritionists worked at Brebes District Health Office determined the occurrence of goiter. The thyroid size was graded according to the joint criteria of WHO, UNICEF and ICCIDD (non-palpable goiter = grade 0, palpable but not visible goiter = grade 1 and palpable and visible goiter = grade 2)[9].

Thyroid stimulating hormone (TSH) levels collected from sub-samples of 69 subjects were measured with a mini VIDAS® (bioMérieux S.A.), a compact automated immunoassay system based on the Enzyme Linked Fluorescent Assay (ELFA) principles at an accredited clinic laboratory. Non-fasting peripheral venous blood samples were obtained in the morning from 09.00 to 11.00. Subjects were categorized suffering from hypothyroidism when the TSH levels were ≥ 4.5 µIU/L[2]. Meanwhile, UIC levels were measured using a method of acid digestion with persulfate ammonium. Spot urine samples were obtained from sub-samples of 66 subjects.

Univariate analysis was used to describe frequencies for categorical data, mean±standard deviation, and range for continuous data. Chi-square test was performed to analyze the association between two variables.

Ethics approval was obtained from the health ethics committee of Faculty of Public Health, Diponegoro University, Semarang, Indonesia. Written permission to conduct this study was obtained from the head of Education Office Brebes District and the head teachers and chiefs of the schools involved. Parents also signed an informed consent form.

FINDINGS

A proportion of female was higher than a proportion of male in three elementary schools. Fathers and mothers educational status were mostly middle or less, respectively 95% and 97%. Meanwhile, as many as 26% of fathers worked as a farmworker and mothers as a farmworker as many as 21%. (Table 1).

Table 1. Characteristics of Subjects

Characteristics	Frequency (%)
Age (years):	
9	6 (6.0)
10	17 (17.0)
11	52 (52.0)
12	25 (25.0)
Sex:	
Male	43 (43.0)
Female	57 (57.0)
Fathers educational status:	
Middle or less	95 (95.0)
High school	5 (5.0)
Fathers occupation:	
Farmworker	26 (26.0)
Non-farmworker	74 (74.0)
Mothers educational status:	

Middle or less	97 (97.0)
High school	3 (3.0)
Mother's occupation:	
Unemployement	33 (33.0)
Farmworker	21 (21.0)
Non-farmworker	46 (46.0)

The overall prevalence of goiter was found to be 53.0%. Prevalence of Grade 1 goiter was 27.0% and that of grade 2 was 26.0%. The results of TSH level measurement on 69 samples demonstrated that as many as 17% of them were categorized suffering from hypothyroidism (TSH > 4.5 μIU/L). Meanwhile, the results of UIC level measurement showed that there was no subject suffering from iodine deficiency (> 100 (μg/L) (Table 2).

Table 2. The occurrence of goiter, hypothyroidism, and median UIC

Characteristics	Frequency (%)
The occurrence of goiter (*n*=100):	
1. Yes	53 (53.0)
2. No	47 (47.0)
Grade:	
1. Grade 0	47 (47.0)
2. Grade 1	27 (27.0)
1. Grade 2	26 (26.0)
Hypothyroidism (*n*=69):	
1. Yes	12 (17.4)
2. No	57 (82.6)
TSH (mean±SD, range)	3,1±1,87 (0,4-11,4)
UIC (median, range) (μg/L) (*n=66*)	346 (192-349)

A proportion of goiter among subjects who had fathers working as a farmworker was equal to 80.8%, two times higher than that of subjects who had fathers working as non-farmworker (43.2%) (Table 3).

Table 3. The occurrence of goiter based on fathers' occupation

Fathers' occupation	The occurrence of goiter		*P*	Prevalence Ratio (95% CI)
	Yes	No		
Farmworker	21 (80.8)	5 (19.2)	0.002*	1.9 (1.3-2.6)
Non-farmworker	32 (43.2)	42 (56.8)		

Significant <0.05

A proportion of hypothyroidism among subjects who had fathers working as a farmworker was equal to 29.4%, two times higher than that of subjects who had fathers working as non-farmworker (13.5%) (Table 4).

Table 4. The occurrence of hypothyroidism based on fathers' occupation

Fathers' occupation	The occurrence of hypothyroidism		*P*	Prevalence Ratio (95% CI)
	Yes	No		
Farmworker	5 (29.4)	12 (70.6)	0.255	2.2 (0.8-6.0)
Non-farmworker	7 (13.5)	45 (86.5)		

DISCUSSION

This study found as many as 53% of elementary school students located in lowland areas suffered from goiter. Brebes is an agricultural area producer of shallot in Central Java province, Indonesia. The farmers usually spray pesticides 2-3 times per week, even every day in the rainy season. The yield rate of shallot in Brebes in 2014 as much as 121.46 quintals/hectare[11].

Goiter, a manifestation of thyroid hyperplasia and increased thyroid vascularity, results from a compensatory increase in the release of thyroid-stimulating hormone (TSH) as a result of lower triiodothyronine (T_4) levels and is traditionally detected and evaluated using inspection and palpation[12]. We used palpation in our study because ultrasonography is cumbersome and costly to carry out[13], and palpation is regarded as an acceptable and simple alternative. Palpation of the thyroid is important in assessing goiter prevalence, which is relatively easy to conduct, and training of personnel to do it[14].

UIC levels greater than 100 µg/L (Table 2) mean that there was no case of iodine deficiency on all research participants. Iodine deficiency early in life impairs cognition and growth, but iodine status is also a key determinant of thyroid disorders in adults. Dietary iodine intake is required for the production of thyroid hormone. Consequences of iodine deficiency include goiter, intellectual impairments, growth retardation, neonatal hypothyroidism, and increased pregnancy loss and infant mortality[15,16]. A main cause of goiter commonly is due to lack of iodine intakes. Iodine is the critical raw material for a process of thyroid hormone biosynthesis. Iodine plays an important role in growth and development, and brain function[17].

There are several accepted methods for the monitoring of population iodine status[18]. Because 90% of ingested iodine is renal excreted, median spot urinary iodine concentrations (UIC) serve as a biomarker for recent dietary iodine intake. Population iodine sufficiency is defined by median UIC of 100–299 µg/L in school-aged children[9]. A source of iodine in the environment depends on a location/geographical factor. Generally, sufferers of goiter are commonly found in highland areas (mountainous regions) because there is a lack of iodine levels in water and soil, where iodine has been washed away by glaciation and flooding[15]. On the other hand, oceans are the world's main repositories of iodine and very little of earth iodine is actually found in the soil. The deposition of iodine in the soil occurs due to volatilization from ocean water, a process aided by ultraviolet radiation. The coastal regions of the world are much richer in iodine content than the soils further inland[19].

IDD has a strong relationship with a geographical factor because it is generally found in highland areas among school age children. This age group is very susceptible to iodine intakes obtained from the environment. School-age children are considered as an appropriate target group for determining iodine deficiency due to their susceptibility to iodine deficiency, easily accessibility as a study group and representativeness of their community society as a whole[20]. Some studies demonstrated that the occurrence of goiter was due to a lack of iodine intake and generally found in highland areas. A study conducted at Kayseri, Turkey, where the goiter is endemic, goiter prevalence was 54.8% and median urinary iodine level was 9.54 µg/dl indicating mild iodine deficiency[21]. The prevalence of goiter among children 6-12 years old in Lay Armachiho Northwest Ethiopia was found to be 37.6%, whereas 70,3% of the subjects had inadequate iodine content (<15 ppm)[20]. A study in high altitude areas of Saudi Arabia revealed the goiter prevalence was 7.4% and about 71% of the participants had UIC less than 100µg/L[22]. Other studies demonstrated that goiter cases were found in areas with sufficient iodine intakes (non-endemic areas) such as coastal or lowland areas. Study at adult more than 18 years old in an iodine-sufficient area in Chengdu China revealed prevalences of goiter was 8.8%[23]. A study by Suhartono in District of Brebes found pesticide exposure as a risk factor for hypothyroidism among women at childbearing age living in an agricultural area, Brebes District, Indonesia[24].

The proportion of goiter and hypothyroidism was higher among farmworkers' children than among non-farmworker's children (Table 4). However, Iodine intakes in all research participants were sufficient. Pesticides might be a risk factor for goiter. A pesticide is a chemical widely used to increase agricultural products and to decrease food-borne or vector-borne diseases[25]. The use of a synthetic pesticide can contaminate soil, water, grass, and other vegetation. In addition to killing the insects or weeds, pesticides can be toxic to a number of other organisms, including birds, fish, beneficial insects, and non-target plants. Insecticides are generally the most acute toxic class of pesticides, herbicides but can also pose a risk to non-target organisms[26]. Pesticide residues leftover from agriculture not only contaminated crops but also the environment, such as ambient air, surface water, and soil. These findings reinforce the concern about pollution by organophosphates in areas surrounding agriculture areas of pesticide use[27]. Ideally, toxic effects of pesticide are on target organisms (pests) but in fact, the toxicity of most of the active ingredients of pesticide is not specific. Therefore, it is very harmful to human health[28].

Pesticides are categorized as endocrine disrupting chemicals (EDCs)[29]. Exposure by EDCs can disrupt thyroid function that is well-known as thyroid disrupting chemicals (TDCs)[30]. Thyroid dysfunction has an impact on growth and development of children[2]. EDCs can bind and activate a variety of hormone receptors and then mimics the action of natural hormones (agonist action). EDCs also can bind to the receptors without activating them. Antagonist action would block and inhibit the action of the receptors. In addition, EDCs also can interfere with the synthesis, transport, metabolism and elimination of hormones, thus reducing the concentrations of natural hormones[31].

CONCLUSIONS

The proportion of goiter and hypothyroidism among children was two times higher in subjects whose fathers as farmworkers than non-farmworkers although the iodine intake was adequate.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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