

ORIGINAL ARTICLE

**“DIAGNOSTIC INSIGHT AND EFFICACY OF FINE-NEEDLE
ASPIRATION CYTOLOGY IN ASSESSING CERVICAL
LYMPHADENOPATHY”**

**AJAY SINGH THAKUR ¹, CHANDRASHEKHAR INDORIA ^{2*}, VISHAL KULKARNI ³,
APURVA AGRAWAL ⁴, ADITI DAS ⁵**

¹ Associate professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur,
Chhattisgarh, India

² Associate professor, Department of Pathology, Bharat Ratna Late Shree Atal Bihari Vajpayee
Memorial Medical College, Rajnandgaon, Chhattisgarh, India

³ Associate professor, Department of Pathology, Rajmata Shrimati Devendra Kumari Singhdeo
Government Medical College Ambikapur, Chhattisgarh, India

⁴ Assistant professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur,
Chhattisgarh, India

⁵ Associate professor, Department of Pathology, Shree Balaji Institute of medical sciences, Raipur,
Chhattisgarh, India

Corresponding Author: Chandrashekhhar Indoria²

Department of pathology, BRLSABVM Government Medical College, Pendri, Rajnandgaon,
Chhattisgarh, India, 491441

Mobile number-- +918818967626, +919406355748

E-mail id—dr.csindoria@gmail.com

Abstract

Background: FNAC is a safe, reliable, cost-effective, and efficient method for initial screening of patients with cervical lymphadenopathy.

Aims: The purpose of this study was to identify cytomorphological features and to evaluate the diagnostic efficacy of FNAC as a screening tool for cervical lymphadenopathy.

Materials and Methods: A study included 952 cases of FNAC, with 215 cases being compared to histological diagnosis. Subsequently, discordant cases, including both false negatives and false positives, were retrospectively re-evaluated. Additionally, a thorough review of previous research on the factors that contribute to misdiagnosis was conducted.

Results: Discordance was found more in benign lesions (12.4%) as compared to malignant lesion aspirates (4.9%). When suspected malignant and malignant group are all classified as cytologically positive, the sensitivity and specificity are 97.3% and 95.8% respectively. Overlapping cytological

features, heterogeneity, unsampled areas and error in interpretation were the primary factors contributing to false positive and false negative diagnosis.

Conclusion: FNAC of cervical lymphadenopathy is a precise, sensitive, and specific initial diagnostic procedure. However False-negative diagnoses are mainly due to issues with the specimens obtained, while false-positive diagnoses are primarily caused by errors in interpretation. Experienced cytopathologists are expected to analyze the outcomes of FNAC while considering the accompanying clinical, radiographic, and laboratory information. In cases where there is ambiguity in the interpretation of these results, additional investigations and ancillary technique are essential to address potential misdiagnoses.

Keyword: FNAC, cervical lymph node, misdiagnoses, false negative, false positive, efficacy.

Introduction

Cervical lymphadenopathy (CLA) is characterized by the enlargement of cervical nodal tissue with a diameter exceeding 1 cm. The occurrence of this serves as an indicator of an underlying pathological condition, whether local or systemic, including infections, medications, autoimmune disorders, and malignancies [1,2]. According to the timeframe involved, cervical lymphadenopathy is categorized into acute lymphadenopathy (lasting 2 weeks), subacute lymphadenopathy (lasting 2-6 weeks), and chronic lymphadenopathy, which includes cases where lymphadenopathy persists beyond 6 weeks. Diagnosing cervical lymphadenopathy through fine needle aspiration cytology is challenging due to the diversity of lymph node lesions, intralesional heterogeneity, and morphological overlap. However, it is a widely accepted, cost-effective, and minimally invasive technique for the rapid cytological evaluation of cervical lymphadenopathy. The current study evaluated the reliability and validity of Fine Needle Aspiration Cytology (FNAC) through a comparative analysis of cytological and histological diagnoses in patients with lymph node enlargement. The study aimed to enhance the accuracy of diagnosing malignant tumors and minimize the occurrence of false-negative and false-positive results. This would contribute to the development of more effective treatment strategies for future patients.

Material and method

Study subjects, sampling, technique and data acquisition

The current study spans six years, covering the period from January 2008 to January 2013. The study was conducted at the Department of Pathology, Pt. J.N.M. Medical College and its associated Dr. B.R.A.M. Hospital in Raipur, Chhattisgarh, India. The prospective study involved selecting cases from patients with cervical lymphadenopathy who were attending various clinical outpatient departments and inpatient facilities. Ethical considerations were duly acknowledged through the acquisition of approval from the institutional ethics committee, and written consent was procured from all individual patients involved in the study. The aspirates were prepared as direct smears. Smear made from the centrifuged deposit of aspirated fluid. Staining of the wet fixed smears was done with Papanicolaou stain/Haematoxylin and Eosin, while air-dried smears were stained with

MGG (May Grunwald and Giemsa) stain. The cases were initially classified into benign lesions and malignant lesions (including those suspicious for malignancy). The final histopathological diagnosis was correlated with the FNAC findings to assess the accuracy of cytodiagnosis.

False negative and false positive diagnoses

Non-diagnostic cases were not included in the analyses. False-negative and false-positive diagnoses were defined as cases in which the results of the fine needle aspiration (FNA) did not correspond with the findings of the final histological examination. A false-negative diagnosis is defined as a situation where lymphadenopathy was initially identified as a benign lesion through fine-needle aspiration cytology (FNAC), but upon histological examination, it was revealed to be a malignant lesion. Conversely, a false-positive diagnosis was described as lymphadenopathy with cytology indicating malignancy (suspicious for malignancy and malignant lesion) that was later found to be a benign lesion upon histological analysis after surgery. The slides from FNAs that resulted in false-negative and false-positive diagnoses were reviewed again to identify the reasons behind the misdiagnoses.

Statistical analysis

Statistical analysis was conducted to evaluate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy. IBM SPSS Statistics (version 19.0) was used for the analysis, and the chi-square test was employed for the primarily categorical variables. The Cohen's kappa (κ) coefficient was employed to evaluate the agreement between the FNA and histopathology results. P value of <0.05 was considered statistically significant.

Result

During the period from January 2008 to January 2013, we conducted a comprehensive review of 952 cases of cervical lymphadenopathy fine-needle aspiration cytology (FNAC). The distribution of benign lesions and malignant cervical lymph node lesions among the total 952 FNACs was as follows: 642 (67.4%) and 310 (32.5%), respectively. Reactive lymphadenitis was the most common benign cervical lymph node lesion, accounting for 43.3% (278/642), followed by chronic granulomatous lymphadenitis at 27.7% (171/642). In malignant cervical lymph node lesions, 68.4% (212/310) of cases were of metastatic carcinoma, followed by non-Hodgkin lymphoma (20.9%, 46/310) [Table 1].

In the present study, both cytology and histopathology were conducted in 215 cases. Out of these, 74 cases had benign cervical lymph node lesions, while 141 cases had malignant lesions. The fine-needle aspiration (FNA) findings were compared with the corresponding histological diagnosis. 87.6% of benign cervical lymph node lesions were consistent with the histopathological diagnosis. In the malignant group, 96.4% of tumors showed agreement with histopathology [Table 2 and 3].

The results of the assessment comparing the findings of fine-needle aspiration cytology (FNAC) with the final histopathology results of the patients are presented in Table 4. Upon inspection of the

aforementioned table, a significant correlation was identified between the two measurements ($\kappa = 0.927$, $p < 0.001$). The test sensitivity was found to be 97.9%, while the specificity was determined to be 95.8%. Based on the results of the FNAC test, the positive predictive value (PPV) for malignancy was 85.6%, while the negative predictive value (NPV) for benign cases was 99.4%.

Table 01 Demographic and clinical data of the study patients

Characterstics			n
FNAC cases (n=952)	Benign lesion (n=642)	Reactive lymphadenitis	278
		Chronic granulomatous lymphadenitis	171
		Tubercular lymphadenitis	109
		Acute suppurative lymphadenitis	44
		Chronic non specific lymphadenitis	32
	Malignant neoplastic lesion (n=310)	Metastatic carcinoma	212
		Non Hodgkin lymphoma	65
		Hodgkin lymphoma	33
	Histopathology cases (n=215)	Benign lesion (n=74)	Chronic granulomatous lymphadenitis
Tubercular lymphadenitis			24
Reactive lymphadenitis/hyperplasia			21
Non specific lymphadenitis			02
Malignant neoplastic lesion (n=141)		Metastatic carcinoma	80
		Non Hodgkin lymphoma	46
		Hodgkin lymphoma	15

Table 02 Comparative analysis of cytological and histological diagnosis of benign cervical lymphadenopathy lesions

S. No	Cytological Diagnosis	No. of Cases whose histopathology was available	Histopathological Diagnosis		False negative cases
			Concordance	Discordance	
1	Reactive lymphadenitis	25	20	05 (01 Metastatic carcinoma, 01 Non Hodgkin)	02 (01 Metastatic carcinoma, 01)

				lymphoma, 03 granulomatous lymphadenitis)	Non Hodgkin lymphoma)
	Chronic granulomatous lymphadenitis	24	22	02 (01 Metastatic carcinoma, 01 TB lymphadenitis)	01 (01 Metastatic carcinoma)
2	Tubercular lymphadenitis	24	22	02 nonspecific lymphadenitis	0
	Total	73	64 (87.6%)	09 (12.4%)	03

Table 03 Comparative analysis of cytological and histological diagnosis of malignant cervical lymphadenopathy lesions

S. No	Cytological Diagnosis	No. of cases	Histopathological Diagnosis		False positive
			Concordance	Discordance	
1	Non Hodgkins lymphoma	42	42	-	0
2	Hodgkins lymphoma	19	15	04 (NHL-03, Reactive lymphadenopathy-01)	01 (01 RLH)
3	Metastatic carcinoma	81	78	03(Granulomatous lymphadenitis--02, TB lymphadenopathy-01)	03
	Total	142	135 (95.1%)	07 (4.9%)	04

Table 04 Conformity of the FNAC and histopathology results of the study patients

PPV, positive predictive value; NPV, negative predictive value; FNR, false-negative rate; FPR, false-positive rate.

Variables		Histopathological diagnosis		Total
		Malignant lesion	Benign lesion	
		n	n	
Cytological diagnosis	Malignant lesion	138 (TP)	04 (FP)	142
	Benign lesion	03 (FN)	70(TN)	73
Total		141	74	215
Statistical analysis Result		Sensitivity		97.3%
		Specificity		95.8%
		Accuracy		96.3%
		PPV		85.6%
		NPV		99.4 %
		Cohen’s Kappa		0.9276
p value		< .00001		

Discussion

Fine-needle aspiration (FNA) serves as an uncomplicated, secure, cost-efficient, and precise diagnostic method for the initial assessment of patients with cervical lymphadenopathy. The primary objective of fine-needle aspiration (FNA) is the preliminary assessment of enlarged lymph nodes. Early FNAC can guide additional testing and evaluation, reduce patient anxiety, and save time, money, and patient morbidity [4]. In order to ensure precise FNAC-based diagnoses, it is essential to maintain the quality and proper processing of the cytologic specimen[5]. Additionally, the utilization of ancillary techniques plays a crucial role in achieving accurate diagnostic outcomes [6]. FNAC has demonstrated effectiveness in diagnosing conditions such as lymphoid hyperplasia, granulomatous lymphadenitis, infectious diseases, and metastatic tumors. It is also valuable for promptly assessing treatment responses without the need for an excisional biopsy [7]. When combined with clinical and radiographic findings, FNAC serves as a diagnostic tool that can help avoid unnecessary surgical procedures and accurately differentiate between benign and malignant

lesions [8]. FNA also provides the best opportunity to collect additional material for flow cytometry analysis [9].

A significant proportion of cervical lymphadenopathies observed in this study were attributed to benign conditions (67.2%), consistent with several previous studies [10, 11, 12]. Narang et al. also showed benign lesions in 61.6% of the lymph nodes [13]. The most common types of benign cervical lymphadenopathy identified were reactive lymphadenopathy, followed by granulomatous lymphadenopathy and tuberculous lymphadenopathy. These results align with the research conducted by Shakya and colleagues [14], which indicated that reactive hyperplasia, tuberculosis, malignancy, and granuloma accounted for 50.4%, 22.4%, 4.8%, and 10% of lymphadenopathy cases, respectively. Among malignant cervical lymph node lesions, metastatic carcinoma was the most common, followed by non-Hodgkin's lymphoma. These findings align with studies conducted by K.R. Anila et al. [15] and Mamta K. et al. [12].

Cytological under-diagnoses (False Negative cases)

The occurrence of false negatives (FNs) varies significantly across different studies, with reported rates ranging from less than 2% to exceeding 20% (16). In our study, we encountered three false-negative cases: two cases of metastatic carcinoma and one case of non-Hodgkin's lymphoma. All slides were reexamined to determine the cause of misdiagnoses. One histologically proven case of metastatic carcinoma partially involved the lymph node with fibrosis and exhibited a polymorphous lymphoid population with low cellularity in cytology, which led to an underdiagnosis. Another metastatic carcinoma was underdiagnosed as granulomatous lymphadenitis due to cytological misinterpretation. A case of non-Hodgkin's lymphoma cytologically shows inflammatory cellularity with scattered large atypical cells misinterpreted as immunoblasts, leading to underdiagnosis. Factors contributing to false negative results can be attributed to sample adequacy, proper smear preparation, and cytological interpretation. It is recommended that fine-needle aspiration cytology (FNAC) procedures be conducted by a trained professional, ideally with immediate feedback on sample adequacy, and with appropriate sample triage. Immediate fixation of smears is crucial due to the high susceptibility of lymphocytes to preservation and air-drying artifacts. The assessment of adequate cellularity in lymph node aspirates can be challenging, particularly when lymphoid lesions are suspected. It is important to emphasize that an adequate sample should not only contain a sufficient number of lymphocytes but also a substantial quantity of well-preserved and well-stained lymphocytes. In a study by Makarenko et al. [17], upon reevaluation of fine needle aspiration cases, 4 out of 6 cases were reclassified from "benign" to "inadequate" due to insufficient well-preserved lymphoid material. In the subsequent cytological interpretation, despite the presence of well-prepared and sufficiently cellular smears, specific situations inherently pose an increased risk of underdiagnosis. These conditions may occur due to malignancies mixed with non-neoplastic cells, any lymphoproliferative disorders featuring a diverse lymphoid population, and concurrent observations that overlap between benign and malignant states [18].

Cytological Over-Diagnoses (false positive cases)

The present study found three false-positive results in FNACs. The initial diagnosis of non-Hodgkin lymphoma based on cytology was later confirmed to be reactive lymphoid hyperplasia upon histopathological examination. Examination of these smears revealed various scattered large atypical lymphoid cells with prominent nucleoli within a reactive lymphoid background. Mendon et al., Hafez et al., and Min En Nga suggested that if the aspiration sample from the reactive node originates from the large germinal center, the presence of a significant number of large cells (centroblasts and dendritic cells) along with a high mitotic count may raise suspicion for malignant lymphoma [18, 19, 20]. Viral lymphadenitis, especially infectious mononucleosis, can present a diagnostic challenge in cytology. It can be confused with non-Hodgkin lymphoma, large cell type, when a substantial number of immunoblasts are present, or misidentified as Hodgkin lymphoma when Reed-Sternberg-like cells are prominent. Landgren et al. proposed that a diagnosis of lymphoma should be considered when immature cells constitute more than 50% of the cell population [18,21]. In two other cases, granulomatous lymphadenitis and tubercular lymphadenitis were misdiagnosed as metastatic carcinoma on cytology. Upon analysis, interpretation errors were found in these cases.

FNAC as a screening modality

In our study, we found that fine-needle aspiration cytology (FNAC) demonstrated a sensitivity of 97.3%, specificity of 95.8%, and diagnostic accuracy of 96.3% when compared to histologic diagnosis, as shown in Table 4. The positive predictive value for a malignant diagnosis using FNAC was 85.6%, and the negative predictive value was 99.4%. Furthermore, statistical analysis revealed a strong agreement between cytological and histological findings, with a kappa value of 0.7135. These findings suggest that FNAC can effectively predict the presence of malignancy, depending on the prevalence of malignancy. The literature review showed significant consistency in the sensitivity and specificity of fine needle aspiration cytology for diagnosing cervical lymph node swelling across various populations and settings [5, 22-26]. For instance, Lee J et al. conducted a study on 432 cases of cervical lymphadenopathy and reported a sensitivity of 97.8% and a specificity of 97.5% [5]. In contrast, Hafez NH et al. found a sensitivity of 90.9%, specificity of 67.2%, and diagnostic accuracy of 82.2% in their evaluation of 157 cases of cervical lymph node swelling [23], which was much lower compared to our study. In the literature, the accuracy rate of lymph node FNAC ranges from 82% to 94.4% [22-26].

Study strengths and limitations

The research conducted in our study is subject to certain constraints, notably its retrospective design and the restriction to a single center. Additionally, the study was hindered by a small sample size, resulting in the exclusion of numerous FNAC cases without accompanying histopathology reports. Moreover, due to logistical challenges such as long travel distances and financial limitations faced by patients, follow-up data was unavailable. Despite these constraints, this study

aims to investigate the correlation between FNAC and related histopathology in diagnosing cervical lymphadenopathy. Furthermore, it evaluates the precision, sensitivity, specificity, positive predictive value, negative predictive value, false negative rate, and false positive rate of fine needle aspiration cytology as a diagnostic tool for cervical lymphadenopathy.

Conclusion

The results of our study have shown that fine-needle aspiration cytology (FNAC) of cervical lymphadenopathy demonstrates a significant level of accuracy, sensitivity, and specificity, allowing for an appropriate initial diagnostic tool. Salivary cytology is a safe, reliable, cost-effective, and efficient method that should be utilized as the primary investigative tool for salivary lesions. Although the ability to characterize specific tumor types is limited due to variations in cytomorphology. False-negative diagnoses were mainly attributed to issues with the specimens obtained, while false-positive diagnoses were primarily caused by errors in interpretation. Experienced cytopathologists are expected to analyze the outcomes of FNAC while considering the accompanying clinical, radiographic, and laboratory information. In cases where there is ambiguity in the interpretation of these results, additional investigations and ancillary techniques are essential to address potential misdiagnoses.

References

1. Sakr M: Cervical:lymphadenopathy.Headand Neck and Endocrine Surgery.2016,163-90.10.1007/978-3-319-27532-1_8
2. Al Qout MM, Al Hamoud M, AlQahtani MS, Alqahtani AY, Asiri AH, Alshahrani AA. The Diagnostic Value of Fine-Needle Aspiration Cytology in Cervical Lymphadenopathy in Correlation to Postoperative Histopathological Results in a Tertiary Care Center in Saudi Arabia. *Cureus*. 2023 Sep 29;15(9):e46210. doi: 10.7759/cureus.46210. PMID: 37905246; PMCID: PMC10613460.
3. Allhiser JN, McKnight TA, Shank JC. Lymphadenopathy in a family practice. *J.Fam Pract*. 1981 ; 12 (1) :27-32. [PubMed]
4. Vasilj A, Katović SK: Fine-needle aspiration cytology of head and neck lymph nodes in a ten-year period-single center experience. *Acta Clin Croat*. 2015, 54:315-8.
5. Ha HJ, Lee J, Kim DY, Kim JS, Shin MS, Noh I, Koh JS, Kim EJ, Lee SS. Utility and Limitations of Fine-Needle Aspiration Cytology in the Diagnosis of Lymphadenopathy. *Diagnostics (Basel)*. 2023 Feb 14;13(4):728. doi: 10.3390/diagnostics13040728. PMID: 36832214; PMCID: PMC9954935.
6. Jin M., Wakely P.E., Jr. Lymph node cytopathology: Essential ancillary studies as applied to lymphoproliferative neoplasms. *J. Cancer Cytopathol*. 2018;126:615–626. doi: 10.1002/cncy.22013. [PubMed] [CrossRef] [Google Scholar]

7. 20. Altınboğa A.A., Yüce G. Fine-Needle Aspiration Cytology in the Diagnosis of Lymph Nodes: Correlation with Histopathological Diagnosis. *Diagn. Value Lymph Node Cytol.* 2019;30 doi: 10.14744/scie.2019.14622.
8. 21. Peker İ.O., Kulaçoğlu S., Eruyar T., Ergül G. Fine needle aspiration cytology of head and neck masses: A cytohistopathological correlation study with emphasis on false positives and false negatives. *Turk. J. Ear Nose Throat.* 2013;23:163–172. doi: 10.5606/kbbihtisas.2013.27048.
9. Gourin C G, Johnson J T (2000) Incidence of unsuspected metastases in lateral cervical cysts. *Laryngoscope* 110(10): 1637-1641
10. . Hirachand S, Lakhey M, Akhter J, Thapa B. Evaluation of fine needle aspiration cytology of lymph nodes in Kathmandu Medical College, Teaching hospital. *Kathmandu Univ Med J (KUMJ)* 2009;7:139-42.
11. Serrano Egea A, Martínez González MA, Pérez Barrios A, Alberti Masgrau N, de Agustín de Agustín P. Usefulness of light microscopy in lymph node fine needle aspiration biopsy. *Acta Cytol* 2002;46:368-9
12. Mamtha K. et al. Utility of fine needle aspiration cytology (FNAC) in evaluation of cervical Indian *Journal of Pathology and Oncology*, April-June 2017;4(2):218-220
13. Narang R, Pradhan S, Singh R, Chaturvedi S. Place of fine needle aspiration cytology in the diagnosis of lymphadenopathy. *Ind J Tub* 1990;37(1):29-31.
14. Shakya G, Malla S, Shakya KN, Shreshtha R. A study of FNAC of cervical lymph nodes. *J Nepal Res Counc.* 2009;7(14):1–5.
15. Anila KR, Nayak N, George PS, Jayasree K. Utility of fine needle aspiration cytology in evaluation of lymphadenopathy - An audit from a Cancer Centre in South India. *Gulf J Oncolog.* 2015 Sep;1(19):50-6. PMID: 26499831.
16. Gupta P, Gupta N, Kumar P, Bhardwaj S, Srinivasan R, Dey P, et al. Assessment of risk of malignancy by application of the proposed Sydney system for classification and reporting lymph node cytopathology. *Cancer Cytopathol.* 2021;129(9):701–18.
17. Makarenko VV, DeLelys ME, Hassserjian RP, Ly A. Lymph node FNA cytology: Diagnostic performance and clinical implications of proposed diagnostic categories. *Cancer Cytopathol.* 2022 Feb;130(2):144–53.
18. Min En Nga Pitfalls in Lymph Node Fine Needle Aspiration Cytology *Acta Cytologica* , DOI: 10.1159/000535906.
19. Nesreen H. Hafez, Neveen S. Tahoun, Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy, *Journal of the Egyptian National Cancer Institute*, Volume 23, Issue 3, 2011, Pages 105-114, ISSN 1110-0362, <https://doi.org/10.1016/j.jnci.2011.09.009>.
20. M.E. Mendon Fine needle aspiration cytology of lymph nodes *Prog Diagn Cytol*, 32 (1999), pp. 453-456
21. O. Landgren, A.P. MacDonald, E. Tani, A. Ost, C. Wedelin A prospective comparison of fine needle aspiration cytology and histopathology in the diagnosis and classification of lymphomas *Hematol J*, 5 (2004), pp. 69-76.
22. The efficacy of lymph node fine needle aspiration cytology. Attard J, Galea J, Betts A. <https://www.um.edu.mt/umms/mmj/PDF/489.pdf> *Malta Med J.* 2015;27:16–21.
23. Reliability of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of cervical lymphadenopathy. Hafez NH, Tahoun NS. *J Egypt Natl Canc Inst.* 2011;23:105–114.

24. Diagnostic value of lymph node fine needle aspiration cytology: an institutional experience of 387 cases observed over a 5-year period. Nasuti JF, Yu G, Boudousquie A, Gupta P. *Cytopathology*. 2000;11:18–31.
25. Cervical lymphadenopathy: a common diagnostic dilemma. Qasmi SA, Kiani F, Malik AI, et al. *J Surg Pak*. 2012;17:76–80.
26. Al Qout MM, Al Hamoud M, AlQahtani MS, Alqahtani AY, Asiri AH, Alshahrani AA. The Diagnostic Value of Fine-Needle Aspiration Cytology in Cervical Lymphadenopathy in Correlation to Postoperative Histopathological Results in a Tertiary Care Center in Saudi Arabia. *Cureus*. 2023 Sep 29;15(9):e46210. doi: 10.7759/cureus.46210. PMID: 37905246; PMCID: PMC10613460.