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Diagnostic Test Fine Needle Aspiration Biopsy (FNAB) Examination on Gold Standard Histopathological Tests for Identification of Colli Lymphadenopathy Patients at RSPAL. Dr. Ramelan Surabaya

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ABSTRACT Colli lymphadenopathy is a common clinical manifestation that requires prompt and accurate diagnosis to differentiate between benign and malignant etiologies. Fine Needle Aspiration Biopsy (FNAB) is widely employed as an initial diagnostic approach due to its simplicity, speed, and cost-effectiveness. However, its diagnostic accuracy compared to the gold standard histopathological examination remains subject to evaluation. This study aimed to assess the diagnostic performance of FNAB against paraffin block histopathology in identifying benign and malignant colli lymphadenopathy at RSPAL Dr. Ramelan Surabaya. A descriptive observational study was conducted using retrospective data from medical records of patients diagnosed with colli lymphadenopathy between January 2019 and March 2022. A total of 66 cases meeting the inclusion criteria were analyzed. Each case underwent both FNAB and histopathological examination. Diagnostic test parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated using 2×2 cross-tabulation. The findings revealed that FNAB had a sensitivity of 80.48%, specificity of 96.15%, PPV of 97.05%, NPV of 75.75%, and an overall diagnostic accuracy of 86.56%. These results indicate that FNAB is a highly specific and reasonably sensitive screening tool for initial diagnosis of colli lymphadenopathy. In conclusion, FNAB offers a practical and efficient method for the preliminary diagnosis of colli lymphadenopathy, with high specificity and diagnostic accuracy. While FNAB may not completely replace histopathological examination, its utility as a front-line diagnostic tool is well supported, especially in resource-limited settings. Further research incorporating additional diagnostic metrics such as likelihood ratios may enhance diagnostic precision in future applications.

INDEX TERMS Colli lymphadenopathy, Fine Needle Aspiration Biopsy, Histopathology, Diagnostic accuracy, Screening test

I. INTRODUCTION

Lymphadenopathy, particularly in the cervical (colli) region, remains a common clinical presentation with a wide array of differential diagnoses, ranging from benign inflammatory processes to malignant neoplasms [1], [2]. Accurate and timely differentiation between these etiologies is essential to guide appropriate therapeutic interventions and reduce morbidity. Excisional biopsy followed by histopathological examination is recognized as the diagnostic gold standard. However, it is invasive, resource-intensive, and often impractical in low-resource settings or for patients with comorbidities [3], [4].

To address these limitations, Fine Needle Aspiration Biopsy (FNAB) has emerged as a minimally invasive, rapid, And cost-effective alternative for evaluating lymphadenopathy [5]–[7]. FNAB allows cytological assessment through aspirated cellular material, aiding in the initial diagnosis of malignancies and infections with relatively high diagnostic yield [8], [9]. Advances such as ultrasound-guided aspiration, rapid on-site evaluation (ROSE), and adoption of standardized cytopathological reporting systems (e.g., the Sydney System) have further enhanced its diagnostic accuracy and clinical utility [10]–[13]. Meta-analyses have reported FNAB sensitivity and specificity for lymphadenopathy ranging from 85% to over 95%, particularly when supported by experienced cytopathologists and adjunctive diagnostic tools [14]–[16].

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Despite these advantages, FNAB is not without limitations. It may yield inadequate samples or inconclusive results, particularly in cases of lymphoma, necrotic tissue, or small lymph nodes [17], [18]. Moreover, FNAB cannot reliably provide architectural context, which is crucial for certain diagnoses like Hodgkin lymphoma or granulomatous diseases [19], [20]. These diagnostic challenges underscore the importance of correlating FNAB results with histopathological findings to evaluate its true clinical value.

In Indonesia, particularly in tertiary-care hospitals, the utilization of FNAB is increasing. However, empirical evidence assessing its diagnostic performance remains limited. Most available studies focus on general lymphadenopathy or are concentrated in urban medical centers such as Yogyakarta or Jakarta [21], [22]. Little is known about the accuracy of FNAB in diagnosing colli lymphadenopathy specifically at RSPAL Dr. Ramelan Surabaya. Thus, there is a pressing need for region-specific data to validate FNAB as a frontline diagnostic tool and to assess its agreement with histopathological outcomes.

This study aims to evaluate the diagnostic test performance of FNAB against gold-standard histopathological examination for colli lymphadenopathy cases at RSPAL Dr. Ramelan Surabaya. By examining sensitivity, specificity, predictive values, and overall accuracy, the research intends to generate localized evidence that supports clinical decision-making and strengthens diagnostic protocols. The key contributions of this study are as follows:

A. LOCAL VALIDATION OF FNAB

This study provides the first quantitative evaluation of FNAB accuracy for colli lymphadenopathy diagnosis at a tertiary-care facility in Surabaya.

B. PROCEDURE-OUTCOME CORRELATION

It explores the relationship between diagnostic accuracy and influencing factors such as sample adequacy, patient age, and diagnostic concordance.

C. BENCHMARKING AGAINST GOLD STANDARDS

The study compares FNAB results directly with histopathology to identify performance gaps and opportunities for improving cytological practices. The remainder of this article is organized as follows:

1. Section II describes the research methodology, including sample selection, data collection, and analytical approach.
2. Section III presents the diagnostic test results.
3. Section IV discusses findings in the context of existing literature.
4. Section V concludes with clinical implications and suggestions for future research.

II. METHODHOLOGY

A. Study Design

This study utilized a retrospective, descriptive-observational design to evaluate the diagnostic performance of Fine Needle Aspiration Biopsy (FNAB) against the gold-standard histopathological examination in the diagnosis of colli lymphadenopathy. The study was conducted at the Anatomical Pathology Laboratory, RSPAL Dr. Ramelan Surabaya, Indonesia. The retrospective nature allowed for the analysis of archived patient records and diagnostic outcomes from an existing hospital database without influencing the diagnostic process or introducing intervention bias [26].

B. STUDY SETTING AND PERIOD

Data were collected from the SIM-RS (hospital information system) database at RSPAL Dr. Ramelan Surabaya. The study covered patients examined between January 2019 and March 2022. This timeframe ensured sufficient data for statistical analysis and reflected recent clinical practices and diagnostic standards.

C. POPULATION AND SAMPLING

The study population included patients presenting with cervical lymphadenopathy, defined clinically as lymph node enlargement greater than 1 cm in diameter. Inclusion criteria were:

1. Patients who underwent both FNAB and subsequent histopathological examination via paraffin block analysis.
2. Patients with complete and legible medical records.
3. Confirmed anatomical localization of the lymphadenopathy to the colli (neck) region. Exclusion criteri patients whose diagnostic process included only FNAB or histopathology, incomplete medical records, and non-cervical lymph node involvement.

Using total sampling, all eligible cases within the defined period were included. After screening 74 cases, 66 patient records met the eligibility criteria and were analyzed. This non-randomized sample was selected to enhance data completeness and eliminate selection bias commonly found in convenience sampling [27].

D. DATA COLLECTION

Patient demographic and diagnostic data were extracted from SIM-RS and verified manually. Variables collected included:

1. Age
2. Year of diagnosis
3. FNAB diagnostic result (benign/malignant)
4. Histopathological result (benign/malignant)

The data were compiled into a standardized database using Microsoft Excel and validated for internal consistency. No direct patient contact or intervention occurred during the data collection process.

E. DIAGNOSTIC PROCEDURES

1. FINE NEEDLE ASPIRATION BIOPSY (FNAB)

FNAB procedures were performed by trained pathologists using a 22- or 23-gauge disposable needle attached to a 10 mL syringe. The lymph node was fixed with one hand, and aspiration was conducted using a single-puncture, multi-directional technique. Aspirated material was smeared on clean glass slides and immediately fixed using 96% alcohol for cytological staining. Staining was conducted using Hematoxylin-Eosin (HE) and Papanicolaou techniques, as per laboratory protocol. The cytological evaluation focused

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on nuclear and cytoplasmic morphology, cellular arrangement, and background features. Diagnoses were categorized as either benign or malignant based on cytomorphologic criteria [28].

2. HISTOPATHOLOGICAL EXAMINATION

Histopathological analysis was conducted using paraffin block-embedded excisional biopsy samples, sectioned at 3–5 µm using a rotary microtome. Standard HE staining was applied. Tissue sections were examined by senior pathologists to establish a definitive diagnosis. These histopathological results served as the reference (gold standard) for evaluating FNAB diagnostic performance [29].

F. DATA PROCESSING AND DIAGNOSTIC ACCURACY TESTING

A 2×2 contingency table was used to classify the FNAB results against histopathology into:

1. True Positive (TP): FNAB and histopathology both diagnosed malignancy.
2. False Positive (FP): FNAB diagnosed malignancy, but histopathology showed benign.
3. True Negative (TN): Both FNAB and histopathology diagnosed benign lesions.
4. False Negative (FN): FNAB diagnosed benign, but histopathology confirmed malignancy.

The following metrics were computed:

1. Sensitivity = TP / (TP + FN)
2. Specificity = TN / (TN + FP)
3. Positive Predictive Value (PPV) = TP / (TP + FP)
4. Negative Predictive Value (NPV) = TN / (TN + FN)
5. Accuracy = (TP + TN) / (TP + FP + TN + FN)

These diagnostic test parameters were calculated using Microsoft Excel 2020 and verified using SPSS version 25. No inferential statistics (e.g., chi-square, regression analysis) were conducted due to the study's descriptive nature [30].

G. QUALITY ASSURANCE

All FNAB and histopathological evaluations were conducted by certified, experienced pathologists. Internal quality control was ensured through double-reading of histological slides in 10% of the cases. Specimen adequacy was ensured during collection and verified microscopically before staining. Inadequate aspirates were repeated prior to diagnostic processing where applicable [31].

H. ETHICAL CONSIDERATIONS

There is no specific information available regarding ethical approval for this study

I. LIMITATIONS

The study was limited by its retrospective design and lack of standardized FNAB reporting frameworks (e.g., the Sydney System or Bethesda System). Additionally, operator variability and procedural heterogeneity could not be fully controlled. These limitations were mitigated through strict inclusion criteria and multi-pathologist confirmation.

III. RESULTS

The results of examination of FNAB and Histopathology data were then tabulated and classified using 2x2 crosstabulation statistics. After the cross tabulation test, the data were processed using a diagnostic test calculation based on the formula for accuracy, sensitivity, specificity, positive predictive value, negative predictive value, calculations with the following details (TABLE 1).

TABLE 1
Cross tabulation 2x2

		Gold standard (Histopatologi Blok Parafin)		
FNAB		**Positive**	**Negative**	**Total**
	Positive	a	b	a + b
	Negative	c	d	c + d
Total		a + c	b + d	Total

Where a is positive (malignant) FNAB examination results and positive (malignant) gold standard is TP (True Positive) b is positive (malignant) FNAB examination results and negative (benign) gold standard = FP (False Positive); c is negative (benignt) FNAB examination results and positive (malignant) gold standard which FN (False Negative), d is positive (malignant) FNAB examination results and negative (beningn) gold standard which FP (False Positive), a + c is TP + FN which the total number of people who are sick (determines the sensitivity value), b + d is FP + TN which the total number of people who are not sick (determines the specitifity value), a + b is TP + FP which the total number of people who test positive (determining a positive predictive value), c + d is FN + TN which the total number of people who test negative (determining a negative predictive value).

a. Sensitivity Diagnostic :
$$= \frac{TP}{TP+FN} \text{ x } 100\% = \frac{33}{33+\mathbf{7}} \text{ x } 100\% = 82{,}5\%$$

b. Specificity Diagnostic :
$$= \frac{TN}{FP+TN} \text{ x } 100\% = \frac{25}{25+\mathbf{1}} \text{ x } 100\% = 96{,}15\%$$

c. Negative Predictive Value :
$$= \frac{TP}{TP+FP} \text{ x } 100\% = \frac{33}{33+\mathbf{1}} \text{ x } 100\% = 97{,}05\%$$

d. Positive Predictive Value :
$$= \frac{TN}{FN+TN} \text{ x } 100\% = \frac{25}{25+\mathbf{7}} \text{ x } 100\% = 78{,}12\%$$

e. Diagnostic Accuracy :
$$= \frac{TP+TN}{Total} \text{ x } 100\% = \frac{33+25}{66} \text{ x } 100\% = 87{,}87\%$$

A. DISTRIBUTION OF THE NUMBER OF CASES OF LYMPHADENOPATHY COLLI THAT WENT THROUGH THE FNAB EXAMINATION IN THE PERIOD 2019 – MARCH 2022.

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Based on the results of the examination data that has been done with tabulation tests and classification of colli lymphadenopathy patients who did FNAB and Histopathology examinations, there were 74 excluded samples. Then obtained a number of 66 samples taken from medical record data (SIM-RS) that meet the research inclusion criteria. Table 2 contains information on the distribution of patients with cases of lymphadenopathy in the period 2019 to 2022 (TABLE 2). Graph of Data Distribution of the number of cases of lymphadenopathy colli that went through the FNAB examination in the period 2019 – March 2022. Based on the sample data obtained during the study period, it showed that from a total of 66 cases of Colli Lymphadenopathy patients who had FNAB performed, 34 cases were found to be malignant with a percentage of 50.77% (FIGURE 2).

TABLE 2
Distribution of the number of cases of lymphadenopathy colli that went through the FNAB examination in the period 2019 – March 2022.

Year	Type Of Tumors		Number
	Benign	Malignant	
2019	9	7	16
2020	10	10	20
2021	10	13	23
2022	3	4	7
Number	**32**	**34**	**66**

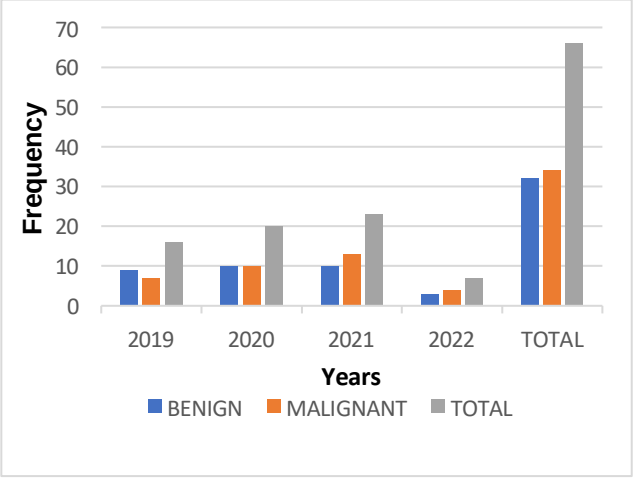


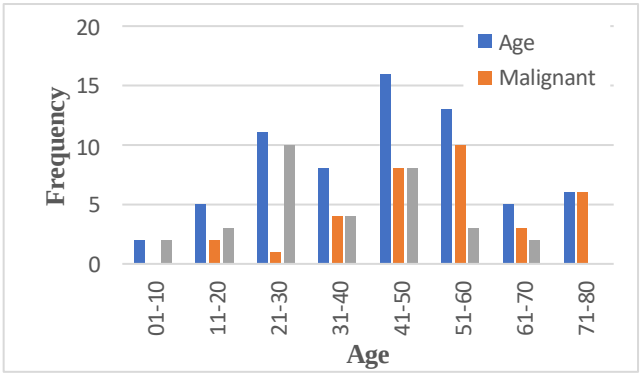
FIGURE 2. **Data distribution of the number of cases of lymphadenopathy colli that went through the FNAB examination in the period 2019 – March 2022.**

B. CLASSIFICATION OF COLLI LYMPHADENOPATHY PATIENTS BY AGE

TABLE 3
Classification of colli lymphadenopathy patients by age

Age	Benign	Malignant	Frequency	Percentage
01-10	0	2	2	3%
11-20	2	3	5	8%
21-30	1	10	11	17%
31-40	4	4	8	12%
41-50	8	8	16	24%
51-60	10	3	13	20%
61-70	3	2	5	8%
71-80	6	0	6	9%
Total	34	32	66	100%

The ages of colli lymphadenopathy patient's classified by TABLE 3 according to the patient's age along with the type of malignant and benign tumors. The total number of benign tumors was 34 and 32 the number of malignant tumors. Patients with colli lymphadenopathy cases when reviewed based on age range, show that the age range of 41-50 years is the age with the highest incidence of colli lymphadenopathy, with a total of 16 cases with a percentage of 24%. The most cases of malignant colli lymphadenopathy that underwent FNAB examination were found in the age range of 51-60 years with a total of 10 cases with a percentage of 20%. Whereas in benign cases, the most FNAB examinations were found in the age range



of 21-30 years with a total of 10 cases with a percentage of 17% (FIGURE 3).

FIGURE 3. **Classification of patients with Colli Lymphadenopathy by age**

On physical examination, adults undergoing primary outpatient examination generally have visible lymph nodes. Although the incidence decreases with age [22]. Patients with lymphadenopathy aged 40 years or more have a malignancy risk of about 4%. Patients under the age of 40 years have a malignancy risk of 0.4%. Lymphadenopathy lasting less than 2 weeks or more than 1 year without progression in size has a very small probability that the etiology is malignancy[18]. Based on studies conducted, the age range of 41-50 has the highest number of colli lymphadenopathy cases that are often found FIGURE 3. In the age range of 51-60 years has the highest number of patients with colli lymphadenopathy malignancy.

According to TABLE 5, it explains that the data obtained were then tabulated and classified using the 2x2 crosstabulation statistic. Details of the tabulation details as in the table. The results of the FNAB examination which were confirmed by histopathological examination found malignancy in 34 cases, and 33 cases were found to be truly malignant/true positive. While 33 cases of benign FNAB examination, only 25 cases were diagnosed as truly benign/true negative histopathologically.

TABLE 5
Patient Data on Colli Lymphadenopathy FNAB Examination and Paraffin Block Histopathology in the 2x2 Crosstabulation table.

		Gold standard (Histopatologi Blok Parafin)		
		Positive	**Negative**	**Total**
FNAB	**Positive**	33	1	34
	Negative	7	25	32
Total		40	26	66

V. DISCUSSION

This study aimed to evaluate the diagnostic performance of Fine Needle Aspiration Biopsy (FNAB) in differentiating between benign and malignant colli lymphadenopathy,

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using paraffin-block histopathology as the gold standard. Among the 66 samples included, FNAB yielded an accuracy of 87.87%, with a sensitivity of 82.5% and a specificity of 96.15%. The positive predictive value (PPV) was 97.05%, while the negative predictive value (NPV) stood at 78.12%. These values affirm that FNAB is a highly specific and reasonably sensitive screening tool for cervical lymphadenopathy.

The relatively high sensitivity demonstrates FNAB's capacity to correctly identify malignant lesions in most patients. However, the presence of 7 false-negative cases, where FNAB failed to detect malignancy confirmed by histopathology, indicates the risk of underdiagnosis. Such false negatives can stem from several factors including sampling errors, inadequate cellular material, or subtle cytological features that mimic benign processes.

Meanwhile, the high specificity and PPV indicate that when FNAB suggests malignancy, it is highly reliable. Only one case in this study was deemed a false positive. This aligns with FNAB's well-established strength in ruling in malignancy, particularly in metastatic tumors where cellular features are distinctive. Nevertheless, the moderate NPV suggests caution when interpreting negative results, especially in high-risk patients. These findings support FNAB as a valuable diagnostic tool, especially for triaging cases before proceeding to more invasive procedures like excisional biopsy. Its benefit being minimally invasive, rapid, cost-effective, and safe enhance its applicability in routine clinical practice.

A. COMPARISON WITH PREVIOUS STUDIES

When compared with similar studies, our findings demonstrate consistency with global trends. A study by Dwianingsih et al. in Yogyakarta reported FNAB sensitivity of 85.88% and specificity of 70.73%, with an overall accuracy of 80.95%. Another study involving 300 cases recorded even higher sensitivity (84.5%) and specificity (99.3%), highlighting the variability based on sample size, operator expertise, and lesion types.

Furthermore, Sushama et al. reported FNAB accuracy values ranging from 78–92%, reinforcing that the technique is highly effective, albeit susceptible to variations due to cytologist experience, sample adequacy, and lesion location [33]. In our study, the rate of false negatives was slightly higher than in some reports. This could be due to limitations such as lack of ultrasound guidance or the absence of rapid on-site evaluation (ROSE), both of which have been shown to improve sample adequacy and diagnostic yield [34]. International guidelines increasingly recommend using standardized classification systems like the Sydney System or the Bethesda System for cytology reporting to improve diagnostic reproducibility and communication among clinicians [35]. These were not employed in this study, which may partly explain variability in interpretation and classification of cytological findings.

Moreover, FNAB is known to be less reliable for primary lymphoid neoplasms, such as low-grade non-Hodgkin lymphomas, due to their overlapping cytological features with reactive hyperplasia. Studies by Makarenko et al. and Domanski emphasized the challenges FNAB poses in such conditions, often necessitating histopathology or immunohistochemistry for definitive diagnosis [36], [37]. Despite such limitations, our specificity and PPV values were among the highest reported, suggesting that FNAB is highly reliable when identifying malignant lesions in the neck region. This reinforces its role as a frontline diagnostic method in both primary and referral hospital settings.

B. STUDY LIMITATIONS AND CLINICAL IMPLICATIONS

While this study offers valuable insights into the utility of FNAB, several limitations must be acknowledged. Firstly, its retrospective design introduces inherent biases, particularly related to data completeness and operator variation. Not all FNABs may have been performed under standardized protocols or by the same practitioner, potentially affecting accuracy.

Secondly, the absence of cytological classification systems such as the Sydney System limited the ability to categorize findings into risk-based tiers. These frameworks not only aid in interpretation but also guide clinical management based on risk of malignancy [35]. Future research should incorporate such classification systems to enhance diagnostic precision and clinical decision-making.

Additionally, the modest sample size (66 cases) and single-center setting limit the generalizability of findings. Multicenter studies involving larger cohorts and a variety of pathologist profiles would offer more robust and representative data. Also, adjunct diagnostic tools such as immunocytochemistry or molecular testing were not utilized, although they could improve accuracy, especially in lymphoma cases [36].

Technical errors remain another concern. Diagnostic discrepancies may arise from the pre-analytical stage (e.g., poor specimen collection), the analytical phase (e.g., staining artifacts, inadequate fixation), or the post-analytical phase (e.g., misinterpretation). As highlighted in prior literature, quality assurance at each phase is vital for diagnostic fidelity [38].

From a clinical perspective, the high specificity and PPV found in this study suggest that FNAB is most reliable in confirming malignancy, making it a valuable tool for surgical triage or oncologic referral. However, its moderate sensitivity and NPV mean that a benign FNAB result should not be the sole basis for ruling out malignancy, particularly in patients with persistent or high-risk features. In such cases, follow-up imaging or excisional biopsy should be pursued.

In terms of resource allocation, FNAB offers a cost-effective diagnostic pathway in environments with limited access to surgical services. Given its quick turnaround and minimal invasiveness, it can expedite patient management, reduce hospitalization, and improve patient comfort. These benefits are particularly relevant in developing healthcare systems such as Indonesia's, where hospital resources may be constrained.

C. IMPLICATIONS FOR FUTURE RESEARCH

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This study provides foundational evidence for the implementation of FNAB as a screening tool in the diagnosis of colli lymphadenopathy in Indonesian tertiary hospitals. Future research should focus on the integration of ancillary techniques such as ROSE and immunocytochemistry to improve diagnostic yield, particularly in challenging cases like lymphoma or tuberculosis. Moreover, prospective studies utilizing standardized reporting systems and comparing FNAB with emerging technologies such as core-needle biopsy or image-guided cytology may further refine the role of FNAB. A cost-effectiveness analysis would also be beneficial to quantify the economic advantages of FNAB over surgical biopsy in both public and private healthcare sectors.

V. CONCLUSION

This study was conducted to assess the diagnostic performance of Fine Needle Aspiration Biopsy (FNAB) in comparison with the gold-standard histopathological examination for identifying benign and malignant cases of colli lymphadenopathy at RSPAL Dr. Ramelan Surabaya. The primary objective was to determine the reliability of FNAB as a frontline diagnostic tool in evaluating cervical lymph node enlargement. The analysis of 66 eligible patient cases revealed that FNAB demonstrated a diagnostic accuracy of 87.87%, a sensitivity of 82.5%, and a specificity of 96.15%. The positive predictive value (PPV) was found to be 97.05%, indicating a high probability that patients with malignant FNAB results truly had malignancies confirmed by histopathology. The negative predictive value (NPV), however, was moderately lower at 78.12%, suggesting that caution should be exercised when interpreting benign FNAB results, particularly in high-risk patients. These findings confirm that FNAB is an efficient, minimally invasive, and cost-effective diagnostic technique that can serve as an initial screening method for patients presenting with colli lymphadenopathy.

However, given the observed false-negative rate, histopathological confirmation remains essential in clinically suspicious cases despite benign cytological findings. The results of this study reinforce existing literature on the diagnostic utility of FNAB, while also highlighting the necessity for procedural standardization, including the use of cytological classification frameworks and image-guided aspiration to enhance diagnostic precision. For future research, prospective studies incorporating larger, multicenter samples and standardized reporting systems such as the Sydney System are recommended. Additionally, integrating ancillary techniques like rapid on-site evaluation (ROSE), immunocytochemistry, or molecular assays may further improve diagnostic accuracy, particularly in cases of lymphoproliferative disorders. Overall, FNAB remains a valuable diagnostic modality in the clinical evaluation of lymphadenopathy, especially within resource-constrained healthcare environments where access to surgical biopsy may be limited.

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DATA AVAILABILITY

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Patient data were obtained from the hospital information system (SIM-RS) of RSPAL Dr. Ramelan Surabaya and are not publicly available due to privacy and ethical restrictions.

AUTHOR CONTRIBUTION

Devan Andhika Putra Pratama contributed to data collection, analysis, and the initial drafting of the manuscript. Anik Handayati supervised the research process, provided methodological guidance, and critically revised the manuscript for intellectual content. Evy Diah Woelansari supported data interpretation, literature review, and final editing of the manuscript. All authors have read and approved the final version of the manuscript.

DECLARATIONS

ETHICAL APPROVAL

Ethical approval for this study is not explicitly documented or reported

CONSENT FOR PUBLICATION PARTICIPANTS

This study used secondary data obtained from hospital medical records. All personal identifiers were removed to ensure patient confidentiality. As the data were anonymized and retrospective in nature, the requirement for individual informed consent was waived by the institutional ethics committee.

COMPETING INTERESTS

The authors declare that there are no competing interests related to the content or publication of this research.

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