



# Tuberculous cervical lymphadenitis: A retrospective cohort study of 632 cases

Poras Chaudhary<sup>1\*</sup>; Bindiya Chaudhary<sup>2</sup>; Amrit kumar gupta<sup>3</sup>; Pute u losu<sup>3</sup>; Romesh Lal<sup>4</sup>

<sup>1</sup>Associate Professor, Department of Surgery, Lady Hardinge Medical College and Associated Dr Ram Manohar Lohia, New Delhi, India

<sup>2</sup>Specialist Dental Surgeon, Sri Sai Dental Care Centre, Khanpur, New Delhi

<sup>3</sup>postgraduate student, Lady Hardinge Medical College and Associated Dr Ram Manohar Lohia, New Delhi, India

<sup>4</sup>Professor of Surgery, Dept of Surgery, Lady Hardinge Medical College and associated Smt. S.K.Hospital & Dr. R.M.L.Hospital, New Delhi

## \*Corresponding Author(s): Poras Chaudhary

Associate Professor, lady Hardinge medical college and associated Dr Ram Manohar Lohia hospital, New Delhi, India

Email: drporaschaudhary@yahoo.com

## Abstract

**Introduction:** With 20% cases, India accounts for the highest tuberculosis burden in the world. Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis in India. Aim of this study is to present our experience on tuberculous cervical lymphadenitis.

**Method:** 32 patients who received standard antituberculous treatment with or without surgical treatment with the diagnosis of tuberculous cervical lymphadenopathy between January 2001 and December 2018 were reviewed retrospectively. Patients with presence of active tuberculous lesion at other sites in association with tuberculous cervical lymphadenopathy, and patients with HIV were excluded. Descriptive statistics were used to summarize the data.

**Results:** Majority of patients presented with periadenitis (198) collar stud abscess (178). Diagnosis could be achieved with fine needle aspiration cytology in 483, excision biopsy was done in 81, and polymerase chain reaction in only 3 cases to achieve correct diagnosis. Sinus failed to heal in 33 patients with antituberculous treatment.

**Conclusion:** No single test gives definite diagnosis. Excision biopsy is reserved for those where FNAC is inconclusive as it is more cost effective than polymerase chain reaction, and excision and primary closure of sinus track gives better cosmetic results.

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**Keywords:** Tuberculous cervical lymphadenitis; A cohort of 632 cases; Standard anti-tuberculous therapy



## Introduction

Tuberculosis is a disease of great public health importance in India. With 20% cases, India accounts for the highest TB burden in the world [1]. While *Mycobacterium tuberculosis* most commonly afflicts the lungs, it also affects lymphoid tissue in the form of lymphadenitis. Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis in India, usually occurring in the cervical region. Source of infection for tuberculosis is a sputum positive (open) case of pulmonary tuberculosis. Mode of infection is direct inhalation of aerosolised bacilli containing droplet nuclei [1]. The cervical lymph nodes are predominantly affected.

*M. tuberculosis* is the most common cause in areas where TB is endemic and bovine TB is well controlled while in developed countries with low rates of TB transmission, non-tuberculous mycobacteria (NTM) are mainly responsible [2]. Tuberculosis affects all ages. Factors that predispose to tuberculosis are: genetic susceptibility, age, immune-competence, stress, nutrition, coexisting illness, poor quality of life, poor housing, overcrowding, undernutrition [1,3].

Tuberculous lymphadenopathy patients usually present with painless lymph node enlargement in early stages and with an abscess or a sinus in late stages and it is easy to diagnose, prevent complications like collar stud abscess and sinus formation and cure tuberculosis. Aim of this study is to present our 15 year experience on tuberculous cervical lymphadenitis.

## Materials and methods

Record of total number of 632 patients who received standard anti-tuberculous treatment with or without surgical treatment with the diagnosis of tuberculous cervical lymphadenopathy in surgical unit 6 at Dr Ram Manohar Lohia hospital, New Delhi between January 2001 and December 2018 were reviewed retrospectively. The data were collected from out-patient department record and DOTS (directly observed treatment, short course) centre at Dr Ram Manohar Lohia hospital. Patients with presence of active tuberculous lesion at other sites in association with tuberculous cervical lymphadenopathy, and patients with HIV were excluded.

Fine needle aspiration cytology (FNAC), culture from discharging sinus, X-ray chest PA view, ultrasonography, haemogram with ESR, Liver and renal function tests, tuberculin test, sputum for acid fast bacilli, excisional lymph node biopsy, polymerase chain reaction which had been performed were evaluated. The clinical examination findings, family history of tuberculosis and parameters including age, gender, diagnostic procedures like FNAC, lymph node excisional biopsy, surgical treatment received in the form of antigravity aspiration, incision and drainage, lymph node excision, exploration and excision of sinus, treatment morbidity and mortality were also evaluated. The protocol was approved by the ethical review board of the institute.

**Statistical analysis:** Descriptive statistics were used to summarize the data.

## Results

There were 341 male and 291 female patients. Their mean age was 26 (range, 14-71) years. Constitutional symptoms suggestive of tuberculosis were present only in 38 patients (table 1). Majority of patients presented with periadenitis (198) collar stud abscess (178). Chest X-ray was done in all the patients and did not reveal any active focus. Tuberculin test was done on all the patients but this test has a little value as a case finding tool as the diagnostic value of this test is invalidated. Polymerase chain reaction (PCR) from FNAC specimen was done in only 3 patients for achieving correct diagnosis. Out of these 96 patients with sinus, in 45 patients, sinus healed completely within 6 weeks of initiation of AKT, and in 18 patients, sinus healed in 14 weeks while in rest of the 33 patients, sinus failed to heal even after 6 months of therapy. In these patients, sinus was then explored and the entire cavity was debrided. Following this procedure, sinus healed in another 14 patients. Nineteen patients were subjected to microbiological culture to rule out non-tuberculous mycobacteria (NTM) as the causative agent as an etiological factor in association with mycobacterial tuberculosis and NTM was not seen in any of the case (table 2). There was no treatment failure and no death (table 3).

**Table 1:** Patient characteristics, ®constitutional symptoms- decreased appetite, fever, fatigue, and night sweats, ∞past history of pulmonary tuberculosis- diagnosed case for which patient took standard anti-tuberculous treatment and got cured.

Patient Characteristics	Number of patients (n=632)	Percent
Age	Range 14-71, mean-26	
Sex	M=341 F=291	53.95 46.05
Socioeconomic status	Low=573 Lower middle=45 Upper middle=14	90.66 7.12 2.22
Family history of tuberculosis	423	66.93
Comorbidity	86	13.60
Presence of constitutional symptoms®	38	6.02
Past history of pulmonary TB∞	102	16.14

**Table 2:** Clinical characteristics, <sup>®</sup>size- transverse diameter of largest lymph node mass, <sup>∞</sup>data presented as mean, <sup>©</sup>data presented as range, No: Number; ATT: Antituberculous Treatment; Hb: Haemoglobin; ESR: Erythrocytic Sedimentation Rate; TLC: Total leukocyte Count, FNAC: Fine Needle Aspiration Cytology; US: Ultrasonography; PCR: Polymerase Chain Reaction; I&D: Incision and Drainage

Clinical Characteristics	No. of patients	Percent
Duration of symptoms before seeking medical advice (days)	34 (range 22-106 days)	
Presence of		
Unilateral lymphadenopathy	496	78.48
Single	477	
multiple		
Bilateral lymphadenopathy	136	21.52
Size <sup>®</sup> of lymph node (at presentation) <sup>∞</sup>		
<3cm	46	
>3cm	586	
Size of lymph node (at 4 weeks of ATT) <sup>∞</sup>		
<3 cm	290	
>3 cm	342	
Involvement of		
Anterior group	603	95.42
Posterior group	29	4.58
Stage at presentation		
Adenitis	48	7.6
Periadenitis	198	31.33
Caseation	112	17.73
Collar stud abscess	178	28.17
Sinus formation	96	15.19
Haematological and biochemical parameters (at initiation of ATT) <sup>©</sup>		
Hb (mg%)	8.2-13.6	
TLC (/cu.mm)	5300-10600	
ESR	58-92	
Serum bilirubin	1-1.5	
SGPT	20-64	
Diagnostic modality		
FNAC	483	76.43
Repeat FNAC (under US guidance)	19	3.00
Mycobacterial culture	33	5.22
Excision biopsy	81	12.82
PCR	03	0.48
Culture from discharging sinus	13	2.06
Cytology from discharging sinus	00	0.00
Identification of atypical mycobacteria	00	0.00
Surgical Treatment		

Antigravity aspiration	178	28.16
Incision and drainage	24	3.80
Secondary closure after I&D	24	3.80
Sinus exploration and excision	33	5.22
Morbidity		
Repeated antigravity aspiration	178	28.16
Delayed wound healing after I & D	14	2.22
Delayed wound healing after excisional lymph node biopsy	16	2.53
Drug induced side effects	12	1.90
No. of patients requiring admission	00	

**Table 3:** Treatment group and response to antituberculous therapy

Treatment group	No. of patients	Percent
Default	54	8.54
Default managed with first line therapy	41	6.49
Default managed with second line therapy	13	2.06
Treatment failure	00	0.00
Complete cure		
AKT for 6 months	556	87.97
AKT for 9 months	76	12.03

**Table 4:** showing treatment categories and sputum examination schedule for extrapulmonary tuberculosis in DOTS chemotherapy in India.

Category of treatment	Type of patient	Regimen®	Pre-treatment sputum	Test at month	IF result is	Then
Category III	New extra-pulmonary, not seriously ill	2 (HRZ) 3	-	2	-	Start continuation phase, test sputum again at 6 months
		4 (HR) 3			+	Re-register the patient and begin category II treatment
Category I	Seriously ill extra-pulmonary	2 (HRZE)3	-	2	-	Start continuation phase, test sputum again at 6 months
		4 (HR) 4			+	Continue intensive phase for one more month, test sputum again at 3, 4 and 7 months

® The number before the letter refers to the number of months of treatment and after the letters refers to the number of doses per week

### Discussion

Tuberculosis is still a matter of great concern in many developing countries including India. In India, this disease affects both low as well as high socioeconomic group, although much more common in low socioeconomic strata. Tuberculous lymphadenopathy is the most common form of extrapulmonary tuberculosis in India. As a clinician, we have observed that most of the patients, both belonging to low as well as high socioeconomic group, of pulmonary TB takes his disease very seriously for two reasons- awareness and a social stigma attached to it. But people in low socioeconomic group do not give serious consideration to any form of extrapulmonary TB, especially tuberculous lymphadenopathy. To increase awareness about tuberculosis, various programmes are in operation in India like National tuberculosis programme which is in operation since 1962. The government of India, WHO and World Bank together reviewed and revised

this programme in the year 1992 [1]. WHO launched the new STOP TB strategy programme in the year 2006.

FNAC, as reported in many studies is the most effective, easy and non-invasive method of confirming diagnosis in tuberculous lymphadenitis [4-6]. In our institute, FNAC was done from all the unilateral or bilateral multiple enlarged lymph nodes to confirm tuberculosis as etiological factor. Out of 632 patients, definitive diagnosis could be made with FNAC in 483 patients. Repeat FNAC was done in rest of the cases under USG guidance and aspirate was also sent for mycobacterial culture, which was helpful in 19 cases, while CT scan was not done in any of the case. Though negative results do not exclude diagnosis of tuberculosis if there is strong clinical suspicion and AKT can be started but confirmation of tuberculosis is important for registration

and initiation of AKT in DOTS centres in India. So, PCR from the FNAC specimen was sent in 3 patients in whom diagnosis could not be achieved with other methods and it confirmed diagnosis. So, it can be recommended that ultrasonography can be done when in doubt about diagnosis as it can directly give clue towards diagnosis with findings like presence of hypoechoic lesion showing necrosis in all tuberculous lesions and presence of other findings like sharp margins, abnormal surrounding tissue, matting and posterior enhancement and also by assisting in guiding the site for FNAC specimen [7]. CT scan is almost never required for diagnosis, so, should not be a part of diagnostic work-up. Gupta et al [7] has concluded in his study that CT helps in better anatomical localization of lymph nodes not usually detected on clinical examination i.e., for screening purpose. Ueda et al [8] has also recommended role CT scan for diagnosis of tuberculous lymphadenitis. Aljafari et al [4] in his study compared FNAC, microbiological methods and PCR in diagnosing tuberculous lymphadenitis and concluded that FNAC has a high false positive rate (38%) and PCR proved to be the most valuable and a diagnostic success of 100% was achieved when FNAC and PCR were combined. Baeket al<sup>9</sup> has recommended PCR for diagnosing tuberculous lymphadenitis. PCR is costly investigation and is not available in most of the government institutes in India, so, in our setting PCR is not cost-effective but it reduces the necessity for excisional biopsy and PCR was done in only 3 patients for achieving correct diagnosis. In rest of the cases, definite diagnosis was achieved with other cost-effective methods. Based on these findings, it can be recommended that in presence of strong clinical suspicion, PCR should be done only in cases where other modalities fail to diagnose tuberculosis.

Excisional lymph node biopsy was required in 84 patients. Though the best way of diagnosing tuberculosis is direct histopathological proof by taking excisional biopsy but it is not done routinely because of treatment remains same and cosmetically a scar can also be avoided. For pulmonary tuberculosis, it is easy to document complete cure. For tuberculous lymphadenopathy, negative histopathology is the best and the only way to document complete cure in tuberculous lymphadenitis after full course of AKT, but it is not done in our institute for this purpose.

It is not uncommon to present for the first time with a tuberculous sinus which is a late feature in natural history of disease. Out of 96 patients who presented with sinus, bacteriological culture was positive in 13 cases (13.5%). Out of these 96 patients, in 45 patients, sinus healed completely within 6 weeks of initiation of AKT, and in 18 patients, sinus healed in 14 weeks while in rest of the 33 patients, sinus failed to heal even after 6 months of therapy. In these patients, sinus was then explored and the entire cavity was debrided. Following this procedure, sinus healed in another 14 patients while 19 patients were then subjected to microbiological culture to rule out NTM as the causative agent as an etiological factor in association with mycobacterial tuberculosis. NTM was not seen in any of the case. These patients were then put on second line therapy for 6 months which resulted in healing of sinus.

For drainage of abscess, repeated antigravity aspiration was done in 178 patients and 24 patients ultimately needed incision and drainage with debridement of the cavity and in all of these patients the wound was secondarily closed after 7 days which gave a better cosmetic result in these patients. In 3 patients, sinus was formed after secondary closure which healed spontaneously after 3 to 4 weeks. So, it can be concluded that

it is better to close the wound after 5-7 days rather than allow it to heal by secondary intention to achieve better cosmetic results. Lymph node size decreased in majority of cases with AKT but in 44 patients lymph node size did not show any significant decrease in size. Persistence of enlarged nodes even after successful therapy represents an immune reaction. In these patients lymphadenectomy was done for cosmetic reason as well for microbiological and pathological confirmation of complete cure. In such cases, culture should always be done and if it is negative, excision of lymph node is indicated only for cosmetic purpose.

The principles of treatment for tuberculous lymphadenopathy are the same as for pulmonary tuberculosis. It has also been demonstrated that TB lymphadenitis can be treated with short-course chemotherapy [10,11]. Convincingly good results have been achieved with standard antituberculous treatment. Tuberculous lymphadenitis is included in category III. Standard AKT was given for 6 months in all the cases. Treatment categories and sputum examination schedule for extrapulmonary tuberculosis in DOTS chemotherapy in India is given in table 4. Extrapulmonary, not seriously ill patients are included in category III and seriously ill extrapulmonary patients are included in category I of treatment schedule. In DOTS, during the intensive phase of treatment a health worker watches as the patient swallows the drug in his presence. During continuation phase the patient is issued medicine in a combipack only for one week and this pack is checked when the patient comes to collect medicine for next week. Liver function tests were done before initiation of AKT and then 4 weekly till the completion of therapy. Surgical treatment for the local lesion was given as and when indicated. All the patients responded well to short course chemotherapy. There was no treatment failure. Only few patients needed to restart first line therapy and some needed second line therapy to which they all responded. Counselling also played an important role in these patients.

NTM results in lymphadenitis relatively more resistant to chemotherapy. We did not come across any case of NTM lymphadenitis in past 13 years. Drugs like newer macrolides, ethambutol, rifampicin have shown some efficacy but in most of the cases of NTM, surgical excision is required [12].

## Conclusion

No single test gives definite diagnosis. Excision biopsy is reserved for those where FNAC is inconclusive as it is more cost effective than polymerase chain reaction. Short course standard antituberculous treatment (DOTS chemotherapy in India) has convincingly shown good results and surgical treatment is often required if the patient presents late and surgery should be done in cases of sinus formation to achieve better cosmetic results.

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