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Original Article

Quality of life in episodic hypoxic children after emergency department or PICU hospitalization

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Abstract

Background Studies on long–term outcomes of hypoxic children after being hospitalized are limited, even though hypoxia is known to affect their quality of life (QoL).

Objective To assess the QoL of children with episodic hypoxia following hospitalization in the emergency department (ED) and pediatric intensive care unit (PICU).

Methods A prospective cohort design study targeting pediatric patients aged 2-7 years with critical illness was conducted at Dr. Cipto Mangunkusumo Hospital. Inclusion criteria are hypoxia patients receiving oxygen therapy, defined from the ratio of partial arterial oxygen pressure and inspired oxygen (PaO_2/FiO_2). The PedsQLTM questionnaire was used to assess QoL at the time of admission and 3 months after hypoxia event. Patients with cerebral palsy, mental retardation, chromosomal abnormalities, liver transplantation, and length of stay ≤24 hours were excluded. Data distribution in numerical form was analyzed using the Kolmogorov-Smirnov test.

Results Forty-six children with a median age of 4 (2-7) years had decreased QoL at 3 months after episodic hypoxia, based on PedsQLTM scores. The physical, emotional, and social domains were significantly decreased ($P<0.01$) compared to QoL at the time of admission. Prior to admission, 78.3% of children had already experienced impaired QoL.

Conclusion Children with episodic hypoxia demonstrated a decline in QoL at 3 months after hypoxia event based on PedsQLTM scores. Specifically, the physical, emotional, and social domains were significantly decreased compared to at the time of admission. **[Paediatr Indones. 2025;65:357-64; DOI: https://doi.org/10.14238/pi65.5.2025.357-64**].

Keywords: *hypoxia; post treatment; pediatrics; quality of life; PedsQLTM*

Hypoxia is a condition of limited oxygen supply at the cellular and tissue levels needed to maintain adequate homeostasis. The term 'hypoxia' can be simplified to decreased oxygen concentration on cells and tissue.[1,2] Several studies have shown that hypoxia is related to changes in brain structure, such as volume atrophy, and reduced gray matter on the amygdala (correlated with behavioral disorders, such as bipolar disorder), hippocampus, anterior cingulate cortex, and prefrontal cortex.[3-5] However, research on long–term outcomes of hypoxic children after hospitalization in the pediatric intensive care unit (PICU) remains limited. Such outcomes may manifest as residual symptoms encompassing physical, cognitive, and behavioral problems. Several studies have shown that up to 50% of individuals experience a decrease in QoL after hypoxia.[6-8]

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Quality of life (QoL) encompasses the physical and psychological characteristics that influence an individual's perception of their environment and satisfaction in life. *Health-Related Quality of Life* (HRQoL) is a subjective perspective on health, including disease and the management of physical, psychological, social functioning, and overall well–being.[9-12] The *World Health Organization* (WHO) established measurement standards of QoL, consisting of physical, mental, and social aspects.[12] *The Pediatric Quality of Life Inventory*™ (PedsQL™), approved by the WHO, is a validated tool for assessing QoL in children and adolescents across various health statuses, including acute and chronic illnesses. The PedsQL™ 4.0 generic module has been used on 25,000 children and parents and translated into 60 languages. The scales demonstrated excellent consistency and clear differentiation among healthy children and those with acute or chronic condition across all age subgroups, showing high internal reliability and strong validity.[13,14] The PedsQL™ 4.0 was translated to Indonesian according to the *Mapi Trust Organization* guidelines for language and cultural adjustments.[13,14]

After PICU hospitalization, children with hypoxia often had lower QoL in social, emotional, physical, and school functioning than healthy children.[6,7,9] A study showed that children using extracorporeal membrane oxygenation (ECMO) or those with congenital heart disease in the cardiac intensive care unit had a lower QoL than healthy population using the PedsQL™.[15] Thus, we aimed to evaluate the QoL of episodic hypoxic children at admission and after hospitalization in the emergency department (ED) and PICU using PedsQL™.

Methods

A cohort study included children hospitalized in Dr. Cipto Mangunkusumo Hospital from November 2021 to April 2022. Subjects were aged 2-7 years with critical disease who received oxygen therapy in the ED and/or PICU. As a national referral center, patients come with various diagnoses. Patients admitted due to respiratory, neurologic, hematologic, or heart disease, as well as those with sepsis, post-operation, and critical illness using opioids and deep sedation were included in this study. Children with cerebral palsy, mental retardation, chromosomal abnormality, liver transplantation, and duration of hospitalization ≤24 hours were excluded. Informed consent was obtained from parents of all subjects. Long-term follow-up on subjects was done during treatment and in follow-up clinics. Data on patient characteristics (age, weight, height, duration of oxygen therapy, and education level) were obtained from medical records.

Hypoxia evaluation was done once at the time of admission by calculating the ratio of partial arterial oxygen pressure and inspired oxygen (PaO_2/FiO_2) (mild ≤300 mmHg; moderate 100-200 mmHg; severe≤100 mmHg) or the ratio of peripheral oxygen saturation and fraction of inspired oxygen (SpO_2/FiO_2) (mild 235-314 mmHg, moderate 150-234 mmHg, or severe <150 mmHg), as a PICU standard. Nutritional status was determined using the 2006 WHO or *2000 Centers for Disease Control and Prevention* (CDC) growth charts.[16,17] Subjects' QoL was assessed by the PedsQL™ questionnaire, which were completed by subjects' parents at admission and 3 months after hypoxia diagnosis. The PedsQL™ consists of 23 items that assess four domains: physical function, emotional function, school function, and social function. Items are reverse scored and transformed to a 0-100 scale (0=100; 1=75; 2=50; 3=25; 4=0), with higher scores representing higher QoL. The score are classified into either decreased or not decreased; impaired (<70) or normal (≥70). The PedsQL™ tool was used to assess the quality of life (QoL) in children with episodic hypoxia. To our knowledge, this is the first study conducted in this specific population.

The pre-and post-QoL data were collected. A normality test was done for numerical data. Paired T-test was used to analyze normally distributed data, while the Wilcoxon test was used for non-normally distributed data. Chi-square test was used to analyze categorical variables and assess associations between groups. Results with $P<0.05$ were considered to be statistically significant. Analyses were performed with *IBM Statistical Product and Service Solutions* (SPSS) *version 26* software. This study was approved by the Ethics Committee of the Faculty of Medicine, University of Indonesia/Dr. Cipto Mangunkusumo Hospital.

Results

Initially, 50 hypoxic children were included in this study. Follow-up monitoring after hospitalization was done in the third month. Four children died during the follow–up period, and were considered dropouts, leaving a total of 46 children for analysis. The median age of subjects was 4 (2-7) years, their median weight was 11.5 (8.2-36.6) kg, and their median height was 91.5 (83-129) cm. Subjects' median duration of O2 therapy was 8 days. Subjects were hospitalized for various underlying diseases, encompassing both respiratory and non-respiratory problems. Most patients had primary diseases such as pneumonia (48.0%), malignancy (35.0%), and/or septic shock (4.3%). Several children had comorbidities such as hydrocephalus on ventriculoperitoneal (VP) shunt, transverse myelitis, epilepsy, thalassemia, or tracheostomy. The general characteristics of study subjects are described in **Table 1**.

The relationship between the PedsQL™ score at the time of admission and subjects' characteristics is described in **Table 2**. Based on PedsQL™ scores, 36 children have impaired QoL, with median age 4 (range 2-7) years. Subjects with normal and impaired QOL had no significant differences in basic characteristics at the time of admission, such as age, duration of O2 therapy, gender, educational level, or nutritional status. Differences between PedsQL™ scores at the time of admission and 3 months after episodic hypoxia were analyzed by Wilcoxon test and are graphically illustrated in **Figure 1**. Notably, there were significant declines in PedsQL™ scores in the physical, emotional, and social domains as well as the overall scores. However, no significant difference was observed in the school domain. **Table 3** shows that significantly more patients had impaired QoL 3 months after hypoxic episodes than at the time of admission.

Analysis of mean PedsQL scores and severity of hypoxic episode using the paired T-test is shown in **Table 4**. Significant decreases in PedsQLTM scores were observed 3 months after hypoxic episode for all 3 categories of hypoxic severity.

Table 1. General characteristics of study subjects

Characteristics	(N=46)
Median age (range), years	4 (2-7)
Median weight (range), kg	11.5 (8.2-36.6)
Median height (range), cm	91.5 (83-129)
Median duration of O2 therapy (range), days	8 (4-41)
Education level, n (%)	
Unschooled	36 (78.3)
Kindergarten	3 (6.5)
Grade 1 elementary school	6 (13.0)
Grade 2 elementary school	1 (2.2)
Nutritional status, n (%)	
Malnutrition	22 (47.9)
Normal nutritio	24 (52.1)
Hypoxia severity, n (%)	
Mild	8 (17.4)
Moderate	19 (41.3)
Severe	19 (41.3)
Underlying disease, n (%)	
Pneumonia	22 (48.0)
Malignancy	16 (35.0)
Septic shock	2 (4.3)
Hypovolemic shock	1 (2.1)
Cardiogenic shock	1 (2.1)
Hemorrhagic shock	2 (4.3)
Tetanus	1 (2.1)
Lung AVM	1 (2.1)

AVM=arteriovenous malformation

Table 2. Analysis of QoL at the time of admission and subjects' characteristics

Parameter	Quality of life (QoL)		P value
	Normal (n=10)	Impaired (n=36)	
Median age (range), years	5 (2–7)	4 (2–7)	0.287*
Median duration of O2 therapy (range), days	6.5 (4–24)	8 (4–41)	0.149*
Gender, n			0.150**
Male	8	18	
Female	2	18	
Education level, n			0.050**
Unschooled	6	30	
Kindergarten	0	3	
Grade 1 elementary school	3	3	
Grade 2 elementary school	1	0	
Nutritional status, n			0.159**
Malnutrition	7	15	
Normal nutrition	3	21	

*Mann–Whitney test (compared to at the time of admission) **Chi-square or Fisher's exact test

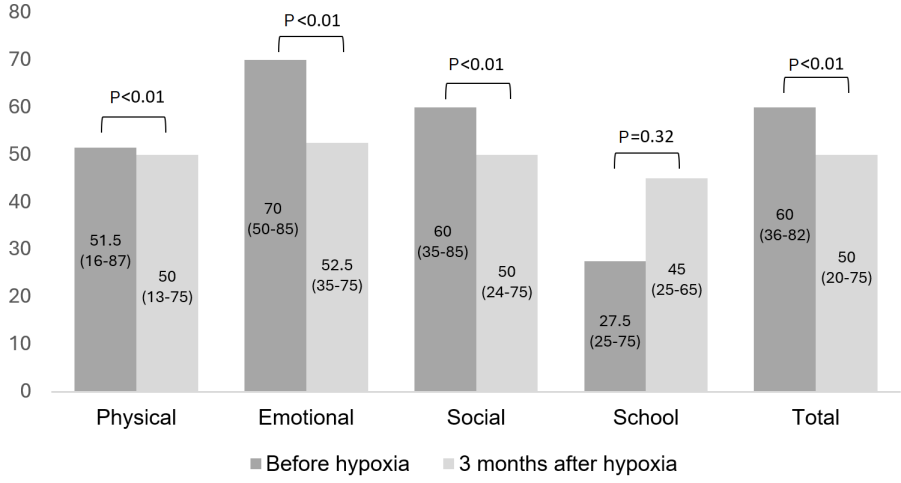

Figure 1. PedsQLTM scores at the time of admission and 3 months after hypoxic episodes, presented in median (range)

Table 3. Analysis of QOL status at the time of admission and 3 months after hypoxia (N=46)

QoL	At admission	3 months after hypoxia	P value
Normal, n (%)	10 (21.7)	3 (6.5)	0.013
Impaired, n (%)	36 (78.3)	43 (93.5)	

Table 4. Analysis of PedsQLTM scores and hypoxic severity at the time of admission and 3 months after hypoxia

Hypoxic severity	(N=46)	Mean PedsQLTM score (SD)		P value
		At admission	3 months after hypoxia	
Mild	8 (17.4)	59.38 (8.26)*	45.75 (11.61)*	<0.01
Moderate	19 (41.3)	63.26 (14.51)*	52.85 (14.48)*	<0.01
Severe	19 (41.3)	55.0 (11.83)*	44.2 (9.75)*	<0.01

Discussion

This pilot study showed a decreased QoL in episodic hypoxic children 3 months after hospitalization in the ED and/or PICU of Dr. Cipto Mangunkusumo Hospital using the PedsQL™ tool. Previous QoL studies using PedsQL™ in Indonesia have been done on children with thalassemia,[18] nephrotic syndrome,[19] acute lymphoblastic lymphoma,[20] HIV,[21] and acyanotic congenital heart disease,[22] but there have been no QoL studies on children with previous hypoxic episodes. At the time of admission, children with normal QoL had a higher median age (5 years) than those with impaired QoL (4 years) in our study. This difference might be attributed to the maturation of organs, systemic function, and adaptation mechanisms to stress. Serebrovskaya et al. stated that autonomic response measurement in older infants had more sympathetic than parasympathetic activation, indicating a better stress response with increasing age.[23]

Subjects' QoL was assessed using the PedsQL™, as collected from parents' reports. At the time of admission, most subjects had impaired QoL (78.3%) due to underlying chronic diseases. A meta-analysis comparing children with and without chronic disease showed that health-related quality of life (HRQOL) was lower in children with chronic conditions, with larger declines in children with spina bifida, osteogenesis imperfecta, cerebral palsy, and neuromuscular disorders.[24] A previous study suggested that children with chronic diseases exhibit lower physical, emotional, social, and school function compared to healthy peers.[25] The relatively high QoL impairment in our study was likely due to the complex and varied cases at the study location, a national referral hospital in the capital city. Further analysis based on hypoxic severity revealed a significant decrease in QoL at the time of admission and 3 months after episodic hypoxia. Despite 78.3% of subjects already having impaired QoL, significant decreases were observed even in mild hypoxia patients after 3 months.

Furthermore, we found a decreased QoL based on PedsQL™ score at 3 months after episodic hypoxia, in concordance with findings from another study on cognitive function and functional disability of patients with trauma, primary oncological and neurological disease, as well as patients who underwent mechanical ventilation, renal transplant, and post-cardiopulmonary resuscitation.[5] Several risk factors influenced this decrease, including disease severity, nutritional status, length of stay, immunization status, comorbidities, and treatment history (antibiotic, steroid, and invasive procedure).[26,27] Our decreased QoL finding was in agreement with a study which found a lower self-reported physical functioning score at three months and one year after PICU discharge.[28] Theoretically, hypoxia reduces pediatric QoL due to inadequate oxygen supply to the brain. The brain relies heavily on oxidative metabolism to maintain function, thus, brain cells are particularly sensitive to hypoxia. When hypoxia occurs, oxidative metabolism decreases, leading to a reduction in ATP supply. Consequently, the brain relocates the energy supply to vital organs and sacrifices other organs.[29-31] Additionally, hypoxia leads to cell damage due to reactive oxygen species (ROS), leading to cellular apoptosis and disrupting cell and organ functions, especially in neuronal cells, which can impair cognitive function, memory, and neuropsychology. This results in abnormalities in brain development, including decreased learning ability, memory, and decision-making skills, as well as increased anxiety, depression, and physical disability.[7,32]

We also found that median PedsQL™ scores at 3 months after hypoxic episode significantly decreased in almost every domain (physical, emotional, social) compared to at the time of admission ($P<0.01$). These findings were similar to several previous studies.[6,7,15] A meta-analysis found that chronic or intermittent hypoxia during development negatively affects behavior and academic achievement.[6] In addition, another study showed that subacute or progressive hypoxic injury causes hippocampal injury and amnesia, which lowers cognitive function, especially in memory, fine motor skills, and executive function ability.[7] In our study, although the median PedsQL™ school domain score increased, the result was not significant, likely due to the small number of school children in our study. Our nutritional status findings were consistent with previous studies, which showed that hypoxia negatively impacted children by impairing QoL, even when their nutritional status was predominantly normal.[6,7,15,27] Due to hypoxia from chronic disease, self-autonomy in daily activities

cannot be achieved; this adversely affects children's learning capabilities.33

Oxygenation is the primary treatment for hypoxia, and appropriate techniques and dosage are crucial to prevent deterioration during critical conditions. Unstable patients require further examinations, such as arterial blood gas analysis, lactate examination, and chest radiography, to determine the appropriate decision regarding the use of oxygen therapy.

This study had strengths and limitations. As a pilot study, this research provides preliminary insight into the QoL of children with episodic hypoxia post-hospitalization. The findings highlight the feasibility of using the PedsQL™ tool in this clinical population and underline the need for further research with a larger sample size to confirm and expand upon these results. The strengths include providing insights into the long–term outcomes of episodic hypoxic children across physical and psychosocial domains. Such studies have been limited, especially in Indonesia. However, the uneven distribution of nutritional status, being predominantly normal, posed a challenge in evaluating its effect on the study's outcomes. Additionally, there were no significant changes in the school domain because of the population age, warranting further analysis in the education subgroup. Lastly, most hypoxic children in our study had pre-existing chronic diseases that impaired their QoL even before they experienced hypoxia. Thus, future research should focus on evaluating the longer-term outcomes of hypoxic children comprehensively.

In conclusion, episodic hypoxic children experience a notable decrease in QoL 3 months after hospitalization compared to their pre-hypoxia status, as assessed by PedsQLTM. The physical, emotional, and social domains were the most affected. Episodic hypoxic children should undergo early screening for physical and psychosocial QoL domains after hospitalization.

Conflict of interest

None declared.

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