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Research Article

Comparison of Nasopharyngeal Carcinoma Treatment Outcome Before and During The COVID-19 Pandemic: Experiences From Dr. Soetomo Hospital In 2017-2022

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ABSTRACT

Nasopharyngeal carcinoma is endemic in Southeast Asia. In Indonesia, the recorded mean prevalence is 6.2/100.000, with 13.000 yearly new Nasopharyngeal carcinoma cases. Observational data suggest that cancer-specific mortality was higher during the COVID-19 pandemic when compared with pre-pandemic levels. This study aims to compare the treatment outcome of nasopharyngeal carcinoma cases before and during the COVID-19 pandemic at Dr Soetomo Hospital in 2017-2022. This study employed a retrospective cross-sectional approach with an observational analytic method. Data is taken secondary from medical records for nasopharyngeal carcinoma patients at Dr. Soetomo Hospital in Surabaya and primary by telephone interview for additional information on the patient's risk factors. The majority of nasopharyngeal carcinoma patients at Dr. Soetomo Hospital were male, elderly,>50 years old, and referral patients (outside Surabaya). In both eras, patients arrived already in stage 4 (advanced stage). However, before COVID-19, more patients were cured and survived before the COVID-19 period in comparison to during the COVID-19 pandemic period. This may be related to delayed treatment caused by COVID-19 policy on social distancing, healthcare regulation during the pandemic, and immunocompromised status.

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INTRODUCTION

Nasopharyngeal carcinoma is endemic in specific regions globally, with a notably high incidence in Southeast Asia. In Indonesia, it ranks as the fourth most prevalent cancer after cervical, breast, and skin cancers, and represents the most common malignancy in the head and neck region. Nationally, the average prevalence rate is documented at 6.2 per 100,000 individuals, with approximately 13,000 new cases reported annually (Adham et al., 2012). Nasopharyngeal carcinoma predominantly originates in the nasopharynx, a tubular region situated posterior to the nasal cavity and connected inferiorly to the oropharynx. Its anatomical proximity to critical structures, including the brain and other vital organs of the head and neck, contributes to a complex clinical profile with higher risks of adverse outcomes and complications. The prognosis for Nasopharyngeal carcinoma is generally poor; global data indicate over 133,000 new cases annually, with associated mortality exceeding 80,000 (Global Cancer Observatory, 2020).

The COVID-19 pandemic impacted cancer treatment worldwide, and recent data suggest increased cancer mortality due to delays in diagnosis and treatment. For Nasopharyngeal carcinoma, the pandemic likely affected patient outcomes, as delayed screenings and treatments led to diagnoses at later stages, posing a serious challenge for optimal management. However, limited research exists on the effects of COVID-19 on Nasopharyngeal carcinoma outcomes in Indonesia, particularly at Dr. Soetomo Hospital. It is known that the COVID-19 pandemic caused global disruptions in cancer care, leading to significant delays in nasopharyngeal carcinoma treatment and contributing to increased severity and mortality rates (Chen, 2020). At Dr. Soetomo Hospital, the reallocation of healthcare resources, hospital bed shortages due to COVID-19, and limited medical supplies exacerbated outcomes for nasopharyngeal carcinoma patients. This shift was followed by the adoption of telemedicine for non-emergency services, including outpatient care, which limited access to essential physical examinations and laboratory assessments (Linjawi et al., 2023).

This study seeks to address this gap by analyzing nasopharyngeal carcinoma treatment outcomes before and during the COVID-19 pandemic (2017–2022), with a focus on its impact on patient staging and treatment efficacy. The findings will enhance understanding of pandemic-related disruptions in nasopharyngeal carcinoma management and provide valuable insights for optimizing cancer care during future healthcare crises.

METHODS

Method and Design of Research

This study employed a retrospective cross-sectional approach with an observational analytic method. Data is taken secondary from medical records for nasopharyngeal carcinoma patients at Dr. Soetomo Hospital in Surabaya and primary by telephone interview for those who can be contacted by phone calls for additional information regarding the patient's risk factors. The data collected were processed using Microsoft Excel and IBM SPSS 26, categorized into groups based on predefined variables, and then presented in the form of graphs and distribution tables. Patients meeting the inclusion criteria were selected via quota sampling using the Lemeshow formula with 22 samples in each group (2017–2019 and 2020–2022). This study was conducted under *Komite Etik Penelitian Kesehatan RSUD Dr. Soetomo Surabaya,* ethical clearance number: 0896/

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KEPK/I/2024. Informed consent was obtained via telephone before starting the interview. The telephone interview was conducted by a single researcher to minimize bias in the results. The interview process began with obtaining informed consent, followed by confirming the patient's identity, and then proceeding with questions related to the patient's demographics and socio-economic background, including ethnicity, smoking habits, dietary habits, and work-related hazards.

Inclusion and Exclusion Criteria

The inclusion criteria for this study were patients with nasopharyngeal carcinoma at Dr. Soetomo Hospital from 2017 to 2022 who finished treatment procedures and had documented pre-treatment and post-treatment TNM staging. The exclusion criteria were patients with incomplete data (such as missing information on sex, age, place of origin, pre-treatment, and post-treatment TNM staging) or those who were lost to follow-up with no post-treatment TNM staging available.

Data Analysis

The data analysis in this study was conducted using an observational analytic approach. Secondary data obtained from medical records were systematically categorized based on predefined variables and subsequently presented as frequency distribution tables. To evaluate associations between categorical variables before and during the COVID-19 pandemic, Pearson's Chi-Square test was applied, specifically examining variables such as sex and place of origin. Additionally, the Mann-Whitney U test was employed to compare differences between two independent groups concerning continuous or ordinal variables, including age, pre-treatment TNM staging, post-treatment TNM staging, and treatment outcomes. These statistical methods were selected to rigorously assess the relationships and differences within the dataset, ensuring the robustness of the findings.

RESULTS

The results showed that there is no significant difference before and during the COVID-19 pandemic, that most of the nasopharyngeal carcinoma patients at Dr. Soetomo Hospital were male, aged over 50, and primarily referred from regions outside of Surabaya. Most patients who came to RSUD Dr. Soetomo, in both periods before and during the COVID-19 pandemic, were already in an advanced stage (stage 4), with p = 0.178. It was found that during COVID-19, early-stage patients at stage 2 were about 23% of the total respondents. This phenomenon was not seen before the COVID-19 pandemic.

Post-treatment patient outcomes in Dr. Soetomo Hospital were similar in both periods before and during the COVID-19 pandemic, in which they were in the advanced stage (stage 4) with p: 0.571 (Table 2). The analysis of treatment outcomes for nasopharyngeal carcinoma patients before and during the COVID-19 pandemic revealed no significant differences, with a p-value of 0.081. However, there was a noticeable trend toward worse outcomes during the pandemic. An interesting result is that almost a third of patients before COVID-19 had recovered completely (27%), whereas during COVID-19, no one reached stage 0; in fact, 14% of cases died. While no nasopharyngeal carcinoma patients were found died before COVID-19. With a Partial response, as the highest rate between both periods.

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Table 1. Nasopharyngeal carcinoma patients' demography at Dr. Soetomo Hospital in 2017-2022

Variables Category	Variables	Before COVID-19 (2017-2019) n1 (%)	During COVID-19 (2020-2022) n2 (%)	p value (significancy)
Sex	Male	17 (77.27)	16 (72.73)	0.728*
	Female	5 (22.73)	6 (27.27)	(not significant)
Age	Teenager: <25 y.o	1 (4.55)	1 (4.55)	0.478**
	Early adulthood: 25-35 y.o	1 (4.55)	-	(not significant)
	Late adulthood: 35-50 y.o	6 (27.27)	10 (45.45)	
	Elderly: >50 y.o	14 (63.63)	11 (50.00)	
Place of Origin	Surabaya	4 (18.18)	1 (4.55)	0.154*
	Outside Surabaya	18 (81.82)	21 (95.45)	(not significant)

*: Pearson's Chi-Square Test

**: Mann-Whitney Test

Table 2. Nasopharyngeal carcinoma patients' staging and treatment outcome at Dr. Soetomo Hospital in 2017-2022

Variables Category	Variables	Before COVID-19 (2017-2019) n1 (%)	During COVID-19 (2020-2022) n2 (%)	Mann-Whitney Test p value (significancy)
Pre-Treatment TNM Staging	Stage 2	-	5 (22.73)	0.178
	Stage 3	6 (27.27)	4 (18.18)	(not significant)
	Stage 4	16 (72.73)	13 (59.09)	
Post-Treatment TNM Staging	Stage 0	6 (27.27)	-	0.571
	Stage 1	1 (4.55)	2 (9.09)	(not significant)
	Stage 2	-	6 (27.27)	
	Stage 3	3 (13.64)	2 (9.09)	
	Stage 4	12 (54.55)	12 (54.55)	
Treatment Outcome	Cured	6 (27.27)	-	0.081
	Partial response	8 (36.36)	10 (45.45)	(not significant)
	Stable	2 (9.09)	6 (27.27)	
	Progress	6 (27.27)	3 (13.64)	
	Death	-	3 (13.64)	

There were three post-treatment nasopharyngeal carcinoma patients reported died during COVID-19, as summarized in Table 3. All of them died due to respiratory failure, with only one who was confirmed case due to have COVID-19. Two of the patients have reached stage 4, while one patient has only reached stage 2 of nasopharyngeal carcinoma.

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Table 3. Post-treatment nasopharyngeal carcinoma patient reported dead

Patient initials	Cause of death	Age	Hospital stays	Place of origin
MT	Respiratory failure + nasopharyngeal carcinoma T4N0M1 post-chemo radiotherapy 35x + pneumonia COVID-19 + metastasis	43 y.o	2 days	Situbondo (outside surabaya)
BEH	Respiratory failure + nasopharyngeal carcinoma T2N1M0 post-chemo + pneumonia + septic shock	42 y.o	4 days	Surabaya
SA	Respiratory failure + nasopharyngeal carcinoma T4N2M0 palliative care + pneumonia + septic shock	55 y.o	1 days	Magetan (outside surabaya)

DISCUSSION

This study highlights key risk factors and socioeconomic influences on nasopharyngeal carcinoma (NPC) in Indonesia, with a notable prevalence among males, consistent with findings from Romdhoni et al. (2023). A major risk factor is smoking, which is more common among Indonesian males than females and may introduce carcinogenic nitrosamines that irritate the nasopharyngeal epithelium (Andriani, 2020). Similarly, as stated by Junianto et al. (2022), high consumption of salted fish in Indonesia, commonly associated with local dishes in maritime regions, is another significant dietary risk factor. Although alcohol consumption is an established risk factor, its impact is less pronounced in Indonesia due to religious prohibitions (Nurprasetia, 2022).

Dr. Soetomo Hospital, located in Surabaya, the capital of East Java Province in Indonesia, serves as one of the premier tertiary referral hospitals in the region. According to *Badan Pusat Statistik Provinsi Jawa Timur* (2024), Surabaya itself is home to approximately 3,088,750 residents as of 2024. However, the broader East Java Province encompasses a population of over 38 million people living in cities and rural areas outside Surabaya. Despite this vast population, the cancer care infrastructure remains heavily concentrated in Surabaya, creating significant disparities in healthcare access for residents in more remote areas. This centralized healthcare system often leads to delayed treatments for patients far from Dr. Soetomo Hospital, contributing to poorer health outcomes. This situation worsened during the COVID-19 pandemic, as transportation disruptions further delayed care, contributing to the increased prevalence of advanced-stage nasopharyngeal carcinoma and poorer health outcomes (Chen et al., 2021). Addressing these inequities is crucial for improving public health in East Java and ensuring timely, equitable care for all residents.

Nasopharyngeal carcinoma at Dr. Soetomo Hospital is frequently diagnosed at advanced stages, such as Stage IV, due to factors like non-specific early symptoms (e.g., nasal congestion, ear issues, headaches) that mimic common conditions and delay medical consultation. The tumor's deep location in the nasopharynx, often hidden in submucosal layers, complicates detection during routine exams. These factors explain the high proportion of NPC cases being diagnosed at advanced stages, when the disease has already spread to nearby structures such as lymph nodes, the skull base, or distant sites (Jiang et al., 2024). During the COVID-19 pandemic,

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there was a significant increase in patients presenting with sore throats, often attributed to heightened awareness of respiratory symptoms and fears of COVID-19 infection. Consequently, a higher number of early-stage nasopharyngeal carcinoma diagnoses were observed during the pandemic era compared to the pre-pandemic era, possibly due to this shift in healthcare-seeking behavior (Taylor et al., 2022).

Research conducted by Chen (2020) highlights how the COVID-19 pandemic disrupted cancer care globally, significantly delaying treatment for nasopharyngeal carcinoma while increasing severity and mortality rates. These phenomena were also observed at Dr. Soetomo Hospital. Key factors contributing to worsening outcomes for nasopharyngeal carcinoma patients included the re-shifting of healthcare resources, reallocation of hospital beds to COVID-19 cases, and severe shortages of medical supplies. At Dr. Soetomo Hospital, non-emergency services were reduced, including outpatient clinic appointments, which were shifted to telemedicine. This shift limited the ability of NPC patients to rely fully on remote care due to the need for physical exams and laboratory work (Linjawi et al., 2023).

A study by Wang et al. (2024) examined the challenges social distancing posed for routine healthcare, noting a shift to telemedicine and significant changes in healthcare infrastructure, which altered patient experiences. In Indonesia, from January to August 2020, about 241 regulations, with 100 focused on Large-Scale Social Restrictions (PSBB), were enacted, requiring citizens to adapt to new healthcare access protocols (Yogadhita et al., 2021). These regulations are explicitly detailed in *Peraturan Pemerintah Republik Indonesia No. 21 Tahun 2020 tentang Pembatasan Sosial Berskala Besar dalam Rangka Percepatan Penanganan Corona Virus Disease 2019*. At Dr. Soetomo General Hospital, PSBB policies prioritized COVID-19 patients, especially those with severe symptoms, in line with government regulations (Permenkes No. 9 Tahun 2020). Additionally, the hospital implemented changes, categorizing care by patient severity to expedite COVID-19 treatment, which led to delays or redirection of non-COVID patients, impacting access for those with cancer and chronic illnesses.

Referring to Linjawi et al. (2023) research findings, during the COVID-19 pandemic, cancer patients faced increased mortality risks, primarily due to their immunocompromised state from treatments like chemotherapy and radiation, which led to more hospitalizations, infections, and higher mortality rates. SARS-CoV-2 also elevated cytokine levels, promoting cancer growth and spread. While COVID-19 vaccines were safe for cancer patients, seroconversion rates were lower than in the general population. Psychological and cellular stressors, including economic hardships and social instability, are linked to Epstein-Barr virus (EBV) reactivation, a process heightened by oxidative stress and radiation exposure (Schmeer et al., 2019). EBV reactivation, further impacted by age, sex, and stress, has been associated with pain and depressive symptoms, especially in females (Bale et al., 2015). Recent research by Hashimoto et al. (2023) indicates that COVID-19 itself may trigger EBV reactivation, contributing to long COVID symptoms. Elevated EBV antibody levels have been observed in COVID-19 patients, particularly those with long COVID, underscoring the complex interactions between COVID-19, immunosuppression, and virus reactivation that affect cancer patient outcomes and recovery trajectories. The limitation of this study was that several subjects could not be contacted to gather additional information

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regarding key factors such as ethnicity, smoking habits, diet, and work-related hazards, which were unfortunately not documented in each patient's medical record.

CONCLUSION

Our study on nasopharyngeal carcinoma patients at Dr. Soetomo Hospital from 2017 to 2022 highlighted several key findings when comparing the pre-pandemic period to the COVID-19 pandemic era. The demographic characteristics of patients remained consistent across both periods, predominantly featuring male, elderly, and referral patients with already in advanced-stage nasopharyngeal carcinoma (stage 4). While the post-treatment outcomes for nasopharyngeal carcinoma before and during the COVID-19 pandemic did not show a significant difference, a greater number of patients achieved remission and survived before the pandemic compared to during the pandemic. This disparity may be attributed to the redirection of medical resources towards COVID-19 cases, as well as factors such as the immunocompromised state of patients, lower seroconversion rates, and the reactivation of the Epstein-Barr virus in nasopharyngeal carcinoma patients.

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