

# The issue of fine needle aspiration cytology in the diagnosis of tuberculous cervical lymphadenitis in Iran

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## RESEARCH

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## ABSTRACT

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### Background

Due to different reports about the value of fine needle aspiration cytology (FNAC) as a simple and minimal invasive diagnostic tool for extra-pulmonary tuberculosis, we attempted to demonstrate the sensitivity of FNAC in patients with cervical tuberculous lymphadenitis in Iran. We wanted to know if fine needle aspiration (FNA) is an accurate method as a first step in diagnosis or not.

### Methods

This study covered a 14 year period identifying 137 patients with a pathological report of granulomatosis in excisional biopsy of lymphadenopathy in two tertiary referral hospitals of Tehran, Iran. The results of fine needle aspiration cytology (FNAC) in 67 patients with tuberculosis cervical lymphadenitis were evaluated.

### Results

The FNA cytology showed granuloma with background necrosis in five patients (7.46 per cent) and granuloma with or without necrosis in 13 patients (19.40 per cent). Patients with positive results of FNAC had a longer duration of

lymphadenopathy compared to other patients.

### Conclusion

In this study, sensitivity of FNAC was reported to be low. The sensitivity of this method was 7.46 per cent (including pathology granuloma with background necrosis) and 19.40 per cent (total cases of granuloma with or without necrosis). It seems that the sensitivity of FNAC is significantly lower in patients with early cervical tuberculosis (TB) lymphadenitis. Combining acid-fast bacillus (AFB) staining and non-culture methods like polymerase chain reaction (PCR) could increase FNA sensitivity in these patients.

### Key Words

Fine needle aspiration cytology, cervical lymphadenitis, tuberculosis

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## What this study adds:

### 1. What is known about this subject?

There is a changing trend in sensitivity of fine needle aspiration in the diagnosis of tuberculosis lymphadenitis.

### 2. What new information is offered in this study?

This study shows that fine needle aspiration is not an accurate method as a first step for the diagnosis of tuberculosis lymphadenitis.

### 3. What are the implications for research, policy, or practice?

We suggest FNA should be combined with PCR or be replaced with excisional biopsy for diagnosis of TB lymphadenitis.

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## Background

Although an estimated incidence rate of tuberculosis (TB) in Iran is comparatively very low amongst all six regions of World Health Organization (WHO) in 2014 (22 case per 100,000 population) it is still one of the major health problems in Iran.<sup>1</sup> Due to the high rate of migration from neighbouring countries, strict control of TB is one of our

health care system priorities.

One of the common causes of all cervical lymphadenopathies is tuberculosis lymphadenitis which is the commonest presentation of extra-pulmonary tuberculosis.<sup>2</sup> In these cases an excisional biopsy of affected lymph nodes, combined with microbial tests is the most reliable diagnostic tool for suspected tuberculosis lymphadenitis.<sup>3</sup> However, it is invasive and time-consuming. Fine needle aspiration cytology (FNAC) is a rapid simple modality and it is minimally invasive, cost-effective, feasible and painless.<sup>4</sup> FNAC is a promising technique which can help diagnosis. It permits treatment to start even before final diagnosis is confirmed with culture or other modalities.<sup>5</sup> Considering the importance of tight control of TB, early detection could be an important step in preventing the pandemic in the country.

Although it is accepted that FANC is a first line diagnostic technique for lymphadenopathies in most conditions,<sup>6</sup> to assess the sensitivity of this method has greater importance in the diagnosis of tuberculosis cervical lymphadenitis. According to different reports from different parts of the world about the sensitivity rate of FNAC, especially at different stages of the disease, this study attempts to demonstrate the sensitivity of FNAC in patients with a definite diagnosis of tuberculous lymphadenitis. Because of changing trends in sensitivity of fine needle aspiration, we suggest that this method cannot be used as an accurate method as a first step in the diagnosis of tuberculosis lymphadenitis.

## Method

This is a retrospective cross-sectional study carried out in Tehran, Iran from March 1999 to March 2013. In this study, all pathology reports of patients with cervical lymphadenopathy who were admitted to Imam Khomeini Complex Hospital and Amir-Alam Hospital, (two major referral centres under coverage of Tehran university of Medical Sciences) were evaluated. Amongst 137 patients 1 confirmed to have caseous necrosis and granulomatosis changes in their pathologies report, there were 39 cases with non-cervical lymphadenopathies, nine outpatient cases and 22 cases with no FNAC reports so these were excluded from the study. Eventually 67 cases were included in the study. The sensitivity of this method was 7.46 per cent (including pathology granuloma with background necrosis: 5/67) and 19.40 per cent (total cases of granuloma with or without necrosis: 13/67). The data was collected from medical files including demographic information, past medical history, clinical examination, laboratory results and

FANC report.

All selected patients were treated with anti-TB drugs for six months. During follow-up or at the end of the treatment, no clinical evidence of recurrence or treatment failure was observed. Continuous and categorical variables were compared using student's t-test and chi-square test respectively. P-value <0.05 was meaningful.

## Results

There were 29 (43.3 per cent) men and 38 (56.7 per cent) women involved in our study. Mean  $\pm$ SD and Median age of patients were  $38.31\pm 16.5$  and 38 years old respectively. Nineteen patients (28.4 per cent) were older than 50 years. The assessment of nationality distribution of patients showed 50 (74.6 per cent) Iranian and 17 (25.4 per cent) Afghan. 55 (82.1 per cent) patients had unilateral and 12 patients (17.9 per cent) bilateral cervical Lymphadenopathy. All patients had a normal chest x-ray and negative HIV Antibody test (HIV Ab). Purified protein derivative test (PPD test) was positive in 59 cases. Duration of lymphadenopathy was from 15 days to two years with a mean of 85 days. Tables 1 and 2 show the distribution of cytology reports according to sex and nationality. Amongst all study cases, 13 patients had classical features of tuberculosis in FNAC reports including granuloma with background necrosis in five patients (7.46 per cent) and granuloma with or without necrosis in 13 patients (19.40 per cent). Mean duration of lymphadenopathy in cases with positive results of FNAC was 291 days. Table 3 shows demographic and characteristic features of patients with cytologic evidence of TB.

A significant correlation was found between nationality and positive FANC reports that showed a higher rate of positive FNAC in Afghan patients based on cytomorphology ( $p < 0.05$ ) (Table 2).

The mean duration of lymphadenitis was significantly longer in cases with positive results of FNAC (P-value <0.05). There was no significant correlation between other variables and FANC reports.

## Discussion

Although Iran is not considered as a high burden country for TB,<sup>1</sup> tight control of TB is one our major problems. Multidrug resistance tuberculosis, increasing human immunodeficiency virus (HIV) infection and migration from neighbour countries to Iran can be a trigger for future pandemics. Clinical features, though indicative of tuberculous etiology, are not adequate for making a definitive diagnosis.

There is a necessity for using rapid, simple, minimally invasive and sensitive methods to the diagnosis of tuberculosis and the answer is FNAC. In one study, comparative analysis showed biopsies had higher diagnostic value than FNA, presumably due to their larger size.<sup>7</sup> However, in the routine clinical setting, aspirates are preferred because taking FNA is less invasive and easier. Hafez et al. in their study in 2011 mentioned although FNAC has some limitations and pitfalls, it is a good first line method for investigating the cases of cervical lymphadenopathy.<sup>8,9</sup> Bezabih et al. conducted a cross-sectional study for assessing the correlation between FNAC and the Ziehl Neelsen staining technique. Their findings suggested using these two methods together in diagnosing tuberculous lymphadenitis to increase the diagnostic accuracy.<sup>9</sup> They reported the overall diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of FNAC technique were 90.9 per cent, 67.2 per cent, 82.6 per cent, and 81.3 per cent, respectively<sup>8</sup> and it varies from 70–100 per cent in studies.<sup>10–12</sup> This study aimed to evaluate the sensitivity of FNAC in the diagnosis of tuberculosis in patients who present with neck lymphadenopathy in Tehran, Iran. Sixty seven patients with lymph node excisional biopsy-proven cervical lymphadenitis due to tuberculosis were evaluated. As a result, the sensitivity of this method was 7.46 per cent (including pathology granuloma with background necrosis) and 19.40 per cent (total cases of granuloma with or without necrosis), respectively. Although in one study the demonstration of granuloma without necrosis in FNAC was compatible with tuberculosis diagnosis in only 23 per cent of patients,<sup>13</sup> another study showed that diagnosis of tuberculosis was established by demonstration of epithelioid granuloma with or without caseation in FNAC even in absence of acid-fast bacillus (AFB).<sup>14</sup> This low sensitivity for FNAC technique reported in this study was not attributed to selection bias because all cases had biopsy-proven tuberculous lymphadenitis.

FNAC is not without limitations. There is the chance of technical as well as interpretative error in the FNA cytologic diagnosis of tuberculosis. Inexperienced pathologists who read the slides may also add to the low sensitivity rate of FNA cytology. Furthermore, fresh and adequate aspirate samples are needed for making a correct cytodiagnosis. So samples may not be representative or adequate.

The mean duration of lymphadenitis was much longer in cases with positive results of FNAC. Indeed aspirates from an early stage lymph node were the main cause of low sensitivity. If lymph node aspiration was done once in the

early stage; the diagnosis is likely to be dismissed as a reactive node.<sup>15,16</sup> Another study showed that re-aspirating after several weeks, and waiting for the development of granuloma, improved the diagnostic efficacy could improve.<sup>16</sup> Unfortunately due to a limited number of examples in spite of the long-term evaluation, lack of more investigations like PCR, culture, and smear in order to increase the sensitivity, the power of our study was affected. It seems that FNA cytology has low sensitivity in early tuberculous lymphadenitis. If this report is confirmed in another study with a larger sample size, it is necessary to use another screening technique to evaluate early cervical lymphadenopathy as a first line modality. We suggest that the FNA method should be combined with PCR or be replaced with excisional biopsy for the diagnosis of TB lymphadenitis.

### Conclusion

In this study, sensitivity of FNAC was reported to be low. It seems that the sensitivity of FNAC is significantly lower in patients with early cervical TB lymphadenitis. Combining AFB staining and non-culture methods like PCR could increase FNA sensitivity in these patients.

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1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
  2. All possible steps have been taken to safeguard the identity of the patient(s).
  3. This submission is compliant with the requirements of local research ethics committees.

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## PEER REVIEW

Not commissioned. Externally peer reviewed.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

## PATIENT CONSENT

The authors, *Hasibi M, Rezaii J, Rasoulinejad M, and Yassin Z*, declare that:

**Table 1: Distribution of cytology findings according to sex**

	Male	Female
Granuloma	3	5
Granuloma with necrosis	2	3
Acute Inflammation	9	10
Chronic Inflammation	7	10
Acute & Chronic Inflammation	3	7
Malignancy	5	3
<b>Total</b>	<b>29</b>	<b>38</b>

**Table 2: Distribution of cytology findings according to nationality**

	Iranian	Afghan
Granuloma	3	5
Granuloma with necrosis	2	3
Acute Inflammation	15	4
Chronic Inflammation	14	3
Acute & Chronic Inflammation	8	2
Malignancy	8	0
<b>Total</b>	<b>50</b>	<b>17</b>

**Table 3: Distribution of variables among tuberculous patients with positive results of FNAC**

Variable		Cases (n)	Percentage
Mean age (year)		13	34.7 (year)
Sex	Male	5	38.5 %
	Female	8	61.5 %
Nationality	Iranian	5	38.5 %
	Afghan	8	61.5 %
Lymphadenopathy	Uni-lateral	10	76.9 %
	Bi-lateral	3	23.1 %
PPD	+	12	92.3 %
	-	1	7.7 %
Mean duration of lymphadenitis 291 (days)			