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The Correlation Between Age of Diagnosis and Quality of Life in Children with Congenital Hypothyroidism: A Cross Sectional Study in A Limited Resource Setting

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ABSTRACT

Background and Objectives: Thyroid hormones have a significant impact on how the brain develops. The quality of life is greatly impacted by early diagnosis. Analyzing the correlation between the age of diagnosis and quality of life in children with congenital hypothyroidism in a setting with limited resources was the aim of this study. ***Materials and Methods:*** A cross-sectional study was performed on 31 children with congenital hypothyroidism who were still under routine control from August 2023 to February 2024. The generic Pediatric Quality of Life Inventory (PedsQL) scale was used to measure quality of life, while age at diagnosis was obtained from the patient's medical record data. The normality test was performed and followed by Spearman analysis. ***Result:*** A total of 15 out of 31 children were aged between 2-4 years old. There were 15 respondents who were successfully diagnosed <6 months. There were 14 children who were diagnosed with central hypothyroidism. The average PedsQL score of 16 children was in the poor category (0-76). Age of diagnosis and quality of life showed abnormal distribution with Asymp. Sig (2-tailed) < 0.05. There was a correlation between age of diagnosis and quality of life (α=0.05, p=0.042, p<α). The Spearman correlation was in the negative distribution (-0,366), so the correlation between age of diagnosis and quality of life was inversely proportional. ***Conclusion:*** In children with congenital hypothyroidism, the age of diagnosis was associated with the quality of life overall, but was not significantly with each quality of life sector.

Keywords: congenital hypothyroidism; child; age of diagnosis; quality of life.

INTRODUCTION

Quality of life in children is very essential to note, especially those with chronic diseases, for example, in children with congenital hypothyroidism. Hypothyroidism is a condition of thyroid hormone deficiency marked with increased serum Thyroid Stimulating Hormone (TSH) and decreased T3 and T4 [24]. The role of thyroid hormones is very important in brain development; therefore, children with hypothyroidism often have symptoms of motor delays, speech delays, and cognitive impairment [25]. The incidence of congenital hypothyroidism varies across countries. Globally, the ratio is 1:3000 to 1:4000 births.

In Indonesia, according to Newborn Screening for Congenital Hypothyroidism (SCH) data from 14 provinces, the prevalence of its occurrence reaches 1:2513 births [10].

Children with congenital hypothyroidism have different ages of diagnosis determined through the newborn Screening for hypothyroidism Congenital (SCH) program, according to clinical conditions. The condition is according to etiology, age of onset in utero, prognosis, and duration of hypothyroidism. At the beginning of detection, only less than 5% of children with positive screening results show mild clinical symptoms of hypothyroidism [24].

It happened because the uneven implementation of SCH in Indonesia only reached less than 10%. It's been a challenge for the government. As a result, there are an average of 51 cases of IQ developmental disorders due to delays in providing early therapy at the age of more than 1.5 years [29].

Previous studies have found that pediatric patients with congenital hypothyroidism who receive early and regular treatment will produce better PedsQL (Pediatric Quality of Life Inventory) scores with a minimum risk of complications than patients with late diagnosis and late treatment [20]. However, another study concluded that age at first treatment did not significantly correlate with PedsQL [18]. Research on treatment management for quality of life in patients with congenital hypothyroidism until now is still inconsistent. In addition, based on the predicted increase in the incidence of congenital hypothyroidism and its harmful side effects on children's brain development, the researchers conducted further research aimed at collecting evidence on the correlation between age at diagnosis and quality of life in children with congenital hypothyroidism at Dr. Soetomo, General Academic Hospital, Surabaya, Indonesia. An explanation of possible factors underlying the effectiveness of early diagnosis in improving patient quality of life will be added.

MATERIAL AND METHOD

We examined 31 children with congenital hypothyroidism who were routinely seen at the Pediatric Endocrinology Clinic, Outpatient Installation, Dr. Soetomo, General Academic Hospital, Surabaya, Indonesia, from August 2023 to February 2024. This study was approved and licensed by the Health Research Ethics Committee of Dr. Soetomo, General Academic Hospital, Surabaya, Indonesia (070/1176/102.6.3.3/Litb/2023). The inclusion criteria included children aged 0 months to 18 years old, routine control at the Pediatric Endocrinology Clinic of Dr. Soetomo, General Academic Hospital and those who agreed to be involved in this study. Pediatric congenital hypothyroidism patients who were undergoing treatment for acute complications in the Pediatric Intensive Care Unit were excluded from the study sample.

The age at diagnosis was obtained from medical records according to the initial symptoms or abnormal serum TSH and FT4 levels. Parents were interviewed about their child's quality of life using the Pediatric Quality of Life Inventory (PedsQL) 4.0 generic scale questionnaire. The PedsQL 4.0 questionnaire provides four age-specific versions that have been validated according to age group. Each age group consists of 23 questions covering four sectors: physical functioning (eight items), emotional (five items), social (five items), and academic (five items). The Scores of each sector were scored based on how often the problem occurred in the patient's daily life, namely: 0 = never, 1 = almost never, 2 = sometimes, 3 = often, and 4 = almost always. All scores on each of those items will be linearly transformed to 0-100, then accumulated and averaged. The quality of life range was classified into 2 categories, namely poor (score 0-76) and good (score 77-100). A normality test was conducted on all data. A Spearman test was performed to analyze the correlation between age and the PedsQL scale. Data was deemed statistically significant if *p*-value <0.05. The results were analyzed with SPSS 26.0 software.

DISCUSSION

The correlation between age of diagnosis and quality of life (PedsQL score) is described in Table 3. The characteristics of the patients are presented in Table 1. The median age at data collection from 31 samples was 24-48 months, while the median age of diagnosis was 0-6 months. We had 51.61% of patients with central congenital hypothyroidism, 38.71% with peripheral congenital hypothyroidism, and 9.68% with subclinical hypothyroidism. Our patients had a poor quality of life (total score PedsQL 0-76).

TABLE 1: Characteristics of the respondent.

CHARACTERISTICS	FREQUENCY (%)
Gender	
Boy	16 (51.61)
Girl	15 (43.39)
Age at data collection (median)(months)	24-48 months
Age of diagnosis (median)(months)	0-6 months
Weight/Height (median), SD	18 (58.06)
Type of hypothyroidism	
Primary hypothyroidism	12 (38.71)
Secondary hypothyroidism	16 (51.61)
Subclinical hypothyroidism	3 (9.68)
Quality of life	
Low (total score: 0-76)	16 (51.61)
High (total score: 77-100)	15 (43.89)

SD: Standard Deviation.

TABLE 2: Characteristics of the parent's respondents.

CHARACTERISTICS	FREQUENCY (%)
Education Level	
Junior high school level	1 (3.22)
Senior high school level	22 (70.97)
College	8 (25.81)

TABLE 3: Correlation between age at diagnosis and quality of life (PedsQL sector).

QUALITY OF LIFE SECTOR (PedsQL)	
Factor	**Age at diagnosis**
Accumulation across sectors	r = -0.366 p = 0.043
Physical function	r = 0.113 p = 0.545
Emotional function	r = -0.055 p = 0.770
Social function	r = -0.009 p = 0.092
Academic function	r = -0.086 p = 0.646

The correlation between age of diagnosis and quality of life of children with congenital hypothyroidism in our study was significant. This can be seen from the Spearman rank test with a significance value of α = 0.05 with the obtained Sig. (ρ=0.043), which means ρ < α (Table 3). This is supported by Figure 1. which shows that the age of diagnosis has an inversely proportional relationship with quality of life. It meant that the lower the age of diagnosis, the higher the quality of life. However, the age of diagnosis did not have significant meaning when correlated separately with each sector of quality of life including physical, emotional, social, and academic functions (Table 3).

This condition occurred because each patient had a pattern of problems that was not exactly the same as other patients. According to the interview results, patients had different conditions and birth problems that gradually developed depending on the parenting of each family. This condition is in line with the time series study theory of Wirawan et al. (2016) there are three important factors that influence the poor prognosis of child development in early childhood, namely history of low birth weight, comorbid diseases that develop according to parenting, and abnormalities in thyroid function [28].

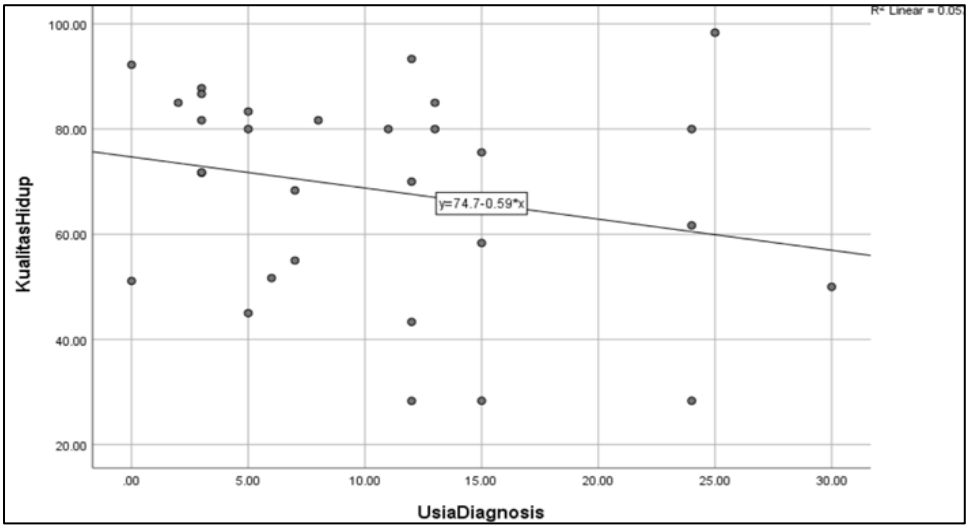

FIGURE 1: Distribution of sample correlation test results.

As listed in Table 1. the final result of the PedsQL total score is in the range of 0-76 (poor quality of life category) at 51.61%. This grouping was in accordance with the theory of Varni et al. (2005) which classifies children's quality of life as poor if the total summary score is <77 [26]. In addition, the poor quality of life in our sample can also be seen from the results of data collection of the patient's nutritional range data (weight/height). A total of 32,26% of samples had a nutritional range below normal, with 9.68% of children being classified as malnourished and 22.58% as undernourished.

Poor quality of life in respondents occurred due to several factors, one of them was due to the high delay in diagnosis (29.58%) (Table 1). This condition occurs because the patient's initial clinical symptoms are still vague due to the residual intake of thyroid hormones from his mother since pregnancy so that the level of TSH increase is not too high [17]. These symptoms will become more obvious over time. The later the detection of symptoms, the more delayed the treatment, the healing process may be prolonged (until 2-4 years old or even more) and the patient's prognosis may worsen. In line with the research of Balhara et al., (2011) that the prognosis of congenital hypothyroidism is determined according to the initial TSH level, then the levels must always be maintained according to the treatment target with regular monitoring every month for up to 6 months of the second therapy to achieve optimal targets [4]. Children with congenital hypothyroidism who have a delayed diagnosis and do not receive prompt correction will continue to have low thyroid hormone levels until their critical period. In our study, almost half of the samples (48.39%) were aged 2-4 years old (Table 1.). This age is classified as a critical period (golden age period) for children to achieve maximum growth and development. This theory is stated by Suryana et al. (2022) that the critical period is the peak of rapid growth and development of children from the womb until 2 years old [23].

Thyroid hormone acts as a development hormone. Therefore, low levels of thyroid hormone are a major cause of decreased quality of life due to physical, educational, social, and emotional developmental barriers in children. In line with Khaleghzadeh et al. (2021), normal levels of thyroxine could support the development of the child's brain as the central nervous system that regulates body control. As a result, children with congenital hypothyroidism will have impaired development of the central nervous system and have the potential to suffer mental retardation [13]. In contrast to the research study from Pulungan et al. (2019), early diagnosis did not have a significant effect on therapy and patient quality of life [18]. Differences in these results may occur due to differences in sample exclusion criteria and quality of life measurement methods, as well as the number of samples taken in our study being more collected.

Therapy for congenital hypothyroidism patients is highly dependent on the initial TSH and fT4 levels in each patient as written in the first diagnosis. These levels are used as the basis for determining the initial drug dose. Patients who have an early diagnosis age usually have low TSH levels because their bodies still store residual thyroid hormones from their mothers. According to previous research, early treatment of congenital hypothyroidism (<13 days) with initial T4 >9.5 mcg/kgBB/day can prevent psychomotor severity [20]. T4 levels in the first 2 years of life have a significant relationship with mental development indices at 2 years old and verbal ability at 6 years old [28]. Based on other studies, children with early detection < 1.5 years old have the possibility of more effective and maximum therapy when compared to other patients with late diagnosis [29].

The lower quality of life scores may also be due to barriers to early detection due to delayed TSH elevation in 51.61% of respondents with central congenital hypothyroidism which was frequently encountered in our study (Table 1). The implementation of Newborn Screening for hypothyroidism Congenital (SCH) is obtained using the examination of the patient's Thyroid Stimulating Hormone (TSH) level. So that it can only be done to establish primary hypothyroidism as a result of an increase in TSH due to positive feedback from a decrease in FT4, unlike the central type of congenital hypothyroidism which is more difficult to detect because the source of the disorder is in the central nervous system so that TSH levels are low [12]. This is also exacerbated by the implementation of SCH in Indonesia is still not fully distributed, the percentage only reaches <2% in all regions of Indonesia, especially in areas that are difficult to access information [18]. The even distribution of screening information is still not valuable if the screening implementation process is still not optimal [2].

Parents' education level influences the age at diagnosis and quality of life of children with congenital hypothyroidism. This is related to hypothyroidism disease which requires higher knowledge to be able to understand the initial symptoms, causes, and consequences of the appearance of the disease. Table 3. shows that the highest level of education of parents or caretakers (70.97%) is senior high school level. The education level of parents or caretakers is very influential in recognizing the early signs and symptoms of congenital hypothyroidism disease. The level of education is an indicator of an individual in pursuing a formal education level which affects a person's ability to seek and process information. According to the theory of Budiman and Riyanto (2018), the higher a person's education, the faster it is to receive and understand information so that the knowledge possessed is also higher [6]. This is also in line with the results of research conducted by Pulungan et al., (2019) that delays in early diagnosis and treatment often occur due to a lack of knowledge about the importance of early detection and timely treatment [18].

CONCLUSIONS

We concluded that age of diagnosis was associated with quality of life in children with congenital hypothyroidism. However, the age of diagnosis was not significantly correlated with each sector in PedsQL because thyroid hormone abnormality due to congenital hypothyroidism is not the single major factor that determines intellectual prognosis, and there are other factors that also play an important role in it.

LIMITATION

However, this study still has some limitations. The study variables were quite limited because in reality there are variations in the comorbid diseases of patients with different prognoses, so this also affects the quality of life score. In addition, primary data collection was only conducted in one healthcare center with a limited number of samples in certain areas. The authors strongly recommend further experimental studies and clinical trials with a variety of parameters and sampling sites to comprehensively evaluate the various predictors affecting the quality of life of children with congenital hypothyroidism.

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