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Association of LMP1 expression and cancer stage of nasopharyngeal carcinoma patients at Dr. Soetomo Regional General Hospital in January 2023 – December 2023

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Abstract

Nasopharyngeal carcinoma (NPC) is the most common multifactorial malignancy of the nasopharynx. Its prevalence rate is the fourth highest among other malignancies in Indonesia, at 1.2 cases per 100,000. The pathogenesis of NPC cases is closely linked to one of its risk factors, Epstein-Barr Virus, specifically the expression of one of its proteins, LMP1, which is found in almost all NPC patient tissue samples. The role of LMP1 (Latent membrane protein 1) has been proven to influence cancer stage that also linked to poor prognosis, overall survival, and metastasis. However, conflicting studies about significance of the relationship between LMP1 and NPC stage were also found. Therefore, this observational analytical quantitative study with a retrospective approach was conducted to clarify the controversy surrounding the relationship between LMP1 and NPC stage. A total of 40 patients met the inclusion criteria. There were 30 males and 10 were female. The dominant age ranged from 41 to 50 years old (32.5%). Thirty-three patients (82.5%) showed LMP1(+) expression, while seven patients (17.5%) were LMP1(-). Most of these NPC patients were in stage IV (75%). Although number of LMP1(+) patient expression was found in most of the patients and seemed increase in late stage of NPC, the correlation with NPC stage from chi-square test was deemed insignificant (p>0.05).

Keywords: Nasopharyngeal Carcinoma; Lmp1; NPC Stage; Epstein-Barr virus; Retrospective study

1. Introduction

Nasopharyngeal carcinoma (NPC) is the most common multifactorial malignancy of the nasopharynx [1] This carcinoma is endemically distributed worldwide, particularly in Southeast Asia, including Indonesia. Its prevalence rate is the fourth highest among other malignancies in Indonesia, at 1.2 cases per 100,000 population and 12,000 new cases per year [2].

The pathogenesis of NPC cases is closely related to one of its risk factors, Epstein-Barr virus (EBV), particularly the non-keratinizing subtype. Furthermore, many NPC patients are also known to have EBV antibodies [3]. EBV infection is not directly associated with tumor induction, but rather with an increased risk of cancer in healthy individuals [4]. More than 95% of adults worldwide have been infected with EBV and are healthy carriers of the virus. Transformation of EBV infection into malignancy can occur due to a combination of viral activation and epigenetics, including the development of genetic lesions in cells caused by carcinogens, dietary components, and genetic immunodeficiencies, making it a multifactorial disease [2].

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The LMP1 protein is found in nearly all tissue samples from premalignant and preinvasive NPC patients [5,6]. The role of LMP1 expression in mediating invasion, angiogenesis, and metastasis, as well as inducing most inflammatory cytokines and chemokines through the NF-κB and STAT3 pathways, which support tumor progression, has also been demonstrated [7]. These various mechanisms include the induction of matrix metalloproteinase (MMP)-9, the activation of ets-1, c-Met, ezrin, and Mucin 1 (MUC1) through inhibition of cell adhesion, as well as the cooperative interaction between IL-6 and laminin [6]. Furthermore, evidence of a correlation between LMP1 and NPC stage is found in the discovery of higher levels of LMP1 expression in NPC with metastasis compared to those without metastasis [8]. Similar discoveries also highlighted positive associations and results between LMP1 expression with overall survival, tumor progression, and poor prognosis [9,10,11].

These referred investigations implicated LMP1 as pivotal oncogenic driver, particularly in NPC stage, albeit there remain contradictory studies: absence of LMP1 expression in NPC cells [12], the absence of a significant relationship between LMP1 expression and histopathological type, tumor grade (T), nodal status (N), distant metastases (M), and staging [13,14]. Moreover, Khabir et al. [15] observed no association between LMP1 expression and visceral metastasis or disease recurrence. Given the conflicting evidence regarding LMP1's role and its purported association with NPC stage, this study aimed to clarify this discrepancy.

2. Material and methods

This study is an observational quantitative study with retrospective approach. The data collection was done by consecutive sampling according to inclusion criteria. The data contains secondary data of LMP1 expression from representative tissue biopsy paraffin blocks of NPC patients from January 2023–December 2023 from the anatomical pathology installation that is assessed quantitatively (positive/negative expression) through immunohistochemistry and NPC patient stage that evaluated by UICC/AJCC 8th Edition (2017) with the 2020 updated version. The data is grouped based on predetermined variables (positive/negative expression of LMP1 and NPC Stage) and patient characteristics (sex and age group). Then, the data were analyzed using bivariate analysis using chi-square test through SPSS program to determine the association between LMP1 expression and NPC stage.

3. Results and discussion

A total of 40 nasopharyngeal carcinoma (NPC) cases that met the inclusion criteria were identified at Dr. Soetomo Regional General Hospital during the period from January 2023 to December 2023.

3.1. Main Characteristic of NPC Patient

Tabel 1 General Characteristics of NPC Patients at Dr. Soetomo Regional General Hospital, January 2023–December 2023

Variable	Category	Frequency	Percentage
Sex	Male	30	75%
	Female	10	25%
Age (years)	10–20	1	2.5%
	21–30	1	2.5%
	31–40	7	17.5%
	41–50	13	32.5%
	51–60	10	25%
	61–70	6	15%
	71–80	2	5%

Previous studies have been conducted to identify biomarkers in NPC patients, particularly those targeting EBV oncogenic proteins, one of which is LMP1, which plays a significant role in tumorigenesis and NPC progression. This study examined LMP1 expression alongside NPC stage between January 2023 and December 2023. The results showed 30 male and 10 female patients, consistent with relevant studies on the male-to-female NPC ratio of 2.9:1 [16].

NPC is more common in men than in women due to differences in risky habits, such as smoking and higher alcohol consumption. Furthermore, the 5-year survival rate is considered better in women, at 84% compared to 78% in men [17] due to intrinsic female biological factors, such as hormones and sex chromosomes [18].

Most NPC patients in this study are in the age of 41–50 years old. This age range aligns with research by Fauzan et al. [19] which found that the disease is most often found between the ages of 35 and 55. This is influenced by genetic factors, environmental factors, or exposure to carcinogenic substances at an early age. Notably, two young male patients, aged 18 and 27, were diagnosed earlier at stage II. These cases of NPC occurring at a young age are likely possible due to a genetic predisposition that is susceptible to NPC development.

3.2. LMP1 Expression of NPC Patient

Tabel 2 LMP1 Expression in NPC Patients at Dr. Soetomo Regional General Hospital, January 2023–December 2023

Variable	Category	Frequency	Percentage
LMP1 Expression	Positive	33	82.5%
	Negative	7	17.5%

The pathophysiology of NPC is also closely associated with the presence of EBV's primary oncogenic proteins, one of which is LMP1, which was detected in NPC patients. This is reinforced by the high number of positive LMP1 expression findings in 82.5% of patients in this study. Negative LMP1 expression was also found in 17.5% of 40 NPC patients. This undetectable expression may be due to low LMP1 levels, which makes IHC (immunohistochemistry) testing incapable of detecting them, as it has sensitivity limit compared to other methods (RT-PCR and Western Blotting). However, even though LMP1 levels are considered low and undetectable, its contribution in mediating NPC development remains remarkable [20].

Furthermore, there are factors other than the oncogenic EBV virus, such as HPV, smoking, alcohol, consumption of salted fish with preservatives (nitrosamines), and exposure to other carcinogens [21]. Additionally, genetic alterations have been found in NPC patients independent of EBV, such as missing alleles on chromosomes 3p21.3 and 9p21, which inactivate tumor suppressor genes (RASSF1A and p16), thus facilitating NPC expansion and progression [22].

3.3. NPC Stage

Nasopharyngeal carcinoma is also a disease that is difficult to detect early due to its deep location and nonspecific symptoms [23]. This leads to other factors contributing to delayed diagnosis: doctors not considering the diagnosis of NPC, doctors suspecting NPC but misdiagnosing it during screening, and some patients refusing screening or not seeking follow-up [24].

Upon initial diagnosis of NPC, patients often complain of unilateral ear problems with tinnitus, such as Eustachian tube obstruction, otitis media effusion, conductive hearing loss, and otalgia [2] due to the NPC mass compressing the torus tubarius. Furthermore, neck masses, nasal obstruction, and headaches may also occur [25]. These symptoms often lead to suspicion of ear problems or upper respiratory tract infections, which are then misinterpreted as dental problems. This led to repeated visits to the ENT doctor over the course of a year due to lack of improvement in the same symptoms, ultimately leading to nasal endoscopy and CT scans to detect the NPC mass [24,26]

Furthermore, nasal endoscopy screening for NPC masses often results in false-negative results due to the inability to visualize the entire fossa of Rosenmüller, so a contralateral examination is recommended [25]. Other false-negative imaging findings include insufficient contrast, capturing fewer than two sections of the nasopharynx, insufficient axial orientation, and the presence of dental artifacts. Furthermore, misinterpretation of sinusitis symptoms can lead the radiologist to focus more on the sinuses and miss the NPC [25]. These false-negative results, which lead to a missed NPC diagnosis, require further examination with MRI, which has been found to have a sensitivity of >90% [27,28].

Tabel 3 Cancer Stage in NPC Patients at Dr. Soetomo Regional General Hospital, January 2023–December 2023

Variable	Category	Frequency	Percentage
Stage	Stage I	0	0%
	Stage II	3	7.5%
	Stage III	7	17.5%
	Stage IV	30	75%

In this study, the largest number of patients, 30 (75%), were diagnosed with stage IV indicating a tendency for late diagnosis, 7 (17.5%) with stage III, and 3 (7.5%) with stage II. Stage is assessed based on the local extent of the cancer from the site of origin (T), the extent of regional lymph node metastases (N), and the presence or absence of distant metastases (M) by UICC/AJCC 8th Edition (2017) with the 2020 updated version. The most common stage in this study was stage IV, indicating distant metastases, consistent with previous studies [29,30,31].

3.4. Association of LMP1 Expression and NPC Stage

It appears that there is an increase in the number of patients with positive LMP1 expression at higher stages. However, a bivariate chi-square analysis showed no significant results ($p>0.05$). The statistically insignificant results in LMP1 expression according to the stage of NPC patients are likely due to the undetectable LMP1 expression on IHC due to low levels of expression. A study by Baizig et al. [32] in Tunisia, a NPC-endemic area, found that LMP1 is associated with NPC, but not all NPC cases showed LMP1 expression. Even with higher NPC stages, LMP1 expression was not always positive.

However, in clinical and biological contexts, LMP1 is an important factor associated with poor prognosis and the proliferation pathway of nasopharyngeal cancer via IGF-1R. Furthermore, LMP1 has been shown to downregulate cell adhesion to other cells and increase cell motility through the activation of ets-1 and c-Met. Ezrin expression, a link between the plasma membrane and the actin cytoskeleton, can also induce the expression of Mucin 1 (MUC1), which plays a crucial role in tumor invasion and metastasis. LMP1 contributes to the worsening of NPC and acts as a tumor driver [33].

Another study by Liu et al. [34] found that antiapoptotic components involved in NPC progression, such as Bcl-2 via the NF-κB pathway, were also upregulated to prevent cytotoxic signals dependent on LMP1 expression. However, other findings suggest that increased Bcl-2 expression is independent of LMP1, as evidence exists that LMP1 silencing does not affect Bcl-2 expression [35]. However, the two work synergistically to increase the severity of NPC [36].

Furthermore, studies by Yang et al. [37] and Murono et al. [38] found that the angiogenesis factor VEGF (vascular endothelial growth factor) is induced by LMP1 expression through upregulation of COX-2 and the JNKs/HIF-1 pathway. However, a study by Challouf et al. [39] found that LMP1 expression did not correlate with blood vessel density or the degree of vascularization in NPC tissue. This suggests that LMP1 does not play a significant role in angiogenesis in NPC. Similar results were found in studies that found increased LMP1 expression with advanced NPC clinical stage, but this remained uncorrelated [40].

Conversely, despite the finding that NPC stage and LMP1 expression were not directly related and did not appear significant, research by Ye et al. [41] still showed a relationship between LMP1 and clinical stage, meaning LMP1 contributes to tumor progression. This was demonstrated by studies of LMP1 expression, which can play a role in the early stages of cancer formation and tumor development [6], especially NPC that is correlated with EBV infection. It can be concluded that LMP1 is not the sole determinant of NPC progression, but remains relevant as a future biomolecular target.

Tabel 4 Cancer Stage and LMP1 Expression in NPC Patients at Dr. Soetomo Regional General Hospital, January 2023–December 2023

NPC Stage	LMP1 Expression			
	Positive		Negative	
	n	%	n	%
Stage II	3	100	0	0
Stage III	6	85.7	1	14.3
Stage IV	24	80	6	20
Total	33	82.5	7	17.5

Table 4 shows LMP1 expression that was found to be higher in patients with stage IV compared to those with stages II and III. Chi-square statistical test using SPSS showed a non-significant association between LMP1 expression and NPC stage ($p>0.05$).

Tabel 5 Chi-square of Cancer Stage and LMP1 Expression in NPC Patients at Dr. Soetomo Regional General Hospital, January 2023–December 2023

	Chi-square		
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	. 816[a]	2	0.665
Likelihood Ratio	1.332	2	0.514
N of Valid Case	40		

4. Conclusion

Nasopharyngeal carcinoma (NPC) in patients at Dr. Soetomo Regional General Hospital between January 2023 and December 2023 was more common in men, with 30 patients between 41–50 years whereas most patients were already in stage IV (75%), indicating a late diagnosis of NPC. Although positive LMP1 expression was found in 82.5% of patients that mostly in the late stage, no significant correlation was found between LMP1 expression and NPC stage. Future research is expected to conduct with a larger and more representative sample size to identify patients with stage I NPC. Furthermore, more sensitive methods for LMP1 expression testing that include interval data are needed to enhance the detection limit for LMP1 and thereby substantially reduce the risk of false-negative findings.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no known conflicts of interest in relation to this manuscript.

Statement of ethical approval

The study was approved by the Ethics Committee of Dr. Soetomo Regional General Hospital.

Statement of informed consent

Written informed consent was obtained from all participants prior to their inclusion in the study.

References

[1] Shah AB, Nagalli S. Nasopharyngeal carcinoma [Internet]. StatPearls - NCBI Bookshelf. 2024.

[2] Adham M, Kurniawan AN, Muhtadi AI, Roezin A, Hermani B, Gondhowiardjo S, et al. Nasopharyngeal carcinoma in Indonesia: epidemiology, incidence,signs, and symptoms at presentation. Chinese Journal of Cancer [Internet]. 2012 Feb 7;31(4):185–96.

[3] Liang T, Chen H, Liu L, Zheng Y, Ma Z, Min L, et al. Antibody profiling of pan-cancer viral proteome reveals biomarkers for nasopharyngeal carcinoma diagnosis and prognosis. Molecular and Cellular Proteomics [Internet]. 2024 Feb 2;23(3):100729.

[4] Su ZY, Siak PY, Leong CO, Cheah SC. The role of Epstein–Barr virus in nasopharyngeal carcinoma. Frontiers in Microbiology [Internet]. 2023 Feb 9;14.

[5] Zhong BL, Zong YS, Lin SX, Zhang M, Liang YJ. Epstein-Barr virus infection in precursor lesions of nasopharyngeal carcinoma. Ai Zheng. 2006 Feb;25(2):136-42.

[6] Nakanishi Y, Wakisaka N, Kondo S, Endo K, Sugimoto H, Hatano M, et al. Progression of understanding for the role of Epstein-Barr virus and management of nasopharyngeal carcinoma. Cancer and Metastasis Reviews. 2017 Aug 17;36(3):435–47.

[7] Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell. 2010;140:883–899. doi: 10.1016/j.cell.2010.01.025.

[8] Ye Q, Li J, Wang X, Zhang X, Lin J, Huo Y, et al. In vivo and in vitro study of co-expression of LMP1 and Cripto-1 in nasopharyngeal carcinoma. Brazilian Journal of Otorhinolaryngology [Internet]. 2019 May 20;86(5):617–25.

[9] Kurniawan AN, Kodariah R, Elisabeth M, Roezin A, Gondhowiardjo S. Evaluation of EBV-LMP1 as prognostic indicator of nasopharyngeal carcinoma in Indonesian patients. Medical Journal of Indonesia [Internet]. 2002 May 1;81.

[10] Hariwiyanto B, Sastrowiyoto S, Mubarika S, Salugu M. LMP1 and LMP2 may be prognostic factors for outcome of therapy in nasopharyngeal cancers in Indonesia. Asian Pac J Cancer Prev. 2010;11(3):763-6

[11] Ye D, Zhu J, Zhao Q, Ma W, Xiao Y, Xu G, et al. LMP1 up-regulates calreticulin to induce epithelial-mesenchymal transition via TGF-B/SMAD3/NRP1 pathway in nasopharyngeal carcinoma cells. Journal of Cancer [Internet]. 2020 Dec 13;11(5):1257–69.

[12] Tabyaoui I, Serhier Z, Sahraoui S, Sayd S, Cadi R, Bennani O, et al. Immunohistochemical expression of latent membrane protein 1 (LMP1) and p53 in nasopharyngeal carcinoma: Moroccan experience. African Health Sciences [Internet]. 2013 Sep 6;13(3).

[13] Yoshizaki T, Horikawa T, Qing-Chun R, Wakisaka N, Takeshita H, Sheen TS, Lee SY, Sato H, Furukawa M. Induction of interleukin-8 by Epstein-Barr virus latent membrane protein-1 and its correlation to angiogenesis in nasopharyngeal carcinoma. Clin Cancer Res. 2001 Jul;7(7):1946-51.

[14] Nur RW, Karlowee V, Prasetyo A. Association Between LMP-1 and p16 Expression with Prognostic Factor of Nasopharyngeal Carcinoma. MAGNA MEDICA Berkala Ilmiah Kedokteran Dan Kesehatan [Internet]. 2023 Feb 1;10(1):9.

[15] Khabir A, Karray H, Rodriguez S, Rosé M, Daoud J, Frikha M, et al. EBV latent membrane protein 1 abundance correlates with patient age but not with metastatic behavior in north African nasopharyngeal carcinomas. Virology Journal [Internet]. 2005 Apr 20;2(1). Available from: https://pubmed.ncbi.nlm.nih.gov/15842731/

[16] Centre for Health Protection, Department of Health - Nasopharyngeal Cancer [Internet]. Available from: https://www.chp.gov.hk/en/healthtopics/content/25/54.html

[17] Utomo AW, Romdhoni AC. Characteristics of patients with nasopharyngeal carcinoma in Dr. Soetomo General Academic Hospital Surabaya. Bali Medical Journal [Internet]. 2023 May 11;12(2):1589–93.

[18] Clocchiatti A, Cora E, Zhang Y, Dotto GP. Sexual dimorphism in cancer. Nature Reviews Cancer [Internet]. 2016 Apr 15;16(5):330–9.

[19] Fauzan A, Susilawati S, Larasati V. The association between clinical characteristics and histopathology of nasopharyngeal carcinoma at Dr. Mohammad Hoesin General Hospital, in 2019-2020. Biomedical Journal of Indonesia [Internet]. 2022 Jan 31;8(1):13–9.

[20] Lo AKF, Dawson CW, Lung HL, Wong KL, Young LS. The role of EBV-Encoded LMP1 in the NPC tumor microenvironment: From function to therapy. Frontiers in Oncology [Internet]. 2021 Feb 25;11. Available from: https://doi.org/10.3389/fonc.2021.640207

[21] Nathania N, Dewi YA, Permana AD. Profile of head and neck cancer patients at Hasan Sadikin Hospital in 2013-2018. Oto Rhino Laryngologica Indonesiana [Internet]. 2021 Jan 2;50(2):141.

[22] Tsao SW, Tsang CM, Lo KW. Epstein–Barr virus infection and nasopharyngeal carcinoma. Philosophical Transactions of the Royal Society B Biological Sciences [Internet]. 2017 Sep 11;372(1732):20160270.

[23] Shah AB, Nagalli S. Nasopharyngeal carcinoma. StatPearls - NCBI Bookshelf. 2024.

[24] Adham M, Rohdiana D, Mayangsari ID, Musa Z. Delayed diagnosis of nasopharyngeal carcinoma in a patient with early signs of unilateral ear disorder. Medical Journal of Indonesia [Internet]. 2014 Mar 11;52.

[25] Wang KH, Austin SA, Chen SH, Sonne DC, Gurushanthaiah D. Nasopharyngeal Carcinoma Diagnostic Challenge in a Nonendemic Setting: Our Experience with 101 Patients. The Permanente Journal [Internet]. 2017 Jun 8;21(3).

[26] Prasad U, Pua KC. Nasopharyngeal carcinoma: a delay in diagnosis. Med J Malaysia. 2000 Jun;55(2):230-5

[27] King AD, Vlantis AC, Bhatia KSS, Zee BCY, Woo JKS, Tse GMK, et al. Primary Nasopharyngeal Carcinoma: Diagnostic Accuracy of MR Imaging versus that of Endoscopy and Endoscopic Biopsy. Radiology [Internet]. 2010 Dec 4;258(2):531–7.

[28] Abdel Khalek Abdel Razek A, King A. MRI and CT of nasopharyngeal carcinoma. AJR Am J Roentgenol. 2012 Jan;198(1):11-8.

[29] Nafisa IM, Utama MS, Sunardi MA, Adibrata AA. Profile of Nasopharyngeal Cancer Patients who Underwent Radiotherapy in Dr. Hasan Sadikin General Hospital Bandung. Indonesian Journal of Cancer [Internet]. 2022 Jun 29;16(2):88.

[30] Paskarani PE, Mahastuti NM, Khosasi SHRistekbrinGoI, Nareswari MD. The Relationship Between Poly-ADP-Ribose Polymerase-1 (PARP-1) Expression with Clinicopathological Characteristics of Nasopharyngeal Carcinoma in Bali, Indonesia. Indonesian Journal of Cancer [Internet]. 2023 Sep 29;17(3):176.

[31] Liemiyah R, Ruspita DA, Naftali Z, Muyassaroh M, Farokah F. Epidemiological characteristics and 3-year overall survival outcome of nasopharyngeal cancer in Central Java: a Single institution Retrospective study. Indonesian Journal of Cancer [Internet]. 2024 Jun 27;18(2):143–55.

[32] Baizig NM, Wided BA, Amine OE, Gritli S, ElMay M. The Clinical Significance of IGF-1R and Relationship with Epstein–Barr Virus Markers: LMP1 and EBERs in Tunisian Patients with Nasopharyngeal Carcinoma. Annals of Otology Rhinology and Laryngology [Internet]. 2020 May 29;129(10):1011–9.

[33] Horikawa T, Yang J, Kondo S, Yoshizaki T, Joab I, Furukawa M, et al. Twist and Epithelial-Mesenchymal Transition Are Induced by the EBV Oncoprotein Latent Membrane Protein 1 and Are Associated with Metastatic Nasopharyngeal Carcinoma. Cancer Research [Internet]. 2007 Mar 1;67(5):1970–8.

[34] Liu T, Zhou L, Li D, Andl T, Zhang Y. Cancer-Associated fibroblasts build and secure the tumor microenvironment. Frontiers in Cell and Developmental Biology [Internet]. 2019 Apr 24;7.

[35] Mei YP, Zhou JM, Wang Y, Huang H, Deng R, Feng GK, et al. Silencing of LMP1 induces cell cycle arrest and enhances chemosensitivity through inhibition of AKT signaling pathway in EBV-Positive nasopharyngeal carcinoma cells. Cell Cycle [Internet]. 2007 Jun 1;6(11):1379–85.

[36] Sheu L, Chen A, Lee H, Hsu H, Yu D. Cooperative interactions among p53, bcl-2 and Epstein–Barr virus latent membrane protein 1 in nasopharyngeal carcinoma cells. Pathology International [Internet]. 2004 Jun 4;54(7):475–85.

[37] Yang L, Liu L, Xu Z, Liao W, Feng D, Dong X, et al. EBV-LMP1 targeted DNAzyme enhances radiosensitivity by inhibiting tumor angiogenesis via the JNKs/HIF-1 pathway in nasopharyngeal carcinoma. Oncotarget [Internet]. 2015 Jan 21;6(8):5804–17.

[38] Murono S, Inoue H, Tanabe T, Joab I, Yoshizaki T, Furukawa M, et al. Induction of cyclooxygenase-2 by Epstein–Barr virus latent membrane protein 1 is involved in vascular endothelial growth factor production in nasopharyngeal carcinoma cells. Proceedings of the National Academy of Sciences [Internet]. 2001 May 29;98(12):6905–10.

[39] Challouf S, Ziadi S, Zaghdoudi R, Ksiaa F, Gacem RB, Trimeche M. Patterns of aberrant DNA hypermethylation in nasopharyngeal carcinoma in Tunisian patients. Clinica Chimica Acta [Internet]. 2012 Jan 29;413(7–8):795–802.

[40] Purwono PB, Romdhoni AC, Rahaju AS, Rahniayu A, Astutik AF, Dewayani A, et al. Expression level of latent membrane protein 1 Epstein-Barr virus in tissue biopsy among different clinical stages of nasopharyngeal carcinoma. Research Square (Research Square) [Internet]. 2024 Oct 21.

[41] Ye D, Zhu J, Zhao Q, Ma W, Xiao Y, Xu G, et al. LMP1 up-regulates calreticulin to induce epithelial-mesenchymal transition via TGF-B/SMAD3/NRP1 pathway in nasopharyngeal carcinoma cells. Journal of Cancer [Internet]. 2020 Dec 13;11(5):1257–69.