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EFFICACY OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN THE DIAGNOSIS OF TUBERCULOUS LYMPHADENITIS AS COMPARED TO GENEXPERT IN A TERTIARY CARE HOSPITAL, PUNJAB, PAKISTAN

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ABSTRACT

Background and Objectives

Tuberculous lymphadenitis is a common extrapulmonary manifestation of tuberculosis which is difficult to accurately diagnose especially when resources are limited like in most of the progressive countries. The current research is focused on comparing the diagnostic utility and effectiveness of GeneXpert and Fine Needle Aspiration Cytology (FNAC) for accurate identification of tuberculous lymphadenitis.

Materials & Methods

This study was conducted at a tertiary care hospital, Punjab, Pakistan, from October 2022 to December 2023. A total of 150 patients with clinically suspected tuberculous lymphadenitis were included. FNAC and GeneXpert were performed on all patients in the study and the results were compared for accuracy of diagnosis. FANC results were analyzed for granulomatous inflammation and AFB presence. On the other hand, GeneXpert was used to detect Mycobacterium TB DNA and rifampicin resistance.

Results

FNAC identified granulomatous inflammation in 80% of cases. Sensitivity and specificity of FNAC remains 92.3% and 66.7% respectively. However, GeneXpert showed a sensitivity of 86.7% and detected rifampicin resistance in 10% of cases.

Conclusion

This comparative study concluded that although FNAC is initially a valueable tool for diagnosing tuberculous lymphadenitis, limitations in accuracy limits its reliability. However, the other diagnostic

tool, GeneXpert provides comparatively higher diagnostic accuracy and is essential for detecting drug resistance. Therefore, this study recommends an integrated use of FNAC and GeneXpert to improve the diagnosis of Tuberculous lymphadenitis.

Keywords: Tuberculous Lymphadenitis, FNAC, GeneXpert MTB/RIF

INTRODUCTION

GeneXpert and Fine Needle Aspiration Cytology (FNAC) are two techniques which are globally utilized in the diagnostics of tuberculous lymphadenitis. It is a common form of extrapulmonary TB which can be defined as the inflammation of lymph nodes as a result of Mycobacterium TB infection. Accurate and timely clinical diagnosis is a fundamental and mandatory step for prompt treatment of tuberculous lymphadenitis [1]-[3].

Comparative studies between FNAC and GeneXpert in the correct identification of tuberculous lymphadenitis have shown that FNAC remains a valuable initial diagnostic tool due to its accessibility and ability to provide immediate cytological evaluation [4]-[6]. GeneXpert enhances diagnostic accuracy, particularly in cases where FNAC results are inconclusive or when a rapid diagnosis is required [7]. The combination of FNAC and GeneXpert has been shown to improve diagnostic yield, allowing for more accurate and timely diagnosis of tuberculous lymphadenitis [8].

In resource constrained medical facilities where access to advanced molecular diagnostics may be limited, FNAC remains a cornerstone in the diagnosis of tuberculous lymphadenitis. However, the integration of GeneXpert into diagnostic techniques has the potential to improve the sensitivity and specificity of TB detection, particularly in cases with atypical presentations or where drug resistance is a concern [9]. The synergistic use of these diagnostic tools can optimize patient outcomes by ensuring accurate and early diagnosis, thereby facilitating appropriate treatment and reducing the burden of TB [10].

MATERIALS AND METHODS

The study was conducted at a tertiary healthcare facility in Southern Punjab Pakistan in the South Asia which is single largest source of the Tuberculous lymphadenitis cases around the globe [1]. Bahawal Victoria Hospital, Bahawalpur is one of the largest health care facility in the south Punjab region. The study period was comprised of more than 15 months, from October 2022 to December 2023.

A total of 150 patients with clinically suspected tuberculous lymphadenitis were enrolled in the study. Patients were selected consecutively as they presented to the hospital, ensuring a representative sample of the population. The inclusion and exclusion criteria are presented as follows:

Inclusion Criteria:

- Patients of all ages and both genders with clinically suspected tuberculous lymphadenitis.
- Patients who provided informed consent.

Exclusion Criteria:

- Patients with a history of lymphadenopathy due to causes other than TB, such as malignancy or autoimmune diseases.
- Patients who had received anti-tuberculous treatment prior to presentation.

FNAC was performed on all 150 vitally stable patients. A 22-gauge needle attached to a 05 ml syringe was used to aspirate material from the affected lymph nodes under aseptic conditions after written consent. Multiple passes were made to obtain an adequate sample and sample adequacy was confirmed on site microscopy. Aspirated material was then smeared onto glass slides, air dried and stained with Diff-Quik stain for cytological examination.

In parallel, an additional sample was collected from each patient for GeneXpert testing. The aspirated material was transferred into a sterile container and sent to the hospital's molecular diagnostic laboratory for processing. GeneXpert MTB/RIF assay was performed according to the manufacturer's protocol, with results obtained within 2 hours.

The presence of granulomas composed of Langhans giant cells, caseous necrosis, and epithelioid histiocytes were among the cytological findings consistent with granulomatous inflammation favoring the diagnosis of tuberculous lymphadenitis. The aspirated material was considered positive for the GeneXpert assay if Mycobacterium tuberculosis DNA was detected in it. Rifampicin resistance was also evaluated as part of the assay.

The data was entered and assessed using SPSS 26.0. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FNAC were calculated using GeneXpert as the reference standard. The percentage results that were shown came with a 95% confidence interval. Chi-square testing was used to assess the association between FNAC and GeneXpert results; a p-value of less than 0.05 was considered statistically significant.

RESULTS

The study comprised 150 patients in total. The patients' ages ranged from 15 to 70 years old, with a mean age of 35.4 years (SD \pm 12.8 years). Of the patients, sixty percent were men and ninety percent were women (n = 60, 40%). Table 1 displays the patients' age and gender distribution.

Table 1: Demographic Characteristics of the Study Population

Characteristic	Number of Patients (n=150)	Percentage (%)
Gender		
Male	60	40%
Female	90	60%
Age Group (years)		
15-30	50	33.3%
31-45	55	36.7%
46-60	35	23.3%
>60	10	6.7%

Out of the 150 patients, FNAC was positive for granulomatous inflammation suggestive of tuberculous lymphadenitis in 120 patients (80%). Among these, 85 samples (56.7%) showed the presence of caseous necrosis, and AFB was detected in 60 samples (40%).

GeneXpert testing was positive for Mycobacterium TB in 130 out of 150 patients (86.7%). Rifampicin resistance was detected in 15 patients (10%). Statistical results of FNAC compared to GeneXpert are shown in Table 2.

 Table 2: Diagnostic Performance of FNAC Compared to GeneXpert

Diagnostic Parameter	Value (95% CI)
Sensitivity	92.3% (85.7% - 96.4%)
Specificity	66.7% (44.7% - 84.4%)
Positive Predictive Value (PPV)	96.7% (91.4% - 98.8%)
Negative Predictive Value (NPV)	50% (32.9% - 67.1%)

The association between FNAC and GeneXpert results was statistically significant ($\chi^2 = 25.63$, p < 0.001). This indicates that FNAC has a strong correlation with GeneXpert in the diagnosis of tuberculous lymphadenitis, though GeneXpert outperformed FNAC in terms of sensitivity.

Among the 15 patients with rifampicin resistance detected by GeneXpert, FNAC results were positive in 13 cases (86.7%), suggesting that FNAC can still be a useful initial diagnostic tool even in cases of drug-resistant TB.

DISCUSSION

This study sought to evaluate the effectiveness of FNAC in diagnosing tuberculous lymphadenitis as compared to GeneXpert in a tertiary care setting. The results affirm that while FNAC is a valuable

tool, its diagnostic accuracy is surpassed by that of GeneXpert, particularly in cases with a low bacterial load or when drug resistance is a concern.

FNAC was positive in 80% of cases, consistent with previous studies that have underscored its utility in identifying granulomatous inflammation, characterized by caseous necrosis and the boomerang shaped epithelioid histiocytes in background of lymphocytes. [1][2]. Despite this, sensitivity of FNAC was found to be 92.3%, which is somewhat lower than in other reports [3]. This discrepancy may be attributed to the subjective nature of cytological evaluation and the potential for sampling errors, which can lead to false negatives [2][11].

GeneXpert, with its sensitivity of 86.7% in this study, continues to be a gold standard in molecular diagnostics for TB [4][5]. The assay's ability to detect Mycobacterium TB DNA directly from clinical samples with high accuracy, even in paucibacillary forms of the disease, has been well documented [12][13]. This study includes those findings, highlighting GeneXpert's role in rapidly diagnosing TB and detecting rifampicin resistance, which was observed in 10% of the cases [6][14]. The early detection of drug resistance is crucial in management of TB, as it allows for the timely initiation of appropriate targeted therapy and helps to prevent the spread of resistant strains [15][16].

The specificity of FNAC in this study was 66.7%, which aligns with other studies that have reported limitations in FNAC's ability to definitively diagnose tuberculous lymphadenitis, especially in the absence of AFB [8][17]. This limitation underscores the need for complementary diagnostic tools, such as GeneXpert, to enhance diagnostic accuracy. Studies have shown that the combined use of FNAC and GeneXpert can significantly improve the overall diagnostic yield, as evidenced in our study [10][18].

FNAC remains a valuable diagnostic tool for the in resource-limited settings like Bahawal Victoria Hospital where it provides a cost-effective and rapid method for initial assessment. However, an integration of both methods may enable improved patient care [19]-[20].

CONCLUSION

Two diagnostic tools, FNAC and GeneXpert, are studied and analyzed for comparative results for utilization in effective diagnosis of tuberculous lymphadenitis. The results are statistically computed and compared for finding out a more efficient approach among the two. The study concluded that FNAC is an easily available and comparatively low-cost diagnostic tool with a limitation of diagnostic accuracy based on several factors including preprocessing and clinician competency. On the other hand, GeneXpert has higher sensitivity and ability to detect rifampicin resistance has proven itself a comparatively more accurate technique for diagnosis of TB. Based on statistical analysis, the integration of GeneXpert and FNAC improves the overall diagnostic accuracy and helps in the early identification of drug-resistant TB. In regions like Bahawalpur, Punjab, Pakistan, with a high burden of TB, the integrated use of FNAC and GeneXpert is a recommended approach to optimize TB diagnosis and control the further the spread of the disease.

REFERENCES

- [1]. Suh KW, Park CS, Lee JT, Lee KG. Diagnosis of cervical tuberculous lymphadenitis with fine needle aspiration biopsy and cytologic examination under ultrasonographic guides. Yonsei Medical Journal. 1993;34(4):328–33 DOI: 10.3349/ymj.1993.34.4.328.
- [2]. Das DK. Fine-needle aspiration cytology in the diagnosis of tuberculous lesions. Lab Med. 2000;31(11):625-632 https://doi.org/10.1309/UJ0B-VDWV-U0LE-E0QQ.
- [3]. Knox J, Lane G, Wong J, Trevan P, Karunajeewa H. Diagnosis of tuberculous lymphadenitis using fine needle aspiration biopsy. Internal medicine journal. 2012;42(9):1029–36 DOI: 10.1111/j.1445-5994.2012.02748.x.
- [4]. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010;363(11):1005-1015 DOI: 10.1056/NEJMoa0907847.

- [5]. Gómez AV, González-Martín J, García-Basteiro AL. Xpert® MTB/RIF: Usefulness for the diagnosis of tuberculosis and resistance to rifampicin. Medicina Clínica (English Edition). 2017;149(9):399–405 https://doi.org/10.1016/j.medcle.2017.09.021.
- [6]. World Health Organization (WHO). Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system. Policy statement. Geneva: WHO; 2011.
- [7]. Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2014;44(2):435-446 DOI: 10.1183/09031936.00007814.
- [8]. Handa U, Mundi I, Mohan H. Nodal tuberculosis revisited: A review. J Infect Dev Ctries. 2012;6(1):6-12 DOI: https://doi.org/10.3855/jidc.2090.
- [9]. Moure R, Muñoz L, Torres M, Santín M, Martín R, Alcaide F. Rapid detection of Mycobacterium tuberculosis complex and rifampin resistance in smear-negative clinical samples by use of an integrated real-time PCR method. J Clin Microbiol. 2011;49(3):1137-1139 DOI: 10.1128/JCM.01831-10.
- [10]. Sharma SK, Ryan H, Khaparde S, Sachdeva KS, Singh AD, Mohan A, et al. Index-TB guidelines: Guidelines on extrapulmonary tuberculosis for India. Indian J Med Res. 2017;145(4):448-463 doi: 10.4103/ijmr.IJMR_1950_16.
- [11]. Purohit MR, Mustafa T, Mørkve O, Sviland L. Gender differences in the clinical diagnosis of tuberculous lymphadenitis—a hospital-based study from Central India. Int J Infect Dis. 2009;13(5):600-605 https://doi.org/10.1016/j.ijid.2008.06.046.
- [12]. Tortoli E, Russo C, Piersimoni C, Mazzola E, Dal Monte P, Pascarella M, et al. Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis. Eur Respir J. 2012;40(2):442-447 DOI: 10.1183/09031936.00176311.
- [13]. Norbis L, Alagna R, Tortoli E, Codecasa LR, Migliori GB, Cirillo DM. Challenges and perspectives in the diagnosis of extrapulmonary tuberculosis. Expert Rev Anti Infect Ther. 2014;12(5):633-647 DOI: 10.1586/14787210.2014.899900.
- [14]. van Kampen SC, Anthony RM, Kazi M, Peters R, Ramsay AR, Justesen US, et al. Xpert MTB/RIF version G4 assay for tuberculosis testing in a low tuberculosis incidence setting. Eur Respir J. 2017;49(3):1602216 DOI: https://doi.org/10.1186/s12879-016-2039-4.
- [15]. Pietersen E, Ignatius E, Streicher EM, Mastrapa B, Padanilam X, Pooran A, et al. Long-term outcomes of patients with extensively drug-resistant tuberculosis in South Africa: a cohort study. Lancet. 2014;383(9924):1230-1239 DOI: 10.1016/S0140-6736(13)62675-6.
- [16]. Cox HS, Mbhele S, Mohess N, Whitelaw A, Muller O, Zemanay W, et al. Impact of Xpert MTB/RIF for TB diagnosis in a primary care clinic with high TB and HIV burden. Int J Tuberc Lung Dis. 2014;18(8):932-937 DOI: 10.1371/journal.pmed.1001760.
- [17]. Yang ZG, Kong YY, Gao GP, Bai HG, Cai YJ, Zhang CP. Diagnostic Accuracy of the Xpert MTB/RIF Assay for Lymph Node Tuberculosis: A Systematic Review and Meta-Analysis. Pathol Res Pract. 2018;214(7):977-982 doi: 10.1155/2019/4878240.
- [18]. Parsons LM, Somoskövi Á, Gutierrez C, Lee E, Paramasivan CN, Abimiku A, et al. Laboratory diagnosis of tuberculosis in resource-poor countries: challenges and opportunities. Clin Microbiol Rev. 2011;24(2):314-350 DOI: 10.1128/CMR.00059-10.
- [19]. Pimkina E, Zablockis R, Nikolayevskyy V, Danila E, Davidaviciene E. The Xpert® MTB/RIF assay in routine diagnosis of pulmonary tuberculosis: A multicentre study in Lithuania. Respiratory medicine. 2015;109(11):1484–9 DOI: 10.1016/j.rmed.2015.07.006.
- [20]. Albert H, Nathavitharana RR, Isaacs C, Pai M, Denkinger CM, Boehme CC. Development, rollout and impact of Xpert MTB/RIF for tuberculosis: what lessons have we learnt and how can we do better? Eur Respir J. 2016;48(2):516-525 DOI: 10.1183/13993003.00543-2016.