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OVERVIEW OF HEMOGLOBIN VALUE ON PRE AND POST RADIOTHERAPY IN PEDIATRIC CANCER PATIENTS: STUDY AT RSUP DR. KARIADI SEMARANG

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ABSTRACT

Background: Cancer is a deadly disease that gets less attention in childhood. One of the manifestations of cancer in children is anemia. As many as 50% of cancer patients will experience anemia. Radiotherapy is one of the last treatments for various types of cancer. Radiotherapy can affect hematopoiesis, thereby reducing hemoglobin production. **Aim:** To describe pre and post-therapy Hb levels in pediatric cancer patients undergoing radiotherapy. **Methods:** This research is a descriptive study with a Cross-sectional design using electronic medical records of as many as seventy eight people and then collecting data in the form of age, gender, patient diagnosis, and hemoglobin levels before and after radiotherapy. **Results:** Pre-radiotherapy and post-radiotherapy hemoglobin levels decreased significantly between the two groups ($p<0.05$). **Conclusion:** There is a significant difference between pre- and post-radiotherapy reduced hemoglobin levels in pediatric cancer patients undergoing radiotherapy.

INTRODUCTION

Cancer is a condition of abnormal cell division in malignant tissue, so it is a deadly disease because it can cause physical and psychological changes during cancer formation and the treatment period.[1,2]

Cancer received less attention in childhood. Cancers that occur in children are grouped by age under 19 years. Based on data from the Royal College of Radiologists and the Children's Cancer and Leukemia Group, there are 1800 cases of cancer in children in the UK that do not receive special attention for treatment.[3] Types of cancer that occur in children are divided into two types, namely blood cancers such as white blood cell cancer (leukemia) and cancers that form from solid tumors such as central nervous system cancer (medulloblastoma), eye cancer (retinoblastoma), and bone cancer (osteosarcoma). The prevalence can be different in each country.[4]

Cancer in children can cause specific clinical manifestations, one of which is anemia. Based on research conducted by Gordon S, more than 50% of cancer patients in children tend to experience anemia, either because of the malignancy itself or after therapy.[5] Anemia is a condition of decreased hemoglobin (Hb) levels in the blood with normal Hb levels around 12 g/dL at 6-11 years old. Anemia in cancer can occur due to the increased production of cytokines in the immune system. Increased cytokines will impact the suppression of erythroid progenitors, iron metabolism, and decreased erythropoietin formation. This event will end in reduced Hb formation and rapid destruction of blood cells resulting in anemia. Anemia causes the transport of oxygen to the tissues to be reduced. Tissue deprived of oxygen is called hypoxia. Tissue hypoxia causes adverse effects on patients because it can accelerate tumor progression and tumor growth becomes aggressive.[6]

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Radiotherapy is a last resort in treating certain types of childhood cancer. Solid tumors such as Osteosarcoma prioritize surgery by looking at the child's age, and blood cancers such as Acute Lymphocytic Leukemia (ALL) prioritize chemotherapy. Radiotherapy is often used in some cases of retinoblastoma in one eye, which is thought to save the other healthy eye.[7,8]

The difference in therapy in various types of cancer is influenced by how radiotherapy works, where radiotherapy works with electromagnetic radiation, which forms a free radical along with oxygen to interact with tumor cells and damage their DNA.[5] Radiotherapy uses oxygen as a radiosensitizer, which plays a vital role in therapy, so radiotherapy's effectiveness decreases in hypoxic conditions.[9] Based on data from the Japanese Cancer Association, of the 62 patients with an average age of 10 years who were identified as having rhabdomyosarcoma of the head and neck, only 17 patients were successfully treated for a period of 5 years.[10]

Not only that, radiotherapy affects normal cells around cancer so that it can interfere with the development of these cells.[2] This can affect the growth and development of children, especially nerve cells that develop most optimally in childhood. Radiotherapy must have a particular dose to properly treat cancer cells and reduce the number of normal cells affected by the surrounding therapy.[11]

In addition to the two things already mentioned, radiotherapy also affects hematopoiesis because it can inhibit the work of bone marrow cells in producing hemoglobin but does not directly affect Hb levels already in the blood, so further research is needed.[12]

Research on the description of hemoglobin levels in pediatric cancer patients with radiotherapy treatment needs to be done to see the initial state of hemoglobin before radiotherapy is carried out. Likewise, in the post-radiotherapy situation, hemoglobin levels are essential to know the relationship with anemia, which can affect the patient's general condition in the treatment process.

Hemoglobin levels of pediatric cancer patients undergoing radiotherapy at RSUP Dr. Kariadi have never been done before. Therefore, this description of hemoglobin levels needs to be done as an early effort to detect anemia which is helpful for pediatric cancer patients before and after undergoing therapy.

This study will investigate the description of Hb levels before and after radiotherapy in pediatric cancer patients undergoing radiotherapy. Therefore, this study aims to describe pre and post-therapy Hb levels in pediatric cancer patients undergoing radiotherapy. This study is expected to help analyze the condition of anemia in pediatric cancer patients before and after undergoing radiotherapy.

METHODS

This reseacrh is a descriptive study with a Cross-Sectional design. The study was conducted in April - May 2022 at Dr. Kariadi Hospital Semarang and has obtained approval from the Diponegoro University Health Research Ethics Commission as stated in the Ethics Statement Letter No.102/EC/KEPK/FK-UNDIP/IV/2022. The accessible population of this study was all pediatric cancer patients at Dr. Kariadi Hospital Semarang from January 2019 - December 2021.

The sample size was 78 people using total sampling technique with inclusion criteria of patients aged 0-18 years, treated with radiotherapy, and the type of cancer originated from solid organs. The exclusion criteria in this study were childhood cancer patients who experienced two types of cancer simultaneously and childhood cancer patients who underwent other therapies simultaneously with radiotherapy, for example chemotherapy.

The study was conducted by collecting data in the form of age, gender, patient diagnosis, and hemoglobin levels before and after radiotherapy. Statistical analysis using SPSS with normality test using Kolmogorov Smirnov because the sample is >50. Furthermore, a paired sample t-test was conducted to determine whether there was a significant difference in hemoglobin levels before and after radiotherapy.

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RESULTS

A total of 78 patient were included in the study. The characteristics of the research subjects can be seen in Table 1.

Table 1. Characteristics of Research Subjects

Variable	n	%
Gender		
Men	50	64%
Women	28	36%
Age (years)		
1-9	46	59%
10-18	32	41%
Pre-radiotherapy hemoglobin levels(mg/dL)		
<12 mg/dL	27	35%
>12 mg/dL	51	65%
Post-radiotherapy hemoglobin levels(mg/dL)		
<12 mg/dL	49	63%
>12 mg/dL	29	37%

Based on the frequency distribution data in Table 1, it shows that there were more male research subjects than female subjects with a wider age range at 1-9 years.

Based on patient diagnosis, the majority of paediatric cancer patients who underwent radiotherapy were diagnosed with medulloblastoma with 13 (17%) patients, followed by glioma with 8 (10%) patients (Table 2).

Table 2. Characteristics of patient diagnosis distribution

Diagnosis	N	Diagnosis	N
Meduloblastoma	13	Basal cell carcinoma	2
Glioma	8	Non-Hodgkin lymphoma	2
Craniopharyngioma	6	Osteosarcoma	2
Retinoblastoma	6	PNET	2
Astrositoma	5	SOL	2
Ependimioma	5	Ewing sarcoma	1
Pinealoblastoma	4	Breast cancer	1
Neuroblastoma	3	Adenoid Carcinoma	1
Rhabdomyosarcoma	3	Oligodendroglioma	1
Wilms tumour	3	Alveolar sarcoma	1
Chordoma	2	Sinovial sarcoma	1
Germinoma	2	Mediastinum Tumour	1

The mean values are shown in Table 3. It is known that the pre-radiotherapy hemoglobin level has a mean value of 12.5 mg/dL. While the post-radiotherapy hemoglobin level has a mean value of 11.6 mg/dL.

Table 3. Relationship test results between pre and post-radiotherapy hemoglobin levels

Group	Mean ± SD	p
Pre-radiotherapy	12.5±2.00	0.002
Post-radiotherapy	11.6±2.14	

Description: *Significant p<0.05

The paired sample t-test found the difference in hemoglobin levels before and after radiotherapy was significant (p<0.05).

DISCUSSION

Based on the results of the study, it shows that the male gender is dominant in experiencing cancer in childhood. This is in accordance with research conducted by Yohanes Adhinata at RSUP Sanglah Bali which stated that childhood cancer patients were more common in men as many as 54% of the 410 patients. Patients at RSUP Sanglah Bali had a diagnosis of acute lymphoblastic leukemia, retinoblastoma and medulloblastoma.[13]

The male dominance in pediatric patients is also proven by Lindsay M's research from the SEER 18 data collection. Of the 71,609 cases, 53% were male with an incidence ratio of 1.19, where most types of cancer are dominated by men except nephroblastoma and malignant melanoma. This is due to hormonal variations such as rapid growth hormone formation in men which causes boys to be diagnosed with cancer more often than girls.[14]

The results of research that has been conducted related to the age of childhood cancer patients show that the majority of patients are aged 7-9 years and the least are aged 16-18 years. The data is in accordance with research conducted by Fithriyah at Dr. Soetomo Hospital which states that the number of childhood cancer patients in the age range of 1-5 years is almost the same as the number of patients in the age range of 6-10 years and 11-15 years, with the number of patients in the age range of 16-18 years being the least.[15]

The results of Sri Mulatsih's research from the Yogyakarta Pediatric Cancer Registry data on pediatric cancer patients are slightly different from the results of this study. Sri Mulatsih's research shows that out of 2,441 patients, the majority of patients were aged 1-5 years (49.7%) followed by patients aged 6-9 years (18.5%) but the appropriate ones are patients aged over 15 years who have the least data. This is due to the existence of BPJS which was valid for the last 5 years before the study was conducted so that many pediatric

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patients were diagnosed with cancer during that period.[16]

Based on the research conducted, from 78 samples, the patient's hemoglobin level decreased from 12.5 mg/dL to 11.6 mg/dL. Furthermore, the data went through the significance test phase with the t-test. The t-test was conducted to test the truth of the research hypothesis regarding the effect of each variable, in this case, the hemoglobin levels before and after radiotherapy. In the t-test, the mean is calculated from the data that has been processed using the SPSS application. The mean obtained is then viewed in the coefficients table for its significance value. Based on the data, the significance value was 0.002, where the value met $p<0.05$, so there was a significant change between pre and post-radiotherapy hemoglobin levels in pediatric cancer patients.[20] Significant in this case means that decreased hemoglobin levels occur in all pediatric cancer patients. From the tests, it can be concluded that there is a recurrence of the theory, which states that the hemoglobin level of pediatric cancer patients undergoing radiotherapy will decrease.

The results of this study are by the findings put forward by Ni Nyoman Ratini at RSUP Sanglah that there is a decrease in hemoglobin levels between pre and post-radiotherapy. Hemoglobin levels in cervical cancer patients decreased rapidly after administration of more than 3000 cGy. This is because radiation can affect the division of pluripotential stem cells in the bone marrow. Pluripotential stem cells play a role in hematopoiesis so that there is suppression of blood cell formation and the number of blood components, including hemoglobin will decrease.[17]

Donny also conducted a similar study on nasopharyngeal cancer patients at RSUP Dr. Kariadi. The patient's hemoglobin level decreased from 11 mg/dL to 8.8 mg/dL after radiotherapy at a dose of 6000 rad. The data obtained were then analyzed using the Post Hoc Test (LSD). The significant result was a significant decrease in hemoglobin levels at each radiation dose except at 2000 and 4000 rad doses. This proves the theory presented by researchers that radiotherapy will affect organs that work in hematopoiesis, such as bone marrow and spleen. Radiotherapy can also directly affect hemoglobin production by inhibiting stem cell mitosis. The amount of indirect hemoglobin decreases significantly when erythrocytes are not radiosensitive because erythrocytes have a longer lifespan than other blood cells. Still, radiation can reduce iron uptake resulting in a reduction in hemoglobin formation.[18]

This study proved that pediatric cancer patients who underwent radiotherapy would experience a decrease in hemoglobin levels. According to Wulandari, radiotherapy damages hemoglobin-forming cells and hemoglobin itself. Radiotherapy works by inducing damage to parts of DNA, for example, single-strand breaks (SSB), double-strand breaks (DSB), base damage, DNA cross-linking, or a local combination of these damages. This DNA damage causes mutations, chromosomal abrasion, and changes in activity, up to apoptosis. Radiotherapy indirectly causes interphase death of blood cells.[19]

CONCLUSION

There is a significant difference in the picture of pre- and post-radiotherapy hemoglobin levels which decrease in pediatric cancer patients undergoing radiotherapy. Hemoglobin is a parameter that can be used to monitor anemia after cancer radiotherapy in children.

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