**Glosains: Jurnal Sains Global Indonesia**
**Volume 7, Issue 3, 1029-1037**
**e_ISSN: 2798-4311**
https://glosains.staiku.ac.id
DOI: doi.org/10.59784/glosains.v7i3.772

# Correlation Between Duration of Docetaxel Administration and Epiphora Severity in Nasopharyngeal Carcinoma Patients

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**Article Info:**

***Article history*:**
Received: May 04, 2026
Revised: June 18, 2026
Accepted: June 23, 2026

***Keywords*:**
Docetaxel; Epiphora; Munk Score; Nasopharyngeal Carcinoma

**Abstract**

**Background:** Docetaxel, an effective chemotherapeutic agent for various cancers, including nasopharyngeal carcinoma, is associated with epiphora as a notable adverse effect.
**Objective:** This study aimed to investigate the correlation between the duration of docetaxel administration and the severity of epiphora, as assessed by the Munk score, in patients with nasopharyngeal carcinoma.
**Methods:** A descriptive cross-sectional study was undertaken at the Ophthalmology Polyclinic of Dr. Mohammad Hoesin Hospital, Palembang, from January to August 2024. The study sample comprised n=25 patients who met the research criteria. Epiphora severity was measured using the Munk score. Statistical analysis was performed using Spearman's rank correlation test.
**Results:** The majority of patients were male (68.2%) and aged ≤50 years (77.3%). Most received an 80 mg docetaxel dose (91%) for six weeks (77.3%). Based on the Munk score, 86.4% of patients had a score of 1, and 13.6% had a score of 2. No significant associations were found between Munk score and gender (p=0.445), age (p=0.578), or docetaxel dose (p=1.000). However, the duration of docetaxel administration was significantly associated with Munk score (p=0.001) and showed a moderate positive correlation with epiphora severity (r=0.626; p=0.001).
**Conclusion:** Patients with a Munk score of 2 received docetaxel for a longer duration. A longer duration of docetaxel administration is associated with a higher Munk score for epiphora in nasopharyngeal carcinoma patients.

**To cite this article:** Erna, R., Sidharta, R., Utama, D. S., & Harahap, D. H. (2026). Correlation between duration of docetaxel administration and epiphora severity in nasopharyngeal carcinoma patients. *Glosains: Jurnal Sains Global Indonesia*, 7(3), 1029–1037. https://doi.org/10.59784/glosins.v7i3.772

## INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a distinct type of head and neck cancer with a unique geographic distribution, showing high prevalence in Southeast Asia, including Indonesia (Salehiniya et al., 2018; Su et al., 2024). Epidemiological studies indicate that NPC incidence is significantly higher in Asian populations compared with Western countries, with peak occurrence typically reported between the ages of 40 and 60 years (Hutajulu et al., 2021; Kanno et al., 2019). Several risk factors have been identified, including Epstein–Barr virus infection, genetic susceptibility, and environmental influences, all of which contribute to the complex pathogenesis of this malignancy (Zuo et al., 2019).

Docetaxel is one of the most widely used chemotherapeutic agents in the management of various malignancies, including nasopharyngeal carcinoma (Liu et al., 2018; Xie et al., 2025). It exerts its antitumor activity by stabilizing microtubules and inhibiting mitotic cell division,

ultimately leading to cancer cell apoptosis (Sebastian & Rathinasamy, 2023). Due to its effectiveness, docetaxel is frequently incorporated into combinationn chemotherapy regimens for NPC patients. However, despite its clinical benefits, docetaxel is associated with a range of adverse effects that may significantly affect patients' quality of life.

Among these adverse effects, ocular complications, particularly epiphora, have been increasingly recognized. Epiphora is defined as excessive tearing resulting from either overproduction of tears or impaired tear drainage (Acır & Cetinkaya, 2025). Previous studies have demonstrated that docetaxel can induce alterations in the ocular surface, including damage to the conjunctival and corneal epithelium, which may contribute to tear film instability (Stjernschantz & Astin, 2019; Stoicescu et al., 2021). In addition, docetaxel has been associated with stenosis of the lacrimal drainage system, further exacerbating tear retention and leading to persistent epiphora (Kim et al., 2012). Epidemiologically, the incidence of epiphora among taxane users has been reported at 55.6 per 10,000 person-years, significantly higher than that among tamoxifen users at 7.9 per 10,000 person-years, underscoring the clinical burden of this complication (Sodhi et al., 2022).

The pathophysiological mechanism underlying docetaxel-induced epiphora is believed to involve chronic inflammation and fibrosis of the lacrimal drainage apparatus. This process is mediated by the release of cytokines and growth factors that promote angiogenesis, fibroplasia, and mucosal remodeling within the lacrimal system (Garg & Zhang, 2017; Yao & Zhang, 2017). Over time, these structural changes may lead to canalicular obstruction, which is considered a key contributor to chronic epiphora in patients receiving docetaxel (Esmaeli et al., 2002).

The incidence and severity of epiphora appear to vary depending on the regimen, frequency, and duration of docetaxel administration. Previous studies have reported that weekly docetaxel regimens are associated with a higher incidence of epiphora compared with three-weekly regimens, suggesting that cumulative exposure plays an important role in the development of this adverse effect (Yamagishi et al., 2014). However, most existing studies have focused on treatment frequency or cumulative dose rather than specifically evaluating the duration of therapy as an independent factor influencing epiphora severity. Additional confounding factors, including concurrent radiotherapy to the head and neck region, concomitant use of other chemotherapeutic agents, and pre-existing ocular conditions, may also significantly influence epiphora development and severity (Soni et al., 2023).

Despite the growing body of evidence on docetaxel-induced ocular toxicity, limited research has specifically examined the relationship between the duration of docetaxel administration and the severity of epiphora in patients with nasopharyngeal carcinoma. This represents an important knowledge gap, particularly in clinical settings where treatment duration may vary depending on patient response and therapeutic protocols. Therefore, this study aims to analyze the correlation between the duration of docetaxel administration and the degree of epiphora, as measured by the Munk score, in patients with nasopharyngeal carcinoma. While cumulative dose and treatment frequency have been studied, duration as an independent factor, separate from cumulative dose, has not been adequately characterized, particularly in NPC patients who may have different exposure patterns compared with breast cancer patients.

## METHOD

This study employed an observational analytic, cross-sectional design to evaluate the correlation between the duration of docetaxel administration and the severity of epiphora in patients with nasopharyngeal carcinoma. The study was conducted at the Ophthalmology Polyclinic of Dr. Mohammad Hoesin Hospital, Palembang, Indonesia, from January to August 2024.

The study population consisted of patients diagnosed with nasopharyngeal carcinoma who were undergoing docetaxel-based chemotherapy. A consecutive sampling technique was used to recruit eligible participants who met the inclusion criteria during the study period. The inclusion criteria were patients aged ≥18 years, currently receiving docetaxel chemotherapy, with no prior history of epiphora before treatment, and willing to participate by providing informed consent. Patients with pre-existing ocular surface disorders, anterior segment infections or inflammation, eyelid abnormalities, or a history of eyelid or lacrimal surgery were excluded from the study.

The primary independent variable in this study was the duration of docetaxel administration, measured in weeks based on patients' chemotherapy records. The dependent variable was the severity of epiphora, assessed using the Munk score, a standardized clinical grading system ranging from 0 to 4, where higher scores indicate more severe tearing. A score of 0 indicates no epiphora, while scores of 1 to 4 represent increasing frequency of tear wiping required by the patient. Data were collected through clinical examination and medical record review. Ophthalmological assessments were performed to evaluate the presence and severity of epiphora. All collected data were recorded in a standardized data collection form to ensure consistency and accuracy.

Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics were used to summarize patient characteristics, including age, sex, docetaxel dose, and duration of therapy. The association between categorical variables and epiphora severity was analyzed using the Chi-square test. The correlation between the duration of docetaxel administration and the Munk score was analyzed using Spearman's rho correlation test, as the data were not normally distributed. A p-value of $<0.05$ was considered statistically significant. Munk score assessments were performed by a certified ophthalmologist to ensure standardized evaluation across all participants.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Dr. Mohammad Hoesin Hospital. All participants provided written informed consent prior to inclusion in the study. To ensure data reliability, all clinical assessments were performed using standardized procedures by trained healthcare professionals. The evaluation of epiphora severity using the Munk score was conducted consistently to minimize inter-observer variability. In cases where discrepancies occurred, reassessment was performed to achieve consensus.

Data management was carried out systematically, including verification and validation to ensure completeness and accuracy. Prior to statistical analysis, data were checked for normality using appropriate tests to determine distribution patterns. This step was essential in selecting the appropriate statistical methods for further analysis. In addition, efforts were made to control potential sources of bias by applying strict inclusion and exclusion criteria. Although this study did not include a control group, the use of a homogeneous study population helped reduce variability and improve internal validity. All patient data were anonymized to maintain confidentiality, and access to the dataset was restricted to the research team. Ethical considerations were strictly adhered to throughout the study process.

Based on a power analysis for Spearman's correlation with a medium effect size ($r = 0.5$), a significance level of $\alpha = 0.05$, and a power of 0.80, the minimum required sample size was estimated at 29 participants. The present study included 25 patients, which represents a limitation acknowledged in the limitations section. The study site, Dr. Mohammad Hoesin Hospital, was selected as it is the primary oncology referral center in Palembang, South Sumatra, offering comprehensive chemotherapy and ophthalmology services, with a documented patient volume sufficient for recruitment within the study period.

## RESULTS AND DISCUSSION

### Results

In this study, the majority of patients were male (68%), with a male-to-female ratio of 2:1. The mean age of nasopharyngeal carcinoma patients was 46.28 years (range, 33–56 years), with patients aged ≤50 years outnumbering those aged >50 years in a ratio of 4:1.

In this study, 22 out of 25 nasopharyngeal carcinoma patients (88%) experienced epiphora. The majority of epiphora patients were male (68.2%), with a male-to-female ratio of 2:1. The mean age of epiphora patients was 47.05 years (range, 33–56 years), with patients aged ≤50 years outnumbering those aged >50 years in a ratio of 3:1.

In this study, 22 out of 25 nasopharyngeal carcinoma patients (88%) experienced epiphora. The majority of epiphora patients were male (68.2%), with a male-to-female ratio of 2:1. The mean age of epiphora patients was 47.05 years (range, 33–56 years), with patients aged ≤50 years outnumbering those aged >50 years in a ratio of 3:1.

Nasopharyngeal carcinoma patients with epiphora requiring wiping less than twice a day (Munk score 1) were the most common group (86.4%) in this study. Only 3 patients (12%) had no epiphora. Similarly, only 3 patients (13.6%) had epiphora requiring wiping 2–4 times a day (Munk score 2). However, no patients with epiphora requiring wiping more than 4 times a day (Munk scores 3 and 4) were found in this study. The majority of nasopharyngeal carcinoma patients received a docetaxel dose of 80 mg (91%) and had received docetaxel for 6 weeks (77.3%).

Nasopharyngeal carcinoma patients with epiphora requiring wiping less than twice a day (Munk score 1) were also the most common group (76%) in this study. Only 3 patients (12%) had no epiphora. Similarly, only 3 patients (12%) had epiphora requiring wiping 2–4 times a day (Munk score 2). However, no patients with epiphora requiring wiping more than 4 times a day (Munk scores 3 and 4) were found in this study. The majority of nasopharyngeal carcinoma patients received a docetaxel dose of 80 mg (92%) and had received docetaxel for 6 weeks (80%).

**Table 1.** Clinical and Demographic Characteristics of Patients with Epiphora (n=22)

| Characteristic | N (%) (n = 22) | Mean±SD<br>Median (Min-Max) |
|---|---|---|
| **Gender** | | |
| Male | 15 (68.2) | - |
| Female | 7 (31.8) | |
| **Age (years old)** | | |
| >50 years old | 5 (22.7) | 47.05±5.56 |
| ≤50 years old | 17 (77.3) | 47.5 (33-56) |
| **Doxetacel Dose** | | |
| 40 mg | 1 (4.5) | 80.0±12.34 |
| 80 mg | 20 (91.0) | 80 (40-120) |
| 120 mg | 1 (4.5) | |
| **Duration Therapy** | | |
| 6 weeks | 17 (77.3) | 7.44±3.14 |
| 12 weeks | 4 (18.2) | 6 (6-18) |
| 18 weeks | 1 (4.5) | |
| **Munk Score** | | |
| 1 | 19 (86.4) | - |
| 2 | 3 (13.6) | |
| 3 | 0 (0) | |
| 4 | (0) | |

Note: Data are presented as n (%) for categorical variables and as mean ± SD or median (min-max) for continuous variables. SD = Standard Deviation.

**Characteristics of the Study Sample Based on the Munk Score**

This study found no differences in gender (p = 0.445), age (p = 0.578), or docetaxel dose (p = 1.000). However, there was a difference in the duration of docetaxel administration according to the Munk score (p = 0.001). All mean docetaxel doses were similar between patients without epiphora and those with epiphora with Munk scores of 1 and 2. However, patients with a Munk score of 2 had the longest and statistically significant duration of docetaxel administration.

**Table 2. Distribution of Patient Characteristics Based on Munk Score**

| Characteristic | Munk Score | | | *P value* |
|---|---|---|---|---|
| | **0** | **1** | **2** | |
| **Gender** | | | | |
| Male | 2 (66,7) | 12 (63,2) | 3 (100) | 0,445[a] |
| Female | 1 (33,3) | 7 (36,8) | 0 (0) | |
| **Age (years old)** | | | | |
| > 50 years old | 0 (0) | 4 (21,2) | 1 (33,3) | 0,578[a] |
| ≤ 50 years old | 3 (100) | 15 (78,9) | 2 (66,7) | |

| Characteristic | Munk Score | | | *P value* |
|---|---|---|---|---|
| | **0** | **1** | **2** | |
| **Duration Therapy — Numerical Data** | | | | |
| Mean ± SD | 6,0 ± 0,0 | 6,63 ± 1,89 | 14,0 ± 3,46 | 0,001[b] |
| Median | 6 | 6 | 15 | |
| Min - Max | 6 - 6 | 6 - 12 | 12 - 18 | |
| **Duration Therapy — Data Categorical** | | | | |
| 6 minggu | 17 (77,3) | 17 (89,5) | 0 (0) | 0,001[a] |
| 12 minggu | 4 (18,2) | 2 (10,5) | 2 (66,7) | |
| 18 minggu | 1 (4,5) | 0 (0) | 1 (33,3) | |

**Description:**
- Categorical data are presented as the number of patients and percentages: *n* (%).
- Numerical data are presented as mean ± standard deviation (Mean ± SD), Median, and Minimum–Maximum Values (Min Max). [a]
- Tested using *Chi-Square Test / Fisher's Exact Test*. [b]
- Tested using *Kruskal-Wallis Test / One-Way ANOVA*. - A *P-value* of < 0.05 is considered statistically significant.

Spearman's rho correlation test revealed a moderate positive correlation between the duration of docetaxel administration and the degree of epiphora based on the Munk score (r = 0.626; p = 0.001). This finding indicates that longer exposure to docetaxel is associated with higher severity of epiphora in patients with nasopharyngeal carcinoma. The correlation was statistically significant (p = 0.001), and its strength was interpreted as moderate according to Cohen's conventions.

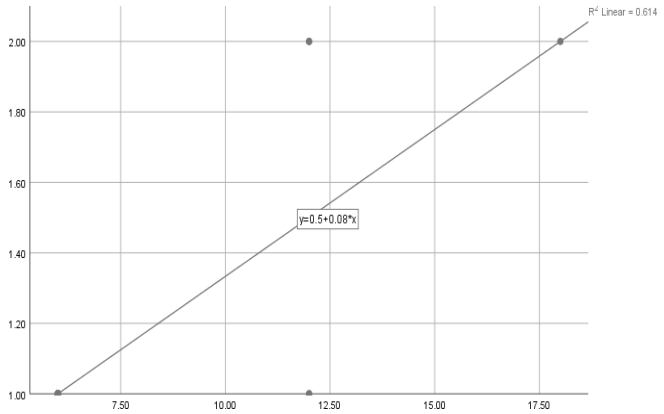


**Figure 1.** Correlation between The Duration of Docetaxel Administration and The Degree of Epiphora**.**

**Table 3.** Correlation between the Duration of Docetaxel Administration and the Degree of Epiphora in Nasopharyngeal Cancer Patients

| **Variable** | **r** | **P value** |
|---|---|---|
| Duration of Docetaxel Administration Munk Score | 0.626 | 0.001* |

*Spearman Rho's.* *p<0.05

The findings of this study indicate that epiphora was a common clinical manifestation among patients receiving docetaxel chemotherapy, with 88% of patients experiencing this condition. Most cases were classified as mild based on the Munk score, suggesting that although epiphora frequently occurs, its severity tends to remain at a lower level during the early duration of therapy.

In terms of treatment characteristics, the majority of patients received a docetaxel dose of 80 mg and underwent therapy for approximately six weeks. This relatively uniform distribution

of dosage may explain the lack of a significant association between docetaxel dose and epiphora severity observed in this study. In contrast, variation in treatment duration showed a statistically significant relationship with the Munk score, indicating that duration may play a more critical role than dosage in influencing epiphora severity.

Furthermore, patients with higher Munk scores tended to have longer durations of docetaxel administration, particularly those receiving therapy for 12 to 18 weeks. This pattern supports the hypothesis that prolonged exposure contributes to the progression of lacrimal drainage dysfunction. Overall, these findings highlight the importance of monitoring epiphora over extended docetaxel treatment courses in patients with nasopharyngeal carcinoma.

**Discussion**

This study found that nasopharyngeal carcinoma (NPC) patients had a mean age of 46.28 years (range, 33–56 years), with a higher prevalence in patients aged ≤50 years. Furthermore, most patients were male (68%), with a 2:1 male-to-female ratio. Consistent with these findings, that most NPC patients were aged ≤50 years and demonstrated a male predominance (Hong et al., 2021; Kanno et al., 2019).

This study found that NPC patients had a mean age of 46.28 years (range, 33–56 years), with a higher prevalence in patients aged ≤50 years. Furthermore, most patients were male (68%), with a 2:1 male-to-female ratio. Consistent with these findings, studies conducted by Hong (2021) and Kanno (2019) reported that most NPC patients were aged ≤50 years and showed a male predominance.

Docetaxel is an effective chemotherapeutic agent; however, it is associated with several adverse effects, including epiphora (Stoicescu et al., 2021). Epiphora severity can be categorized using the Munk score, ranging from 0 (no epiphora) to 4 (constant epiphora or requiring wiping more than 10 times per day). Higher scores indicate more frequent tearing episodes (Stoicescu et al., 2021). In this study, 86.4% of patients with epiphora had a Munk score of 1 (wiping fewer than 2 times per day), and 13.6% had a score of 2 (wiping 2–4 times per day). Supporting this finding, Sodhi (2022) demonstrated in a large pharmacoepidemiologic cohort study that taxane-based chemotherapy, including docetaxel, was associated with a significantly increased risk of epiphora (adjusted HR = 5.15; 95% CI: 2.79–9.54) compared with tamoxifen users, reinforcing the need for careful ocular monitoring during treatment. Furthermore, Stoicescu (2021) emphasized that ocular toxicities from chemotherapeutic agents, including epiphora, are frequently underrecognized and that ophthalmologic evaluation should be integrated into standard oncology care. Importantly, concurrent radiotherapy, commonly administered in head and neck cancer patients, represents a significant confounding factor that may independently contribute to lacrimal drainage dysfunction and should be considered in interpreting these findings.

This study confirms a significant association between the duration of docetaxel administration and the severity of epiphora in NPC patients. This finding is consistent with the proposed mechanism that docetaxel may induce damage to the lacrimal drainage system, which over time may lead to canalicular or nasolacrimal duct stenosis and epiphora (Stoicescu et al., 2021).

The cumulative dose of docetaxel, which is closely related to treatment duration, has been reported to be higher in patients with canalicular stenosis (Esmaeli et al., 2002). Comparisons with previous studies showing less frequent tearing with triweekly versus weekly docetaxel administration support the idea that exposure frequency and duration may influence epiphora severity (Yamagishi et al., 2014). Esmaeli (2002) also reported significantly higher cumulative docetaxel doses in patients with canalicular stenosis. These findings reinforce the importance of monitoring epiphora severity in patients receiving docetaxel, particularly during prolonged treatment.

This study provides scientific evidence on the association between the duration of docetaxel administration and epiphora severity, offering important clinical implications for NPC patients regarding this potential adverse effect. Therefore, improved communication, education, and counseling regarding docetaxel-associated epiphora are necessary for both patients and healthcare providers.

In addition, from a clinical perspective, early detection and routine ophthalmologic

evaluation are essential for patients undergoing docetaxel chemotherapy to prevent progression to more severe lacrimal drainage disorders (Limura et al., 2026). Collaboration between oncologists and ophthalmologists should be strengthened to ensure optimal patient management and to preserve quality of life during treatment (Stoicescu et al., 2021). Additional limitations include: (1) selection bias due to consecutive (non-probability) sampling, which may limit representativeness; (2) lack of control for concurrent radiotherapy, a major confounder in NPC patients; (3) absence of a priori sample size calculation, reducing statistical power; (4) non-blinded Munk score assessment, which may introduce observer bias.

This study also has several limitations that should be acknowledged. The relatively small sample size and single-center design may limit generalizability. In addition, the case series approach restricts causal inference. Other factors such as cumulative dose, concomitant therapy, and individual susceptibility were not fully analyzed and may influence outcomes. Future studies with larger sample sizes, multicenter designs, and longitudinal follow-up are recommended to further explore the relationship between docetaxel exposure and epiphora severity. The use of objective diagnostic tools, such as lacrimal irrigation or imaging-based assessment, may also provide more robust evidence regarding underlying mechanisms.

Furthermore, the findings emphasize the clinical importance of recognizing epiphora as a potentially progressive adverse effect associated with prolonged chemotherapy exposure. Although most patients experienced mild symptoms, the observed trend toward increased severity with longer treatment duration suggests the need for preventive strategies. Early intervention, including patient education, symptomatic management, and timely referral to ophthalmology services, may reduce the risk of long-term complications and improve overall outcomes. Integrating ophthalmologic assessment into routine oncology care may facilitate early detection of lacrimal drainage dysfunction, enhance patient safety, and support adherence to chemotherapy by minimizing treatment-related discomfort.

This study indicates a statistically significant moderate positive correlation between the duration of docetaxel administration and epiphora severity in NPC patients. Patients with longer chemotherapy duration tended to have higher Munk scores, suggesting an association between prolonged exposure and increased ocular toxicity. However, these findings should be interpreted with caution due to the small sample size (n = 25), cross-sectional design, non-probability sampling, and lack of control for major confounders such as concurrent radiotherapy. Early ophthalmologic monitoring and interdisciplinary collaboration between oncologists and ophthalmologists are recommended. Future multicenter prospective studies with larger samples are needed to validate these findings.

This study demonstrates a statistically significant moderate positive correlation between the duration of docetaxel administration and epiphora severity in NPC patients. Patients with longer chemotherapy duration tended to experience higher Munk scores, indicating more severe epiphora. These findings highlight the importance of treatment duration as a contributing factor to ocular side effects in cancer patients. Early identification and regular monitoring are essential to prevent complications and preserve quality of life during chemotherapy. Integrating routine ophthalmologic evaluation into oncologic care may improve early detection and enable timely intervention, thereby minimizing progression of lacrimal drainage disorders and supporting better treatment adherence.

Further studies with larger sample sizes, multicenter designs, and longer follow-up periods are recommended to validate these findings and explore additional factors such as cumulative dose and patient susceptibility. In addition, this study emphasizes the need for increased awareness among healthcare providers regarding ocular toxicities associated with docetaxel therapy. Recognizing epiphora as an early clinical indicator of lacrimal system involvement may facilitate timely intervention and prevent progression to more severe conditions. Preventive strategies, patient education, and routine ophthalmologic monitoring should be integrated into standard oncology care protocols to improve outcomes and quality of life. Ultimately, these findings provide a foundation for future research aimed at developing targeted interventions to reduce chemotherapy-induced epiphora.

## CONCLUSION

This study demonstrated a statistically significant moderate positive correlation between the duration of docetaxel administration and the severity of epiphora in patients with nasopharyngeal carcinoma. Patients who received docetaxel for a longer duration tended to have higher Munk scores, indicating more severe epiphora symptoms. In contrast, no significant associations were observed between epiphora severity and gender, age, or docetaxel dose. These findings suggest that treatment duration may play a more important role than dosage in the development of docetaxel-associated epiphora.

The results highlight the importance of routine ophthalmologic monitoring during prolonged docetaxel therapy to facilitate early detection and management of ocular complications. Early intervention and interdisciplinary collaboration between oncologists and ophthalmologists may help prevent progression of lacrimal drainage disorders and improve patients' quality of life. Further multicenter studies with larger sample sizes and prospective designs are recommended to validate these findings and explore additional contributing factors, including cumulative dose, concurrent therapies, and individual susceptibility to ocular toxicity.

## ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the Department of Ophthalmology and the Department of Oncology at Dr. Mohammad Hoesin Hospital, Palembang, Indonesia, for their support and assistance during data collection and clinical evaluation. The authors also thank all patients who voluntarily participated in this study and contributed valuable information to the research process. Their cooperation was essential for the successful completion of this study.

## AUTHOR CONTRIBUTION STATEMENT

R.E. contributed to the study conceptualization, research design, data collection, clinical assessment, data interpretation, and manuscript preparation. R.S. contributed to methodology development, data analysis, and manuscript review. D.S.U. contributed to supervision, validation of research findings, and critical revision of the manuscript. D.H.H. contributed to data interpretation, literature review, manuscript editing, and final approval of the manuscript. All authors read, reviewed, and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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