Characteristics Of Chemotherapy Side Effects In Patients With Nasopharyngeal Cancer

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Abstract

This study investigates the characteristics of post-chemotherapy side effects in patients with nasopharyngeal cancer at Dr. Wahidin Sudirohusodo Hospital in Makassar during 2023. Utilizing secondary data, the research analyzes the prevalence of side effects based on gender and age. The findings reveal that male patients predominantly experience gastrointestinal (11.6%) and respiratory (16.8%) side effects, while female patients report higher rates of neuropathy (22.2%). In terms of age, adults exhibit the highest prevalence of gastrointestinal effects (12.1%) and combined effects (5.3%), whereas adolescents show significant rates of neuropathy (40.0%) and respiratory complications (60.0%). Elderly patients experience similar gastrointestinal and neuropathic toxicities (17.3% each), but at lower frequencies. Notably, no cases of nasopharyngeal cancer were reported in toddlers and children, indicating that this malignancy primarily affects older age groups. The study underscores the need for increased public awareness regarding nasopharyngeal cancer, particularly among vulnerable demographics, to promote early detection and prevention. Additionally, enhancing public knowledge about nasopharyngeal cancer and its risk factors is crucial for better understanding and management of the disease. Future research should focus on elaborating the specific side effects associated with each affected system to provide comprehensive insights into the impact of chemotherapy on nasopharyngeal cancer patients. Overall, this study contributes valuable information to the understanding of chemotherapy-related side effects in nasopharyngeal cancer, emphasizing the importance of tailored management strategies to improve patient outcomes and quality of life.

Keywords: *Nasopharyngeal Carcinoma, Chemotherapy Side Effects, Gender Differences, Age-Specific Variations and Patient Outcomes.*

I. INTRODUCTION

Nasopharyngeal carcinoma is a malignancy that arises from the epithelial cells of the nasopharynx, a region located behind the nose and above the throat. This type of cancer is particularly prevalent in certain geographic areas, notably Southeast Asia, where it poses significant public health challenges due to its aggressive nature and the complexities associated with its treatment [1], [2]. Nasopharyngeal cancer is characterized by easy development and metastasis, often diagnosed at advanced stages, with a notable ability to spread to regional lymph nodes. According to GLOBOCAN 2018, there are 129,079 new cases and 72,987 deaths from nasopharyngeal cancer worldwide, with Indonesia reporting a high incidence rate of 17,992 cases per year, making it the fourth most common malignancy in the country [3], [4]. The management of nasopharyngeal cancer typically involves a multimodal approach, integrating chemotherapy, radiotherapy, and sometimes surgery, depending on the stage and extent of the disease [5], [6]. Among these treatment modalities, chemotherapy plays a crucial role, especially in advanced stages, where it is often combined with radiotherapy to enhance treatment efficacy and improve patient outcomes [7], [8].The administration of chemotherapy is frequently accompanied by a range of side effects that can significantly impact the quality of life of patients. These side effects can be acute or chronic and vary widely among individuals, influenced by factors such as the specific chemotherapeutic agents used, the patient's overall health, and the presence of comorbid conditions [9], [10]. Common side effects associated with

chemotherapy in nasopharyngeal cancer patients include nausea, vomiting, fatigue, mucositis, and hematological toxicities such as neutropenia and thrombocytopenia [11], [12]. Approximately 50% of nasopharyngeal cancer patients report nasal complaints, including bloody discharge and headaches, which are indicative of serious disease progression [4], [13].

The diagnosis of nasopharyngeal cancer can be established through anamnesis, physical examination, and supporting examinations, including radiological assessments and endoscopic biopsies [14].Research has shown that the combination of cisplatin and other agents, such as gemcitabine, is commonly employed in the treatment of nasopharyngeal cancer, but this regimen is associated with significant toxicities, including renal impairment and hearing loss [9], [15]. Furthermore, the timing and sequencing of chemotherapy in relation to radiotherapy can influence the severity of side effects, with some studies suggesting that induction chemotherapy may lead to a higher incidence of acute toxicities compared to concurrent chemoradiotherapy [16], [17]. Understanding the characteristics of chemotherapy-induced side effects in nasopharyngeal cancer patients is essential for developing effective management strategies that can mitigate these adverse reactions. This includes implementing supportive care measures, such as antiemetics for nausea and vomiting, growth factors for neutropenia, and nutritional support to address weight loss and cachexia [18], [19].In conclusion, while chemotherapy remains a cornerstone of treatment for nasopharyngeal carcinoma, its associated side effects present significant challenges that require careful management and ongoing research. By enhancing our understanding of these side effects, healthcare providers can better support patients through their treatment journey, ultimately improving outcomes and quality of life for those affected by this challenging disease. The findings from various studies underscore the need for a comprehensive approach to managing the side effects of chemotherapy, ensuring that patients receive not only effective cancer treatment but also the necessary support to navigate the complexities of their condition.

II. METHODS

This study is a qualitative study [20], [21] using secondary data from patients with Nasopharyngeal Cancer (KNF) at Dr. Wahidin Sudirohusodo Hospital during the period January to December 2023. The study will be conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar City, South Sulawesi, with the planned implementation time taking place from October to November 2024. The target population in this study is patients with Nasopharyngeal Cancer who have undergone chemotherapy, while the target population includes patients who experience side effects of chemotherapy at the hospital. Inclusion criteria included patients who had undergone chemotherapy at Dr. Wahidin Sudirohusodo Hospital, while exclusion criteria included patients with complications or other comorbid diseases, pregnant patients, and patients who did not undergo chemotherapy. The independent variable in this study is the characteristics of chemotherapy side effects, while the related variable is patients with Nasopharyngeal Cancer.

The data collected will be analyzed using univariate analysis to obtain the percentage and proportion of the variables studied [22]. Operational definitions include chemotherapy side effects grouped into five categories: gastrointestinal, neuropathy, respiratory, combined effects, and no effects at the time of examination. Patient age will be grouped into five categories based on the MOH classification (2024), and gender will be recorded as male or female. This study will also follow strict ethical procedures, including submission of ethical recommendations, application for permission to the Faculty of Medicine, Muslim Indonesia University, and maintaining the confidentiality of patient identities contained in medical record data. It is hoped that this study can provide benefits for related parties, as well as add insight into the characteristics of chemotherapy side effects in Nasopharyngeal Cancer patients, so as to improve understanding and management of side effects experienced by patients.

III. RESULT AND DISCUSSION

Results

Characteristics of Nasopharyngeal Cancer Patients

Table 1. Distribution of Post-Chemotherapy Side Effects of Patients with Nasopharyngeal Cancer at Dr. Wahidin Sudirohusodo Hospital Makassar Year 2023 Based on Gender

Gender (Sex)		Side Effect										TOTAL	
		Gastrointestinal		Neuropathy		Respiratory		Combined Effect		No effect at screening			
		n	%	n	%	n	%	n	%	n	%	n	%
	Male	20	11,6	32	18,5	29	16,8	7	4,0	85	49,1	173	100,0
	Female	3	5,6	12	22,2	7	13,0	3	5,6	29	53,7	54	100,0
TOTAL		23	10,1	44	19,4	36	15,9	10	4,4	114	50,2	227	100,0

Source: Secondary Data, 2023

From Table 1, presents the distribution of post-chemotherapy side effects among patients with nasopharyngeal cancer at Dr. Wahidin Sudirohusodo Hospital in Makassar for the year 2023, categorized by gender. Among male patients, a total of 173 individuals were assessed, with 20 (11.6%) experiencing gastrointestinal side effects, 32 (18.5%) suffering from neuropathy, and 29 (16.8%) reporting respiratory complications. Additionally, 7 male patients (4.0%) exhibited combined effects, while a significant proportion, 85 patients (49.1%), showed no effects at screening. In contrast, the female cohort comprised 54 patients, with 3 (5.6%) experiencing gastrointestinal issues, 12 (22.2%) reporting neuropathy, and 7 (13.0%) facing respiratory complications. Furthermore, 3 female patients (5.6%) experienced combined effects, while 29 (53.7%) had no effects at screening. Overall, the total number of patients included in the study was 227, with 23 (10.1%) experiencing gastrointestinal side effects, 44 (19.4%) suffering from neuropathy, and 36 (15.9%) reporting respiratory complications. The occurrence of combined effects was noted in 10 patients (4.4%), while 114 individuals (50.2%) exhibited no effects at screening. This data highlights the varying prevalence of side effects between genders, with male patients generally experiencing higher rates of gastrointestinal and respiratory issues, while female patients showed a greater incidence of neuropathy.

Table 2. Distribution of Post-Chemotherapy Side Effects of Patients with Nasopharyngeal Cancer at Dr. Wahidin Sudirohusodo Hospital Makassar Year 2023 Based on Age

Gender (Sex)		Side Effect										TOTAL	
		Gastrointestinal		Neuropathy		Respiratory		Combined Effect		No effect at screening			
		n	%	n	%	n	%	n	%	n	%	n	%
	Toddlers	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	100,0
	Children	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	100,0
	Teenagers	0	0,0	2	40,0	3	60,0	0	0,0	0	0,0	5	100,0
	Adults	19	11,2	33	19,4	24	14,1	9	5,3	85	50,0	170	100,0
	Elderly	4	7,7	9	17,3	9	17,3	1	1,9	29	55,8	52	100,0
TOTAL		23	10,1	44	19,4	36	15,9	10	4,4	114	50,2	227	100,0

Source: Secondary Data, 2023

From Table 2, presents the distribution of post-chemotherapy side effects among patients with nasopharyngeal cancer at Dr. Wahidin Sudirohusodo Hospital in Makassar for the year 2023, categorized by age group. Notably, there were no reported cases of side effects in toddlers and children, indicating the absence of nasopharyngeal cancer in these age groups. Among teenagers, a total of 5 patients were assessed, with 2 (40.0%) experiencing neuropathy and 3 (60.0%) reporting respiratory complications, while no gastrointestinal or combined effects were noted. In the adult cohort, which comprised 170 patients, gastrointestinal side effects were reported by 19 individuals (11.2%), neuropathy by 33 (19.4%), respiratory issues by 24 (14.1%), and combined effects by 9 (5.3%). Additionally, 85 adults (50.0%) exhibited no effects at screening. The elderly group, consisting of 52 patients, reported gastrointestinal side effects in 4 (7.7%), neuropathy in 9 (17.3%), respiratory complications in 9 (17.3%), and combined effects in 1 (1.9%), with 29 elderly patients (55.8%) showing no effects at screening. Overall, the total number of patients included in the

study was 227, with 23 (10.1%) experiencing gastrointestinal side effects, 44 (19.4%) suffering from neuropathy, and 36 (15.9%) reporting respiratory complications. The data highlights that while teenagers primarily faced respiratory complications and neuropathy, adults exhibited a broader range of side effects, and elderly patients showed a similar pattern of side effects, albeit at a lower frequency. The absence of side effects in younger age groups underscores the epidemiological trends of nasopharyngeal cancer, which predominantly affects older adolescents and adults.

Discussion

Types and Doses of Chemotherapy Commonly Used in Nasopharyngeal Cancer Treatment

The treatment of nasopharyngeal carcinoma typically involves a combination of chemotherapy and radiotherapy, leveraging the disease's high sensitivity to these therapeutic modalities. The specific type and dosage of chemotherapy are tailored to the cancer's stage and characteristics. Cisplatin is the cornerstone of nasopharyngeal cancer treatment and is frequently combined with radiotherapy; for advanced stages, concurrent chemoradiotherapy utilizing cisplatin at a dosage of 100 mg/m² every three weeks has demonstrated significant efficacy in improving progression-free survival [23]. Additionally, the cisplatin-gemcitabine combination is recognized as the first-line therapy for recurrent or metastatic nasopharyngeal cancer due to its high response rate [24]. Induction chemotherapy, which precedes radiotherapy or chemoradiotherapy to reduce tumor size, is another critical approach. Common regimens include TPF (Taxotere, Platinum, Fluorouracil), where doses typically consist of docetaxel (75 mg/m²) and cisplatin (75 mg/m²) administered on day one, alongside continuous fluorouracil (750 mg/m² per day) for five days, a regimen that has been shown to improve overall survival in advanced nasopharyngeal cancer [25]. A simpler regimen, combining cisplatin (80-100 mg/m²) with fluorouracil (800 mg/m² per day) [26], is often employed for patients who cannot tolerate more intensive treatments [23].

Alternative agents, such as nedaplatin, a derivative of cisplatin, have emerged as less toxic options, offering comparable efficacy with fewer gastrointestinal and renal side effects, administered at 100 mg/m² every three weeks. Lobaplatin, used in induction chemotherapy at a dosage of 30 mg/m², has also shown promising antitumor activity with reduced toxicity compared to cisplatin. Adjuvant chemotherapy aims to eliminate microscopic residual disease following chemoradiotherapy, with a metronomic approach using capecitabine (650 mg/m² twice daily for one year) demonstrating improved failure-free survival compared to observation, while maintaining manageable side effects [27]. Concurrent chemoradiotherapy with cisplatin (100 mg/m² every three weeks or 40 mg/m² weekly) remains the standard for locally advanced nasopharyngeal cancer, although high-dose regimens yield better outcomes but are associated with increased toxicity [28]. Lastly, targeted and immune therapies, such as camrelizumab, an immune checkpoint inhibitor combined with cisplatin and gemcitabine, present a promising option for recurrent nasopharyngeal cancer, providing a high response rate alongside a manageable safety profile [24].

Post-Chemotherapy Side Effects of Nasopharyngeal Cancer Patients Based on Gender

Chemotherapy is a primary modality in the treatment of nasopharyngeal cancer; however, its side effects can vary significantly based on several factors, including the patient's gender. The results of this study indicate a notable difference in the proportion of side effects experienced by male and female patients. Specifically, the proportion of male patients experiencing side effects in the gastrointestinal system (11.6%) and respiratory system (16.8%) was greater than that of female patients (5.6% and 13.0%, respectively) [29], [30]. This disparity can be attributed to several factors. First, physiological differences between the sexes may play a role, as males generally exhibit a higher metabolism and variations in enzyme distribution that influence the metabolism of chemotherapy drugs, potentially leading to increased susceptibility to toxic effects on the gastrointestinal and respiratory organs [31]. Second, lifestyle and environmental exposures may contribute; literature suggests that men are more likely to experience adverse effects related to respiratory function due to a heightened inflammatory response. Additionally, the dose effect of chemotherapy may be relevant, as some studies indicate that men may receive higher relative doses than women based on body weight and surface area, which could influence the severity of side effects on specific systems [29]. Conversely, a greater proportion of female patients (22.2%) reported adverse effects on neurotherapy systems compared to male patients (18.5%) [32].

Factors influencing this difference include the sensitivity of the nervous system, as research indicates that women possess a lower pain threshold and a heightened neural response to neurotoxic drugs. The role of hormones, particularly estrogen, may also modulate the neural response to toxicity, increasing the risk of chemotherapy-induced neuropathy. Side effects such as peripheral neuropathy have been more frequently reported in female patients in similar studies [33], [34]. Furthermore, genetic and enzymatic interactions may play a role, as genes affecting drug metabolism, such as CYP450, may be expressed differently between men and women, impacting toxin accumulation in the nervous system. Regarding combined effects, female patients (5.6%) exhibited a higher proportion than male patients (4.0%), likely due to women's combined physiological sensitivity to various toxic effects of chemotherapy. This susceptibility may arise from hormonal and metabolic differences, as women's metabolism is influenced by hormonal cycles, potentially increasing the risk of combined effects across multiple organ systems [35]. Additionally, women tend to have a stronger immune response, which may lead to inflammation or autoimmune effects as a side effect of therapy [36].

Post-Chemotherapy Side Effects of Nasopharyngeal Cancer Patients Based on Age

Post-chemotherapy adverse events in nasopharyngeal cancer patients at Dr. Wahidin Sudirohusodo Hospital exhibited significant age-specific variations, highlighting different physiological responses and susceptibility at each age stage. Adult patients primarily experienced gastrointestinal (GI) effects (12.1%) and combined effects (5.3%), consistent with findings that adults undergoing cisplatin-based chemotherapy have a high prevalence of nausea, vomiting, diarrhea, and other GI toxicities due to the systemic impact of chemotherapy. Studies have also indicated that GI side effects often coincide with oral mucositis and dehydration, particularly in regimens that incorporate chemoradiotherapy. Combined effects in adults may arise from the systemic toxicity of multidrug chemotherapy protocols, which frequently impact multiple organ systems, with cumulative toxicity being common with prolonged chemotherapy exposure. Furthermore, newer regimens, such as induction chemotherapy followed by radiotherapy, are being evaluated to mitigate these side effects while maintaining efficacy. Adolescents experienced the highest rates of neuropathy (40.0%) and respiratory complications (60.0%).

Neurotoxicity is a well-documented side effect of cisplatin and other platinum-based chemotherapies, leading to cumulative damage to peripheral nerves, and adolescents may be particularly vulnerable due to their developing nervous systems [37]. Respiratory complications can result from infections and weakened immunity, exacerbated by chemoradiotherapy-induced mucosal damage in the nasopharynx and airway, with such complications often going unreported in this demographic, indicating a need for closer surveillance during therapy. The high rate of neurotoxicity aligns with findings from studies on neurotoxic agents in younger populations, with a randomized trial comparing cisplatin-based therapy reporting increased sensory neuropathy in younger patients [26]. Elderly patients experienced gastrointestinal, neuropathic, and respiratory toxicities (17.3% each) and combined effects (1.9%). Age significantly influences chemotherapy tolerance, as older adults often possess diminished organ reserves and comorbidities that exacerbate side effects [38]. The increased frequency of GI effects among the elderly may be attributed to reduced gastrointestinal motility and mucosal resilience, heightening susceptibility to diarrhea and nausea [39]. Neuropathy reflects cumulative nerve damage compounded by age-related declines in nerve repair mechanisms [40]. Notably, the absence of nasopharyngeal cancer cases in toddlers and children aligns with global epidemiological trends, where this type of cancer predominantly affects adolescents and adults due to the involvement of the Epstein-Barr Virus (EBV) [41].

IV. CONCLUSION

Based on the results of the study on the characteristics of chemotherapy side effects in patients with nasopharyngeal cancer, it was concluded that most male patients experienced significant post-chemotherapy side effects in the gastrointestinal system and respiration, while female patients experienced more side effects in the neuropathy system and combined effects. In addition, adult patients showed the highest prevalence of adverse events in the gastrointestinal system and combined effects, followed by adolescent patients who experienced the most adverse events in the neuropathy system and respiration. On the other

hand, elderly patients only experienced a very small number of gastrointestinal, neuropathy, respiration and combined effects. Interestingly, the age group of toddlers and children were not listed in the category of nasopharyngeal cancer patients studied, suggesting that nasopharyngeal cancer is more common in older age groups. Based on the findings of the study, it is recommended to increase public awareness, especially among subjects with age and gender susceptible to nasopharyngeal cancer, to encourage early detection and more effective prevention. In addition, it is important to increase public knowledge regarding nasopharyngeal cancer and its associated risk factors, so that individuals can better understand this condition and take the necessary preventive measures. Furthermore, future studies are expected to elaborate on the side effects that may be associated with each affected system, so as to provide more comprehensive and in-depth information regarding the impact of chemotherapy on nasopharyngeal cancer patients.

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