

Health-Related Quality of Life Assessment in Children with Cancer Using Pediatric Quality of Life Inventory™ in Ulin Hospital Banjarmasin

ABSTRACT

Aims: Cancer in children can adversely affect their quality of life. Evaluation of health related quality of life (HRQoL) during the process of treatments is important for recognition of acute dysfunction related to therapy and disease. The aims of this study was to assess the HRQoL of cancer children with using the Pediatric Quality of Life Inventory™ (PedsQL™) and to assess the influence of cancer type dan duration of treatment to their quality of life.

Methodology: This cross-sectional study was conducted at the age of 2-18 years of pediatric cancer patient in the Children Haematology Oncology's Ward at the Ulin Hospital Banjarmasin from November to Desember 2022. Subject and their parents were assessed using the PedsQL™ Generic Core Scales and Cancer Module, which consist of parent-report and/ or child-report.

Results: A total number of 59 children participated in this study, mean age 8.4 years old, 38 (64.41%) were male. Non solid tumor represented 62.5% of the sample, with the highest percentage for leukemia (62.71%). Parent had reports about having lower quality of life on the assessment than their children ($p < 0.05$). Children with solid tumor had more problem in procedural anxiety than non solid tumor, and HRQoL children with duration of therapy more than 1 year was significantly better than the children who had duration of therapy less than 1 year on pain and hurt domain ($p < 0.05$).

Conclusion: Children cancer in Ulin Hospital Banjarmasin have low quality of life based on parent reports, especially in school function. Children cancer with solid tumor had more problem in procedural anxiety, and also shorter duration of therapy had more problem in pain and hurt. Special care and psychosocial support to children and their parent is needed to improve their HRQoL during treatment.

Keywords: Health-related quality of life, cancer, children

1. INTRODUCTION

Cancer is a serious disease that threatens the children health in the world, because every year there is an increase in the number of new sufferers. The highest incidence of cancer occurs at the age of 2-3 years and begins to decrease at the age of 9 years, and increases again in adulthood. Cancer in children is more common in males than females. The most common type of cancer found in children is leukemia [1,2].

Although the prospects for survival are currently high for pediatric patients with cancer, encountering this life-threatening condition can severely impair the quality of life for patients and their parents. In addition, the long duration of therapy and the possible side effects of medication are troubling for pediatric patients, parents, and other family members. In the early and intermediate phases of treatment, children may experience unpleasant side effects such as nausea and vomiting, mucositis, fatigue, bleeding and infection. Behavioral and emotional problems in children can arise. The toxic nature of medications can have long-term adverse effects in children including impaired intellectual functioning, neuroendocrine disorders, cardiotoxicity, reproductive disorders and secondary malignancies [3].

Cancer management is not measured based on the child's physical health, but also by achieving a good quality of life spiritually and psycho-socially. Children with cancer can experience physical disabilities, mental disorders, and impaired social functioning as a result of the malignancy of cancer and side effects of treatment [4]. Many children with cancer can enjoy normal lives, but have poor health status and cognitive and emotional disorders [5].

Multidimensional construct composed of the patients' perceptions of the impact of disease and treatment on his or her functioning in a variety of aspects of life, including physical, psychological and social health domains is defined as health-related quality of life (HRQOL). Children with cancer and their families often feel sadness, disappointment, stress, depression, and anxiety so that an assessment of the HRQOL of children with cancer and family members can determine actions that can improve their quality of life [2]. According to a previous study conducted by Anggreini et al, the HRQoL of children with blood cancer is lower than children with solid tumors and the assessment of the HRQoL of children with cancer is lower based on parent report rather than the child report of child's own assessment. Other studies report that children with blood cancer, especially leukemia, initially show a decrease in HRQoL, but will increase with treatment. However, according to the National Cancer Institute, during the late stages of the disease and 6 months before the end of life, children with blood cancer have significantly lower HRQoL compared to patients with solid tumors. The results of Sand et al's research gave the same results as the results of parent report of the HRQoL of children was lower than child report themselves [1].

Assessment of the HRQoL of children with cancer is needed in order to describe the HRQoL of children with cancer. The Pediatric Quality of Life Inventory™ (PedsQL™) is an instrument for measuring the quality of life for children, developed over 15 years by Varni et al (1998). PedsQL™ has 2 modules: generic and specific disease. Generic PedsQL™ is designed for use in various health conditions of children, this instrument can distinguish the QoL of healthy children from children who suffer from an acute or chronic disease. Specific disease PedsQL™ have been developed for malignancy, asthma, arthritis, childhood diabetes, cystic fibrosis, sickle cell disease, cerebral palsy and cardiology [6].

This study aims to compare the HRQoL of children with cancer based on the assessment of parents and children, as well as assess the HRQoL of children with cancer based on the type of cancer (solid tumor and non-solid tumor) and duration of treatment using the PedsQL™ 4.0 Generic Core Scale (Generic Scale) and PedsQL™ 3.0 cancer module (Cancer Scale) questionnaires.

2. MATERIAL AND METHODS

2.1 Study Design

This research is a cross sectional study. The sample cases in this study were all pediatric patients with cancer and their parents at Pediatric Hematology Oncology Ward at Ulin Hospital, Banjarmasin, Indonesia, from November to December 2022, with the same inclusion and exclusion criteria. The inclusion criteria included all pediatric patients with cancer, aged 2-18 years, along with accompanying parents. Exclusion criteria included pediatric patients with mental retardation, cerebral palsy, frail conditions, and parents who did not want to be involved in the study. Data collected by interviewing questionnaire.

2.2 Study Tool

The instrument used in this study was a questionnaire in the form of a PedsQL™ 4.0 Generic Core Scale (Generic Scale) and 3.0 Cancer Module (Cancer Scale).

PedsQL™ 4.0 Generic Core Scale (Generic Scale) is an instrument that can be used and is valid, based on age group, which consists of 23 points grouped with assessment sub-scales including:

- 1) Physical function
- 2) Emotional function
- 3) Social Function
- 4) School Functions

PedsQL™ 3.0 Cancer Module (Cancer Scale) is a multidimensional tool that can be used to assess the impact of disease and management on the quality of life of pediatric patients with cancer, based on age groups, with assessment sub-scales including:

- 1) Pain and aches
- 2) Nausea
- 3) Procedural anxiety
- 4) Treatment anxiety

- 5) Worried
- 6) Cognitive problems
- 7) Perceived physical appearance
- 8) Communication.

Each item of the instrument is consisting of a 5-point Likert scale (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem. Then we transformed the scale to an equivalent score from 0 to 100, where 0 denoted the poorest quality of life and 100 denoted the greatest quality of life. Primary data collection was obtained from filling out the Generic Scale and Cancer Scale questionnaires where the researcher directly interviewed the patient and the patient's parents for 15-20 minutes. We classified the subject to : a) Cancer groups : solid tumor and non-solid tumor. b) Treatment duration : low duration represented less than 1 year and high duration denoted to more than 1 year.

2.3 Data Entry and Analysis

Data were analyzed using SPSS version 27 for Windows. The normality data were first tested with one-sample Kolmogorov-Smirnov test. Continuous variables are presented as mean \pm SD (standard deviation). Comparisons between variables were performed using Mann-Whitney (non parametric). *P* value < 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

In this study, 59 pediatric patients with cancer in the Pediatric Hematology Oncology Room at the Ulin Hospital, Banjarmasin, were involved from November 2022 to December 2022. All study subjects met the inclusion criteria and aged 2 to 18 years, along with their parents who were willing to take part in the study.

Table 1. Demographic and medical characteristics of the study subjects (n=59)

Characteristic	n	%
Gender :		
1. Male	38	64.41
2. Female	21	35.59
Child age in year :		
1. 2-4 year-group	13	22.03
2. 5-7 year-group	18	30.51
3. 8-12 year-group	15	25.42
4. 13-18 year-group	13	22.03
Mean \pm SD (range) :	8,4 \pm 4,5	
Type of Malignancy :		
1. Solid Tumor	22	37.29
- NHL (Non-Hodgkin Lymphoma)	3	
- Nephroblastoma	3	
- Retinoblastoma	5	
- Soft Tissue Carcinoma	2	
- Liposarcoma	1	
- Adenocarcinoma Ovarii	1	
- Adenocarcinoma Testis	1	
- Teratoma	1	
- Ewing Sarcoma	1	
- Squamous Cell Carcinoma	1	
- Rhabdomyosarcoma	1	
- Osteosarcoma	2	

2. Non Solid Tumor	37	62.71
- Acute Lymphoblastic Leukemia (ALL)	31	
- Acute Myeloblastic Leukemia (AML)	6	

Treatment Duration :

1. Low Duration	37	62.71
2. High Duration	22	37.29

Table 1 showed that most of the pediatric patients with cancer in this study were male (64.41%). The mean age of the research subjects was 8.4 ± 4.5 years. The age distribution is even in all age group with mean \pm SD (range) : $8,4 \pm 4,5$. Most of the types of cancer suffered by the subjects of this study were non-solid tumors (ALL & AML) in 37 people (62.71%). The results of this study are the same as Anggreini et al with the average age of all subjects being 7.6 years and Fihriyah et al's research with the highest age group in the 6-10 year age group [1,19]. Non solid tumor (leukemia) is the most common type of cancer found in this study. This is in accordance with data from the Indonesian Cancer Registration System (SriKanDi) for 2005-2007 which shows that the estimated incidence of cancer in children is 9 per 100,000 children with leukemia, which is the highest cancer in children (2.8 per 100,000) [2]. These results are also in line with the results of Adinatha et al's study which showed that 58.5% of pediatric patients with cancer consisted of leukemia, where Acute Lymphoblastic Leukemia was the most common hematological malignancy found in children, covering 41% of the total, followed by other solid tumor types [20].

Table 2. Scale Description for Generic Scale : Child Report and Parent Report

Domain	Parent Report			Child Report			P value
	Mean \pm SD	Min	Max	Mean \pm SD	Min	Max	
1. Physical Function	61.49 \pm 19.68	12.50	96.88	70.65 \pm 22.33	15.63	100.00	0.001*
2. Emotional Function	60.25 \pm 21.20	25.00	100.00	77.28 \pm 19,11	40.00	100.00	<0.001*
3. Social Function	62.71 \pm 19.83	20.00	100.00	71.63 \pm 21.42	15.00	100.00	0.018*
4. School Function	52.67 \pm 15.25	25.00	80.00	66.07 \pm 13.14	45.00	100.00	<0.001*
Total score	59.58 \pm 15.53	19.38	91.72	71,09 \pm 16.41	26.88	100.00	

* = Significant ($p < 0.05$)

Table 2 shows the mean total QoL score from the Generic Scale based on parent report in this study was 59.58 (± 16.75). Meanwhile, the mean total HRQoL score based on child report in this study was 71.09 (± 16.41). The HRQoL domain with the lowest score among the four assessed domains is the School Function, both from parent and child report of Generic Scale. Varni et al reported that the normal HRQoL of children if the total summary score was >70 [21]. The mean value of the total score for children with cancer based on parent report in this study was below the normal HRQoL. Meanwhile, based on the child report, the mean value of the total score is above the normal HRQoL. Research by Brown reports that psychosocial functioning, physical functioning, emotional functioning, social functioning, and school functioning are defined as poor if the score is <80 [22]. When viewed from each assessment domain, all assessment domains are below 80. So it can be said that specifically, the score of physical function, emotional function, social function, and school function is poor. According to Sitaresmi et al, patients will still feel worried about the side effects of chemotherapy and cancer healing because many cancer patients who suffer side effects are broken or die during treatment. They also concerns side effects and chances of recovery, thus impacting the HRQoL of pediatric patients with cancer [23].

Based on statistical tests, the mean values of the four HRQoL domains were assessed using the Generic Scale between parent and child assessments in table 2 found differences in the domain of physical function, emotional function, social function, and school function (P Value: <0.05). The results of this study are in line with research conducted by Susanto et al which stated that there were differences in the assessment of quality of life between parents and children's assessments, where parents' ratings were found to have a lower score than children's assessments [4]. These results are also consistent with the results of Irmawati et al's research which stated that quality Child survival was higher than parents reported for the domains of treatment anxiety, cognitive problems, and the total scale. Meanwhile, procedure anxiety, worry, and pain scored low in both children's and their parents' reports [24]. The results of Sand et al.'s research also yielded the same results with the results of parents' assessments of children's quality of life lower than those of the children themselves [25]. Parents' attention to their children can affect the assessment of the HqoL, where parents who are anxious and depressed tend to score a lower quality of life regardless of what the child actually feels. Assessment of the HqoL of children is better done together with parents and children as a source of information [4].

Table 3. Comparison Means Score of HRQoL (PedsQL™ 3.0 Cancer Modul) between Medical Characteristics: Parent Report

Domain	Solid Tumor (Mean ± SD)	Non Solid Tumor (Mean ± SD)	P Value	Low Duration (Mean ± SD)	High Duration (Mean ± SD)	P Value
1. Pain and Hurt	64.77	65.88	0.949	60.81	73.30	0.037*
2. Nausea	60.00	64.59	0.353	60.68	66.59	0.220
3. Procedural Anxiety	35.23	62.39	0.016*	46.40	62.12	0.132
4. Treatment Anxiety	57.20	72.30	0.111	64.41	70.45	0.651
5. Worry	73.11	60.59	0.259	60.59	73.11	0.226
6. Cognitive Problem	63.39	55.90	0.292	59.80	56.84	0.504
7. Perceived physical appear	58.71	63.51	0.619	59.23	65.91	0.597
8. Communication	52.27	57.66	0.122	55.86	55.30	0.380

* = Significant ($p < 0.05$)

Table 3 demonstrated the HQoL of children with cancer between solid tumors and non-solid tumors, and also between treatment duration. Eight assessments were assessed using the Cancer Scale with the lowest average results in children with solid tumors in the domain of procedural anxiety, while the lowest average in children with non-solid tumors was in the domain of cognitive problems. It was found that there was a difference in the procedural anxiety domain (P Value < 0.05) between pediatric patients with solid and non-solid cancer, where pediatric patients with solid cancer had a higher level of procedural anxiety than non-solid types of cancer. This is because the procedural therapy that must be undertaken by pediatric patients with solid cancer is more diverse than non-solid, including surgery and radiotherapy. So that children with solid cancer tend to be more anxious about the procedures they are undergoing.

Hilda et al's study found that there was no significant difference in the assessment of HQoL of pediatric patients with cancer between hematological malignancies and solid cancer [26]. Meanwhile, the results of Susanto et al's study obtained the results that the assessment of HQoL in pediatric patients with leukemia was reported to be better than physical function and psychosocial compared to lymphoma and solid tumors [4]. Research Landolt et al and Meeske et al also stated that patients with brain tumors reported lower than patients with leukemia. Differences in protocols in each institution can also affect HQoL of pediatric patients with cancer [27,28]. These results are different from the study of Anggreini et al who obtained results that HQoL of children with blood cancer was lower than solid tumors [1]. Other studies reported that children with blood cancer, especially leukemia, initially showed a decrease in HQoL, but would increase with time of medication. However, according to the National Cancer Institute, during the late stages of the disease and 6 months before the end of life, children diagnosed with blood cancer have significantly lower quality of life compared to patients with solid tumors [29].

Table 3 also demonstrated HQoL assessment of children with cancer between treatment duration < 1 year and > 1 year. Eight domains assessed using the Cancer Scale showed higher HQoL scores for children with duration of treatment > 1 year compared to children with cancer who underwent treatment duration < 1 year, except for the domains of cognitive problems and communication problems. Based on statistical tests the mean value of parent report of eight domains assessed by duration of treatment found that there was a significant difference in the pain and hurt domain (P Value < 0.05), but there was no significant difference in the other domains. This analysis shows that pediatric patients with cancer who have undergone treatment for less than 1 year have higher pain and hurt problems compared to patients who have undergone treatment for more than 1 year.

This study is in line with the research of Susanto et al who also obtained the result that the duration of the disease affects the HQoL of pediatric patients with cancer. The study said emotional function appeared better in the group with a longer treatment period. In this condition, the patient and his parents may have entered a better acceptance phase and solved the problems they faced together [4]. Vlachioti et al stated that children with leukemia, especially during the initial treatment period after an established diagnosis and in the first month of therapy, have a major impact on their HQoL. This is due to the aggressive chemotherapy protocol and the complications of the chemotherapy. Interestingly, there was a marked improvement in the HQoL of pediatric patients with leukemia, observed during the first year after the diagnosis of leukemia. Contrary to the case of children with brain tumors, the chemotherapy they underwent was not too aggressive, so their HQoL was not greatly affected during the initial period of cancer diagnosis and the first year of treatment. HQoL

will begin to decline after 1 year of treatment where there is a decrease in physical, cognitive, emotional, and social functions [29].

Cancer is an unintentional cause of death in children. Data taken from the International Incident of Childhood Cancer (IARC) total incidence rates usually range between 70-160 per million children. The most common type of childhood cancer is leukemia, which comprises about 80% of childhood cancers in most populations [30]. Assessment of HQoL in children with chronic diseases, one of which is cancer, is still not routinely carried out in Indonesia. In fact, cancer management is not measured based on the child's physical health alone, but also by achieving a good overall quality of life.⁴ Many children who suffer from cancer can enjoy a normal life, but their health status is poor and cognitive and emotional disturbances are found [20].

In pediatric patients with cancer, the disease and the effects of the therapy given will affect HQoL of the child and family so that the assessment of HQoL in patients and families is very important. The PedsQL™ instrument is one of the recommended and validated tools for assessing HQoL of children with cancer based on the assessment of the parents and the child himself. Giving cancer therapy in childhood can cause physical, social, emotional and school problems so that it can have an impact on quality of life which is affected by health problems [19,31]. The participation of pediatric patients with cancer and their parents in decision making and treatment planning is increasingly being developed. Assessment of HQoL of pediatric patients with cancer is an important thing to do. Their views regarding physical, psycho-emotional, and social functioning may be useful for the health facility concerned in improving health services.

4. CONCLUSION

There are differences in the HQoL of children with cancer based on parent and child report in the four domains assessed using the Generic Scale, where the mean value of the total HQoL score for children with cancer based on parent report is poor. Meanwhile, based on the child's assessment, the average score for the total HQoL is good.

In the study assessed using the Cancer Scale, it was found that the lowest average score in the group of children with solid tumor cancer was the domain of procedural anxiety, while the lowest average in children with non-solid tumors was the domain of cognitive problems. There is no difference in the HQoL of children with cancer based on the type of cancer (solid and non-solid tumor) in the eight domains assessed using the Cancer Scale.

In this study there were limitations to the number of samples, the small variation in the characteristics of the research subjects, and the short time spent on the research. Further research is needed to look for other factors that we have not examined which are related to the HQoL of pediatric patients with cancer.

CONSENT

Informed and written consent was taken from all parents of the children in the study with the guidelines of ethical committee.

ETHICAL APPROVAL

Ethical approval was obtained from the Institutional Review Board/Ethics Committee at Ulin Hospital Banjarmasin, Indonesia.

REFERENCES

1. Anggreini MS, Supit DM. Quality of Life in Children with Cancer using Pediatric Quality of Life Inventory in Abdul Wahab Sjahranie Hospital Samarinda. *Sari Pediatri*. 2022;24(3):151–6.
2. Kementerian Kesehatan RI. Pedoman penemuan dini kanker pada anak. Kementerian Kesehatan RI; 2011.h.1-49. Indonesian.

3. Savage EO, Riordan A, and Hughes. Quality of life in children with acute lymphoblastic leukaemia - A systematic review. *European Journal of Oncology Nursing*. 2009;13:36-48.
4. Susanto IY, Soedjatmiko, and Putra ST. Assessment of health-related quality of life in children with cancer using PedsQLTM (a preliminary study). *Paediatrica Indonesiana*. 2009;49:330-46.
5. Pickard AS, Topfer LA, and Feeny DH. A Structured Review of Studies on Health-Related Quality of Life and Economic Evaluation in Pediatric Acute Lymphoblastic Leukemia. *Natl Cancer Inst Monogr*. 2004;33:102–125.
6. Varni JW, Seid M, Kurtin PS. Pediatric health-related quality of life measurement technology : A Guide for Health Care Decision Makers. *JCOM* 1999;6:33-40.
7. American Cancer Society. What Is Cancer? 2022. Accessed 12 November 2022. Available: <https://www.cancer.org/treatment/understanding-your-diagnosis/what-is-cancer.html>
8. Feliciano SV, Santos MO, Pomdo-de-Oliveira MS. Cancer Incidence and Mortality among Children and Adolescents: a Narrative Review. *Revista Brasileira de Cancerologia* 2018;64(3):385-391
9. American Cancer Society. What Are the Differences Between Cancers in Adults and Children? 2022. Accessed 12 November 2022. Available: <https://www.cancer.org/cancer/cancer-in-children/differences-adults-children.html>
10. Kliegman RM, Geme JS. *Nelson Textbook of Pediatrics*. Elsevier S. Philadelphia: 2011.
11. Lupo PJ, Spector LG. Cancer Progress and Priorities: Childhood Cancer. *Cancer Epidemiol Biomarkers Prev* 2020;29:1081–94.
12. Karimi M and Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference?. *Pharmacoeconomics* 2016;34(7):645-9.
13. Sekartini R, Maharani P. Penilaian Kualitas Hidup Anak : Aspek Penting yang Sering Terlewatkan. IDAI 2015. Accessed 12 November 2022. Available: <https://www.idai.or.id/artikel/seputar-kesehatan-anak/penilaian-kualitas-hidup-anak-aspek-penting-yang-sering-terlewatkan>.
14. Eiser C, Morse R. A Review of Measures of Quality of Life for Children. *Archives of Disease in Childhood* 2001;84(3): 205-11.
15. Muhaimin I, Utomo B, Utoyo DB, Kurniati N, Anugrahini T, Utami F, dan Zuliatie E. Instrumen Pengukuran Kualitas Hidup Anak Terinfeksi HIY. *Jurnal Kesehatan Masyarakat Nasional* 2011; 6(3):726-32.
16. Varni IW, Seid M, Rode CA. The PedsQL™: Measurement Model for the Pediatric Quality of Life Inventory. *Medical Care* 1999;37(2):726-39.
17. Hilda, Lubis B, Hakimi, Siregar OR. Quality of Life in Children with Cancer and Their Normal Siblings. *Paediatr Indones* 2015;55(5):243-7.
18. Varni JW. The PedsQL™ Measurement Model for The Pediatric Quality of Life Inventory™. Accessed 12 November 2022. Available: http://pedsq.org/about_pedsq.html
19. Fithriyah I, Konginan A, Maramis M, Mahajuddin M, Muhdi N. The Epidemiology of Pediatric Cancer in The Palliative Care Unit at Dr. Soetomo General Hospital Surabaya. *J Berk Epidemiol* 2020;8:65-71.
20. Aditnatha Y dan Ariawati K. Gambaran Karakteristik Kanker Anak di RSUP Sanglah, Bali, Indonesia Periode 2008-2017. *Intisari Sains Medis* 2020;11(2):575-81.
21. Varni JW, Burwinkle TM, Seid M. The PedsQL as a Pediatric Patient-Reported Outcome: Reliability and Validity of the PedsQL Measurement Model in 25.000 Children. *Expert Rev Pharmacoecon Outcomes Res* 2005;5:705-19.
22. Brown L. The Healthy Families Program Health Status Assessment (PedsQL) Final Report. Sacramento, CA : Managed Risk Medical Insurance Board; 2004.
23. Sitaresmi MN, Mostert S, Gundy CM, Sutaryo, Veerman AJP. Health-related Quality of Life Assessment in Indonesian Childhood Acute Lymphoblastic Leukemia. *Health and Quality of Life Outcomes* 2008;6:96.
24. Irmawati M, Irwanto, Cahyadi A. Penilaian Kualitas Hidup Anak Penderita Kanker. *Jurnal Ners* 2012;7(2):148–52.
25. Sand P, Kleiberg AN, Kljajić M, Lannering B. The Reliability of The Health Related Quality of Life Questionnaire PedsQL 3.0 Cancer Module in a Sample of Swedish Children. *BMC Pediatr*. 2020;20:1-8.
26. Hilda, Lubis B, Hakimi, Siregar OR. Quality of Life in Children with Cancer and Their Normal Siblings. *Paediatr Indones* 2015;55(5):243-7.
27. Landolt M, Vollrath M, Niggli F. Health-Related Quality of Life in Children with Newly Diagnosed Cancer: a One Year Follow-up Study. *Health Qual Life Ourcomes* 2006;4:63-70.

28. Meeske K, Katz ER, Palmer SN, Burwinkle T, Varni JW. Parent Proxy-reported Health-related Quality of Life and Fatigue in Pediatric Patients Diagnosed with Brain Tumors and Acute Lymphoblastic Leukemia. *Cancer* 2004;101:16-25.
29. Vlachioti E, Matziou V, Perdikaris P, dkk. Assessment of Quality of Life of Children and Adolescents with Cancer During Their Treatment. *Jpn J Clin Oncol.* 2016;46:453-61.
30. Stiller, CA. Epidemiology and Genetics of Childhood Cancer. *Oncogene* 2004;23:6429-44.
31. Hegazy A, Al Bar H, Alamri SH, Almahmoudi FA, Al Ghamdi WS, Abdulgader E. Quality of Life in Pediatric Cancer Patients. *J Adv Med Med Res* 2019;30:1-11.

UNDER PEER REVIEW