

Directly observed treatment short course in immunocompetent patients of tuberculous cervical lymphadenopathy treated in revised national tuberculosis control programme

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ABSTRACT

Background: Prospective observation analysis to evaluate the cure in tuberculous cervical lymphadenopathy with directly observed treatment short course category III (DOTS CAT III) treatment as per revised national tuberculosis control program (RNTCP) at a tertiary care hospital in AP, India, from October 2007 to September 2009. These cases were followed up for period of 22 months. **Materials and Methods:** Total 1521 tuberculous cases were screened in KIMS both pulmonary and extra pulmonary cases out of which 146 cases were tuberculous lymphadenitis. Fifty cases of tuberculous cervical lymphadenopathy were included after diagnostic and treatment algorithm and fine needle biopsy or excision biopsy. Patients below 5 yrs, immunocompromised, having diabetes mellitus, pulmonary tuberculosis and with other co-morbid conditions were excluded from the study. All patients were put on DOTS CAT III as per RNTCP guidelines. Follow-up was done every 2 months till 6 months for 1) Constitution symptoms 2) Weight gain or loss 3) Appetite gain or loss 4) Regression of lymph nodes or increase 5) Compliance 6) Side effects 7) Failures by demonstration of organism by direct smear, culture or histopathological examination. **Results:** In this study, lymph node regression was found in 78% at the end of 2 months, 94% at the end of 4 months and 96% at the end of 6 months, 9 patients had regression in size though the nodes were palpable, 2 had no regression but fresh lymph nodes appeared on the same side and sinus discharge was present, culture was negative in these cases. Two cases had immune reconstitution syndrome, constitutional symptoms disappeared and showed clinical improvement. Four cases were subjected for surgical intervention. **Conclusion:** DOTS CAT III is effective in the treatment of tuberculous cervical lymphadenopathy. Compliance was good with minimal, minor side effects, only two had immune reconstitution syndrome and two had sinus formation; they were referred for surgical intervention, and follow-up of 22 months did not show any relapses.

KEY WORDS: Biopsy, cervical lymphadenopathy, DOTS, immune reconstitution syndrome, tuberculosis

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INTRODUCTION

Tuberculosis Control Programme was operating since 1962 but World Health Organization (WHO) has declared global

emergency for tuberculosis in 1993 and directly observed short course treatment (DOTS) was introduced in 1997 for all patients.^[1]

Tuberculous lymphadenitis without HIV and diabetes mellitus is considered as pauci bacillary and non-serious form of illness, hence WHO, IUATLD has recommended DOTS CATIII treatment with Rifampicin, Isoniazid, and Pyrazinamide.^[2] Only in complicated cases Ethambutol is added to the regimen.

At present, there are only few studies about the efficacy and cure of tubercular cervical lymphadenopathy with DOTS CAT III.^[3]

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At the end of 6 months treatment assessment was made on 1) Clinical grounds, i.e., constitutional symptoms 2) Regression of lymph node size 3) Fine needle and excision biopsy direct smear, culture and histopathological examination. Only few studies are in the literature. This study was aimed and designed to observe the efficacy of 6 months DOTS CAT III, its compliance, side effects, and cure with biopsy and culture.

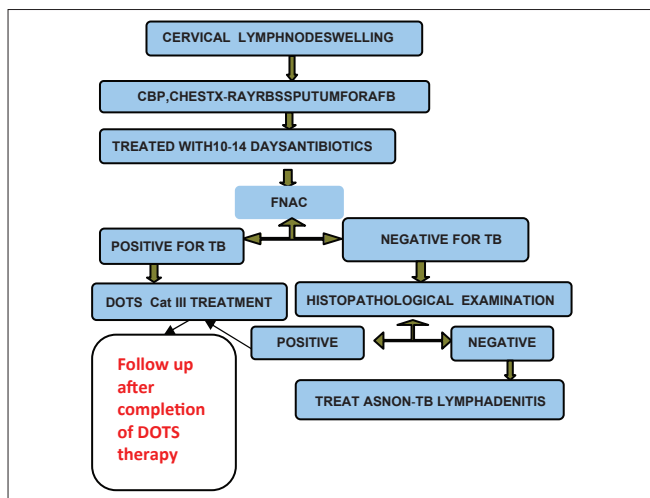
MATERIALS AND METHODS

50 cases of cervical lymphnode swellings were subjected to diagnostic algorithm as per RNTCP [Flow chart 1].

In Revised National Tuberculous Control Programme (RNTCP) DOTS CAT III was recommended as standard treatment for a period of 6 months, which included 2 months intensive phase with 1) Rifampicin, 2) Isoniazid, and 3) Pyrazinamide; only in complicated cases Ethambutol was added and 4 months of continuous phase with Rifampicin and Isoniazid. These drugs were given thrice weekly under supervision in rural health centres and the cases were followed up. Patients who have completed 6 months regular chemotherapy with 90% of the dose was declared as completed or cured only on clinical grounds.

In our present study, inclusion and exclusion criteria was based on

1. All cases which are confirmed as tuberculous cervical lymphadenitis by direct smear, culture, or histopathological examination (After diagnostic and treatment algorithm followed RNTCP guidelines).
2. All patients who had HIV, diabetes mellitus, pulmonary tuberculosis co-morbid conditions and children below 5 years were excluded from the study
3. Follow up was done during the treatment for DOTS CAT III patients at the end of 2 months, 4 months, and 6 months for; 1) constitutional symptoms a) fever present or absent b) appetite gain or loss c) weight



Flow chart 1: Algorithm for the treatment of tuberculous cervical adenitis

- gain or loss; 2) regression of lymph nodes size; 3) compliance; and 4) side effects; 5) therapeutic failure by the demonstration of organism either by direct smear, culture, or histopathological examination by fine needle aspiration biopsy or excision biopsy.
4. After the end of 6 months DOTS therapy treatment, follow-up was done for 22 months period, and no relapses were reported in our study of 50 cases.

RESULTS

50 cases of cervical lymphadenitis were confirmed tuberculosis by fine needle aspiration biopsy or excision biopsy after diagnostic algorithm and cases were followed up. Majority (36%) of the patients were in the age group of 5-14 yrs, followed by 22% of the patients who were in the age group of 15-24yrs [Figure 1]. 44% of the patients were males and 56% were females; Study showed slight female predominance with 1:1.27 ratio [Figure 2]. 74% of the patients had multiple swellings, and 36% of patients had single swelling [Figure 3]. Only 26% of the patients had matting of the lymph nodes, whereas 74% had discrete lymph nodes [Figure 4]. 19 patients (38%) lymph nodes on the right side of the neck are involved, 18 patients (36%) lymph nodes on the left side of the neck were involved and in 13 patients (26%) bilateral involvement was seen [Figure 5]. 32% of the patients had constitutional symptoms [Figure 6]. Only 8% of the patients had sinus formation [Figure 7]. 76% of the patients were diagnosed by FNAC and 24% of the patients required excision biopsy and histopathological examination for the diagnosis [Figure 8].

Lymph node regression was found in 78% at the end of two months of treatment, in 94% at the end of 4 months and in 96% at the end of six months of treatment [Table 1].

76% of the patients reported drug reactions like nausea, vomiting at first follow-up, only 14% had drug reactions at the end of 4 months of treatment and none reported at the end of the treatment [Figure 9].

At the end of the treatment, 78% of the patients had complete regression of the lymph nodes, whereas 22% of the patients had palpable lymph nodes at the end of the treatment. In 39 patients the nodes regressed completely, while 9 patients had regression in size though the nodes were still palpable. Rest two patients had no regression or increase in size but fresh nodes appeared on the same side in one of the patients who also had discharging sinus through out the treatment [Figure 10].

Table 1: The lymphnode size at regular follow up (N=45)

Lymph node size	At first followup n (%)	At second followup n (%)	At the end of treatment n (%)
Increased	02 (04)	0	0
Decreased	39 (78)	47 (94)	48 (96)
Remained same	09 (18)	03 (06)	02 (04)

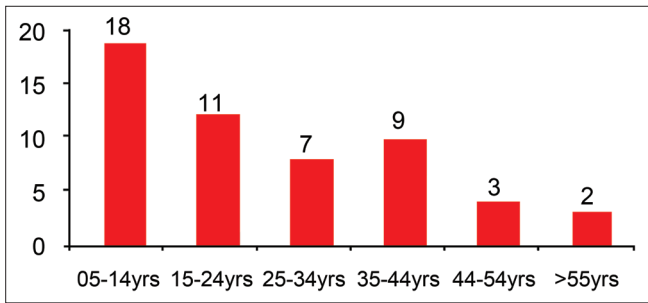


Figure 1: Age distribution of the patients, (N=50)

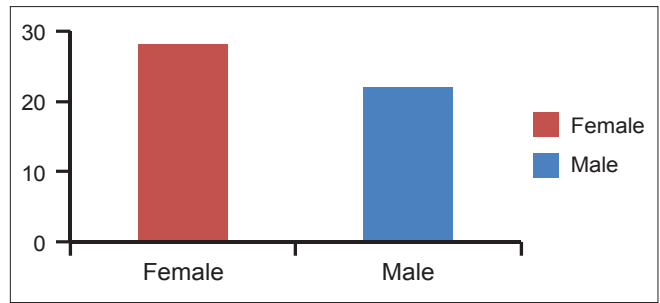


Figure 2: Gender distribution (N=50)

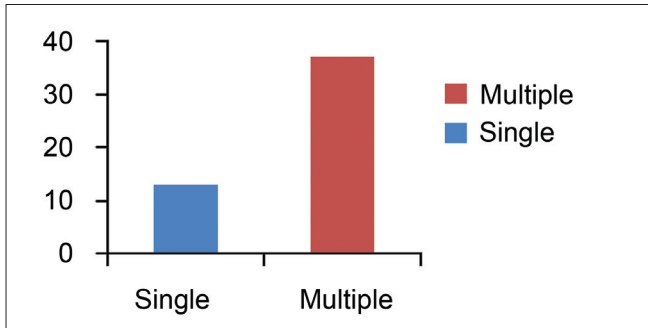


Figure 3: No. of swelling (N=50)

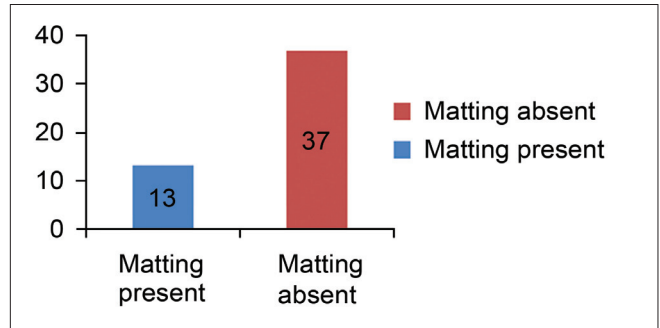


Figure 4: Distribution of matting (N=50)

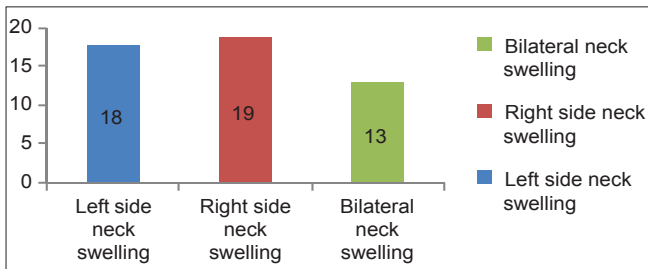


Figure 5: Anatomic distribution of swelling (N=50)

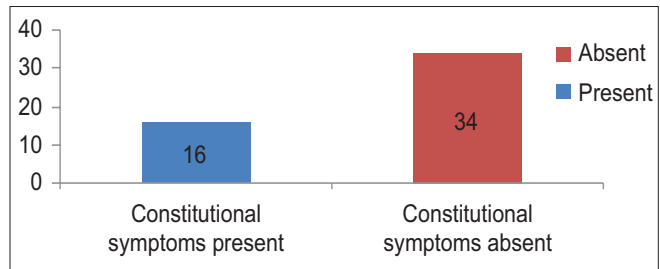


Figure 6: Distribution of constitutional symptoms (N=50)

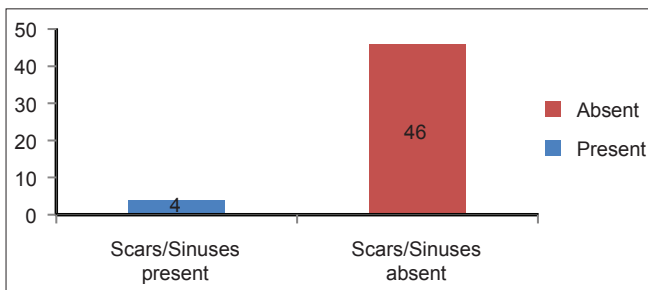


Figure 7: Distribution of scars/ sinuses (N=50)

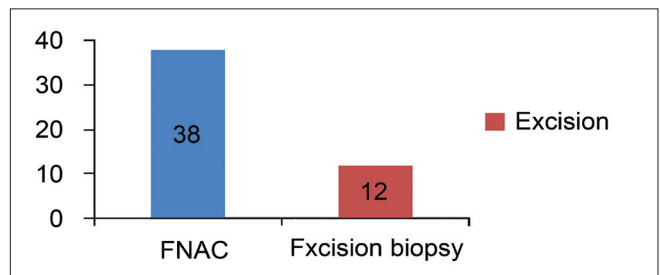


Figure 8: The method of diagnosis

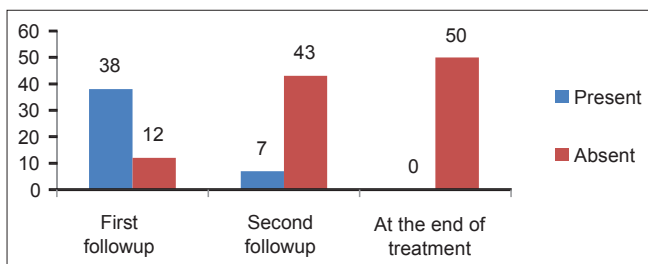


Figure 9: Distribution of drug reaction

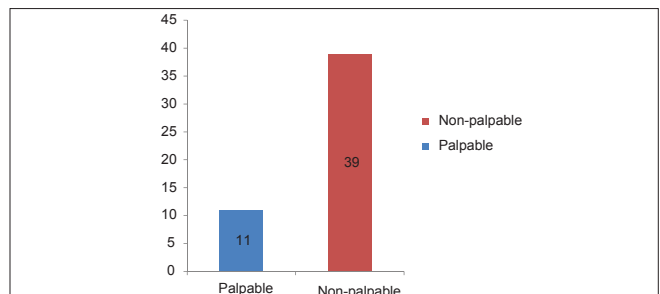


Figure 10: The lymph node status at the end of the treatment (N=50)

DISCUSSION

Mycobacterium tuberculosis infection occurs in human beings by inhalation, ingestion, and inoculation. Majority of infections occur by inhalation hence pulmonary infection is the common mode of presentation. Spread of infection occurs either by hematogenous route, lymphatics, or by contiguity. Only 10 to 20% present with extra pulmonary tuberculosis.^[4,5]

In our study group, all 50 cases were confirmed cases of tuberculous cervical adenitis, which were placed on diagnostic algorithm and FNAB or excision biopsy was done to establish the diagnosis.

As the case is not diagnosed by sputum examination but requires fine needle aspiration biopsy and excision biopsy for histopathological diagnose and even culture, which are not available in local setting (DOTS centre) often land in tertiary care centres where expert guidance of the medical college where professors are available.

Tuberculous cervical lymphadenitis can occurs in any age group but more common in 10 to 30 yrs. In our study also they were between 5-45 yrs of age (90%).^[6,7]

Lymphadenopathy is more common in female patients.^[8,9] Even in our study, female outnumbered the males with 56% to 44% with a ratio of 1:1.27, which can be compared to the study results of Jha *et al.*^[7]

Constitutional symptoms were present in only in about 16 cases (32%) while in other studies these are reported to vary from 33 to 85%.^[10-12]

In the present study single lymph node was present in 13 cases (26%) and 37 cases (74%) had multiple swellings in the neck, 18 cases (36%) were on the left, 19 cases (38%) were on the right side and 13 cases (26%) were on both sides of the neck, matting was present in 13 cases (26%), scarring was seen in 4 cases (8%) and 46 cases (92%) no scarring, only 4 cases (8%) of them had sinus formation.

Diagnosis could be established by either FNAC in 38 (76%) of the cases or excision biopsy in 12 (24%) of the cases. Patients were put on treatment with DOTS. Lymph node regression was complete in 96% of the cases, 78% at the end of 2 months, 94% at the end of 4 months and 96% at the end of 6 months.

At the end of the treatment, 39 cases (78%) had lymph nodes that were not palpable and 11 (22%) cases had palpable nodes though regressed in 9 cases. Rest two had no regression, infact fresh new nodes appeared on the same side. These nodes were aspirated and direct smear and culture was done (no bacilli could be grown) culture was negative. These patients had probable immune

reconstitution syndrome responded partially to steroid therapy but referred to surgeon for further management. A study from Jain *et al.* had referred 8 cases to surgical intervention.^[13]

Adverse reactions were seen in 38 (76%) cases and were absent in 12 (24%) cases. Nausea and vomiting were present. No serious side effects like hepatotoxicity, renal toxicity were noticed at the end of treatment. Defaulter rate was nil (0%) in our study, while Jain *et al.* reported it to be 3.36%.^[13] Compliance was good but it is only small number to comment.

In our study success rate at the end of DOTS CAT III treatment in tuberculous lymphadenopathy was 96%, whereas the study from Jain *et al.* reported 71.86%^[13] and other study from Ajmer reported 63%.^[3]

After the end of 6 months DOTS therapy treatment, the cases were followed up for 22 months; out of 50 cases there were no relapse cases were reported in our study, whereas a study from van Loenhout-Rooyackers *et al.* reported the relapse rate as 3.3% out of 422 cases;^[14] they used daily regimen instead of DOTS therapy.

DOTS CAT III was safe and effective chemotherapy in the treatment of tuberculous cervical lymphadenitis. Compliance was good with minimal, minor side effects. Two cases developed immune reconstitution syndrome, and for follow up of 22 months after DOTS treatment no relapses were reported. Large multi-centric study is required to support the community based management.

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