

Study of Cases of Multi-Drug Resistant Tuberculosis in Cervical Tuberculous Lymphadenitis

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Abstract

Introduction: Lymph nodes are organs which are present in regions of neck, chest, abdomen, and groin. Neck consists of 300 lymph nodes nearly 2/3rd of overall lymph nodes that are there in body. Lymphadenopathy is course of disease and this course involves lymph nodes that are anomalous in uniformity and dimension. Lymphadenitis relates to lymphadenopathies which are caused because of inflammatory pathology. Among the different infective and inflammatory conditions of cervical lymphadenopathy, the commonest cause is tuberculous lymphadenitis. It is a commonest form of extra-pulmonary tuberculosis since tuberculosis is chief health-related problem because of social and economic issues. Tuberculosis is a disease of great antiquity and has even been found in Egyptian mummies. Multidrug-resistant tuberculosis (MDR-TB) is tuberculosis due to organisms which show resistance to both isoniazid and rifampicin, with or without resistance to other anti-TB drugs.

Objective: To determine incidence of Drug resistant Tuberculosis in cervical tuberculous lymphadenitis and to determine response of treatment of Drug resistant Tuberculosis.

Materials and Methods: It is an observational, prospective hospital based study in 52 patients carried out at Sheth L.G Hospital in Ahmadabad in 2 years span. Proper history and clinical evaluation were done. According to the new NTEP guidelines, the pus of each of these patients included in the study were sent for CBNAAT in falcon tube. The expert MTB/RIF technique was performed in the machine kept at Microbiology Department of Narendra Modi Medical College. Results regarding sensitivity of bacilli against rifampicin are produced using this technique within 2 hours. Results thus obtained, were analysed.

Results: There were 52 cases of cervical tuberculous lymphadenopathy in which 14 cases were of drug-resistant tuberculosis. In the present study of gene Xpert, Rifampicin sensitive Tuberculosis which includes Drug sensitive tuberculosis was detected in 73.15% while Rifampicin resistance in 26.9%. Out of 14 cases of drug resistant tuberculosis, 85.71% cases showed treatment success, 7.14% cases were defaulters, 7.14% were lost to follow up.

Conclusion: The emergence of MDR-TB has been attributed to factors such as nonadherence to treatment, inappropriate treatment regimens, drug malabsorption, poor drug quality, lack of health

education, delay in initiation of treatment, resistance to additional drugs and a poor health infrastructure for effective delivery of treatment.

Keywords: Cervical Lymph node, Extra pulmonary tuberculosis, USG, FNAC, Histopathology

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Introduction

Lymph nodes are organs which are present in regions of neck, chest, abdomen, and groin. Neck consists of 300 lymph nodes nearly 2/3rd of overall lymph nodes that are there in body [1].

Lymphadenopathy is course of disease and this course involves lymph nodes that are anomalous in uniformity and dimension. Lymphadenitis relates to lymphadenopathies which are caused because of inflammatory pathology [1].

Cervical lymphadenopathy is most commonly localized to inflammatory processes in the neck and nearby areas. Among the different infective and inflammatory conditions of cervical lymphadenopathy, the commonest cause is tuberculous lymphadenitis. It is a commonest form of extra-pulmonary tuberculosis since tuberculosis is chief health-related problem because of social and economic issues [2]. In India, about 15 to 20% of Extra pulmonary tuberculosis occurs in immune-competent patients and 50% of cases were reported in HIV-positive individuals. Among them lymph node TB (35%), genitourinary TB (9%), cerebrospinal, abdominal, skin, etc. accounts for 26% cases [3].

Tuberculosis is a disease of great antiquity and has even been found in Egyptian mummies. Estimates suggest that worldwide 10 million people develop tuberculosis annually [4].

Multidrug-resistant tuberculosis (MDR-TB) is tuberculosis due to organisms which show resistance to both isoniazid and rifampicin, with or without resistance to other anti-TB drugs. With an estimated 4,80,000 new cases

developing every year multidrug-resistant tuberculosis is one of the greatest public health challenges worldwide. Multidrug-resistant tuberculosis is much more common in patients who have previously been treated for tuberculosis [5]. Newly diagnosed are also at risk due to either spontaneous mutations or transmission of drug-resistant strains. The risk of transmission of resistant strains from close contacts is increasing day-by-day because of the growing burden of MDR-TB patients. WHO estimates that there were 6,00,000 new cases with resistance to rifampicin – the most effective first-line drug, of which 4,80,000 had MDR-TB [6].

Aim & objective

1. To determine incidence of Drug resistant Tuberculosis in cervical tuberculous lymphadenitis at L.G Hospital, Narendra Modi Medical College.
2. To determine response of treatment of Drug resistant Tuberculosis.

Material and methods

1. **Study Design:** Prospective Observational Study
2. **Sample size:** 52
3. **Study Area:** Sheth L.G Hospital and Narendra Modi Medical College, Maninagar, Ahmedabad.
4. **Study Subjects:** All patients who were diagnosed for cervical tuberculosis in otorhinolaryngology department and who were on anti-tuberculosis treatment at NTEP DOTS Centre in L.G Hospital, Maninagar or to referral centre as prescribed by DOTS centre at L.G hospital.

Inclusion criteria

1. All the case of Tuberculosis of cervical lymphadenitis diagnosed and treated at L.G Hospital, Narendra Modi Medical College.

Exclusion criteria

2. Patient not willing to participate in study.
3. Patient with lymphadenopathy other than Tuberculosis cervical lymph node.

It is an observational, prospective hospital-based study in 52 patients carried out at Sheth L.G Hospital in Ahmadabad in 2 years span. Proper history and clinical evaluation were done. According to the new NTEP guidelines, the pus of each of these patients

included in the study were sent for CBNAAT in falcon tube. The expert MTB/RIF technique was performed in the machine kept at Microbiology Department of Narendra Modi Medical College. Results regarding sensitivity of bacilli against rifampicin are produced using this technique within 2 hours. Results thus obtained, were analysed.

Results

Out of 150 cases of cervical lymphadenopathy admitted in otorhinolaryngology department at Sheth L.G hospital, Maninagar, Ahmedabad, there were 52 cases of cervical tuberculous lymphadenopathy in which 14 cases were of drug-resistant tuberculosis.

Table 1: Etiology Of Cervical Lymphadenopathy

Etiology	Present study (n=150)		Gautam Biswas <i>et al</i> study (2012) [7] (n=423)	
	No	%	No	%
Tuberculous lymphadenitis	52	34.66%	192	49.5%
Secondary metastasis	5	3.33%	90	21.28%
Reactive hyperplasia	30	20%	42	9.92%
Lymphoma	4	2.6%	30	7.09%
Chronic granuloma	19	12.66%	15	3.54%
Non-specific lymphadenitis	20	13.33%	24	12%
Reactive lymphadenitis with Abscess	20	13.33%	42	9.92%
Total	150	100%	423	100%

In the present study of 150 cases, most common cause for cervical lymphadenopathy was tuberculous lymphadenitis (34.66%). In Gautam Biswas *et al.* [7] study most common cause for cervical lymphadenopathy was tuberculous lymphadenitis (49.5%) which was similar to our study. Most common site of lymph node involvement was neck and tuberculosis were the most common infectious cause for lymphadenitis.

In our study most affected age group of cervical tuberculous lymphadenopathy is 21 to 30 years (44%). In Wilson's series [8] of 100 cases the common age group of patients were in the 2nd and 3rd decade. In S.P. Pamra

series [9] of 322 cases the commonest age group affected were 2nd and 3rd decades with 25% and 35%.

The incidence of cervical tuberculous lymphadenopathy was more in females. In the study of sex incidence, Males 36.5%, and Females 63.4%. The incidence was more in male than our study in, S.K. Sen's series [10] 58.6% and S.D. Pamra series [9] 57.08%. The increased incidence in females may be because of the wide prevalence of malnourishment. Lack of education, early marriage, pregnancy, large families, and poor socioeconomic conditions [11].

In the present study 57.7% of the patients belonged to low socio-economic group, 36.5% belonged to the middle socio-economic group. Only 5.8% of patients belonged to the higher socio-economic group. In Dr. Gannansekhar series [8] (2006) disparate to our study most common 46% patients belonged to middle socio-economic group and 44% belonged to the middle socio-economic group. Only 10% were of the higher socio-economic group.

In this study, there was no definite history of contact with tuberculosis in 80.8% of cases.

A definite history was obtained in only in 19.2% of cases. In Dr. Gannansekhar series [8] (2006) of tuberculous cervical lymphadenopathy of 50 cases (82%) had no history of contact with tuberculosis, 80% had definite history of contact with tuberculosis.

Majority of present study patients reported level 4 of cervical lymph node i.e., in 46%. followed by level 5 lymph node i.e., in 15.34%. In Dr. Gannansekhar series [8], commonly level 4 of cervical lymph node in 40%, followed by level 3 and level 4 in 28%.

Table 2: Presenting Symptoms Of Study Series

Symptoms	Present study (n=52)		Dr. Gannansekhar <i>et al</i> (2006) [8] (n=50)	
	No	%	No	%
Swelling in neck	52	100%	50	100%
Fever	14	26.9%	15	30%
Local site pain	07	13.5%	03	6%
Sore throat	01	1.9%	01	2%
Cough	05	9.5%	01	2%
Loss of appetite	25	48.07%	20	40%
Loss of weight	30	57.7%	20	40%
Inguinal swelling	02	3.8%	05	10%
Axillary swelling	02	3.8%	05	10%
Old sinus scars	03	5.8%	01	2%

In the present study, most common presenting complains were swelling in neck (100%) associated with fever (26.9%), loss of appetite (48.07%). Loss of weight (57.7%). Similar to our study in Dr. Gannansekhar [8] series (2006), the most common symptoms were swelling in neck (100%) associated with fever (30%). Loss of appetite (40%), loss of weight (40%).

In the present study the incidence of active tuberculosis was 9.6% in chest radiography finding. The highest incidence was found in Dr. Gannansekhar's series [8] (16%).

Table 3: Distribution of Lesions on Ultrasonography

Ultrasonography	Present study (n=52)		Dr. Maya <i>et al</i> (2019) [2] (n=61)	
	No	%	No	%
Cervical lymphadenopathy with tubercular aetiology	4	7.7%	45	73.77%
Cervical lymphadenopathy with abscess	11	21.15%	2	3.3%
Tuberculous/Koch's Abscess	29	55.76%	3	4.9%
Necrotic cervical lymphadenopathy	8	15.38%	6	9.8%

In the present study of Ultrasonography, most of the patients reported with Koch's Abscess i.e., in 55.8% of the patients followed by cervical lymphadenopathy with abscess in 11 cases (21.15%). In Dr.Maya [2] series, a majority of patient reported with cervical lymphadenopathy i.e., in 63.9% followed by necrotic cervical lymphadenopathy 9.8%.

Table 4: Distribution of Lesions on FNAC (Fine Needle Aspiration Cytology)

FNAC	Present study (n=52)		Subash Khadka <i>et al</i> (2015) [11] (n=52)	
	No	%	No	%
Chronic Granulomatous lymphadenitis	1	1.9%	10	19.23%
Tubercular lymphadenitis	6	11.5%	30	57.69%
Acute inflammatory lesion	5	9.6%	1	1.9%
Tuberculous abscess	40	76.9%	11	21.15%

Fine needle aspiration cytology, majority of the patients reported Koch's abscess i.e., in 76.9%, followed by Tubercular lymphadenitis in 11.5%. In Subash Khadka [11] series of fine needle aspiration cytology, majority of patients reported tubercular lymphadenitis in 44.8%, followed by Koch's abscess in 16.4%.

In the study of histopathological diagnosis, majority of the patients reported with Koch's Abscess in 78.8%. In Dr.Maya [2] series, majority of patients reported tuberculous lymphadenitis in 62.3%.

The first national anti-tuberculosis drug resistance survey (NDRS) revealed that 28% of TB patients were resistant to any drugs (22% among new and 36.82% among previously treated).

Table 5: Gene Xpert

Gene Expert	Present study (n=52)	Gujarat Series <i>et al</i> (2002-07) [12] (n=1047)
Rifampicin sensitive low	33 (63.55%)	680 (65%)
Rifampicin sensitive medium	5 (9.6%)	187 (17.86%)
Rifampicin resistance	14 (26.9%)	180 (17.2%)

In the present study of gene Xpert, Rifampicin sensitive Tuberculosis which includes Drug sensitive tuberculosis was detected in 73.15% while Rifampicin resistance in 26.9%. Isoniazid sensitivity was not done who were already rifampicin resistant. Rifampicin resistance considered as surrogate marker of drug resistant tuberculosis as practically most of rifampicin resistant bacilli are resistant to isoniazid [13]. In Gujarat series [12], 82.86% patients found rifampicin sensitive tuberculosis while rifampicin was resistant 17.2% patients like our study.

Table 6: Treatment of Tuberculosis In Cervical Lymphadenitis

Regimen	Cases (n=52) (%)
HRZE (Isoniazid, rifampicin, pyrazinamide, ethambutol)	38 (73%)
Shorter regimen (Inj. Kanamycin, Ethionamide, moxifloxacin, clofazimine, isoniazid, rifampicin, ethambutol)	10 (19.23%)
Longer regimen (bedaquiline, clofazimine, linezolid, cycloserine, levofloxacin, pyridoxine)	2 (3.8%)
HRE with Lfx (Isoniazid, rifampicin, ethambutol, levofloxacin)	2 (3.8%)

In the treatment of tuberculosis in cervical lymphadenitis, out of 52 patients, 38 patients were put on routine anti-tuberculous chemotherapy and 14 patients were of drug resistant cervical tuberculous lymphadenopathy.

Patients who were recurrent case of cervical tuberculous lymphadenopathy had higher incidence of drug resistance (61.11%) as compared to drug resistance seen in cases presenting for first time (8.8%). Drug resistant tuberculosis is more prevalent in relapse cases [14].

In the present study treatment completion rate is 68.42% in Drug sensitive Tuberculosis. Treatment completion rate of Drug resistant tuberculosis is 12 (85.71%).

Table 7: Treatment Outcome

Treatment outcome	Drug sensitive tuberculosis	Drug resistant Tuberculosis
Relapse	9 (23.68%)	0
Defaulter	2 (5.26%)	1 (7.14%)
Failure(Lost to follow up)	1 (1.92%)	1 (7.14%)
Success	26 (68.42%)	12 (85.71%)
Total	38 (100%)	14 (100%)

In the present study of 52 cases, out of 38 cases drug sensitive cervical tuberculous lymphadenopathy, 68.42% cases showed treatment success, 23.68% cases were relapses, 5.26% were defaulters and 1.92% cases were lost follow-up. Out of 14 cases of drug-resistant tuberculosis, 85.71% cases showed treatment success, 7.14% cases were defaulters, 7.14% were lost to follow up.

Motivation to patients and psychological counselling was integral part of the treatment. Early recognition of drug-resistant tuberculosis cases with prompt treatment, diligent follow up and continuous patients' motivation led to the successful outcome of the treatment.

Discussion and Conclusion

- In our study the commonest cause of cervical lymphadenopathy was tuberculous lymphadenitis (34.66%) followed by reactive hyperplasia (20%).
- Most affected age group of cervical tuberculous lymphadenopathy was 21-30 years (44%), followed by 11-20 years (21%).

- A total of 52 patients recruited in this study with Male to Female ratio was (1:1.5).
- 57.7% of patients in this series were from low income group.
- A definite history of contact with tuberculosis was obtained in only 44.24% in this study.
- The most common complaint was unilateral neck swelling. Most common associated complain was weight loss in 57.7% of patients, followed by evening rise of temperature in 26.9% of patients.
- Level 4 was most common level of cervical lymph node involvement in tuberculosis and drug resistant tuberculosis (46%).
- Evidence of active pulmonary tuberculosis along with cervical tuberculous lymphadenopathy in chest radiography was in 9.6% cases only.
- In ultrasonography, 55.76% reported with Koch's/ tuberculous abscess.
- In fine needle aspiration cytology, most common diagnosis was Koch's abscess in 76.9% of cases followed by tuberculous

lymphadenitis in 11.5% and acute inflammatory lesions in 9.6%.

- In histo-pathological report, most common diagnosis was Koch's abscess in 78.8%, followed by tuberculous lymphadenitis in 21.2% of patients.
- Gene Xpert study shown that rifampicin sensitive tuberculosis detected in 63.55% of cases and rifampicin resistant detect in 26.9%. Anti-tuberculous treatment was started in rifampicin low and medium sensitivity patients. Drug-resistant tuberculosis treatment was started in rifampicin-resistant patients that lasted for 12-18 months.
- After the confirmation of diagnosis, out of 52 patients, 38 patients of cervical tuberculous lymphadenopathy have started anti-tuberculous chemotherapy which consist of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for 6 months. The remaining 14 patients were of Drug-resistant tuberculosis. 10 patients were put on Shorter drug regimen (Inj. Kanamycin, Ethionamide, moxifloxacin, clofazimine, isoniazid, rifampicin, ethambutol) for 9 to 11 months, 2 patients on All-over longer regimen (bedaquiline, clofazimine, linezolid, cycloserine, levofloxacin, pyridoxine) for 18 months and 2 patients with slow recovery on routine anti tuberculous drug were put on anti-tuberculous drug along with levofloxacin, Patients showed good response to chemotherapy as evidenced by regression in size of the cervical lymphnodes, improvement in appetite, increase in weight and general health of the patients.
- Patients who were recurrent cases of cervical tuberculous lymphadenopathy had higher incidence of drug resistance (61.11%) as compared to drug resistance seen in case presenting for first time (8.8%).

- Treatment success rate of Drug resistant cervical tuberculous lymphadenopathy was 85.71% and Drug sensitive tuberculous lymphadenopathy was 68.42%.

Drug-resistant tuberculosis has widespread health, social, and economic ramifications and its emergence threaten gains already made at national and global levels in TB care and control.

The incidence of drug resistant tuberculosis in cervical lymphadenitis was 14 out of total 52 patients of cervical tuberculous lymphadenopathy which was 26.9%. Treatment success rate of patients treated with drug resistant tuberculosis regimen was 23.07%.

The emergence of MDR-TB is a global problem which is threatening to destabilize the best efforts of TB control. It has been attributed to factors such as non-adherence to treatment, inappropriate treatment regimens, drug malabsorption, poor drug quality, lack of health education, delay in initiation of treatment, resistance to additional drugs and a poor health infrastructure for effective delivery of treatment. However, even if good drugs are available without a properly functioning DOTS plus programme, it may not show good results. To manage MDR-TB in poor economic settings, the WHO and its partners launched the DOT- Plus initiative to develop a global policy to provide technical assistance to DOTS programme and also to enable access to second-line drugs under rational use.

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