Long-term effects of chemotherapy in children with cancer

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Long-term effects of chemotherapy in children with cancer

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Abstract

Background: Cancer is a non-communicable disease that poses a health problem worldwide, including in Indonesia, affecting not only adults but also children. The most commonly used cancer therapy is chemotherapy, yet it still has effects that can impact children both physically and psychologically
Purpose: To identify the frequently experienced impacts of chemotherapy on children based on assessments conducted by parents at the "Estella" Children's Cancer Center, Prof. Dr. Kandou Hospital.
Method: This research utilized a quantitative descriptive method. The sampling technique employed was consecutive sampling, involving a total of 41 respondents. The study was conducted during the period of July-August 2023. Data was gathered using the Chemotherapy-Symptom Assessment Scale (C-SAS), comprising 23 questions. Data analysis utilized frequency distribution.
Results: The research findings indicated that 80.5% of children experience alopecia (hair loss), and 80% of children considered nausea and vomiting as the most disruptive physical effects of chemotherapy, with mood swings being identified as the most disruptive psychological effect.
Conclusion: Parents need to pay attention to the effects of chemotherapy to enhance the quality of life for their children during their chemotherapy treatments. It is hoped that the results of this research can be utilized by parents to manage the effects of chemotherapy on pediatric cancer patients.

Keywords: Cancer; Children; Effect of Chemotherapy.

INTRODUCTION

Cancer is one of the non-communicable diseases that is a public health concern globally, including in Indonesia. It affects not only adults but also children. The number of child cancer patients comprises around 3%-5% of all cancer cases and stands as the second largest cause of death for children aged 5-14 years. Every year, more than 175,000 children worldwide are diagnosed with cancer, and an estimated 90,000 among them succumb to it, resulting in a cancer mortality rate of 50%-60% (Ministry of Health of the Republic of Indonesia, 2020). There are several common types of cancer among children aged 0-18 years, namely leukemia (11.6%), brain tumors (7.02%), *osteosarcoma* (4.41%), *nasopharyngeal carcinoma* (3.5%), *lymphoma* (2.83%), *retinoblastoma* (2.8%), soft tissue and solid tumors (2.4%), *hepatoma* (1.81%), wilms tumor/kidney cancer (1.58%), and testicular cancer (1.25%) (Anggreini & Supit, 2022).

Cancer treatment in children includes chemotherapy, biological therapy, radiation, *cryotherapy*, bone marrow transplantation, and peripheral blood stem cell transplantation. However, the most common treatment for children is chemotherapy. Continuous chemotherapy treatment, apart from its therapeutic effects, can also lead to side effects. These side effects encompass physical problems such as infections, bleeding, fatigue,

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weakness, hair loss, *mucositis*, nausea, vomiting, diarrhea, constipation, decreased appetite, *neuropathy*, *hemorrhagic cystitis*, urinary retention, facial swelling due to fluid retention, and sleep disturbances. Besides physical issues, children undergoing chemotherapy also experience psychosocial problems like mood disturbances, anxiety, loss of confidence, decreased self-perception, depression, and behavioral changes that impact a child's reluctance to attend school. These effects influence the physical, psychological, and social aspects, affecting the overall quality of life for children (Ranailla, Mardhiyah, & Hidayati, 2016).

Chemotherapy is the primary treatment for children with cancer. Chemotherapy has proven to help around 85% of children survive for 5 years, and some among them even achieve complete recovery. The goal of chemotherapy is to alleviate tumor-related symptoms, enhance overall quality of life, and prolong the time before tumor progression (Katzung, 2012).

RESEARCH METHOD

This research was conducted at the "Estella" Children's Cancer Center, Prof. R.D Kandou Hospital in Manado from June to August 2023. The study follows a quantitative approach with a quantitative descriptive research design. The research sample consisted of 41 parents of children diagnosed with cancer and undergoing chemotherapy. The research measurement instrument utilized the Chemotherapy-Symptom Assessment Scale (C-SAS) questionnaire for Parents, comprising 24 statements about the impact of chemotherapy on children using the Gutman scale (Brown, Sitzia, Richardson, Hughes, Hannon, & Oakley, 2001). The questionnaire was completed by parents in the presence of the researcher during the questionnaire administration. From the 24 statements, each respondent received a score ranging from 0 to 24. The accumulation of these scores was categorized into two groups: scores ≤12 indicated mild impact, while scores ranging from 13 to 18 indicated severe impact. Data analysis was conducted using descriptive statistics presented in tabular form. This research obtained approval and recommendation from the Ethics Commission of the Prof. Dr. Prof Dr Roembajan Deil Kandou Manado Central Public Hospital, indicated by certificate No. 082/ECKEPK-KANDOUVV2023, dated June 23, 2023.

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RESEARCH RESULTS

Table 1. Characteristics of Respondents (N=41)

Variables	Results
Age (n/%)	
(Mean ±SD)(Range)(Year)	(6.93 ±4.268)(1-18)(Year)
0-4	13/31.7
5-7	11/26.8
8-12	13/31.7
13-18	4/9.8
Gender	
Male	28/68.3
Female	13/31.7
Types of Cancer	
CML (*chronic myeloid leukemia*)	31/75.6
Wilms tumor (*nephroblastoma*)	2/4.9
Eye cancer(*retinoblastoma*)	2/4.9
Blood cancer(*lymphoma*)	2/4.9
Ovarian tumor(*ovarian tumor*)	2/4.9
Benign tumor(*teratoma*)	1/2.4
Bone cancer(*osteosarcoma*)	1/2.4
Cancer Diagnosis	
≤1 year	27/65.9
>1 year	14/34.1
Last Chemotherapy	
0-1 week	22/53.6
1-2 week	12/29.3
2-3 week	5/12.2
3-4 week	2/4.9

In Table 1, the data shows a mean of 6.93 with a standard deviation of 4.268 across an age range of 1 - 18 years. Furthermore, respondents aged 0-4 years accounted for 31.7%, those aged 5-7 years accounted for 26.8%, those aged 8-12 years accounted for 31.7%, and those aged 13-18 years accounted for 9.8%.

Regarding gender distribution, male respondents comprised 68.3%, while female respondents comprised 31.7%. Regarding the types of cancer among respondents, those suffering from Chronic Myeloid Leukemia (CML) accounted for 75.6%, Wilms tumor (nephroblastoma) accounted for 4.9%, Retinoblastoma (eye cancer) accounted for 4.9%, Lymphoma (blood cancer) accounted for 4.9%, Ovarian tumor (ovarian tumor) accounted for 4.9%, Teratoma (benign tumor) accounted for 2.4%, and Osteosarcoma (bone cancer) accounted for 2.4%.

In terms of the time when cancer was diagnosed for the first time, respondents diagnosed within ≤1 year constituted 65.9%, while those diagnosed >1 year constituted 34.1%.

Additionally, concerning the time since the last chemotherapy session among respondents, those within the 0-1 week bracket accounted for 53.6%, 1-2 weeks accounted for 29.3%, 2-3 weeks accounted for 12.2%, and 3-4 weeks accounted for 4.9%.

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Table 2. The effect of chemotherapy in children with cancer (N=41)

Parameters	Results (f/%)
Hair loss	33/80.50
Mood swings	32/78.05
Nausea and vomiting	32/78.05
Weak and fatigue	32/78.05
Decreased appetite	28/68.29
Weight loss	28/68.29
Experiencing skin and nail issues such as dry skin, darkening, and changes in nails.	21/51.22
Sleep disturbances	19/46.34
Pain	19/46.34
Mouth and throat problems	19/46.34
Having infection symptoms such as fever, cough and flu	18/43.90
Short breath	14/34.15
Diarrhea	14/34.15
Constipation	14/34.15
Tingling sensation in the hands and feet	11/26.83
Worrisome and anxiety	5/12.20

In Table 2, the impact of chemotherapy is outlined as follows: experiencing hair loss at 80.50%, changes in mood at 78.05%, pre- and post-chemotherapy nausea and vomiting at 78.05%, feeling weak and fatigued at 78.05%, decreased appetite at 68.29%, weight loss at 68.29%, skin and nail issues such as dry and darkened skin at 51.22%, sleep disturbances at 46.34%, experiencing pain at 46.34%, having mouth and throat problems at 46.34%, showing signs of infection like fever, cough, flu at 43.90%, shortness of breath at 34.15%, experiencing diarrhea at 34.15%, constipation at 34.15%, tingling sensation in the hands/feet at 26.83%, and feeling anxious or worried at 12.20%.

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Table 3. Therapies and their side effects

Therapy(s)	Administration	Side Effect(s)
L-Asparaginase (Elspar)	IM (Intramuscular), IV (Intravenous)	Allergic reactions, fever, nausea/vomiting, anorexia, weight loss, arthralgia, and drug toxicity.
Mechlorethamine (Nitrogen Mustard, Mustargen)	IV (Intravenous)	Nausea/vomiting (30 minutes to 8 hours thereafter), hair loss, and local phlebitis.
Mercaptopurine (6-MP, Purinethol)	PO (Peroral)	Nausea/vomiting, diarrhea, anorexia, stomatitis, bone marrow depression (4 to 6 hours later), immune suppression, dermatitis, and liver dysfunction (rarely).
Methotrexate (MTX, Amethopterin)	PO (Peroral), IV (Intravenous), IM (Intramuscular), IP (Intraperitoneal)	Nausea/vomiting (severe at high doses), diarrhea, mucosal ulceration (2 to 5 days later), bone marrow depression (10 days later), immune suppression, dermatitis, photosensitivity, hair loss, toxic effects including: hepatitis (fibrosis), osteoporosis, nephropathy, pneumonitis.
Procarbazine (Matulene)	PO (Peroral)	Mild nausea/vomiting, bone marrow depression (3-4 weeks later), weakness, dermatitis, myalgia, arthralgia, stomatitis, neuropathy, hair loss, and diarrhea.
Vinkristin (Oncovin) and Vinblastin (Velban)	IV (Intravenous)	Neurotoxicity (milder with vinblastine) such as paresthesia, ataxia, weakness, foot drop, hyporeflexia, constipation (spastic ileus), hoarseness (paralysis of the vocal cords), abdominal, chest, jaw pain, mental depression, fever, mild nausea/vomiting, bone marrow depression, and hair loss.
Cytosine Arabinoside (Ara-C, Cytosar, Cytarabine, Arabinosyl Cytosine)	IV (Intravenous), IM (Intramuscular), SK (Sytostatics),IP (Intraperitoneal)	Mild nausea/vomiting, bone marrow depression (7 to 14 days later), mucosal ulceration, immune suppression, and hepatitis.
Cyclophosphamide (Cytoxan, CTX, Neosar)	PO (Peroral),IM (Intramuscular), IV (Intravenous)	Nausea/vomiting (3 to 4 hours later), bone marrow depression (10 to 14 days later), hair loss, hemorrhagic cystitis, stomatitis (rare), hyperpigmentation, and infertility.
Dakarbazin (Dtic-Dome)	IV (Intravenous)	Nausea/vomiting (especially after initial administration), bone marrow depression (7 to 14 days later), hair loss, flu-like syndrome, burning/sense of fear.

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DISCUSSION

Every patient experiences different effects after chemotherapy, depending on the child's body response and resistance to medications. Moreover, the type of drugs administered during chemotherapy also yields different effects on patients (Ruggiero, Rizzo, Catalano, Coccia, Triarico, & Attiná, 2018).

Research results indicated that the most common impact felt by children undergoing chemotherapy for cancer was hair loss (*alopecia*). This occurred because chemotherapy drugs that fought cancer cells could also damage normal cells. One of the normal cells susceptible to this damage is the hair follicle cell, where chemotherapy agents infiltrated the hair follicle, leading to hair loss. Hair loss typically starts within 1-2 weeks after chemotherapy, but it regrows around 1-2 months after chemotherapy ends, although the texture and consistency might slightly differ from the previous hair (Herfiana, & Arifah, 2019; Hidayati, 2017). However, according to parents, hair loss experienced by children isnot too bothersome, but for girls, they generally feel shy to play with their friends as they no longer feel as beautiful without their hair. Additionally, nurses explain before chemotherapy that the lost hair will grow back, comforting the children. Managing hair loss in cancer patients, according to (Kruse, & Abraham, 2018), involves maintaining hair cleanliness with shampoo, gentle combing, and using wigs or headscarves for girls during hair loss. Hair usually regrows 3-6 months after chemotherapy (Kruse, & Abraham, 2018).

Nausea and vomiting lead to anorexia and reduced appetite, affecting weight. Weight changes in children with cancer can be multifactorial and complex. Weight loss in these children can reach up to 60%. Cancer treatment can induce loss of appetite. Changes in taste and food smell due to chemotherapy make children unable to enjoy their meals, causing refusal to eat. Metabolic changes related to anorexia can lead to *cachexia* (a health disorder causing extreme weight loss and muscle wasting), likely due to prolonged imbalance in body energy and energy availability. Food mismatching with the child's hunger worsens their nutrition intake, leading to weight loss (McCulloch, Hemsley, & Kelly, 2018).

Lack of nutrition intake, especially calories, reduces energy supply to cells, causing weakness in the body (Ranailla, Mardhiyah, & Hidayati, 2016). Research results show that most children undergoing chemotherapy complain of weakness and fatigue. Chemotherapy-induced fatigue in patients can be caused by anemia, nutritional deficiency, and lack of sleep. Fatigue felt by patients is an unusual and unpleasant tiredness leading to sadness and irritation that affects the patient's role and activities within the family. However, support from family and friends can assist patients in overcoming the weakness they feel (Spichiger, Rieder, Müller-Fröhlich, & Kesselring, 2012). Nutritional intake deficiency can also reduce protein and albumin levels. Protein, used to build the body's immunity and repair damaged cells, decreases in the body, making children prone to infections (Ranailla, Mardhiyah, & Hidayati, 2016). Several infections can occur in children, including fever, flu, cough, mouth ulcers, and mucositis. Mouth ulcers are caused by damage to mucosal cells in the digestive tract, resulting in sores along the digestive tract, even in the mouth, known as mouth ulcers, significantly affecting a child's appetite. Therefore, parents can take steps to address anorexia in children, such as providing non-stimulating, soft, soupy foods, brushing teeth gently, and advising children to gargle with NaCl and using local anesthetics (Wong, Hockenberry, Rodgers, & Wilson, 2001).

Mucositis in pediatric cancer patients undergoing chemotherapy typically begins with redness and irritation in the mouth and throat, progressing to the mucous membrane of the cheeks, gums, tongue, palate, and throat. Chemotherapy-induced pediatric mucositis is divided into several phases. The first phase is called the vascular phase, where chemotherapy drugs in this phase damage normal mucosal cell DNA, causing cell injuries. Damaged cells release reactive oxygen species (ROS), harmful agents that damage tissues. Tissue damage creates pro-inflammatory agents like cytokines, tumor necrosis factors, interleukin 1 (IL-1), and their activity (Novrianda, & Arif, 2017) leading to the epithelial and inflammatory phases. In this phase, ulceration occurs and can have adverse consequences if the treatment is not proper.

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It is stated that children with blood cancer are more likely to experience mucositis than children with solid tumors because most chemotherapy agents for blood cancer have a high mucositis rate, chemotherapy cycles are more frequent than other patients, and the immunosuppression in children with blood cancer is usually more severe, leading to a lower immune system. Mucositis will cause various disturbances, such as physical and functional issues. Physiological disruptions include lesions, ulcers, excessive inflammation, pain, and infections. Bacteria, fungi, and viruses originating from lesions can lead to systemic infections. Functional disruptions encompass difficulty chewing, swallowing, and speaking (Novrianda, & Arif, 2017).

Weight management includes accurate and precise weight recording, input and output monitoring, and nutritional status assessment. Children with better nutrition can generally tolerate treatment and fight infections. Good nutrition is essential for children to achieve normal growth and development, while poor nutrition (excessive or deficient) can have negative impacts on drug actions, increase drug toxicity, alter treatment responses, and raise long-term risks. Things parents can do include maintaining the child's meal timing accuracy and regularity, stopping all activities when the child is eating, and providing snacks (McCulloch, Hemsley, & Kelly, 2018; Ardi, 20

During cancer treatment, children experience many side effects related to chemotherapy. Side effects experienced by children include nausea and vomiting, loss of appetite, anorexia, pain, fatigue, bone marrow suppression (anemia, leukopenia, and thrombocytopenia), alopecia, mucositis, sleeping problems, and neurological issues. The effects of chemotherapy depend on the drug characteristics (Ruggiero, Rizzo, Catalano, Coccia, Triarico, & Attiná, 2018; Hasibuan, Lubis, Rosdiana, Nafianti, & Siregar, 2019).

Anti-emetic therapy administered to patients feeling nauseous after chemotherapy involves the administration of anti-emetic drugs such as ondansetron combined with dexamethasone before starting chemotherapy to prevent children from experiencing nausea and vomiting after chemotherapy (Gibson, & Soanes, 2008). Pediatric patients experiencing CINV typically employ non-pharmacological techniques, coping mechanisms in the form of family social support, and distractions like watching TV as the most effective strategies. For pharmacological management, they still use guidelines to manage nausea and vomiting (McCulloch, Hemsley, & Kelly, 2018). Research findings by (Gerçeker, Yildirim, Sülün, Bektaş, Özdemir, & Malbora, 2022) found that the majority of children (43.9%) experienced weight loss. Patients at risk of malnutrition and nutritional deficiencies are tho ged 13-18 years.

One of the commonly complained side effects of chemotherapy by parents is pain. Pa ommonly occurs in children with cancer and is the most common symptom. Pain in children with cancer undergoing chemotherapy is an effect of treatment that usually occurs in progressive diseases nearing the end of life. Cancer pain is a combination of nociceptive pain (visceral and/or somatic), inflammation, and neuropathic pain. Administration of analgesic drugs should be adjusted according to pain characteristics and severity levels. One drug in cancer treatment for pain symptoms is opioids. Pain experienced by children with cancer usually presents as sharp, stabbing pain. Handling pain in children should align with pain assessment results. Several measures are taken for pain management such as providing analgesics (according to patient pain levels), radiotherapy, and anesthesia techniques. Pain can cause negative psychological impacts that affect the quality of life. Therefore, proper pain management should be considered for patients to feel more comfortable (McCulloch, Hemsley, & Kelly, 2018). Complaints of pain in children with cancer can disrupt sleep. Symptoms often complained of by 35-40% of pediatric cancer patients are sleep disturbances. Lack of sleep is associated with sleep time or sleep quality. Children's sleep time is around 9-10 hours in 24 hours. Sleep evaluation includes the duration within 24 hours, duration of awakenings at night, and changes in sl before and during illness. Sleep disturbances can have a negative impact on physiological and cognitive growth. The most common sleep disturbances are an increased number and duration of awakenings at night. Sleep disturbances can lead to fatigue, irritability, and reduced quality of life during the day, which can negatively impact growth. Sleep disturbance management can be done by reducing nighttime noise levels, reviewing vital signs, managing pain,

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and nausea (Kaleyias, Manley, & Kothare, 2012; Handayani, & Udani, 2016).

Cancer patients commonly experience mood changes such as anxiety, fear, anger, and even depression. Mood assessment and psychiatric disease examination in pediatric cancer patients are recommended by the Comprehensive Cancer Network. The prevalence of mood changes is significantly higher in pediatric cancer patients (Dietrich, & Parsons, 2018). Children, especially teenagers, report emotional symptoms like sadness, depression, anxiety, fear, and worry during treatment, while younger children may feel angry because they donot know how to express their feelings. Children are expected to have effective ways to undergo chemotherapy to avoid behavioral problems. Research by (Sposito, Silva-Rodrigues, Sparapani, Pfeifer, de Lima, & Nascimento, 2015) suggests several ways to improve children's mood, such as achieving happiness by engaging in entertaining and enjoyable activities, managing pain through pharmacological and non-pharmacological means, engaging in religious activities to boost hope and belief in the child's recovery process, thereby reducing the suffering felt by the child. Moreover, parents are encouraged to always accompany their children to make them feel cared for and loved during the treatment process. The most troubling behavioral disturbance reported by parents is the sense of anger and mood swings. The causes of anger and mood swings stem from the continuous treatment that exhausts the children, limiting their ability to play as they wish. Additionally, most children undergoing chemotherapy cannot attend school, thus lacking friends to talk or play with. Family relationships and economic status can also contribute to emotional disturbances in children (Ranailla, Mardhiyah, & Hidayati, 2016).

CONCLUSION

The impact of chemotherapy on children with cancer heavily depends on the child's condition. Some of the most dominant effects include baldness, mood swings, nausea and vomiting, weakness and fatigue, decreased appetite, weight loss, skin problems, mouth sores, sleep difficulties, pain, diarrhea, shortness of breath, and anxiety. The most disruptive effects during chemotherapy are usually nausea and vomiting along with mood swings.

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