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Retrospective study on nasopharyngeal cancer (RENOCS): outcome management of in-hospital patients

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ABSTRACT

Background: Nasopharyngeal carcinoma (NPC) is distinct from other head and neck cancers in terms of epidemiology, clinical presentation, biological markers, carcinogenic risk factors, and prognostic factors. However, there is only a small amount of information available on NPC in Indonesia, where the recorded mean prevalence is 6.2/100,000 and there are 13,000 new cases reported annually. Numerous treatments are used, and it's important to pinpoint the risk factor that contributes to a poor prognosis. The aim of this study is to look at the outcomes of nasopharyngeal cancer patients who were hospitalized at a referral hospital based on their characteristics and laboratory results.

Methods: Data from medical records were analyzed to conduct a retrospective study. Up to 785 patients who were hospitalized at a single referral hospital from 2018 to 2022 and received a nasopharyngeal cancer diagnosis were included. Data were statistically and descriptively analyzed.

Results: Chronic kidney disease, education level, and tumor, node, metastasis (TNM) classification was associated with patient outcomes ($p < 0.05$). The results of the multivariate analysis showed that there were significant differences in the variables of chronic kidney disease and pre-treatment albumin levels. Therefore, people with nasopharyngeal cancer who have chronic kidney disease have a 12,151 chance of mortality.

Conclusion: In Indonesia, there is a critical need for efforts to identify NPC as early as possible. These should include public education to increase awareness of the comorbidity status, especially chronic kidney disease to prevent poor outcomes.

Keywords: nasopharyngeal cancer, hospital, patient, laboratory results, outcome.
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INTRODUCTION

Nasopharyngeal cancer (NPC) is still a type of cancer that is a global burden. Nasopharyngeal carcinoma is a type of multifactorial disease that primarily affects the general population in South China, Southeast Asia, and North Africa.[1] Although in certain areas Nasopharyngeal Carcinoma (NPC) is rare in Arab countries, its incidence is increasing due to increased exposure to various risk factors.[2] A study identified nasopharyngeal cancer from Southeast Asia. This study found that the highest incidence and death rates were in Malaysia, Singapore, Indonesia, Vietnam, and Brunei.[3] The incidence of these cases reached 176,500 globally in 2019. Indonesia has a record as the country with the third highest death rate due to nasopharyngeal cancer, reaching 3,220 deaths in 2019.[4] Nasopharyngeal cancer is one of the most common cancers in men in Indonesia besides lymphoma.[5] The prevalence of nasopharyngeal cancer in Indonesia is 6.2/100,000, with nearly 13,000 new cases, but this is a small proportion that has been documented. Nasopharyngeal cancer is the most common head and neck cancer (28.4%), with a male-female ratio of 2:4, and is endemic in Java.[6]

Various studies have found that patients with nasopharyngeal cancer have poor survival rates. Patients come to the hospital in an advanced stage.[7] A survey conducted by Dwijayanti et al, 2020 found the survival rate for nasopharyngeal cancer patients was around 31.08 months. Another study found that the 5-year overall survival rate was 38.6% after receiving neoadjuvant chemotherapy, followed by chemoradiation.[8] A trend towards better survival was found in the subset of patients who sought treatment early. The survival rate and quality of life (QoL) of NPC patients are closely related because each can affect the other negatively or positively.[9]

To support survival, patients need to be supported with optimal hospital health care. One of them is inpatient care. Various factors that exist during pre-treatment, during-treatment, and post-treatment can affect the prognosis, survival, and QoL of NPC patients.[9] Strategies to provide the best outcome in nasopharyngeal cancer patients have been carried out but the results have varied.[10] It is necessary to identify the patient's character which leads to a poor prognosis so that it can be anticipated earlier. Various treatment options for nasopharyngeal cancer patients in hospitals do not fully promise

the best results. Based on this background, this study aims to analyze the outcome of nasopharyngeal cancer patients after hospitalization at a referral hospital based on the characteristics and laboratory results.

METHODS

Type of research and population

This research is a retrospective study. The population in this study were patients with a diagnosis of nasopharyngeal cancer at Dr. Soetomo General Hospital, East Java Indonesia throughout 2018-2022.

Inclusion and exclusion criteria

The inclusion criteria in this study were patients diagnosed with nasopharyngeal cancer in 2018-2022 who were hospitalized and had complete data. Incomplete medical record data and outpatients were not included in the study. Data obtained from as many as 785 patients were analyzed.

Data collection

The data used is secondary data from 2018-2022. The hospital is a referral hospital in East Java, Indonesia. Researchers accessed medical records of nasopharyngeal cancer patient care. Data accessed included sex, age, Eastern Cooperative Oncology Group (ECOG) score, length of stay, comorbid status including type 2 diabetes mellitus, hypertension, and chronic kidney disease, type of treatment, routine medical examinations, risk factors such as alcohol, cigarettes, and smoked fish, body mass index (BMI), staging, and laboratory results before and after treatment.

Data analysis

Data were analyzed descriptively and statistically. Data on the characteristics of the respondents were analyzed using the Chi-square and Fisher's exact tests. Laboratory data were analyzed using the Mann-Whitney test. The difference could be significant if the p-value <0.05. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows 25.

RESULTS

A total of 785 patients with nasopharyngeal cancer were analyzed. Table 1 shows the characteristics of the patients and the outcomes that occurred. The results showed that more than half of the respondents were male patients aged less than 50 years. Most do not have type 2 diabetes mellitus, hypertension, or chronic kidney disease. Almost all respondents had an ECOG score of 0-1, length of stay less than 7 days, checked regularly, received chemotherapy and radiation, and did not use alcohol. More than half are smokers and consume smoked fish. Most had a BMI of less than 25 and were diagnosed with stages III and IV. In this study, it was found that chronic kidney disease, education level, and tumor, node, metastasis (TNM) classification was associated with patient outcomes ($p < 0.05$). The results of this study found that sex, age, comorbidities such as diabetes mellitus type 2 and hypertension, ECOG score, length of stay, routine medical examinations, type of therapy received, smoking status, alcohol, and smoked fish consumption, and cancer stage were not related to patient outcomes ($p \geq 0.05$).

Table 2 shows the laboratory results and outcomes that occurred. The results of statistical tests showed that there were significant differences in the levels of K, SGPT, and platelet before treatment in survivors and non-survivors ($p<0.05$). There were significant differences in the levels of albumin, Na, SGPT, creatinine clearance (CrCl), leukocyte, and platelet after treatment in survivors and non-survivors ($p<0.005$). Only SGPT and platelet both before and after showed significant differences.

Table 3 shows the results of the multivariate analysis. The results of the analysis showed that there were significant differences in the variables of chronic kidney disease and pre-treatment albumin levels. People with nasopharyngeal cancer who have chronic kidney disease (CKD) have a 12,151 chance of mortality.

DISCUSSION

The results of this study found that certain characteristics and certain laboratory results were associated with patient outcomes. It was found that chronic kidney disease was associated with patient outcomes ($p <0.05$). This is related to the condition of the kidneys and chemotherapy in nasopharyngeal cancer patients. Kidney failure usually causes chemotherapy to be delayed or interrupted without complete treatment.[10-11] Nephrotoxicity is a common side effect of many chemotherapeutic agents. The agents most frequently associated with chemotherapy-associated nephrotoxicity are methotrexate, semustine, streptozocin, mithramycin, and cisplatin. Certain chemotherapeutic agents have adverse effects on the kidney and urothelium that can be visualized radiographically, including cystic changes, interstitial nephritis, papillary necrosis, urothelial changes, hemorrhagic cystitis, acute tubular necrosis, infarction.[12]

The results of this study found that gender, age, comorbidities such as diabetes mellitus and hypertension, ECOG score, length of stay, routine medical examinations, type of therapy received, smoking status, alcohol and smoked fish consumption, and cancer stage were not related to patient outcomes. This is in contrast to other studies. Research conducted by Hutajulu et al, 2021 found age, educational status, ECOG index, stage, and first treatment modality were independent predictors of survival time.[13] This is supported by other research. Strong independent prognostic factors for NPC are sex and age. Males are disadvantageous compared to females in overall survival at 5 years and may occur in situations younger than 45 years.[14] In this research, almost all respondents received chemotherapy and radiation. The results of previous studies found that the overall prognosis and 5-year survival rate have improved with the advent of better radiotherapy techniques. There has been an increase from 25% to 40% historically to around 70% in modern medicine at the 5-year survival rate.[15]

The results show that certain electrolytes such as K before treatment, albumin, Na, SGPT, CrCl, leukocyte, and platelet after treatment are associated with patient outcomes. These results are not following the results of Gao et al, 2018 found that albumin before therapy is a potential predictive biomarker to evaluate survival in NPC patients but is not an independent predictor.[16] One of the most common complications in cancer patients is electrolyte disturbances. These disturbances can be associated with

Table 1. Characteristics of nasopharyngeal cancer patients and the outcomes

Characteristics	Outcome				Total	p-value
	Survivor		Non-survivor			
	n	%	n	%		
Sex						
Male	512	65.22	35	4.46	547	0.991
Female	222	28.28	16	2.04	238	
Total	734	93.50	51	6.50	785	
Age						
<50 years	397	50.57	34	4.33	431	0.054
>50 years	337	42.93	17	2.17	354	
Total	734	93.50	51	6.50	785	
ECOG score						
0-1	722	91.97	51	6.50	773	0.444
2	12	1.53	0	0.00	12	
Total	734	93.50	51	6.50	785	
Length of stay						
< 7 days	685	87.26	47	5.99	732	0.457
>7 days	49	6.24	4	0.51	53	
Total	734	93.50	51	6.50	785	
Diabetes mellitus type 2						
Yes	143	18.22	12	1.53	155	0.603
No	591	75.29	39	4.97	630	
Total	734	93.50	51	6.50	785	
Hypertension						
Yes	171	21.78	16	2.04	187	0.223
No	563	71.72	35	4.46	598	
Total	734	93.50	51	6.50	785	
Chronic kidney disease						
Yes	7	0.89	3	0.38	10	0.022*
No	727	92.61	48	6.11	775	
Total	734	93.50	51	6.50	785	
Routine medical examinations						
Routine	721	91.85	51	6.50	772	0.415
Not a routine	13	1.66	0	0.00	13	
Total	734	93.50	51	6.50	785	
Therapy type						
Chemotherapy only/ radiation only	149	18.98	10	1.27	159	0.537
Radiation and chemotherapy	585	74.52	41	5.22	626	
Total	734	93.50	51	6.50	785	
Alcohol consumption						
Yes	17	2.17	2	0.25	19	0.353
No	717	91.34	49	6.24	766	
Total	734	93.50	51	6.50	785	
Tobacco						
Yes	397	50.57	34	4.33	431	0.109
No	337	42.93	17	2.17	354	
Total	734	93.50	51	6.50	785	
Smoked fish consumption						
Yes	399	50.83	29	3.69	428	0.773
No	335	42.68	22	2.80	357	
Total	734	93.50	51	6.50	785	

Characteristics	Outcome				Total	p-value
	Survivor		Non-survivor			
	n	%	n	%		
BMI						
< 25 kg/m²	642	81.78	49	6.24	691	0.074
>25 kg/m²	92	11.72	2	0.25	94	
Total	734	93.50	51	6.50	785	
Cancer stage						
I-II	107	13.63	7	0.89	114	0.532
III-IV	627	79.87	44	5.61	671	
Total	734	93.50	51	6.50	785	
Education level						
Primary school	0	0	1	0	12	0.000*
Junior high school	219	28	21	3	240	
Senior high school	467	59	28	4	495	
Other	48	6	1	0	49	
Total	734	93.50	51	6.50	785	
Insurance type						
No insurance	21	3	0	0	21	0.390
Public insurance	713	91	51	6	764	
Total	734	93.50	51	6.50	785	
Marital Status						
Married	533	68	42	5	575	0.219
Single	124	16	4	1	128	
Widow/Widower	77	10	5	1	82	
Total	734	93.50	51	6.50	785	
T classification						
T1	38	5	3	0	41	0.985
T2	152	19	10	1	162	
T3	169	22	11	1	180	
T4	375	48	27	3	402	
Total	734	93.50	51	6.50	785	
N classification						
N0	70	9	6	1	76	0.002*
N1	184	23	8	1	192	
N2	286	36	14	2	300	
N3	190	24	21	3	211	
N4	3	0	2	0	5	
Total	734	93.50	51	6.50	785	
M classification						
M0	626	80%	44	6%	670	0.938
M1	21	3%	2	0%	23	
M2	1	0%	0	0%	1	
MX	86	11%	5	1%	91	
Total	734	93.50	51	6.50	785	

*Significant with p<0.05

worsening outcomes, affecting the quality of life, likelihood of receiving anticancer drugs, and survival. They may provoke significant morbidity, with multiple organ dysfunction, and rarely cause life-threatening conditions. These changes usually involve serum levels of sodium, potassium, calcium, and magnesium. The causes of electrolyte disturbances are often multifactorial, so it is not always possible to identify and correct the cause.[17] The most commonly occurring derangement is hyponatremia, while hypercalcemia, hypokalemia, and hypophosphatemia are also encountered.[18]

The results of the statistical analysis found that platelet levels before and after showed significant differences between patients who survived and died. Increased cancer incidence and poor survival are indicated by increased platelet counts. As diagnostic approaches, there is an increase

Table 2. Comparisons of laboratory results with outcomes

Laboratory test	Pre mean (min-max)	p-value	Post mean (min-max)	p-value
Albumin	3.69(2.30-5.20)	0.562	3.86(1.80-106.00)	0.000*
GDA	118.70(12.00-347.00)	0.365	114.56(3.60-347.00)	0.668
BUN	11.48(0.89-115.00)	0.502	13.47(0.80-118.00)	0.223
SC	2.14(0.20-974.00)	0.348	2.20 (0.09-974.00)	0.091
Na	138.41(4.2-155.00)	0.876	137.76(45.00-189.00)	0.024*
K	4.66(2.60-123.00)	0.001*	4.60(2.20-138.00)	0.105
Cl	99.68(1.20-123.00)	0.275	99.70(8.70-144.00)	0.282
SGOT	29.77(9.00-307.00)	0.779	34.777(6.00-440.00)	0.068
SGPT	31.76(6.00-237.00)	0.032*	31.71(4.00-280.00)	0.011*
Calcium	9.34(3.90-102.00)	0.672	9.39(0.70-102.00)	0.276
CrCl	91.00(1.51-266.00)	0.162	92.23(4.15-226.00)	0.010*
Hb	12.69(4.80-17.10)	0.279	11.90(5.00-115.00)	0.089
Leukocyte	29.90(1.68-15650.00)	0.543	14.98(1.59-4220.00)	0.002*
Platelet	360.86(11.70-902.00)	0.002*	330/44(32.00-754.00)	0.043*
Neutrophil	14.28(0.00-92.40)	0.324	13.05 (0.28-104.00)	0.140

*Significant with p<0.05

Table 3. Multivariate analysis results

Variable	B	S.E	Wald	p-value	Exp (B)	95% CI	
						Lower	Upper
Length of Stay	.003	.088	.001	.972	1.003	.844	1.192
ECOG SCORE	-.652	2.380	.075	.784	.521	.005	55.316
Sex(male)	.592	.482	1.508	.219	1.808	.703	4.652
Age	-.023	.017	1.955	.162	.977	.946	1.009
Diabetes mellitus (yes)	.394	.543	.528	.467	1.484	.512	4.297
Hypertension (yes)	.069	.499	.019	.890	1.072	.403	2.849
Chronic kidney disease (CKD)	2.497	1.261	3.922	.048*	12.151	1.026	143.912
Therapy type			2.495	.287			
Therapy (radiation only)	-.422	.586	.518	.472	.656	.208	2.069
Therapy (chemotherapy only)	-2.115	1.481	2.040	.153	.121	.007	2.198
Check up (routine)	-18.557	9098.063	.000	.998	.000	.000	.000
Alcohol (yes)	1.302	1.043	1.557	.212	3.676	.476	28.412
Tobacco (yes)	.162	.522	.096	.757	1.176	.423	3.271
Smoked fish (yes)	.544	.515	1.114	.291	1.723	.627	4.731
BMI	-.002	.014	.019	.889	.998	.971	1.026
Hb	-.184	.143	1.650	.199	.832	.628	1.102
Leukocyte	-.028	.043	.432	.511	.972	.893	1.058
Platelet	.000	.002	.055	.815	1.000	.996	1.003
#Neut	.009	.025	.120	.729	1.009	.961	1.058
Albumin	-1.450	.506	8.203	.004*	.235	.087	.633
GDA	.011	.007	2.570	.109	1.011	.998	1.024
BUN	-.034	.040	.738	.390	.966	.894	1.045
SK	-.470	.829	.322	.571	.625	.123	3.171
Na	.054	.030	3.269	.071	1.055	.996	1.118
K	.023	.014	2.502	.114	1.023	.995	1.053
Cl	-.009	.021	.182	.669	.991	.952	1.032
SGOT	.007	.004	2.665	.103	1.007	.999	1.015
SGPT	.012	.012	1.096	.295	1.012	.989	1.036
Calcium	-.030	.049	.380	.538	.970	.882	1.067
CrCl	-.001	.008	.022	.883	.999	.984	1.014
Cancer stage (I-II)	-.011	.798	.000	.989	.989	.207	4.728

Variable	B	S.E	Wald	p-value	Exp (B)	95% CI	
						Lower	Upper
T	-.014	.312	.002	.965	.986	.535	1.817
N	.188	.222	.717	.397	1.207	.781	1.866
M	-.266	1.105	.058	.810	.766	.088	6.686
Education Level			3.152	.369			
Education level(primary)	19.574	40192.970	.000	1.000	316737211.937	.000	.000
Education level (junior)	1.088	1.165	.873	.350	2.969	.303	29.132
Education level (senior)	.392	1.177	.111	.739	1.480	.147	14.876
Health insurance (yes)	18.518	6352.623	.000	.998	110236159.863	.000	.000
Married status			3.865	.145			
Married (married)	-.729	.705	1.070	.301	.482	.121	1.920
Married (single)	-1.822	.942	3.742	.053	.162	.026	1.024

in the platelet count in many types of cancer, including colon, lung, ovarian, and stomach. Higher peak platelet counts were found in patients who died of their cancer within 3 years of diagnosis than in those who survived. Elevated platelet count is a potential prognostic measure for cancer-specific survival.[19] An increase in the platelet count is associated with a cancer diagnosis within 10 years after the blood test. These results were found in a case-control study of Ontario residents who underwent 1 or more routine complete blood count tests.[20] Compared with a low platelet count, a high platelet count was significantly and independently associated with poor distant metastasis-free survival (DMFS) rates in radiotherapy patients.[21]

The results of the statistical analysis found that SGPT before and after showed significant differences between patients who survived and died. This can be related to the occurrence of metastases. Symptoms associated with metastases are rarely seen and the most significant spread includes the liver and lungs. Research examining liver function (using markers like SGPT) in children with leukemia found that although there was a sharp increase during chemotherapy remission, it was temporary and produced deleterious effects on the liver.[22] Determining the cause of abnormal liver function tests in cancer patients undergoing chemotherapy is one of the most difficult problems faced by doctors. Hepatotoxicity from chemotherapy often results from unexpected or idiosyncratic reactions.[23]

The results of the analysis showed that there were significant differences in the variables of chronic kidney disease and pre-treatment albumin levels. People with nasopharyngeal cancer who have chronic kidney disease have a 12,151 chance of mortality. Pretreatment serum albumin levels provide useful prognostic significance in cancer.[24] Other findings suggest that pre-diagnostic serum albumin is inversely and linearly associated with cancer risk among the Chinese population.[25] Early assessment of the serum albumin level in patients and their improvement in the serum albumin level may suggest that there are beneficial effects after chemotherapy.[26] This study uses secondary data that can cause bias when collecting data. Research also has not been able to learn deeper into the treatment process that influences patient outcomes. Future research can explore the type of therapy given and the outcomes obtained if patients are found with laboratory results and certain characteristics.

CONCLUSION

Chronic kidney disease, education level, and TNM classification was associated with patient outcomes. There were significant differences in the levels of K, SGPT, albumin, Na, SGPT, CrCl, leukocyte, and platelet before treatment in survivors and non-survivors. In addition, there were significant differences in the variables of chronic kidney disease and pre-treatment albumin levels. People with nasopharyngeal cancer who have chronic kidney disease have a 12,151 chance of mortality.

CONFLICT OF INTEREST

The authors affirmed that there were no conflicts of interest in this study.

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ETHICAL CLEARANCE

This study has obtained ethical clearance from the Research Ethics Committee of Faculty of Medicine, Universitas Airlangga, Dr. Soetomo General Academic Hospital Surabaya with reference letter number 1183/LOE/ 301.4.2/I/2023.

AUTHOR CONTRIBUTION

All authors contributed equally in this research and publication of this manuscript.

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