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Thyroid Abnormalities Profile of Children Aged 0-1 Years Through Biomarker Examination

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Abstract

Thyroid disorder is a non-communicable disease that has the potential to become a public health problem. One endocrinological abnormality that is often found in children is hypothyroidism, which is a condition due to reduced or no production of thyroid hormones. The aim is to evaluate the profile of thyroid abnormalities in children aged 0-1 years at RSAB Harapan Kita by reviewing the results of biomarker examination. Retrospective research design using secondary data at Harapan Kita Hospital Jakarta. The total of medical record was 157 data from January 2015-August 2016. Data analysis of TSH and fT4 biomarker examination results. Diagnosis of thyroid abnormalities can be done by stimulating thyroid hormone (TSH) biomarker examination, free thyroxine (fT4) which is useful as a biomarker for monitoring, detection, or therapy as early as possible in infants or children who are suspected or have experienced growth and development disorders. The study found 51% Euthyroidism, 23% subclinical hypothyroidism, 13% TSH mediated hyperthyroidism condition, 5% secondary hypothyroidism, 4% primary hypothyroidism, and 4% subclinical hyperthyroidism. From medical records, 20.4% were diagnosed with hypothyroidism, 12.7% developmental disorders, 20.1% down syndrome and 40.8% with a diagnosis of other diseases. The diagnosis of thyroid disorder, especially hypothyroidism, is found at 4-12 months of age as much as 22.8% and 8.9% at the age of 0-3 months. These results show that if management or follow-up of treatment and therapy in patients do not do early can cause permanent retardation of growth and mental development. One of the keys to the success of the treatment of children with thyroid disorders is by early detection through laboratory tests and treatment before children are one year old.

Keywords: Thyroid Abnormalities, Age 0-1 Years, fT4, TSH

1. Introduction

Hypothyroid prevalence in Indonesia is not known with certainty. Results of Basic Health Research (Riskesdas) 2007 found 2.7% of men and 2.2% of women had high TSH levels that showed suspicion of hypothyroidism (Pusdatin Ministry of Health: 2015). The results of Wibowo's research, A: 2013 on 398 school-age children with different levels of endocrine deficiency of iodine found high TSH levels as much as 9% and low fT4 1.8%. Research conducted by Purwanti, KD: 2008 on early detection of congenital hypothyroidism with Neonatal TSH and neonatal fT4 examination in West Nusa Tenggara against 100 samples of umbilical cord blood spots showed a prevalence of 1: 2,500-4,000 in the areas of West Lombok and East Lombok as moderate to heavy endemic areas. Based on the results of congenital hypothyroid screening (SHK) from 2000– 2014 in several selected locations in Indonesia, positive cases were found in the proportion of 0.4 per 1,000 of newborns (Public Health Ministry of the Ministry of Health: 2015).

Indonesia has not had data of congenital hypothyroidism cases nationally. Congenital hypothyroid data in Indonesia can only be obtained from RSUP Dr. CiptoMangunkusumo Jakarta and Hasan Sadikin Hospital Bandung. The medical record review at these Hospitals endocrine pediatric clinics in 2012-2013 showed that more than 70% of congenital hypothyroid patients were diagnosed after 1 year of age so that they had permanent mental retardation. Only 2.3% can be recognized before the 3 months of age and treatment can minimize the retardation of growth and development (Ministry of Health, 2014: 8; Pusdatin Ministry of Health: 2015). Some of these cases were diagnosed late so that they had impaired growth and motor development and intellectual impairment.

Diagnosis of thyroid disease can be done by examining thyroid stimulating hormone (TSH), free thyroxine (fT4), T3 and T4, as monitoring, detection, or therapy as early as possible in infants or children who are suspected or have experienced growth and development disorders Symptoms in hypothyroid patients are usually not very clear, therefore TSH, T4, and fT4 examinations are needed (Stockigt, J, 2003). Errors in diagnosing hypothyroidism can result in a variety of undesirable effects by thyroid hormone therapy, while basic illnesses are actually undiagnosed (Purnamasari, 2007). Estimates of sensitive fT4 and TSH can be used for diagnosis of thyroid disease and to follow up on patients that receive T4 replacement or anti-thyroid drug therapy (Susanto, R, 2009)

2. Method

The study used a retrospective design using secondary data. A total of 157 data that met the inclusion criteria were records of laboratory examination results of biomarkers of thyroid function based on clinical diagnosis and follow-up of neonatal screening tests and medical records for children aged 0-1 year at Harapan Kita Hospital in January 2015 - August 2016. This amount is more than the expected sample size (minimum 92 samples). The data obtained in the study were analyzed descriptively and correlated.

TSH and fT4 test

The Enzyme *Linked FluorescenceImmuno Assay* (ELFA) technique was used for TSH and fT4 examination with Immuno Analyzer (VIDAS). Calibration, using the calibrator provided in the kit and performed every time opening a new reagent after the lot master data has been entered in the tool. Calibration must be done every 14 days. The calibration curve results for the instrument and compensates for possible minor variations in the test signal during the kit's storage period. The calibrator, which was identified, tested in duplo. The calibrator value must be in the RFV "Relative Fluorescence Value" range. The sensitivity and specificity of VIDAS® TSH and fT4 are 100%.

This study has received approval from the Ethics Commission for Health Research at the Health Ministry of Health Polytechnic Jakarta III No. 068/KEPK-PKKJ3/05/2016 before the data collection, informed consent was previously submitted to the Hospital and the data obtained would be kept confidential by not discussing it out of the research team. Descriptive data and test based on time, gender, TSH and fT4 levels.

3. Results

The mean result of basic laboratory examination of thyroid function was TSH, fT4 in children 0-1 years in Harapan Kita Hospital, as in Table 1

Table 1. Average Value of TSH Levels, fT4 by Age

Variable	Mean and Standard Intersection (X ±SD)		
	0-3 months	4-12 months	Referral Value*
TSH (uIU/mL)	8.83 ± 13.16	5.79 ± 9.79	0.27-4.70
fT4 (pmol/L)	18.11 ± 5.18	16.25 ± 5.80	10.60-19.40

** Normal reference values based on VIDAS® TSH dan fT4

Thyroid Stimulating Hormone (TSH) functions to stimulate the production of thyroid hormones T4 and T3 through their receptors on the surface of the thyroid cell. If T3 and T4 levels increase, TSH production will be suppressed so that there will be a decrease in T3 and T4 levels. Triiodothyronine (T3) is a thyroid hormone in the blood with small levels, has a shorter work than T4. Thyroxine (T4) in the bloodstream can form free T4 and bound to protein.

In this study, 157 respondents conducted TSH and fT4 checks at the same time. There were only a few respondents that carried out T3 and T4 together with TSH and fT4, so that researcher could not meet the number of samples. Based on this idea, then in this study researcher only convey the results of TSH and fT4 examination for children aged 0-1 years.

Characteristics of respondents based on age, gender, and clinical diagnosis found the number of children aged 0-3 months as much as 27.4% and ages 4-12 months 72.6% (Table 2). When referring to Permenkes RI No.78 of 2014 concerning Congenital Hypothyroid Screening (SHK), screening examinations are used to sort infants HK suffers from babies who are not HK sufferers at the age of 48-72 hours. It aims to detect as early as possible the presence of congenital disorders. Laboratory testing and treatment before a child reaches 1 month old is the key to successful treatment of children with HK. The lack of number examinations in children 0-3 months is likely because Harapan Kita Hospital is a National Referral Hospital which in the era of BPJS, the treatment is started from primary services so that patients who are treated at RSAB Harapan Kita are referrals patients from various regions.

Table 2. Characteristics of subjects based on time, sex and clinical diagnosis

Characteristics	N	%
Usia		
0 - 3 months	43	27.4
4 - 12 months	114	72.6
Gender 0-3 months		
Male	29	18.5
Female	14	8.9
Gender 4-12 months		
Male	71	45.2
Female	43	27.4
Clinical Diagnosis		
Hypothyroidism	32	20.4
Developmental Disorders	20	12.7
<i>Down syndrome</i>	41	26.1
Other diseases	64	40.8

Clinical diagnosis of requests for examination of TSH and fT4, three are mostly due to hypothyroidism (20.4%), *Down syndrome* (26.1%), developmental delay (12.7%) and due to other causes (40.8%).

Table 3. Frequency distribution of interpretation of biomarker results based on age and approach to thyroid abnormalities based on interpretation of examination results of TSH and fT4 levels with n = 157

Variable	Age 0-3 months				Age 4-12 months			
	Male		Female		Male		Female	
	N	%	N	%	N	%	N	%
Eutiroid	12	7.6	7	4.4	36	22.9	25	15.9

Hypothyroid	3	1.9	0	0	3	1.9	0	0
Subclinical Hypothyroidism	7	4.5	4	2.5	13	8.3	12	7.6
Secondary Hypothyroidism	0	0	0	0	4	2.5	4	2.5
Subclinical Hyperthyroidism	0	0	2	1.3	5	3.2	0	0
Hyperthyroidism mediated by TSH	8	5.1	0	0	11	7.0	1	0.6

(Data Source: RSAB Harapan Kita Jakarta, January 2015-Agustus 2016)

Description: Eutiroid: normal TSH, normal ft4; Hypothyroidism: high TSH, low ft4; Subclinical hypothyroidism: high TSH, normal ft4; Secondary hypothyroidism: normal TSH, low ft4; Subclinical hyperthyroidism: low TSH, normal ft4, TSH-mediated hyperthyroidism: high ft4 with high TSH

Table 4. Correlation levels of Pearson test results on the relationship between TSH and ft4 levels by age

Variable	0-3 months	4-12 months	p value (sig (2-tailed))
TSH dan ft4 levels	-.344*	-.264**	
TSH levels and gender	-.216	-.128	.001
T4 levels and gender	-.307*	-.124	

Pearson test, * level of correlation was significant at α 0.05; ** level of correlation is significant at α 0.01

The results of the bivariate analysis illustrate a significant relationship with negative patterns between TSH and ft4 when related to age and sex. The result of the correlation coefficient is medium.

4. Discussion

In the Guidelines of the American Thyroid Association, it was stated that the selection of appropriate laboratory tests would allow diagnosis of thyroid abnormalities in many patients. The first line test that can be selected is TSH, because TSH is a sensitive indicator of thyroid abnormalities. Enhancement of thyroid hormone causes negative feedback on the pituitary gland so that TSH levels decrease, vice versa. TSH examination only cannot be used if abnormalities occur at the level of the pituitary gland. So we need another thyroid examination. The next option is an ft4 examination, and then if it is necessary should be added with the total of T3 examination. In general, all three of these examinations are requested at once, but because the price is quite expensive at this time the determination of free thyroxine (free T4 / ft4) and TSH as a basic examination of the diagnosis of thyroid function abnormalities (Laboratory Corporation of America, 2014; Dwi, Ratna S. 2014)

Thyroid hormone testing including immunological examinations is quite often requested by the clinician but it is not a routine checkup and only requested if there is a suspicion of thyroid abnormalities. Interpretation of the results of laboratory examination of thyroid function is done through understanding pathophysiology, history of illness from a suspected disorder. Not all thyroid abnormalities show abnormalities in thyroid function, and there are also asymptomatic in hyperthyroidism and subclinical hypothyroidism. The results of the analysis of thyroid hormones can help in diagnosis (Martin I, Surks, et al., 2004).

Decreased ft4 levels and increased TSH levels in 4% of respondents indicated primary hypothyroidism. Abnormalities occur in the thyroid gland, both anatomically and physiologically. If normal ft4 and increase of TSH levels are obtained in the age of the neonates, this abnormality condition is caused by congenital hypothyroidism, but it can also because a normal variant found in 23% of respondents that is called subclinical hypothyroidism. Congenital hypothyroidism suspicion increases when TSH levels > 40 uIU / mL are obtained. Respondents with TSH levels of 20-40 uIU / mL are still necessary to re-examine to confirm the results.

In 5% of respondents experienced a decrease in fT4 accompanied by a decrease in TSH levels. The diagnosis for this condition is secondary hypothyroidism or central. Abnormalities occur in the location of the central nervous system (pituitary or hypothalamus). To distinguish whether the pathology is located in the hypothalamus or pituitary can be examined thyroid releasing hormone (TRH) levels. Central hypothyroidism is often followed by other pituitary hormone disorders such as growth hormone, cortisol, gonadotropins. In central hypothyroid disorders, further investigation is needed to look for pituitary hormone abnormalities above. Symptoms such as growth disorders, palstokiziz and central nervous system problems need to be known to help diagnosis. Some things can cause normal fT4 levels followed by decreased TSH levels. This condition is called subclinical hyperthyroidism which may be due to side effects of drugs and normal variants. Some drugs can cause side effects suppressing TSH secretion. A very small decrease in TSH needs to be watched as a normal variant (Schteingart, David E. 2006).

According to Batubara (2005, 2010), hypothyroid cases are more commonly found in girls than boys with a ratio of 2: 1. In this study, in contrast to the results of previous studies, there were 63.7% male and 36.3% female who were spread with several thyroid abnormalities as shown in Figure 2. This shows the possibility that RSAB Harapan Kita is a referral hospital. So, the number of boys does not describe the ratio as delivered by Batubara: 2010. Women's risk is higher than boy's, and this is because girls have two allelic copies with two X chromosomes while boys only have one allele copy with one X chromosome. Therefore the risk of hypothyroidism is higher in girls.

At the age range of 4-12 months, the results were not different from the age of 0-3 months, and namely male are more than females (Kapelari K et al., 2008). According to the Ministry of Health (2014), more than 70% of patients with thyroid disorders and more because of hypothyroidism was diagnosed after 1 year of age so that they have permanent mental retardation (Hashemipour M et al., 2009). From the results of this study, the diagnosis of hypothyroidism is mostly found in the age of 0-3 months, and this shows that management or follow-up of treatment or therapy for hypothyroid patients can be done early so can minimize growth retardation and permanent mental development. The key to the success of treatment of children with hypothyroidism is by early detection through laboratory tests and treatment before the child is 1 year old. Thus early detection in preventing the occurrence of treatment delays is important, if it does not immediately detect or treated the children will run into an overall physical growth disruption and mental development retardation that cannot be restored, because permanent hypothyroidism requires lifelong treatment and special treatment (Ministry of Health, 2014, Cebeci, A.N et al., 2013).

5. Conclusion

One of the keys to the success of treatment of children with thyroid disorders is by early detection through laboratory tests and treatment before the child is 1 year old. To be more meaningful, it is expected that further research can be carried out in a primary way to obtain examination results from biomarkers of thyroid function over T3 and T4 so that the profile of thyroid abnormalities can be established.

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