

Relation Between Therapy Compliance and Quality of Life in Children with Hypothyroidism: A Cross Sectional Study

Sylvia Sherlinda¹, Nur Rochmah^{2,3*}, Deasy Ardiany^{4,5}, Hermina Novida^{4,5}

¹Faculty of Medicine, Universitas Airlangga, Surabaya

²Department of Child Health, Faculty of Medicine, Universitas Airlangga, Surabaya

³Department of Child Health, Dr. Soetomo General Academic Hospital, Surabaya

⁴Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya

⁵Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya

E-mail: sylvia.erlinda-2021@fk.unair.ac.id; nur-r@fk.unair.ac.id;
deasy.ardiany@fk.unair.ac.id; hermina-n@fk.unair.ac.id

*Corresponding author details: Nur Rochmah; nur-r@fk.unair.ac.id

ABSTRACT

Background: Hypothyroidism in children is the most common congenital endocrine problem and the most common preventable cause of mental retardation in children. Other than that, many growth and development problems also frequently cause a lot of negative impacts in children with hypothyroidism. Hypothyroidism is included as a chronic progressive disease, so good therapy compliance is needed to achieve a good quality of life. **Objective:** This study aims to analyze the relation between therapy compliance and quality of life in hypothyroidism children. **Method:** This research uses an analytical observational method to determine the relation between two variables, namely therapy compliance and quality of life in children with hypothyroidism in a cross-sectional study in a population and at a certain time. Research subjects were chosen using the consecutive random sampling method from all hypothyroidism pediatric patients at the Children's Endocrinology Clinic, Regional General Hospital Dr. Soetomo, in accordance with the research criteria. Interviews with questionnaires were conducted with parents/guardians of children with hypothyroidism regarding therapy compliance and quality of life. **Result:** From the result of this research, the value obtained from a statistical test regarding the significance and closeness of the relation between variables using the Spearman correlation coefficient (with a significance level of $p < 0.05$) is 0.001. This means that the research hypothesis is proven, namely that there is a relation between therapy compliance and quality of life in hypothyroidism children.

Keywords: hypothyroidism; children; therapy compliance; quality of life.

INTRODUCTION

Hypothyroidism is a clinical condition where thyroid hormone in the body is not sufficient [1]. This hormone has important roles in regulating metabolism, growth, and other body functions [2]. In children, hypothyroidism is one of the most common endocrine disturbances that happen [3]. Unfortunately, parents are still startled to know about that, and only a small amount of them have high levels of awareness and knowledge about hypothyroidism in children, even though it has impacts on stunted physical growth and mental retardation that cause a reduction in human resource quality as the next generation [4]. Although the impacts of children's hypothyroidism can be prevented by early diagnosis and good therapy compliance, until now the study of the relation between therapy compliance and quality of life in children is still controversial among the public [5].

Despite the fact that the incidence of hypothyroidism increases with age and is more common at the age of 60 and above, hypothyroidism in children cannot be ignored since it is one of the main causes of intellectual disability in the whole world [5, 6]. According to the Department of Child Health at Ninewells Hospital and Medical School, the prevalence of children's hypothyroidism is 0,135%, or 135:100.000 [7]. In general, infants' hypothyroidism is congenital hypothyroidism, while the acquired hypothyroidism becomes more common with increasing age and usually appears at age 9–11 and hardly appears at age before 4 [8]. Congenital hypothyroidism is 85% caused by thyroid dysgenesis, namely abnormality of thyroid gland development in the womb, and the other 10%-15% is caused by thyroid dysharmonogenesis, namely abnormality of thyroid hormone number of production in the womb [9].

The main cause of acquired hypothyroidism is an autoimmune condition called Hashimoto's thyroiditis which, in certain areas, can be caused by iodine deficiency [10].

Depending on the causes of hypothyroidism in children, the diagnosis and type of hypothyroidism will affect the medication and long-term outcome for them. Therefore, screening in newborns is very important, which can be carried out through laboratory tests by checking thyroid hormone levels using blood samples. Health Minister Regulation Number 25 Year 2014 about Child Health Efforts and Health Minister Regulation Number 78 Year 2014 about Congenital Hypothyroidism Screening have stated that hypothyroidism screening has already been the standard service for all newborns as a promotive and preventive attempt [11, 12]. The Ministry of Health has relaunched the program through the Circular Letter Year 2022 about "The Obligation of Congenital Hypothyroidism Screening for Newborns in Health Service Facilities Providing Childbirth Assistance in order to Improve Quality of Indonesian Children." [13]

Apart from not being very visible and appearing gradually, the symptoms of hypothyroidism are non-specific and similar to other health problems, so they are often ignored [14]. This causes hypothyroidism, probably undetected for ages, while a delay in diagnosis can result in more symptoms and a worse prognosis for the children [15]. Low levels of awareness and knowledge of the parents about the urgency and benefits of hypothyroidism screening, as well as the impacts and dangers of hypothyroidism itself, cause frequent delays in diagnosis and non-compliance therapy, which results in permanent damage for the children [16]. Therapy compliance in children with hypothyroidism is influenced by the role of parents, especially the willingness to do the early diagnosis by screening and compliance with regular control [16]. The result of research in Bahia, Brazil, shows that continuous thyroid hormone replacement therapy with levothyroxine will reverse metabolic changes and thus prevent damage to the children's central nervous system [17]. As a chronic disease that needs long-life therapy, surely therapy compliance in congenital hypothyroidism patients will also be very difficult to achieve due to the patient's assumption as "difficult" and socioeconomic factors [18]. In previous studies, no research has been conducted that specifically examines and analyzes the relation between therapy compliance and quality of life in hypothyroidism children. Therefore, this study aims to determine how compliance with levothyroxine therapy in children with hypothyroidism affects their quality of life.

METHOD

This study uses analytical observational methods to determine the relation between two variables, namely therapy compliance and quality of life in children with hypothyroidism, in a cross-sectional manner in a population and at a certain time.

Samples were taken using the consecutive random sampling method. All hypothyroidism pediatric patients at the Children's Endocrinology Clinic Regional General Hospital Dr. Soetomo are the population that was selected to be the sample when they met the research criteria. Pediatric patients who met the research criteria were taken as samples until the minimum sample size was met. The data collection procedure in this study was carried out through interviews in the form of questionnaire questions to parents of hypothyroidism children. The data in this study is primary data from interviews in the form of questionnaire questions to parents of hypothyroidism children. The data that has been collected was then analyzed using the Spearman correlation coefficient because the distribution is not normal. Next, the data was processed statistically using Statistical Product and Service Solution (SPSS).

RESULT AND DISCUSSION

The basic characteristics of the patients are shown in Table 1. Of the 30 research samples, 56.67% were male and 43.33% were female. The majority of patients are toddlers, followed by preschoolers and schoolchildren. 76.67% of patients had diagnosis ages that met the standard, and the rest did not meet the standard. The most common type of hypothyroidism is primary hypothyroidism, followed by secondary hypothyroidism. 46.67% of patients did not have congenital abnormalities, while 53.33% had congenital abnormalities such as Down syndrome, congenital heart disease, autism spectrum disorder, micropenis, palatoschisis, semantic syndrome, crouzon syndrome, Erb's palsy, and neurological disorders.

TABLE 1: Basic Characteristics.

Characteristic	Number (%)
Gender	
Male	17 (56,67%)
Female	13 (43,33%)
Age	
Toddler	15 (50%)
Preschooler	8 (26,67%)
Schoolchildren	7 (23,33%)
Diagnosis Age	
≤1-year-old	23 (76,67%)
>1-year-old	7 (23,33%)
Hypothyroidism Type	
Primary	16 (53,33%)
Secondary/Central	14 (46,67%)
Congenital Abnormality	
None	14 (46,67%)
Down syndrome	3 (10%)
Congenital heart disease	3 (10%)
Autism spectrum disorder	2 (6,67%)
Micropenis	2 (6,67%)
Palatoschisis	2 (6,67%)
Semantic syndrome	2 (6,67%)
Crouzon syndrome	1 (3,33%)
Erb's palsy	1 (3,33%)
Neurological disorder	1 (3,33%)

Patient therapy compliance is shown in Figure 1. Of the 30 research samples, 50% had low therapy compliance, 36.67% had moderate therapy compliance, and 13.33% had high therapy compliance. These results are in line with research in Saudi Arabia, where the largest number of patients had a low level of therapy compliance, followed by those with a medium level of therapy compliance, and the fewest were those who had a high level of therapy compliance [19]. Therapy compliance is difficult to achieve in chronic diseases whose treatment is prolonged or permanent due to several factors, namely the level of education and socio-economic conditions of the patient's parents, which directly influence the patient's parents' understanding of the benefits, timeliness, and dosage, as well as concern for treatment [20]. Apart from that, people's difficulties in accessing hospitals or health care facilities can also affect compliance with treatment, where compliance with treatment of chronic diseases in developed countries is estimated to reach half of the population, while compliance with treatment of chronic diseases in developing countries is much lower [21].

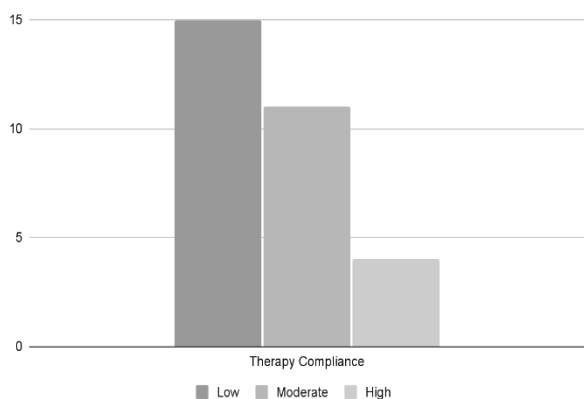


FIGURE 1: Therapy Compliance in Children with Hypothyroidism.

The patient's quality of life is shown in Figure 2. Of the 30 study samples, 53.33% had a poor quality of life, while 46.67% had a good quality of life. These results are in line with research by van der Sluijs Veer et al., which states that children with hypothyroidism have a worse quality of life compared to the normal population in cognitive, motor, social, positive and negative emotional functions, and autonomy [22]. This is because thyroid hormones have a crucial role in body metabolism, growth, and neurological development, which results in children with hypothyroidism experiencing problems in various sectors, such as physical function, emotional function, social function, and academic function [23].

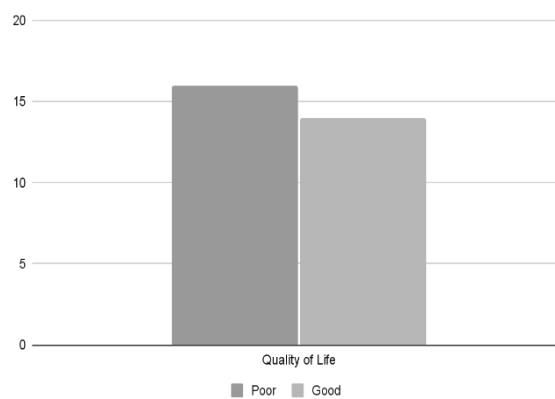


FIGURE 2: Quality of Life in Children with Hypothyroidism.

The results of the normality test using Kolmogorov-Smirnov obtained a Sig value. is 0.023 for therapy compliance and 0.031 for quality of life, where the results are <0.05, which means that the distribution is not normal. Because the distribution is not normal, the data is processed using Spearman coefficient correlation to carry out statistical correlation tests. The Spearman correlation coefficient value between therapy compliance and quality of life is 0.565, which is positive, meaning that therapy compliance and quality of life are directly proportional, where the higher the therapy compliance, the higher the quality of life, and the lower the therapy compliance, the lower the quality of life. The sig value. is 0.001, which is <0.05, so it is concluded that there is a significant relation or correlation between therapy compliance and quality of life. Therefore, it is proven that there is a significant relation between compliance with therapy and quality of life in hypothyroidism children.

The relation between therapy compliance and patient quality of life is shown in Figure 3. Of the 30 research samples, 36.67% had low therapy compliance and poor quality of life, 13.33% had low therapy compliance and good quality of life, 13.33% had moderate therapy and poor quality of life, 23.34% had moderate therapy compliance and good quality of life, 3.33% had high therapy compliance and poor quality of life, and 10% had high therapy compliance and good quality of life. This shows that therapy compliance affects the quality of life in pediatric patients with hypothyroidism. Research in Auckland suggests that early diagnosis through neonatal screening followed by aggressive high-dose hormonal treatment in the first 3 years provides excellent neurocognitive and developmental outcomes in congenital hypothyroidism patients [24]. According to research by Ramadhan et al., non-compliance to therapy is the most common cause of failure of thyroxine therapy, which results in hypothyroidism that does not heal [25]. Research conducted by Almeida et al. also showed that patients with thyroid disorders who were noncompliant with therapy had more symptoms of depression, anxiety, and poorer quality of life [26].

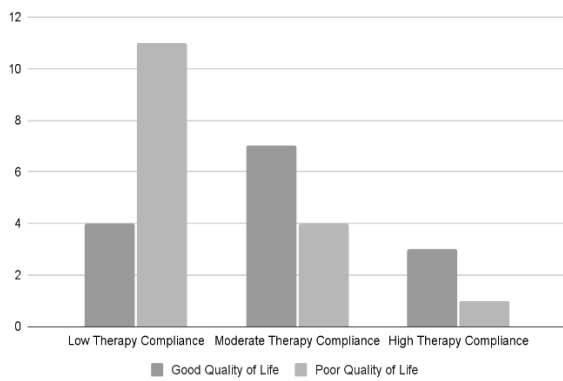


FIGURE 3: Relation Between Therapy Compliance and Quality of Life in Children with Hypothyroidism.

CONCLUSION

Based on the results of this research, several conclusions can be drawn as follows: Therapy compliance in hypothyroidism children as measured using the MMAS-8 Questionnaire had a median value of 6.25 ± 5.25 , where 50% had a high level of therapy compliance, 36.67% had a medium level of therapy compliance, and 13.33% had a low level of therapy compliance. Quality of life in hypothyroidism children as measured using the PedsQL 1.0 and PedsQL 4.0 questionnaires has a median value of 74.17 ± 76.66 , where 53.33% have a poor quality of life and 46.67% have a good quality of life. There is a significant relation between therapy compliance and quality of life in hypothyroidism children, but there are only a few significant relations between each sector of therapy compliance and each sector of quality of life in hypothyroidism children.

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REFERENCES

- [1] National Institute of Diabetes and Digestive and Kidney Diseases (2021). Hypothyroidism (underactive thyroid). National Institute of Diabetes and Digestive and Kidney Diseases. Available at: <https://www.niddk.nih.gov/health-information/endocrine-diseases/hypothyroidism>.
- [2] Shahid, M.A., Sharma, S. and Ashraf, M.A. (2023). Physiology, Thyroid Hormone. Nih.gov. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK50006/>.
- [3] Ghaemi, N., Bagheri, S., Elmi, S., Mohammadzade Rezaee, S., Elmi, S. and Erfani Sayyar, R. (2015). Delayed Diagnosis of Hypothyroidism in Children: Report of 3 Cases. Iranian Red Crescent Medical Journal, 17(11), p.e20306. doi:<https://doi.org/10.5812/ircmj.20306>.
- [4] Bernal, J. (2022). Thyroid Hormones in Brain Development and Function. [online] Nih.gov. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK285549/>.
- [5] Bowden, S.A. and Goldis, M. (2021). Congenital Hypothyroidism. PubMed. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK558913/>.
- [6] Leng, O. and Razvi, S. (2019). Hypothyroidism in the older population. Thyroid Research, 12(1). doi:<https://doi.org/10.1186/s13044-019-0063-3>.
- [7] Hunter, I. (2000). Prevalence and aetiology of hypothyroidism in the young. Archives of Disease in Childhood, 83(3), pp.207-210. doi:<https://doi.org/10.1136/adc.83.3.207>.
- [8] Calabria, A. (2024). Hypothyroidism in Infants and Children - Pediatrics. MSD Manual Professional Edition. Available at: <https://www.msdmanuals.com/professional/pediatrics/endocrine-disorders-in-children/hypothyroidism-in-infants-and-children>.
- [9] Rimoin, D., Pyeritz, R. and Korf, B. (2013). Emery and Rimoin's Principles and Practice of Medical Genetics | ScienceDirect. Sciencedirect.com. Available at: <https://www.sciencedirect.com/book/9780123838346/emery-and-rimoin-s-principles-and-practice-of-medical-genetics>.
- [10] Mincer, D.L. and Jialal, I. (2023). Hashimoto Thyroiditis. Nih.gov. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK459262/>.
- [11] Indonesian Ministry of Health. Ministreal Decree No. 25 Issued in 2014. Available at: <https://regulasi.bkpk.kemkes.go.id/detail/ffb9b802-9f1b-4d14-a945-2fa830ac0db0/>
- [12] Indonesian Ministry of Health. Ministreal Decree No. 78 Issued on 2014. Available at: <https://gizikia.kemkes.go.id/assets/file/pedoman/PMK%20No.%2078%20ttg%20Skinnin%20Hipotiroid%20Kongenital.pdf>
- [13] Circular Letter of Indonesian Ministry of Health Issued in 2022. Available at: <https://www.scribd.com/document/600528080/SE-Kewajiban-Pelaksanaan-SHK>
- [14] Jansen, H.I., Boelen, A., Heijboer, A.C., Bruinstroop, E. and Fliers, E. (2023). Hypothyroidism: The difficulty in attributing symptoms to their underlying cause. Frontiers in Endocrinology, 14(1). doi:<https://doi.org/10.3389/fendo.2023.1130661>.

- [15] AlAwaji, M.I. and Alhamwy, R.H. (2023). The Impact of Hypothyroidism on the Quality of Life of Adults in Riyadh, Saudi Arabia. *Cureus*, 15(4). doi:<https://doi.org/10.7759/cureus.37636>.
- [16] Ez, Z., Mahgoub, E., Adly, R., Rabie, B., Elsadik, A., Mohammed, S. and Elazez, A. (2022). Mothers' Knowledge and Practice regarding Care of their Children with Congenital Hypothyroidism. *Journal of Nursing Science -Benha University*, 3(1), p.2022. Available at: https://jnsbu.journals.ekb.eg/article_214285_1406d30efaf3c2567e8a01c4334f4f92.pdf.
- [17] Brito, L.N.S., Andrade, C.L.O. de and Alves, C. de A.D. (2021). ADHESION TO TREATMENT BY CHILDREN WITH CONGENITAL HYPOTHYROIDISM: KNOWLEDGE OF CAREGIVERS IN BAHIA STATE, BRAZIL. *Revista Paulista de Pediatria*, 39. doi:<https://doi.org/10.1590/1984-0462/2021/39/2020074>.
- [18] Kvarnström, K., Westerholm, A., Airaksinen, M. and Liira, H. (2021). Factors Contributing to Medication Adherence in Patients with a Chronic Condition: A Scoping Review of Qualitative Research. *Pharmaceutics*, 13(7). doi:<https://doi.org/10.3390/pharmaceutics13071100>.
- [19] Alofi, R.M., Lujain Alrohaily, Jan, R.A., Alsaedi, S.L., Fai Anas Mahrous and Alreefi, M.M. (2023). Adherence to Levothyroxine Treatment Among Patients With Hypothyroidism in Madinah, Saudi Arabia: A Cross-Sectional Study. *Cureus*. doi:<https://doi.org/10.7759/cureus.40686>.
- [20] Gast, A. and Mathes, T. (2019). Medication Adherence Influencing Factors—an (updated) Overview of Systematic Reviews. *Systematic Reviews*, 8(1). doi:<https://doi.org/10.1186/s13643-019-1014-8>.
- [21] Brito, L.N.S., Andrade, C.L.O. de and Alves, C. de A.D. (2021). ADHESION TO TREATMENT BY CHILDREN WITH CONGENITAL HYPOTHYROIDISM: KNOWLEDGE OF CAREGIVERS IN BAHIA STATE, BRAZIL. *Revista Paulista de Pediatria*, 39. doi:<https://doi.org/10.1590/1984-0462/2021/39/2020074>.
- [22] van der Sluijs Veer, L., Kempers, M.J., Maurice-Stam, H., Last, B.F., Vulsma, T. and Grootenhuis, M.A. (2012). Health-related quality of life and self-worth in 10-year-old children with congenital hypothyroidism diagnosed by neonatal screening. *Child and Adolescent Psychiatry and Mental Health*, 6(1), p.32. doi:<https://doi.org/10.1186/1753-2000-6-32>.
- [23] Molewijk, E., Fliers, E., Koen Dreijerink, Ad van Dooren and Heerdink, R. (2024). Quality of life, daily functioning, and symptoms in hypothyroid patients on thyroid replacement therapy: A Dutch survey. *Journal of Clinical & Translational Endocrinology*, 35, pp.100330–100330. doi:<https://doi.org/10.1016/j.jcte.2024.100330>.
- [24] Albert, B., Heather, N., Cutfield, W., Webster, D., Gunn, A., Jefferies, C., Wouldes, T., Roberts, C., Tregurtha, S., Stewart, H., Mathai, S., Derraik, J. and Hofman, P. (2013). Neurodevelopmental outcomes are normal in congenital hypothyroid children diagnosed early and treated aggressively over the first three years. *International Journal of Pediatric Endocrinology*, 2013(S1). doi:<https://doi.org/10.1186/1687-9856-2013-s1-o23>.
- [25] Ramadhan, A. and Tamilia, M. (2011). Treatment-refractory hypothyroidism. *Canadian Medical Association Journal*, 184(2), pp.205–209. doi:<https://doi.org/10.1503/cmaj.110994>.
- [26] Almeida, C., Antonio, M., Costa, A., Alves, F., Vaneska Spinelli Reuters, Patrícia Oliveira Teixeira, Ferreira, C., Cristina, A., Bianca Oliveira Melo, de, B., Alexandre Buescu and Vaisman, M. (2007). Subclinical hypothyroidism: psychiatric disorders and symptoms. *SciELO*, 29(2), pp.157–159. doi:<https://doi.org/10.1590/s1516-44462007000200013>.