ORIGINAL ARTICLE

Growth of Infants Aged 0-12 Months in Severe Iodine Deficient Areas

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ABSTRACT In Indonesia, iodine deficiency remains a public health problem and iodine deficiency disorder (IDD) Control Programs are not optimally implemented. This situation might affect the growth and development of young infants living in iodine deficient areas. Eight hundred and eight infants aged 0-12 months in 5 severe iodine deficient subdistrics in West Java, were studied to assess their linear growth. Using the US National Center for Health Statistics (NCHS) age reference standards, there were 14.7% of infants with Z-score below 2 SD of the mean for normal height, defined as stunted. Using the local standards there were 8.2% of infants with stunted growth. The percentage of stunted infants were significantly higher with increasing age. The stunted infants among goitrous mothers were higher compared to those among non-goitrous mothers. It was concluded that a relatively high percentage of linear growth impairment in this study might be attributable to iodine deficiency or other factors. The infants of mothers with goiter were at higher risk of being stunted. **[Paediatr Indones 1999; 39:268-277]**

Introduction

Normal growth and development are finely regulated by a complex interaction of hormonal influences, tissue responsiveness, and nutrition. Metabolic and genetic signals can modulate these responses. Thus many non-genetic factors can also impair growth. Consequently, the evaluation of the growth of children is a sensitive indicator of their general health. The measurements of height and weight is an essential part of the physical examination to determine if a child's health is normal.[1] Thyroid hormones

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are required for normal growth and development and for maintenance of a normal metabolic state. Protein synthesis and the efficient utilization of oxygen in the production of high-energy phosphate bond are necessary for growth and appropriate amounts of thyroid hormones permit these biochemical processes to occur.[2]

Iodine is the essential constituent of thyroid hormones. In geographic areas with iodine deficiency, dietary intakes of iodine are limited, thyroid hormone synthesis is inadequate and secretion declines, resulting in a wide spectrum of conditions-termed as iodine deficiency disorders (IDD).[3] The most important are mental and physical retardation, endemic cretins, impaired reproductive outcome and goiter.[4] Infants who develop a deficiency of thyroid hormone have increasingly slow bodily growth and delayed skeletal maturity, affecting the linear growth. In Indonesia, there are still many areas of iodine deficiency spreading throughout the country. IDD control programs through distribution of oral iodized oil has been prioritized for pregnant and lactating mothers, women of child-bearing age, and infants from birth to 1 year. The use of iodized salt is being promoted for a long term control program.[5] Recent study indicates that in the Province of West Java there are certain areas in some subdistricts still iodine deficient.[6] Subtle forms of intellectual and physical growth impairment which can disappear with iodine supplementation are known to occur in otherwise "normal" people living in areas where iodine deficiency is severe, implying that a large proportion of people living in iodine deficient areas are at risk of developing IDD. The present study was conducted to assess growth of young infants in severe iodine deficient areas in West Java.

Methods

This study was performed from October to December 1997. The study subjects consisted of mothers and their infants from some villages in the area of 5 severe iodine deficient subdistricts: Kertasari, Pagelaran, Maja, Bojong and Pangkalan in the district of Bandung, Cianjur, Majalengka, Purwakarta and Karawang, respectively. Subjects were selected through a multistage sampling method. Eligible infants were 0-12 months old, born in the study villages and without any disorders contributing to stunted growth. Age definition was: zero months; from birth up to 15 days, one month; from 16 days up to 45 days, 2 months; from 46 days up to 75, etc. Written informed consents were obtained from parents and guardians before enrollment.

The study design was a cross sectional. A special form was prepared for this study. In addition to infant's chronological age, data were recorded that could be useful in evaluating physical growth. Body weight and crown-heel length (height) were measured using standardized equipment and procedures. The United States National Center for Health Statistics (NCHS) standard[7] was used as reference standards for weight and height/chronological age. The Z-score was calculated as the number of standard

deviation from the median of the NCHS reference table for normal height. Data from the Nutrition Research and Development Center (Department of Health, Republic of Indonesia) cross sectional study on growth in Bogor, were used for comparison.[8] Mother's thyroid gland was examined using methods recommended by WHO.[9] Particular emphasis was placed on clinical evidence of congenital hypothyroidism and cretinism. Information on infant feeding, oral iodine supplementation and iodinated salt consumption could also be obtained.

Data processing was carried out by using computerized SPSS 7.5 programs. Anthropometric data were analyzed by descriptive statistical methods. Chi-squared test when appropriate was used to analyze differences. For two by two table, the relative risk was also calculated.

Results

A total of 820 infants from 20 villages in the severe iodine deficient areas were recruited. Twelve infants did not meet the study criteria, those were 10 infants with a history of suspected severe intrauterine growth retardation, one with Down syndrome, and one with bilateral coxa vara.

Subject characteristics

Eight hundred and eight infants were enrolled in the study. Four hundred fifteen (51.4%) were male and 393 (48.6%) were female. There were no infants aged zero month available and none showed any signs and symptoms of congenital hypothyroidism or cretinism. Ninety four (11.6%) infants received oral iodized oil. Seven hundred and seventy seven (96.2%) infants were breast fed. Goiter were noted in 25 mothers (3.1%), six hundred and three (74.6%) mothers previously received oral iodized oil. Iodinated salt was used by 80% of mothers. Among 777 lactating mothers, 75.4% received iodine supplementation.

Attained linear growth

As 90.9% of the infants were born at home and 70% deliveries were assisted by traditional birth attendants, not all infants had birth weight and birth length measured and recorded. Using the NCHS reference standards, 119 (14.7%) infants were found to have stunted growth and using the local standards there were 8.2%. When body weight was analyzed against stature corrected for nutritional cause of stunted, no wasted stunted infants were identified. Table 1 shows growth of infants according to three anthropometric indices.

Table 1. Attained growth according to 3 indices: weight (W) and height (H) for chronological age (CA) and weight for height

	Indices					
Growth	Weight/CA		Height/CA		W/H	
	N	%	N	%	N	%
Normal	782	96.8	689	75.3	808	100
Impaired	26	3.2	119	14.7	0	0
Total	808	100	808	100	808	100

Even though the mean values for height among the age groups (Table 2) were within age reference ranges, when this data were expressed in the growth curve it is clearly seen that the growth of male infants, group 1, 2, 3 month do not differ much from the standard, but after wards the differences become prominent approaching the -2 SD line (Figure 1). Figure 2 shows linear growth curve of female infants fluctuating up to 6 months and decreased more form 6 to 12 months of age. The mean standardized Z-score are provided in Table 3. It ranged from 0.16 to -1.65.

Table 2. Height (mean±SD) of the studied infants, the NCHS and the local standard

	MALE								FEMALE							
	Studied infants			NCHS		Local standard			Studied infants			NCHS		Local standard		
Age	N	X	SD	X	SD	N	X	SD	N	X	SD	X	SD	N	X	SD
1.	35	53.7	4.07	54.6	2.4	216	53.8	2.40	35	53.5	4.75	53.5	2.3	168	52.9	2.19
2.	37	58.9	4.51	58.1	2.6	367	57.5	2.69	25	56.5	2.74	56.8	2.4	337	55.9	2.32
3.	32	58.8	4.41	61.1	2.6	436	60.4	2.70	31	58.8	4.55	59.5	2.5	400	58.9	2.58
4.	30	60.8	3.98	63.7	2.7	414	62.8	2.40	35	60.0	2.62	62.0	2.5	413	61.2	2.31
5.	41	62.1	1.96	65.9	2.7	383	64.8	2.44	35	63.6	4.55	64.1	2.6	386	63.1	2.25
6.	45	63.9	3.07	67.8	2.7	328	66.6	2.71	40	64.7	3.58	65.9	2.7	354	64.5	2.17
7.	34	65.2	3.50	69.5	2.7	280	67.8	2.71	30	65.5	5.40	67.6	2.6	295	66.1	2.46
8.	33	67.8	3.93	71.0	2.6	274	69.0	2.56	29	66.3	2.84	69.1	2.7	260	67.2	2.88
9.	30	68.6	2.41	72.3	2.7	222	70.3	2.35	33	66.9	3.39	70.4	2.8	214	68.5	2.53
10.	33	68.5	2.26	73.6	2.7	181	71.5	3.13	35	68.6	3.25	71.8	2.7	161	69.7	2.32
11.	32	69.8	5.97	74.9	2.6	161	72.6	2.79	23	69.8	6.99	73.1	2.8	144	70.7	2.76
12.	33	71.5	3.17	76.1	2.7	120	73.3	2.77	42	69.8	5.14	74.3	2.8	111	71.9	2.58

Table 3. Z-score (Mean and standard deviations) by age group

Age (mo)	Height/CA		
	N	X	SD
1	70	-0.17	1.89
2	62	0.16	1.53
3	63	-0.20	1.75
4	65	-0.69	1.26
5	76	-0.50	1.32
6	85	-0.72	1.25
7	64	-0.73	1.31
8	62	-0.61	1.07
9	63	-1.31	1.04
10	68	-1.21	2.01
11	55	-0.63	1.57
12	75	-1.65	1.04

Association analysis

To explain the association between several variables (maternal and infant characteristics) and the stunted growth, the Mantel-Haenszel test was used, which is displayed in Table 4. These variables included infant's sex and age, breast feeding, maternal goiter status, history of maternal iodized oil supplementation and the use of iodized salt. As the outcome of interest is rare, the odds ratio (OR) is approximately the same as the relative risk (RR).

Table 4 shows independent variables that had a significant association with the occurrence of stunted growth, are mother's goiter status, infant's age and lactating mothers who previously received iodine supplementation. On the order hand gender, breast feeding, iodine supplementation and iodine salt consumption was not related to the stunted growth.

To describe the way the stunted growth is influenced by those independent variables we used multiple logistic regression analysis. Variables with $p<0.25$ were included into the model because these variables may contribute to the regression model in unforeseen ways due to complex interrelationship among them. The results are presented in Table 5.

Table 4. The association between independent variables and the occurrence of stunted growth

Independent Variables		Stunted (n=119)		Non-Stunted (n=689)		Total	RR	P Value
		N	%	N	%			
Maternal characteristics								
Goiter grade	00	111	14.2	672	85.8	783	1.00	0.002
	1A	5	26.3	14	73.6	19	1.85	
	1B	1	33.3	2	66.7	3	2.35	
	02	2	63.7	1	33.3	3	4.49	
Maternal iodine Supplementation								
▪ Yes		95	15.8	508	84.2	603	1.00	
▪ No		24	11.9	181	88.1	205	0.75	0.903
The use of iodized salt:								
▪ Yes		103	15.4	543	84.1	646	1.00	0.226
▪ No		10	7.5	123	92.5	133	0.48	
▪ Do not know		6	20.7	23	79.3	29	1.34	
Infants characteristics								
Sex: Male		62	14.9	353	85.1	415	1.00	0.861
Female		57	14.5	336	85.5	393	0.97	
Age (months):	1-3	15	7.7	180	92.3	195	1.00	0.000
	4-6	22	9.7	204	90.3	226	1.26	
	7-9	33	17.8	156	82.2	189	2.31	
	10-12	49	24.7	149	75.3	198	3.2	
Iodine supplementation								
▪ Yes		15	16.0	79	84.0	94	1.00	0.295
▪ No		104	14.6	610	85.4	714	0.91	
Breast feeding								
▪ Yes		115	14.8	662	85.2	777	1.00	0.770
▪ No		4	12.9	27	87.1	31	0.87	
Iodine supplementation to lactating mother								
▪ Yes		8	13.3	508	86.7	586	1.00	0.040
▪ No		37	19.4	154	80.6	191	1.46	

R= reference value, i.e., RR (relative risk)=1.00

Table 5. Logistic regression analysis between independent variables and the occurrence of stunted growth

Var	B	SE	Wald	Df	Sig	Exp(B)
Goiter grade	-06615	0.3048	4.7172	1	0.0299	0.5161
Age group	-0.4301	0.0930	21.3826	1	0.000	0.6504
The use of iodized salt	-0.7504	0.4076	3.3892	1	0.0456	2.1178
Iodine supplementation	-0.0692	0.1348	0.2636	1	0.6077	1.0716
Lactating mothers previously received iodized oil	-0.5281	0.3349	2.4866	1	0.1148	0.5897
Constant	2.8161	0.4350	41.9023	1	0.0000	-

Discussion

The major goals in the prevention of IDD has been to prevent mental impairment, cretinism and goiter. The technologies available at present for the correction of iodine deficiency are iodinated oil. Iodinated oil has now shown to be effective in Asia (Nepal, Indonesia) and in Africa where there have been great difficulties with the distribution of iodinated salt. Iodinated oil is indicated for severe IDD and for moderate IDD until salt can be effectively distributed.[10,11]

This study showed that iodine supplementation had not covered all infants and mothers. Suboptimal coverage and not sustainable iodine supplementation in the same iodine deficient areas in West Java was also reported by Abunain et al.[6] These findings might contribute to the negative association between iodine supplementation and impairment of infant's growth. In the univariate analysis oral iodized oil previously given to the lactating mothers had a significant association with the stunted growth ($p<0.05$), whereas breast feeding itself did not. Gushurt et al[12] reported that iodine intake was significantly related to the iodine content of the breast milk.

If we assumed that stunted growth was due to iodine deficiency, our results would support the prioritizing of iodine supplementation to the lactating mothers. However in the logistic regression the odds ratio for the variable was lower than in the univariate analysis (1.46 vs 0.59), indicating that there was a confounding factor contributing a significant result in the former analysis. On the contrary the logistic regression analysis yielded a high odds ratio for the use of iodized salt, that is 2.12 which means that the use of iodized salt will decrease the incidence of stunted infant by 2 times. Iodized salt has been successful in developed countries (Switzerland and the USA) and in some developing countries (Guatemala, Colombia).[10]

Iodized salt has much greater cost-effectiveness and coverage. Unfortunately in Indonesia both the supply of and demand for iodized salt are limited. Annual National Household Survey (1995) findings indicated that less than 60% of the salt consumed at the household level was iodized to adequate level. It seemed that the consumption of iodized salt in the household should be more intensively promoted.

Since goiter is the most important as a marker for more serious consequences of iodine deficiency-the tip of iceberg-, suboptimal IDD prevention could eliminate or decrease major IDD problems (cretin and goiter), but would not correct the milder IDD forms such as subclinical hypothyroidism. By definition, patients with subclinical hypothyroidism are asymptomatic. However, careful evaluation may reveal some clinical abnormality, indicating that such a disorder may not be as subclinical as previously thought.[13] Stunted growth without any other signs and symptoms of hypothyroidism might be considered as subclinical hypothyroid status. The prevalence of goiter among the mothers in this study was 3.1% and the occurrence of stunted infants was significantly higher in this group of mothers. Therefore goiter could not be considered as only a compensation mechanism to iodine deficiency, but perhaps those goitrous mothers had already suffered from a certain degree of thyroid hormone insufficiency.

The standard deviation values for the NCHS reference data are recommended to be used for calculating SD score (Z-score). The use of Z-score in Indonesia is recommended by Department of Health Republic of Indonesia.14 The reference limit of Z-score of below -2SD height for chronological age is defined as stunted. Using the local standards (results of growth study on 8177 healthy infants aged 0-12 months in Bogor district West Java), the stunted growth was found much lower (8.2%) than using the NCHS standard. In Bolivia a study on the effects of oral iodized oil on somatic growth in school-age children[15] showed that height and weight increased in all children, but the mean height and weight for each age were substantially less than those published for normal Americans. I was unable to find any previous reports of growth comparisons in young infant in severe iodine deficient areas.

Most IDD researches focused on the effects of IDD on mental development, as brain maldevelopment due to thyroid hormone deprivation is hardly or not restorable by optimizing the hormone supply in a later stage.[16] The development of other organs is (much) less dependent on thyroid hormone, and usually a (partial) catch-up occurs when the thyroid hormone supply is restored later on. According to my observation in the villages where iodine deficiency is prevalent (mountainous rural areas), the environmental factors would not permit the expected catch-up growth to occur. Accordingly any hazardous effect such as iodine deficiency which will interfere the infant's growth potential should also become our concern.

This study is limited in that biochemical indicators of iodine and thyroid status were not available, therefore the relatively high percentage of stunted infants might be attributable to iodine deficiency or to other factors. It seemed that infants of goitrous mothers were at higher risk of being stunted. These data can be used to increased IDD

awareness. The linear growth of those infants living in iodine deficient areas should be monitored and height measurement can be easily performed even in an Integrated Health Service Posts (Posyandu), by non-professional health workers. Further research included thyroid stimulating hormone (TSH) assay is warranted to achieve definite conclusions.

Acknowledgments

This study was sponsored by WHO Collaborating Center for Perinatal Care, Maternal and Child Health. I would like to thank for Professor Anna Alisjahbana as the chairperson of the Collaborating center; Ryadi Fadil MD, Maria Ekawati MD, Restu Pudjadi, for technical assistance; Drs. Hadyana Sukandar MSc, Meita Damayanti MD, and Hartawan for analyzing the data; Renny Faridha for help with manuscript preparation.

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