

ABSTRACT

Background: *Nasopharyngeal carcinoma (NPC) is a head and neck malignancy arising in the epithelium of the nasopharyngeal tube. Nasopharyngeal carcinoma (NPC) is a relatively rare malignancy worldwide, ranking 23rd in global incidence, but shows a distinct geographic concentration in East and Southeast Asia. Indonesia ranks second globally for NPC cases, with over 18,000 new diagnoses in 2022, highlighting a significant regional burden. Phosphatase and tensin homolog that is deleted in chromosome ten (PTEN), suppresses tumors by negative regulation of the PI3K/AKT/mTOR signaling pathway thus inhibiting the growth, proliferation, and survival of the carcinoma, including NPC. An association has also been made in previous studies stating that tumor invasion and metastasis, both of which are characteristics of an aggressive tumor, are more prevalent with decreased PTEN expression.*

Objectives: *The aim of this study is to examine the proportion of PTEN tumor suppressor gene expression in different tumor sizes and the involvement of regional lymph nodes in Nasopharyngeal Carcinoma.*

Materials and Methods: *Samples used in this study were Formalin-Fixed, Paraffin- Embedded (FFPE) tissues of NPC patients (n=34). The study detected the expression in PTEN tumor suppressor gene on the tumor samples through the use of immunohistochemistry (IHC) staining. Data for the tumor size and regional lymph nodes were collected from dr. Sardjito General Hospital medical records. Data analysis was performed using chi square-test to determine proportion of PTEN tumor suppressor gene expression in different tumor sizes and the involvement of regional lymph nodes in Nasopharyngeal Carcinoma.*

Results: *The proportion of PTEN expression showed no statistically significant difference in either tumor size and regional lymph node metastasis (tumor size: $P=0.271$; regional lymph node metastasis: $P=0.465$) in nasopharyngeal carcinoma.*

Conclusions: *There is no difference in the proportion of PTEN expression in nasopharyngeal carcinoma tissue in tumor size and regional lymph node metastasis staging.*

Keywords: *Nasopharyngeal carcinoma, PTEN, tumor suppressor gene, Tumor size, Regional Lymph Nodes, immunohistochemistry (IHC) staining*

ABSTRAK

Latar Belakang: *Nasopharyngeal carcinoma (NPC)* merupakan keganasan pada kepala dan leher yang timbul dari epitel pada saluran nasofaring. *Nasopharyngeal carcinoma (NPC)* tergolong sebagai keganasan yang relatif jarang ditemukan di seluruh dunia, menempati urutan ke-23 dalam insidensi global, namun menunjukkan konsentrasi geografis yang khas di Asia Timur dan Asia Tenggara. Indonesia menempati peringkat kedua secara global untuk kasus NPC, dengan lebih dari 18.000 diagnosis baru pada tahun 2022, yang menyoroti beban penyakit yang signifikan di kawasan ini. *Phosphatase and tensin homolog that is deleted in chromosome ten (PTEN)* berperan sebagai penekan tumor melalui regulasi negatif terhadap jalur *PI3K/AKT/mTOR*, sehingga menghambat pertumbuhan, proliferasi, dan kelangsungan hidup karsinoma, termasuk NPC. Beberapa studi sebelumnya juga menunjukkan bahwa invasi dan metastasis tumor yang merupakan karakteristik tumor agresif lebih sering ditemukan pada ekspresi *PTEN* yang menurun.

Tujuan: Penelitian ini bertujuan untuk menilai proporsi ekspresi gen penekan tumor *PTEN* pada berbagai ukuran tumor dan keterlibatan kelenjar getah bening regional pada *Nasopharyngeal Carcinoma*.

Bahan dan Metode: Sampel yang digunakan dalam penelitian ini berupa jaringan *Formalin-Fixed, Paraffin-Embedded (FFPE)* dari pasien NPC ($n=34$). Penelitian ini mendeteksi ekspresi gen penekan tumor *PTEN* pada sampel tumor melalui pewarnaan *immunohistochemistry (IHC)*. Data mengenai ukuran tumor dan kelenjar getah bening regional diperoleh dari rekam medis Rumah Sakit Umum Pusat dr. Sardjito. Analisis data dilakukan menggunakan *chi square-test* untuk menentukan proporsi ekspresi gen penekan tumor *PTEN* pada berbagai ukuran tumor dan keterlibatan kelenjar getah bening regional pada *Nasopharyngeal Carcinoma*.

Hasil: Proporsi ekspresi *PTEN* tidak menunjukkan perbedaan yang bermakna secara statistik baik terhadap ukuran tumor maupun metastasis kelenjar getah bening regional (ukuran tumor: $P=0.271$; metastasis kelenjar getah bening regional: $P=0.465$) pada *nasopharyngeal carcinoma*.

Kesimpulan: Tidak terdapat perbedaan proporsi ekspresi *PTEN* pada jaringan *nasopharyngeal carcinoma* berdasarkan ukuran tumor dan stadium metastasis kelenjar getah bening regional.

Kata kunci: *Nasopharyngeal carcinoma*, *PTEN*, gen penekan tumor, ukuran tumor, kelenjar getah bening regional, pewarnaan *immunohistochemistry (IHC)*

INTRODUCTION

1. Background

With the earliest recorded case going back to the late 1900s, nasopharyngeal carcinoma continues to be a devastating diagnosis until this day (Abdullah et al., 2020). Nasopharyngeal carcinoma also known as NPC, is a squamous cell malignancy arising in the epithelium of the nasopharyngeal tube (Badoual, 2022). NPC is a relatively rare cancer globally, with an estimated 120,434 new cases and 73,482 deaths reported in 2022, ranking 23rd and 21st respectively in global cancer incidence and mortality (Sung et al., 2021). However, the prevalence of NPC shows regional differences, with high incidence rates observed in East and Southeast Asia. Indonesia ranks second globally in NPC incidence and sixth nationally among all cancer types, reporting 18,385 new cases and 12,949 deaths in 2022. The burden of NPC is especially notable in regions with large populations of southern Chinese ancestry, where the disease exhibits family clustering and genetic predisposition, alongside environmental and viral exposures (Abdullah et al., 2020). In Indonesia, NPC accounts for approximately 28.4% of all head and neck cancers (Romdhoni et al., 2023), making it one of the most aggressive and prevalent malignancies after cervical and breast cancer. NPC is rarely diagnosed in the early stages as the symptoms are ambiguous, this in turn causes bad prognosis if the patient receives treatment when diagnosed at an advanced stage. Good or bad prognosis is often determined by these key points: (i) tumor stage, (ii) histopathological type, (iii) involvement of the lower neck lymph nodes, and (iv) tumor extension to intracranial spaces (Sekarutami et al., 2020).

Nasopharyngeal Carcinoma commonly originates from what is known as the *Rosenmüller Fossa*, situated inferior to the cranial base lined with pseudostratified ciliated columnar epithelium (Abdullah et al., 2020). The World Health Organisation (Badoual, 2022) classified NPC into: (i) non-keratinizing NPC, (ii) keratinizing NPC and (iii) basaloid NPC, with non-keratinizing NPC as the most common. Most of these NPC cases are strongly correlated to the Epstein-Barr virus or human herpesvirus 4, which