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Risk Factors Associated with Chemotherapy Response in Nasopharyngeal Carcinoma: A Cross-Sectional Study from a Tertiary Referral Center in Indonesia

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Abstract

Nasopharyngeal carcinoma (NPC) is a type of cancer commonly found in the head and neck, with the highest incidence in Asia. This study aims to analyze the influence of risk factors on chemotherapy response in NPC patients at Dr. M. Hoesin Hospital Palembang. The sample consisted of 65 NPC patients who underwent chemotherapy during the 2022–2023 period, selected using consecutive sampling. The variables studied include age, gender, histopathological classification, cancer stage, body mass index (BMI), and comorbidities. Chemotherapy response, as the dependent variable, was assessed using the RECIST (Response Evaluation Criteria in Solid Tumors) criteria. Data were collected from patient medical records and analyzed using SPSS software with univariate, bivariate (Chi-Squared test), and multivariate (multinomial logistic regression) analysis. The results showed that comorbidities were significantly associated with chemotherapy response, while age, gender, stage, histopathological classification, and BMI did not show significant relationships. Multivariate analysis indicated that age 30-50 years and stage IVA tended to influence chemotherapy response, although it did not reach statistical significance. In conclusion, managing comorbidities is an important factor in the success of chemotherapy in NPC patients, and this study suggests the need for a more holistic approach to treatment by considering other risk factors that may influence therapy outcomes.

Keywords: Nasopharyngeal Carcinoma (NPC), Chemotherapy Response, Regression Analysis, Risk Factors

1. Introduction

Nasopharyngeal carcinoma (NPC) is one of the most common malignancies occurring in the head and neck region. This tumor originates from the epithelial cells lining the surface of the nasopharynx, with the primary location typically found in the fossa of Rosenmüller. The nasopharynx, being part of the upper respiratory tract, has a unique structure lined by ciliated columnar and squamous epithelium, making it vulnerable to external exposures. NPC exhibits a highly variable geographical distribution. The highest incidence is recorded in Asia, accounting for 83.3% of all global cases. Indonesia ranks second after China in terms of NPC case numbers, with 18,835 reported cases, placing it sixth among all malignancies in the country, despite ranking only 23rd globally.[1–4]

The etiology of NPC involves a complex interaction between genetic, environmental, and infectious factors, particularly the Epstein-Barr virus (EBV). The consumption of certain foods, such as salted fish, smoking habits, and poor oral hygiene, is also considered major contributing factor in the development of this disease. Given Indonesia's highly heterogeneous population, the variation in risk factors across regions becomes more pronounced, requiring region-specific approaches in both prevention and treatment.[2,4–6]

The response to chemotherapy in NPC patients is influenced by various risk factors such as age, sex, clinical stage, BMI,

and comorbid status. Age is often regarded as a critical prognostic factor in previous studies, as younger age is typically associated with better physiological tolerance to treatment, including chemotherapy. Regarding sex, some studies have shown that androgens may promote tumor development, while estrogen in females may exert protective effects by suppressing tumor growth.[7] Patients with comorbidities tend to have poorer treatment responses compared to those without comorbid conditions.[4,8–11]

Dr. M. Hoesin General Hospital in Palembang serves as a referral center for NPC treatment, particularly in the South Sumatra region. However, to date, there is limited data on the influence of various risk factors on chemotherapy response among the local patient population. Most available literature remains general or focuses on national-level populations without specifically evaluating the conditions of patients in particular regions with differing demographic and clinical characteristics. Therefore, a more contextual and locally based study is needed to accurately describe the relationship between risk factors and chemotherapy success in NPC patients. The findings of this study are expected to support treatment strategy evaluation tailored to the patient profile in the Palembang area and improve survival rates among NPC patients.

2. Method

This study employed an analytical observational design with a cross-sectional approach to analyze the relationship between risk factors and chemotherapy response in NPC patients at Dr. M. Hoesin General Hospital, Palembang, which was selected due to the high prevalence of NPC in the region. Ethical approval was obtained from the Health and Medical Research Ethics Committee of Universitas Sriwijaya (protocol number: 250-2024). The study population included all patients diagnosed with NPC and undergoing chemotherapy at the hospital during 2022–2023. The sample was selected using a consecutive sampling technique. Inclusion criteria were patients diagnosed with NPC, complete medical records regarding the studied variables, and those who had undergone chemotherapy during the study period. Exclusion criteria included patients who received treatments other than chemotherapy for NPC and those who did not complete the chemotherapy regimen. Independent variables analyzed in this study included age, sex, histopathological classification, disease stage, BMI, and comorbidities, while the dependent variable was chemotherapy response (CR, PR, NC, PD). Chemotherapy response was assessed based on the Response Evaluation Criteria In Solid Tumors (RECIST), referring to changes in the size of target lesions on imaging before and after treatment. Data were collected from patient medical records and analyzed using SPSS. Univariate analysis was used to describe sample characteristics, bivariate analysis using the Chi-squared test to evaluate the relationship between risk factors and chemotherapy response, and multivariate analysis using multinomial logistic regression to assess the simultaneous effects of risk factors on various chemotherapy response categories. Other potential confounding variables, such as Epstein-Barr Virus (EBV) infection status, could not be analyzed due to limitations in the available medical record data.

3. Result

This study involved 65 patients diagnosed with NPC who underwent chemotherapy at Dr. M. Hoesin General Hospital, Palembang, during the 2022–2023 period. The baseline characteristics of these patients are presented in Table 3.1. Most patients were in the 30–50-year age group (56.9%), with a predominance of male patients (70.8%). The majority had WHO histopathological classification type II (49.2%) and were diagnosed at stage IVA (50.8%). Most patients had a normal body mass index (64.6%) and no comorbidities (93.8%).

Table 3.1. Univariate Analysis

Variable	Frequency	
	n	%
Age		
<30 years	11	16.9%
30-50 years	37	56.9%
51-70 years	17	26.2%
>70 years	0	0%
Sex		
Male	46	70.8%
Female	19	29.2%
Histopathological Classification		
WHO type I	6	9.2%
WHO type II	32	49.2%
WHO type III	27	41.5%
Stadium		
I	0	0%
II	8	12.3%
III	18	27.7%
IV A	33	50.8%
IV B	6	9.2%
Body Mass Index (BMI)		
Severely underweight	5	7.7%
Underweight	8	12.3%
Normal	42	64.6%
Overweight	5	7.7%
Obese	5	7.7%
Comorbidity		
Present	4	6.2%
Absent	61	93.8%
Chemotherapy Response		
Complete Response (CR)	22	33.8%
Partial Response (PR)	13	20%
No Change (NC)	14	21.5%
Progressive Disease (P)	16	24.6%

Bivariate analysis was conducted using the Chi-Squared test to examine the relationship between independent variables and the dependent variable. The results of the bivariate analysis are presented in Table 3.2, which shows that most independent variables did not have a statistically significant association with chemotherapy response ($p > 0.05$). However, a significant association was found between comorbidity status and chemotherapy response ($p = 0.005$). Patients with comorbidities tended to have a different distribution of treatment

responses compared to those without comorbidities, particularly in the categories of partial response and progressive disease.

Multivariate analysis using multinomial logistic regression, as presented in Table 3.3, revealed that none of the variables reached statistical significance. Nevertheless, there was a trend indicating that patients aged 30–50 years were more likely to achieve a complete response (CR), while those diagnosed with stage IVA disease tended to experience progression toward the progressive disease (PD) category. Although these trends did not reach statistical significance ($p > 0.05$), they warrant further investigation in future studies with larger sample sizes.

Table 3.2. Chi-Squared Test Results of Risk Factors and Chemotherapy Response in NPC Patients

Variable	Chemotherapy Response in NPC Patients								p
	Complete Response		*Partial Response*		*No Change*		*Progressive*		
	n	%	n	%	n	%	n	%	
Age									
<30 years	5	22.7%	3	23.1%	1	7.1%	2	12.5%	0.543
30-50 years	9	40.9%	7	53.8%	10	71.4%	11	68.8%	
51-70 years	8	36.4%	3	23.1%	3	21.4%	3	18.8%	
>70 years	0	0%	0	0%	0	0%	0	0%	
Sex									
Male	15	22.7%	10	23.1%	9	64.3%	12	75%	0.866
Female	7	40.9%	3	23.1%	5	35.7%	4	25%	
Histopathological Classification									
WHO type I	1	4.5%	2	15.4%	0	0%	3	18.8%	0.308
WHO type II	12	54.5%	7	53.8%	5	35.7%	8	50%	
WHO type III	9	40.9%	4	30.8%	9	64.3%	5	31.3%	
Stadium									
I	0	0%	0	0%	0	0%	0	0%	0.318
II	2	9.1%	2	15.4%	2	12.5%	2	12.5%	
III	8	36.4%	3	23.1%	1	37.5%	6	37.5%	
IV A	12	54.5%	6	46.2%	10	31.3%	5	31.3%	
IV B	0	0%	2	15.4%	1	18.8%	3	18.8%	
Body Mass Index (BMI)	1	4.5%	1	7.7%	1	7.1%	2	12.5%	0.511
Severely	3	13.6%	1	7.7%	3	21.4%	1	6.3%	
underweight	16	72.7%	9	69.2%	8	57.1%	9	56.3%	
Underweight	0	0%	2	15.4%	2	14.3%	1	6.3%	
Normal	2	9.1%	0	0%	0	0%	3	18.8%	
Overweight									
Obese									
Comorbidity									
Present	0	0%%	0	0%	0	0%	4	25%	0.005
Absent	22	100%	13	100%	14	100%	12	75%	

Table 3.3. Multinomial Logistic Regression Results

Predictor Variable		B	Exp(B)	p	95%CI
Complete	Intercept	1.729		1.000	
Response (CR)	Sex = Male	0.131	1.140	0.909	[0.119; 10.887]
	Sex = Female	0b	.	.	.
	HC = WHO I	17.502	39902339.311	0.997	[0.000; .c]
	HC = WHO II	1.373	3.948	0.129	[0.671; 23.245]
	HC = WHO III	0b	.	.	.
	Stadium = II	18.641	124599129.35	0.996	[0.000; .c]
	Stadium = III	19.727	369424830.16	0.996	[0.000; .c]
	Stadium = IV A	17.446	37731289.172	0.996	[0.000; .c]
	Stadium = IV B	0b	.	.	.
	C = Yes	-4.868	0.008	1.000	[0.000; .c]
	C = No	0b	.	.	.
	BMI = 0	-20.335	1.474E-9	0.997	[0.000; .c]
	BMI = 1	-20.579	1.155E-9	0.997	[0.000; .c]
	BMI = 2	-18.487	9.361E-9	0.997	[0.000; .c]
	BMI = 3	-37.550	4.923E-17	0.996	[0.000; .c]
	BMI = 4	0b	.	.	.
	Age = 0	1.071	2.918	0.527	[0.106; 80.708]
	Age = 1	-1.975	0.139	0.076	[0.016; 1.226]
	Age = 2	0b	.	.	.
Progressive (P)	Intercept	18.737		0.997	
	Sex = Male	0.505	1.657	0.711	[0.115; 23.890]
	Sex = Female	0b	.	.	.
	HC = WHO I	19.369	258066864.74	0.997	[0.000; .c]
	HC = WHO II	1.102	3.012	0.321	[0.342; 26.515]
	HC = WHO III	0b	.	.	.
	Stadium = II	-1.660	0.190	0.469	[0.002; 16.915]
	Stadium = III	0.598	1.818	0.742	[0.051; 64.215]
	Stadium = IV A	-2.513	0.081	0.097	[0.004; 1.570]
	Stadium = IV B	0b	.	.	.
	C = Yes	16.018	9043734.332	0.998	[0.000; .c]
	C = No	0b	.	.	.
	BMI = 0	-18.235	1.204E-8	0.997	[0.000; .c]
	BMI = 1	-20.376	1.415E-9	0.997	[0.000; .c]
	BMI = 2	-19.142	4.861E-9	0.997	[0.000; .c]
	BMI = 3	-20.105	1.855E-9	0.997	[0.000; .c]
	BMI = 4	0b	.	.	.
	Age = 0	1.168	3.215	0.581	[0.051;
	Age = 1	0.552	1.737	0.693	203.397]
	Age = 2	0b	.	.	[0.112; 26.902]
					.
Partial	Intercept	0.115		1.000	
Response (PR)	Sex = Male	0.832	2.299	0.516	[0.186; 28.424]
	Sex = Female	0b	.	.	
	HC = WHO I	18.257	84889131.437	0.997	[0.000; .c]
	HC = WHO II	0.963	2.619	0.309	[0.409; 16.755]
	HC = WHO III	0b	.	.	.
	Stadium = II	0.424	1.527	0.842	[0.024; 98.829]
	Stadium = III	1.109	3.301	0.554	[0.077;
	Stadium = IV A	-0.816	0.442	0.586	119.187]
	Stadium = IV B	0b	.	.	[0.023; 8.354]

C = Yes	-2.404	0.090	.	.
C = No	0b	.	.	[0.090; 0.090]
BMI = 0	-2.069	0.126	1.000	.
BMI = 1	-3.188	0.041	1.000	[0.000; .c]
BMI = 2	-0.689	0.502	1.000	[0.000; .c]
BMI = 3	-1.213	0.297	1.000	[0.000; .c]
BMI = 4	0b	.	.	[0.000; .c]
Age = 0	2.365	10.369	0.212	.
Age = 1	-0.458	0.633	0.709	[0.260; 436.138]
Age = 2	0b	.	.	[0.057; 6.999]
				.

Histopathological Classification = HC, Comorbidity = C. 0b indicates the reference category with parameters set to zero. A dot (".") means the statistic is not computed as a reference variable statistic. The ".c" in [0.000; .c] signifies that part of the confidence interval could not be estimated due to unstable or perfect separation of cases.

4. Discussion

Based on the univariate analysis, the 30–50 years age group constituted the majority of NPC cases, accounting for 56.9% of the total sample. This finding aligns with previous studies that reported a higher incidence of cancer in the productive age group. The <30 age group contributed only 16.9%, indicating a relatively lower risk of NPC among younger individuals, possibly due to a shorter duration of exposure to risk factors such as accumulated genetic mutations or prolonged environmental exposures in older individuals. Moreover, no patients over 70 years of age were found in this study, consistent with findings by Yang and Chang, who reported a decline in NPC incidence after age 60.[6,12–14]

Distribution by sex revealed that male patients were more commonly affected by NPC compared to females, with a ratio of 2.42:1. This is consistent with earlier studies reporting male-to-female ratios ranging from 2:1 to 3.5:1. The disparity is likely associated with greater exposure to risk factors in males, such as smoking habits and contact with certain chemicals, as well as hormonal influences. Some studies suggest that androgens promote tumor progression, while estrogen in females may provide a protective effect against NPC.[15–17]

In this study, most patients were diagnosed with WHO histopathological classification type II (49.2%). This type is more prevalent in countries with a high incidence of NPC, including those in Southeast Asia, as reported by Pandit et al. In addition, the majority of patients were diagnosed at stage IVA, indicating a tendency for late diagnosis. This is consistent with Jiromaru's study, which noted that most NPC cases are diagnosed at stage III or IV, largely due to the nonspecific nature of NPC symptoms.[18–20]

Patient distribution by BMI showed that most patients fell into the normal category (64.6%), which is consistent with several studies reporting no direct correlation between BMI and NPC occurrence. However, some studies suggest that patients with higher BMI may have better survival rates compared to those who are underweight. Regarding comorbidity status, 6.2% of patients had comorbid conditions such as hypertension, acute kidney injury, and tuberculosis, in line with other research showing associations between hypertension and NPC. Furthermore, certain chemotherapy agents have been reported to increase the risk of acute kidney injury in patients. As

for chemotherapy response, this study showed that 33.8% of patients achieved complete response (CR), 20% partial response (PR), 21.5% no change (NC), and 24.6% progressive disease (P). These findings contrast with studies by Lian et al. and Zhang, who reported that most patients initially experienced partial response followed by complete response.[10,21–23]

Bivariate analysis showed that variables such as age, sex, histopathological classification, disease stage, and BMI were not significantly associated with chemotherapy response in NPC patients. Although age is often regarded as a risk factor in NPC occurrence, its impact on chemotherapy response may be more complex, influenced by other conditions such as immune status, metabolic capacity, and the presence of comorbidities. This study also indicated that male and female patients had statistically comparable responses to chemotherapy. Thus, treatment approaches can be applied neutrally, regardless of sex. While histopathological type is important in tumor classification, it was not significantly associated with chemotherapy response in this sample. Other studies have shown that histopathological classification may influence treatment response, but without strong statistical significance. BMI also showed no significant relationship with chemotherapy response ($p = 0.511$), in line with previous studies reporting no clear link between BMI and chemotherapy outcomes in NPC.[23–27]

This study found no significant association between disease stage and chemotherapy response ($p = 0.318$), which contrasts with other studies that identify cancer stage as a major prognostic factor in treatment response. Although cancer stage is critical in determining the prognosis and response to chemotherapy in NPC patients—with more advanced stages generally linked to poorer outcomes—this discrepancy underscores the multifactorial nature of treatment response. Comorbidity status was found to be significantly associated with chemotherapy response ($p = 0.005$). This finding is consistent with the biological mechanisms of disease, as comorbidities may reduce the body's ability to tolerate and respond to treatment effectively by limiting treatment options, increasing the risk of side effects, or necessitating dose reductions. These factors ultimately affect the efficacy of chemotherapy, emphasizing the importance of managing comorbid conditions to improve treatment outcomes.[11,28,29]

Multivariate analysis using multinomial logistic regression revealed that patients aged 30–50 and those with stage IVA disease tended to exhibit different responses to chemotherapy, although these findings did not reach statistical significance ($p > 0.05$). Patients aged 30–50 years were less likely to achieve complete response compared to older patients (OR = 0.139; 95% CI: 0.016–1.226; $p = 0.076$). Although not statistically significant, the OR < 1 suggests a trend toward a negative effect on CR, indicating that while younger age is often associated with a better prognosis, in NPC, older age may be linked to improved chemotherapy outcomes. This may relate to other contributing factors such as comorbidities and the body's capacity to tolerate treatment.[30,31]

Patients with stage IVA disease were less likely to experience progressive disease compared to those with stage IVB (OR = 0.081; 95% CI: 0.004–1.570; $p = 0.098$). This is consistent with studies

showing that stage IVB represents the most advanced disease and is more often associated with poor treatment response, whereas patients with stage IVA tend to have more stable disease or minimal tumor size change. Although the finding did not reach full statistical significance, it highlights the need for a better understanding of chemotherapy response variations based on cancer stage.[31,32]

Other variables such as sex, histopathological classification, BMI, and comorbidities did not show significant associations with chemotherapy response. This lack of significance may be due to limitations such as the relatively small sample size, the single-center nature of the study, and the absence of analysis of important biological variables such as EBV infection status, oncogene expression, and chemotherapy regimen details. Therefore, future studies with prospective designs, larger sample sizes, and multidimensional approaches are needed to strengthen these findings.[33,34]

5. Conclusion

Based on the findings of this study, it can be concluded that age, sex, histopathological classification, and body mass index (BMI) did not show a significant effect on chemotherapy response in nasopharyngeal carcinoma (NPC) patients at Dr. M. Hoesin General Hospital, Palembang. Comorbidities, such as hypertension and acute kidney injury, were found to have a significant impact on chemotherapy outcomes, with patients having comorbid conditions tending to experience poorer responses to treatment. Multivariate analysis also revealed that age and disease stage appeared to be associated with chemotherapy response, although these associations did not reach statistical significance. This study faced several limitations, including patients who did not complete chemotherapy according to the treatment schedule or failed to attend follow-up visits, which may have affected the validity of outcome data. Additionally, the relatively small sample size and the lack of analysis of other important variables—such as Epstein-Barr virus (EBV) infection status, genetic factors, and chemotherapy regimen types—limit the generalizability of the findings. Nevertheless, this study provides important insights into the influence of risk factors on chemotherapy response among NPC patients. Future research should aim to further explore other potential determinants of treatment outcomes, including genetic and viral factors such as EBV infection. Moreover, health promotion efforts should be strengthened to raise public awareness about the importance of regular follow-up after chemotherapy to ensure optimal patient outcomes.

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