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RESEARCH ARTICLE

Thrombocytopenia after treatment for nasopharyngeal carcinoma: a comparison of radiotherapy and chemoradiotherapy

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ABSTRACT

Nasopharyngeal carcinoma (NPC) arises from the nasopharyngeal epithelium. Radiotherapy is the mainstay for locoregional NPC, while concurrent chemoradiotherapy is standard for advanced locoregional disease. Both modalities can affect hematopoiesis and alter platelet counts, but comparative data on treatment-related thrombocytopenia are limited. We retrospectively reviewed medical records of 66 NPC patients treated at Dr Kariadi General Hospital between 2016 and 2023. Collected variables included age, sex, histopathological type, stage, and platelet counts before and after therapy. Descriptive statistics summarised patient characteristics. Paired T-tests were used to evaluate within-patient changes in platelet count pre- versus post-treatment. The association between treatment modality (radiotherapy vs chemoradiotherapy) and occurrence of thrombocytopenia was assessed using the Chi-Square test. Most patients were male (75.8%) and ≥40 years old (75.8%). WHO type 3 histology comprised 83.3% of cases; stage IVA was the most common stage (42.4%). Mean platelet counts decreased from 364.18 × 103/µL to 248.76 × 103/µL after radiotherapy, and from 390.18 × 103/µL to 209.24 × 103/µL after chemoradiotherapy. Thrombocytopenia occurred in 5/33 patients (15.2%) receiving radiotherapy and 13/33 patients (39.4%) receiving chemoradiotherapy. In this cohort, NPC predominantly affected males ≥40 years with WHO type 3 histology and stage IVA disease. Both radiotherapy and chemoradiotherapy were associated with reductions in platelet count, with a higher observed incidence of thrombocytopenia following chemoradiotherapy. Prospective studies with larger samples are warranted to confirm these findings and to identify risk factors for clinically significant thrombocytopenia.

1. Introduction

Nasopharyngeal carcinoma (NPC) is a malignancy of the nasopharyngeal epithelium, classically arising from the fossa Rosenmüller, with propensity to metastasise to regional lymph nodes and distant sites (Sinha & Gajra, 2024). Common presenting symptoms include neck masses, nasal congestion, epistaxis, hearing impairment, diplopia, and weight loss; frequent signs are bloody nasal discharge, nasal obstruction, unilateral conductive hearing loss, tinnitus, otalgia, and otorrhea (Shah & Nagalli, 2022; Stan *et al.,* 2022).

NPC incidence shows marked geographic variation: the highest rates occur in Guangdong Province, southern China (≈20–40 per 100,000) (Adham *et al.,* 2012), while in Indonesia the prevalence is reported at 6.2 per 100,000, ranking NPC among the five most common cancers (WHO, 2020). Although the aetiology is not fully understood, Epstein–Barr virus (EBV) infection, genetic susceptibility, and environmental exposures are major contributors (Chang *et al.,* 2021).

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Histopathologically, NPC is classified as keratinising squamous cell carcinoma (WHO type 1), non-keratinizing squamous cell carcinoma (differentiated, WHO type 2; undifferentiated, WHO type 3), and, less commonly, basaloid squamous cell carcinoma (Shah *et al.,* 2020; Sharif *et al.,* 2020).

Radiation therapy remains the primary treatment for locoregional NPC without distant metastasis. Ionising radiation produces reactive species (H+, OH–) that damage DNA, causing double-strand breaks, crosslinks, and base modifications, thereby leading to tumour cell death (Widiastuti, 2019). For advanced locoregional disease, concurrent chemoradiotherapy is standard; systemic chemotherapy (commonly platinum-based regimens) potentiates radiotherapy efficacy by increasing cancer cell radiosensitivity and enabling delivery of effectively higher tumoricidal doses (Rallis *et al.,* 2021).

Both radiotherapy and chemoradiotherapy adversely affect the hematopoietic system. Radiation can damage bone marrow, inducing apoptosis, hematopoietic stem cell (HSC) differentiation and senescence, and stromal injury, resulting in reduced platelet production. Chemotherapy similarly perturbs hematopoiesis via direct cytotoxicity and cytokine-mediated dysfunction, leading to thrombocytopenia that may impair hemostasis and, in severe cases, cause life-threatening bleeding (Gao *et al.,* 2023; Jinna & Kandhar, 2023).

Clinical studies have reported treatment-related cytopenias in NPC: paclitaxel–cisplatin regimens have been associated with leukopenia and thrombocytopenia (Audina *et al.,* 2019), and declines in haemoglobin, neutrophil, and platelet counts have been documented after the same regimen (Zulkarnain *et al.,* 2017). Evidence also indicates a risk of severe thrombocytopenia during chemoradiotherapy (Hu *et al.,* 2022). Given these findings, this study aims to compare the incidence of thrombocytopenia in NPC patients treated with radiotherapy alone versus concurrent chemoradiotherapy using a paclitaxel-cisplatin regimen.

2. Materials and Methods

Study design and setting

This cross-sectional study used secondary data extracted from medical records at Dr Kariadi General Hospital, Semarang. Data collection and analysis were performed from August to October 2023 for patients treated between 2016 and 2022.

Participants and sampling

Consecutive non-probability sampling was used to identify eligible patients. Inclusion criteria were age 18–70 years; histologically confirmed nasopharyngeal carcinoma; receipt of either radiotherapy alone or concurrent chemoradiotherapy using a paclitaxel–cisplatin regimen; and availability of complete medical records including pre- and post-treatment platelet counts. Exclusion criteria were concurrent viral infections or other systemic diseases likely to affect platelet counts.

Variables and outcomes

Primary outcome: thrombocytopenia, defined as platelet count $<150 \times 103/\mu L$. Secondary outcomes: mean change in platelet count from pre-treatment to post-treatment, occurrence of grade ≥3 thrombocytopenia, treatment interruptions attributed to cytopenia, and transfusion events (if available). Primary independent variable: treatment modality (radiotherapy vs chemoradiotherapy). Covariates: age, sex, WHO histology, and stage.

Statistical analysis

Analyses were performed using SPSS Statistics version 25. Continuous variables are presented as mean ± standard deviation (SD) or standard error (SE); categorical variables are presented as counts and percentages. Test assumptions for normality using Shapiro–Wilk and homogeneity of variance using Levene tests showed the data were distributed normally and had homogeneous variances. Within-group pre- to post-treatment platelet changes were evaluated using Paired T-tests. The incidence of thrombocytopenia between radiotherapy and chemoradiotherapy groups was compared using the Chi-Square test. A two-sided $p<0.05$ was considered statistically significant.

3. Results

Sixty-six NPC patients met inclusion criteria (33 received radiotherapy and 33 received concurrent chemoradiotherapy. Patient characteristics are summarised in Table 1. Most patients were ≥40 years (50/66, 75.8%), male (44/66, 66.7%), WHO type 3 (55/66, 83.3%), and stage IVA (28/66, 42.4%).

Platelet counts (mean ± SD) before and after therapy are shown in Table 2. In the radiotherapy group, mean platelet count decreased from $364.18 \pm 17.82 \times 103/\mu L$ to $248.76 \pm 17.66 \times 103/\mu L$. In the chemoradiotherapy group, mean platelet count decreased from $390.18 \pm 22.90 \times 103/\mu L$ to $209.24 \pm 23.05 \times 103/\mu L$.

Normality (Shapiro–Wilk) and homogeneity of variance (Levene) assumptions were met, permitting paired t-tests. The within-group reductions in platelet count were statistically significant for both radiotherapy (mean difference $115.24 \times 103/\mu L$; $t = 4.913$; $df = 32$; $p < 0.001$) and chemoradiotherapy (mean difference

Table 1. NPC Patient Characteristic

Variable	Radiotherapy (n)	Chemoradiotherapy (n)	Total (n, %)
Age			
• < 40 years	8	8	16 (24.4)
• ≥ 40 years	25	25	50 (75.8)
Gender			
• Male	21	23	44 (66.7)
• Female	12	10	22 (33.3)
Stage			
• I	4	3	7 (10,6)
• II	3	6	9 (13.6)
• II	9	7	16 (24.2)
• IVA	14	14	28 (42.4)
• IVB	3	3	6 (9.1)
• Histopathological type			
• WHO 1	0	0	0 (0)
• WHO 2	7	4	11 (16.7)
• WHO 3	26	29	55 (83.3)

Table 2. Platelet count before and after therapy

Therapy	Mean	n	SD	SE
Radiotherapy				
• Before	364.18	33	16 (24.40)	17.82
• After	248.76	33	50 (75.80)	17.66
Chemoradiotherapy				
• Before	21	23	44 (66.7)	22.897
• After	12	10	22 (33.3)	23.046

Table 3. T-test results on platelet count before and after therapy

Therapy	Mean	Std.Deviation	T test	df	Sig.(2-tailed)
Radiotherapy	115.24	134.956	4,913	32	0.000
Chemoradiotherapy	180.939	136.138	7.635	32	0.000

Table 4. The incidence of thrombocytopenia after therapy

Outcome	Radiotherapy (n ,%)	Chemoradiotherapy (n, %)	Total
Thrombocytopenia			
• Yes	5 (15.2)	13 (39.4)	18 (27.3)
• No	28 (84.8)	20 (60,6)	48 (72.7)
Total	33	33	66 100)

180.94 ×1003/μL; t = 7.635; df = 32; p < 0.001) (Table 3).

Thrombocytopenia (platelets <150 ×103/μL) occurred in 5/33 patients (15.2%) in the radiotherapy group and 13/33 patients (39.4%) in the chemoradiotherapy group (Table 4). Chi-square analysis showed a significant association between treatment modality and thrombocytopenia (Pearson $\chi 2 = 4.889$; df = 1; p = 0.027). No expected cell counts were <5. The Chi-Square test for thrombocytopenia in both radiotherapy and chemoradiotherapy. No cell has an expected count of less than 5, and the minimum expected count is 9.00. The Asym Sig. value is 0.027 < 0.05, indicating a significant difference between the types of therapy and the occurrence of thrombocytopenia.

4. Disscussion

In this cohort of 66 NPC patients, most were aged ≥40 years (50, 75.8%), male (44, 66.7%), had WHO type 3 histology (55, 83.3%), and were diagnosed at stage IVA (28, 42.4%). These demographic and clinicopathologic patterns are consistent with prior reports from endemic and regional centres. Yao *et al*. (2021) found the highest proportion of NPC cases in the 40–49-year age group (38.4%) at Sun Yat-Sen University Cancer Centre, and similar age distributions were reported at Dr Cipto Mangunkusumo General Hospital (Adham *et al.,* 2012). The predominance of older productive-age patients may reflect carcinogen exposure during active working years and a long latency between exposure and disease onset, as well as interactions between environmental risk

factors and genetic susceptibility that impair immune control of EBV (Fauzan *et al.,* 2022).

Male predominance in our series accords with large institutional series (Yao *et al.,* 2021; Tan *et al.,* 2018). Higher male risk is often attributed to greater exposure to carcinogens and lifestyle factors; sex-related biological differences (including hormonal influences and receptor expression) may also contribute to disparities in incidence and prognosis (Yu *et al.,* 2022).

The overwhelming predominance of WHO type 3 histology is typical of endemic regions and mirrors large institutional findings (Yao *et al.,* 2021; Reffai *et al.,* 2021). Endemic areas show higher anti-EBV IgA titers and frequent detection of EBV gene products and monoclonal viral genomes in tumours, supporting an EBV-driven pathogenesis and clonal expansion of EBV-infected cells (WU *et al.,* 2018).

The high proportion of patients presenting with stage IVA reflects delayed detection and referral, as reported in other Indonesian series (Susetiyo *et al.,* 2022; Asnir *et al.,* 2020). Diagnostic delays likely stem from both patient factors (low symptom recognition and delayed help-seeking) and health-system factors (limited recognition and referral of nonspecific early symptoms at primary care level) (Al-Azri *et al.,* 2016).

Both treatment modalities in this study were associated with significant declines in platelet counts. After radiotherapy alone, mean platelet count fell from 364.18 ×103/μL to 248.76 ×103/μL; similar declines after radiotherapy have been reported (Romdhoni *et al.,* 2020). Radiation-induced bone marrow injury, characterised by HSC apoptosis, skewed differentiation, stromal damage, and ROS-mediated HSC ageing, provides a biologic mechanism for reduced megakaryopoiesis and subsequent thrombocytopenia (Shao *et al.,* 2014).

The chemoradiotherapy group exhibited a larger mean platelet decline (390.18 ×103/μL to 209.24 ×103/μL), and a higher incidence of thrombocytopenia compared with radiotherapy alone. Prior work has documented significant cytopenias after paclitaxel–cisplatin regimens (Zulkarnain *et al.,* 2017; Audina *et al.,* 2019), and reports of severe thrombocytopenia during chemoradiotherapy exist (Hu *et al.,* 2022). Mechanistically, paclitaxel interferes with microtubule dynamics, induces apoptosis in marrow progenitors (via p53 and CDKI pathways), and impairs proliferative capacity (Bagby, 2004; Barabas *et al.,* 2008). Cisplatin produces DNA crosslinks and enhances ROS formation, triggering mitochondrial apoptotic cascades in hematopoietic progenitors (Kumar *et al.,* 2010). The combined marrow toxicity of concurrent chemoradiation likely explains the greater platelet nadir and higher rates of thrombocytopenia observed.

Study limitations include the retrospective design, modest sample size, and lack of standardisation or adjustment for potential confounders (age, sex, histology, stage, baseline platelet differences, and comorbidities). We did not perform multivariable adjustment due to limited event counts, and detailed data on transfusions, bleeding events, or timing of nadir platelet counts were incomplete. These limitations restrict causal inference and the generalizability of findings. Future prospective studies should standardise baseline covariates, include larger samples, capture serial platelet trajectories and clinical bleeding outcomes, and compare different chemotherapy regimens to delineate regimen-specific hematologic risks.

5. Conclusions

In this single-center retrospective cohort, NPC patients were predominantly ≥40 years, male, WHO type 3, and diagnosed at stage IVA. Both radiotherapy and concurrent paclitaxel–cisplatin chemoradiotherapy were associated with significant declines in platelet counts; chemoradiotherapy was linked to a higher incidence of thrombocytopenia than radiotherapy alone. Prospective, adequately powered studies that adjust for clinical covariates and examine regimen-specific toxicity are needed to guide monitoring and supportive-care strategies.

Conflict of interest

The authors declare that they have no conflicts of interest.

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