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Initial Screening of Thyroid Function Test in Premature and Term Infants at General Hospital Dr. Zainoel Abidin Banda Aceh

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Abstract: *Congenital hypothyroidism (CH) is the most common cause of mental retardation which can be prevented by early diagnosis and treatment. Premature infants have a higher risk of developing HK than term infants. Screening for CH in every newborn is important, however, in premature babies screening for CH using the TSH examination is often found to have normal levels in the first week of examination. This study is a cross sectional study where the research sample amounted to 62 infants who were divided into 2 groups, namely premature babies (n = 31) and term infants (n = 31). Statistical analysis used is Independent sample t test and Mann-Whitney U test. This study aims to assess the comparison of thyroid function (FT4 and TSHs) between premature infants and term infants at the first examination in the age range of 2 -6 days. The results showed that 90% (28/31) premature infants had hypothyroxinemia with lower FT4 levels than term infants (18.70 ± 6.50, 95% CI). TSHs levels in premature infants were higher than term infants (5.70 ± 5.27, 95% CI). This study concluded that FT4 is better at detecting thyroid function disorders in premature infants while TSHs are better at detecting abnormal thyroid function in term infants.*

Keywords: *Congenital hypothyroidism; congenital hypothyroidism in preterm baby; thyroid function in preterm baby; congenital hypothyroidism screening*

I. Introduction

Screening for congenital hypothyroidism (HK) in neonates is an important preventive measure. Congenital hypothyroidism is one of the preventable causes of mental retardation. Hypothyroidism that is not intervened early can lead to severe mental retardation (Chung, 2019; Hallet, 2011) Thyroid hormone plays an important role in the growth and development of the central nervous system (CNS), which affects the migration of neuron cells, increases myelogenesis, and affects cell metabolism throughout the body.

The incidence of HK is higher in premature babies and low birth weight babies (LBW) compared to normal babies.1.4Immature development of the hypothalamic-pituitary axis causes a delay in the increase in thyroid stimulating hormone (TSH) so that HK is not diagnosed (Chung, 2019; Watson, 2018; Chung, 2009). Premature infants have a greater risk of thyroid function disorders such as HK, hypothyroxineemia and hyperthyrotropinemia compared to term infants (Chung, 2017; Srinivasan, 2011; McGrath, 2019).

The majority of developed countries have conducted screening programs for HK in neonates and about 95% of neonates with HK do not show typical signs and symptoms at birth. Through the HK screening program carried out on infants, infants will receive early therapy so that they can improve the prognosis, especially in the development of the neurological system (Yati, 2017; LaFranchi, 1999).

According to the Regulation of the Minister of Health of the Republic of Indonesia number 78 of 2014, specimen collection for HK screening in special circumstances is carried out 2 or 3 times depending on gestational age and severity of disease. Conditions that are included in a special category are babies who are at risk of experiencing transient HK such as premature babies (gestational age less than 37 weeks), babies with low and very low birth weight, babies being treated in the Neonatal Intensive Care Unit (NICU) and twins. Especially those of the same sex. The first specimen was taken at 48-72 hours, the second was taken at 2 weeks or 2 weeks after the first collection, while the third was taken when the baby was 28 days old or before the baby was sent home. Rovet et al (2003) stated that the examination of thyroid function in infants can be done until the age of 6 days.

TSH examination in newborns cannot detect central hypothyroidism. Normal TSH levels are often found in premature infants with HK at the first examination (Chung, 2009). Thyroxin hormone levels in premature infants are still low due to various factors such as the influence of maternal T4 hormone, immaturity of the hypothalamic-pituitary axis, lack of response of the thyroid gland to TSH and immaturity of tissue deionization. Peripheral. The majority of European countries and Japan currently use HK screening using the FT4 examination both in term infants and in premature infants (Iqbal, 2017).

Based on the exposure of the data above, the researcher is interested in assessing the comparison of thyroid function in the form of FT4 and TSHs between premature babies and term infants at the first examination, which is in the age range of 2 to 6 days. It is hoped that this assessment of thyroid function can be used as the basis for further thyroid function tests, especially in premature infants. Prevention of growth disorders caused by HK in infants, especially premature infants.

II. Research Methods

This study is an observational study with a cross sectional design to determine the comparison of thyroid function in premature infants and term infants during the first examination Zainoel Abidin Banda Aceh. The sample in this study was taken with a consecutive sampling technique. In this technique, the sample is all patients who meet the inclusion and exclusion criteria. The sample size in this study was 62 samples. Inclusion criteria were infants aged 3-6 days who were born or referred to RSUDZA, premature infants with gestational age <37 weeks and birth weight 500-<2500 grams and term infants with gestational age 37-42 weeks and birth weight 2500- 4000 grams.

The independent variable in this study was gestational age which was measured using the New Ballard Score (NBS). Gestational age was divided into term infants and premature infants. The dependent variable was the results of FT4 and TSHs examinations.

Descriptive data in the form of subject characteristics, namely the categorical scale (gender, gestational age and delivery history) and numerical scale (birth weight). The normality of the data was tested using the Saphiro-Wilk test.Comparative analysis between numerical variables using unpaired (independent) t-test if the data is normally distributed. If the data is not normally distributed, use a non-parametric test, namely Mann Whitney. The data is processed using the Statistical Package for the Social Science (SPSS) version 23 computer program. The data will be displayed in the form of text, tables or graphs.

III. Results and Discussion

3.1 Results

a. Basic Characteristics of Research Samples

Table 1. Basic Characteristics of Samples of Preterm and Term Infants

Variable	Baby Group	
	Premature N (%)	**Enough Moon N (%)**
Gender		
Man	16 (51.6)	15 (48.4)
Woman	15 (48.4)	16 (51.6)
Birth Weight Category		
Low birth weight	22 (71.0)	-
Very Low Birth Weight	8 (25.8)	-
Very Very Low Birth Weight	1 (3,2)	-
Gestational Age Category		-
Very Preterm (28-31 weeks)	11 (35.5)	-
Moderate to Late Preterm (32-36 weeks)	20 (64.5)	-

This study involved 31 premature babies and 31 term babies, respectively. There are 3 basic characteristic variables that are considered from the sample of babies in this study, namely gender, birth weight category and gestational age category. % in the group of premature infants and 48.4% compared to 51.6% in the group of term infants. While the categories of birth weight and gestational age were only observed in the group of premature babies. There are 3 categories of birth weight in premature infants in this study, namely low birth weight, very low birth weight and very low birth weight. Among the three categories, more than 70% of premature babies in this study had low birth weight. Furthermore, there are about 25% other premature babies who have very low birth weight. Meanwhile, premature babies with very low birth weight were only 1 person (3.2%). The gestational age group in premature infants in this study consisted of two categories, namely very preterm or gestational age between 28 to 31 weeks and the category of moderate late to preterm with a gestational age range of 32 to 36 weeks. More than 64% of premature babies in this study belonged to the second category (moderate late to preterm) or had a gestational age of 32 to 36 weeks. While the rest are included in the very preterm category. The gestational age group in premature infants in this study consisted of two categories, namely very preterm or gestational age between 28 to 31 weeks and the category of moderate late to preterm with a gestational age range of 32 to 36 weeks. More than 64% of premature babies in this study belonged to the second category (moderate late to preterm) or had a gestational age of 32 to 36 weeks. While the rest are included in the very preterm category. The gestational age group in premature infants in this study consisted of two categories, namely very preterm or gestational age between 28 to 31 weeks and the category of moderate late to preterm with a gestational age range of 32 to 36 weeks. More than 64% of premature babies in this study belonged to the second category (moderate late to preterm) or had a gestational age of 32 to 36 weeks. While the rest are included in the very preterm category.

b. Rate Comparison FT4 and TSHs in the Group of Term Infants and Premature Baby

Table 2. Comparison of FT4 and TSHs Levels between the Groups of Term Infants and Premature Infants

Variable	Premature baby (n=31)	Full term baby (n=31)	*P-value*
FT4	18.70±6.50	20.80 ± 7.77	0.254
TSHs	5.70±5.27	4.25±4.27	0.257

Table 2 showed that the mean FT4 level in the preterm group was lower than the term infant group but not statistically significant (p>0.05). On the other hand, the average TSHs level in the preterm group was slightly higher than the term infant group but not statistically significant (p>0.05).

c. Levels of FT4 and TSHs in Premature Babies Based on Birth Weight

Table 3. Levels of FT4 and TSHs in Premature Infants Based on Birth Weight

Variable	Low birth weight n=22	Very low birth weight n=8
FT4	20.32 ± 6.48	14.89 ± 5.19
TSHs	6.45±5.78	3.21±2.83

Table 3 showed that the mean FT4 level in the group of premature infants with very low birth weight was lower than that of premature infants with low birth weight. The average level of TSHs in the group of premature infants with very low birth weight was also lower than in the group of premature infants with low birth weight.

d. Levels of FT4 and TSHs in Premature Babies by Gestational Age

Table 4. Levels of FT4 and TSHs in Premature Infants Based on Age Gesbag

Variable	**Preterm infants with moderate to late preterm gestational age**n=20	**Premature babies with very preterm gestational age**n=11
FT4	18.87 ± 5.22	18.40±8.65
TSHs	5.98±5.43	5.19±5.17

Table 4 showed that the mean FT4 level in the group of premature infants with very preterm gestational age was lower than that of preterm infants with moderate to late preterm gestation. On the other hand, the mean TSHs level in the group of premature infants with very preterm gestational age was higher than the group of preterm infants with moderate to late preterm gestational age.

e. Comparison of Incidence Rates FT4 and TSHs are not Normal in the Group of Term Infants and Baby Premature

Table 5. Comparison of Abnormal FT4 and TSHs Levels in the Group of Term Infants and Premature Infants

Variable	Premature baby n=31 (%)	Full term baby n=31 (%)	*P-value*
FT4	28 (90.32)	4 (12.90)	<0.001
TSHs	0 (0.00)	11 (35.48)	<0.001

Based on Table 5, it is known that of the 31 samples of premature infants examined in this study, 28 of them or with a percentage of 90.32 had levels ofFT4 with the abnormal category compared to term infants, the number of which had levels of FT4 there are only 4 people who are not normal or with a percentage of 12.90 ($p<0.001$). Furthermore, the number of term infants with TSHs levels in the abnormal category was 11 infants or with a percentage of 35.48 compared to preterm infants who all had normal TSHs levels ($p<0.001$).

3.2 Discussion

Congenital hypothyroidism (HK) is a deficiency of thyroid hormone caused by the thyroid gland is not fully formed, not formed at all, or there is a disorder of thyroid hormone production or function that is acquired from birth. Congenital hypothyroidism can be lifelong (permanent) or temporary (transient) (Julia, 2018). Congenital hypothyroidism is the most common cause of mental retardation that can be prevented by early diagnosis and treatment. Diagnosis and treatment in the first few weeks of life can prevent neurodevelopmental disability. Compared to term infants, premature infants have a higher risk of developing HK.40Factors that predispose to HK in premature infants are immaturity of the hypothalamic-pituitary axis, immaturity of thyroid hormone metabolism, deficiency iodine.

This study is the first study to assess the comparison of thyroid function test results between premature and term infants at the first examination at RSUDZA Banda Aceh. FT4 and TSHs examinations are used as modalities in establishing the diagnosis of hypothyroidism. TSH alone in newborns cannot detect central hypothyroidism, while FT4 alone cannot detect subclinical hypothyroidism (Chung, 2009).

This study involved 62 infants who were divided into 2 groups, namely the group of term infants and the group of premature infants. Premature babies were regrouped based

on gestational age and birth weight. This study found that the mean FT4 level in the preterm group was lower than the term infant group (18.70 versus 20.80 but not statistically significant (p 0.254). Although this study found the average FT4 level among premature infants and term was not statistically different, but if it was associated with a normal reference value of FT4 in premature infants, 90% of premature infants were found to have hypothyroxinemia (28/31). There is a percentage difference baby with rateFT4 and TSHs significant abnormality category (p-value<0.001) between preterm and term infants. The difference in the reference value between premature and term infants causes FT4 levels which are still within normal limits in term infants to be low in premature infants. Term ($p < 0.05$). A study by Sharma et al (2019) found that FT4 levels in preterm infants were lower than in term infants at first examination ($p < 0.05$). The difference in FT4 results may be due to differences in gestational age and birth weight in the study. Clemente et al (2007) explained that premature infants with a gestational age of 27-29 weeks had lower FT4 levels compared to premature infants with a gestational age of 30-35 weeks. The average level of TSHs in the premature infant group was actually higher than the term infant group but not statistically significant. It is associated with the reference value of TSHs in premature infants, although TSHs levels in premature infants are higher, but these values are still within the normal range. This result is in line with research conducted by Iqbal et al. (2017) that found no significant difference in TSHs levels between premature infants and term infants, although TSHs levels in premature babies is higher. Sharma et al (2019) and Murphy et al (2004) also found a non-significant difference in TSH levels between preterm and term infants (p 0.076).

Average FT4 levels in the preterm group with very low birth weight lower than those with premature baby with low birth weight. Rmean TSHs levels in the infant group premature births with very low birth weight are also lower than the premature infant group with low birth weight. This is in line with research conducted by Frank et al. (1996) who found that premature infants with very low birth weights had lower FT4 levels than premature infants with low birth weight and term infants. Based on this study, it was found that lower FT4 levels in premature infants with very low birth weight did not increase the risk of permanent hypothyroidism. FT4 levels will improve with increasing gestational age. Low FT4 levels are associated with sick euthyroid syndrome caused by stress and non-specific disease, so serial thyroid function tests are needed to assess thyroid function in premature infants with low birth weight and very low birth weight.

Rmean FT4 levels in the preterm group with very preterm gestational age is lower than premature infants with moderate to late preterm gestational age. In line with research conducted by Sharma et al (2019), FT4 levels in premature infants are directly proportional to gestational age. The higher the gestational age, the higher the FT4 level. Sharma et al (2019) found that premature infants near 37 weeks' gestation had normal FT4 levels. On the other hand, rmean TSHs levels in the infant group premature with premature with a higher very preterm gestational age than the premature infant group with moderate to late preterm gestation. The higher TSH levels in premature babies according to La Franchi (1999) can be caused by the process of restoring thyroid hormone to normal values. This recovery process is characterized by an increase in TSH levels (5-15 mU/L). A study conducted by Chung et al (2009) also found an increase in TSH levels in premature infants (10 U/ml) compared to term infants.

IV. Conclusion

The FT4 examination can be used as a screening for HK in premature infants compared to term infants. The TSHs examination can be used as a screening for HK in term infants.

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