Evaluation of Incidence, Treatment and Clinical outcomes of Tuberculous Lymphadenitis at Dinajpur Medical College Hospital

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This study was done to evaluate the incidence, treatment and clinical outcomes of tuberculous (TB) lymphadenitis at Dinajpur Medical College Hospital, Dinajpur. For this purpose patients' records were reviewed to identify patients with confirmed diagnosis of TB lymphadenitis between January 2009 and December 2010. Of 1,548 tuberculosis cases, 109 (7.0%) patients had TB lymphadenitis. The mean age was 36.48±12.87 years. Among risk factors for TB lymphadenitis and diabetes mellitus were seen in 17 (15.6%) and 11(10.0%) patients, respectively. Cough and fever were the most frequently reported symptoms. In a majority of cases (n=90, 82.5%) positive results were obtained for fine needle aspiration (FNA). Directly observed therapy was given to all patients. Sixty-two (56.9%) patients were successfully treated, and 5(4.6%) patients died during the treatment. There was no increase in the incidence of TB lymphadenitis over the 1-year study period. The incidence was slightly higher in male than female gender. Diabetes mellitus were the most commonly reported risk factors. FNA is the most reliable diagnostic test

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Introduction

Tuberculosis, a deadly bacterial infection, can spread to other body tissues and organs through the blood stream and the lymphatic system.[1] With the global increase in the incidence of human immunodeficiency virus (HIV) there has been a steady increase in extrapulmonary tuberculosis as exemplified in the United States[2] and Bangladesh,[3] where 21% of extrapulmonary tuberculosis cases were associated with HIV infection.[3] Tuberculous (TB) lymphadenitis also known as scrofula (King's Evil)[4] was first described 3,000 years ago and is one of the common forms of extrapulmonary tuberculosis. In areas where tuberculosis is endemic, TB adenitis is a common cause of lymphadenopathy.[5] The cervix is the most common site of TB adenitis, while other sitesinclude intrathoracic, intra-abdominal, and occasionally, axillary, inguinal and intramammary.[6,7] TB lymphadenitis comprises 30–50% of extrapulmonary tuberculosis cases in the US,[5] and 33.5% in Bangladesh.[8] A wide excision and prolonged antituberculosis therapy were the only available treatment options in the 20th century,[9] but now a short course of rifampicin has been used successfully.[10]

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In Bangladesh, tuberculosis is among the top five communicable diseases with an incidence rate of 62.56 per 100,000 and a mortality rate of 5.37 per 100,000.[11] Pulmonary tuberculosis has been the center of attraction for the researchers for a number of years.[13] However, only a handful of studies[14] have been reported on extrapulmonary tuberculosis, especially, TB lymphadenitis. The current study was designed to expand our current knowledge and to gather baseline data on the incidence, diagnosis, complications, management and treatment outcomes of tuberculous lymphadenitis in a teaching hospital.

Methods

The study protocol was approved by the Dinajpur Medical Hospital. Informed consent was taken from the subjects before performing needle biopsy test.

A total of 1,548 cases were registered for tuberculosis treatment from 1st January 2009 to December 2010 at the Department of Medicine, Dinajpur Medical College. This center is a tertiary level reference center for respiratory diseases in Dinajpur district. All patients with a confirmed diagnosis of TB lymphadenitis were included in the study. For those who had completed treatment, data were obtained from medical records while, for those undergoing treatment data were collected during the course of the treatment. From each medical case file, the patient history, physical findings, chest radiographs and laboratory investigation were reviewed in order to obtain maximum information about the type and severity of TB. In addition, demographic factors, lifestyle (smoking habit and alcohol use) and clinical characteristics were recorded. Among clinical characteristics co-morbid medical complications like diabetes mellitus and HIV, medications for therapy and therapeutic outcomes were recorded.

Categories of Patients for Registration on Diagnosis

a. New patient - a patient who has never had treatment for tuberculosis or has taken anti-tuberculosis drugs for less than 1 month;
b. relapse - a patient who was previously treated for tuberculosis and was declared cured or treatment completed, and later diagnosed with bacteriologically positive (smear or culture) tuberculosis;
c. failure - a patient who, while on treatment, had positive sputum smear at 5 months or later during the course of treatment; return after default: a patient who returned to treatment with positive bacteriology, following interruption of treatment for 2 months or more; transfer in: a patient who was transferred from another tuberculosis registry to continue treatment.

Diagnosis

Diagnosis of tuberculosis and extrapulmonary tuberculosis were based on the World Health Organization definitions.[15,16] For tuberculosis the patient was bacteriologically confirmed, or was diagnosed by a clinician. Extrapulmonary tuberculosis such as pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges, diagnosis was based on one culture positive specimen, histological or strong clinical evidence consistent with active extrapulmonary tuberculosis, followed by a decision by a clinician to treat with a full course of antituberculosis chemotherapy.

The diagnosis of TB lymphadenitis was based on fine-needle aspiration (FNA) biopsy. The diagnosis was also supported by tuberculin skin test, sputum culture for acid-fast bacilli. However, to further ensure the diagnosis of HIV-positive patients and those with the co-morbid diabetes mellitus records from the medical, infectious and venereal diseases clinics were traced and reviewed.

Treatment Outcome
A patient who was sputum smear-negative in the last month of treatment and on at least one previous occasion was assumed to be cured. A patient who was sputum smear-positive at 5 months or later during treatment was categorized as treatment failure. A patient who had completed treatment but who did not meet the criteria to be classified as cured or failure was categorized as treatment completed. A patient who died for any reason during the course of treatment was categorized as dead. A patient whose treatment was interrupted for 2 consecutive months or more was categorized as defaulter. A patient who was transferred to another recording and reporting unit and for whom the treatment outcome was not known was categorized as transferred out. As a whole the sum of patients cured and those who completed treatment was categorized as treatment success.

Data Analysis
The data were analyzed using the statistical software SPSS version 16. The data with quantitative variables are expressed as mean (±SD) and range while the qualitative variables were estimated by frequency and percentage. Furthermore, nonparametric statistics (i.e. X^2 and Fisher's exact test) were used to find out the association among the variables. p values less than 0.05 were considered significant.

Results
Patient Demographics
The demographics of the patients are given in table I. Of the 1,548 patients, 109 (7.04%) had TB lymphadenitis, of whom 58(53.2%) were males and 51 (46.8%) females. The mean age of patients with TB lymphadenitis was 36.48 ±12.87 years (7–72). Incidence of TB lymphadenitis was highest among the age group of 21–30 years (29.4%) and the difference was statistically significant (p = 0.007). Of these 14 (82.35%) were males. The incidence of TB lymphadenitis within the HIV-infected group of patients was found to be statistically significant among male patients (p = 0.006).

Clinical Symptoms
A majority of patients (n = 83, 76.15%) reported cough, 80 (73.39%) fever (53.21%) and night sweats (58%). However, loss of weight and loss of appetite were more significantly reported by female than male patients. Details of the reported symptoms are listed in table II.

Diagnosis
Of the 109 patients, 90 (90.8%) were diagnosed by using FNA, followed by chest radiography (n=87, 79.8%) and erythrocyte sedimentation rate (n=86, 78.9%) as given in table III. The majority were diagnosed as hilar/paratracheal (n=93, 85.32%), followed by lymphatic cervical (n=12, 11%), lymphatic axillary (n=3, 2.75%),and lymphadenopathy in the neck (n = 1, 0.9%).

Management and Outcomes
All patients received directly observed therapy for a minimum of 9 months (range 9–14 months). 2EHRZ+6H2R2 was the therapeutic combination used for the majority (n=22, 20.2%) of the patients. Details about the therapeutic combinations used are given in table IV. Based on the clinical outcome the duration of intensive phase was increased to 3 months in 29 (26.6%) patients. Sixty-two (56.9%) of the patients were successfully treated. In 9 (8.2%) patients treatment failed and 5 (4.6%) patients expired during the course of therapy.

Table I: Demographic information of the 109 patients with TB lymphadenitis statistical significance

Demographic variables			p value
Mean age	All	36.4±12.87 (7–72)	
	Male	39±11.7 (17–72)	
	Female	32 ±13.3 (7–63)	0.197
Gender	Male	58 (53.2)	
	Female	51 (46.8)	0.197
Location	Hospital	100 (91.7)	
	Prison	9 (8.3)	0.09
Age, years	<20	8(7.3	
	21–30	32 (29.4)	
	31–40	20 (18.3)	
	41–50	18 (16.5)	
	51–60	21 (19.3)	
	>60	10 (9.2)	0.007*
Smoker	Yes	36 (33.0)	
	Ex-smoker	6 (5.5)	0.000*
Alcohol	Yes	10 (9.2)	
	Ex-drinker	5 (4.6)	0.014*

Table II: Symptoms reported by 109 patients with TB lymphadenitis

Symptoms	Male (n = 58)	Female (n = 51)	Total (n = 109)	p value
Night sweat	31 (53.4)	27 (52.9)	58 (53.2)	0.958
Cough	45 (77.6)	38 (74.5)	83 (76.1)	0.707
Sputum	27 (46.6)	21 (41.2)	48 (44.0)	0.827
Shortening of breath	19 (32.8)	15 (29.4)	34 (31.2)	0.707
Fever	43 (74.1)	37 (72.5)	80 (73.4)	0.851
Swelling of lymph nodes	8(13.8)	17 (33.3)	25 (23.0)	0.015*
Fatigue	2 (3.4)	2 (3.9)	4 (3.7)	0.097
Loss of appetite	32 (55.2)	40 (78.4)	72 (66.1)	0.002*
Loss of weight	29 (50.0)	40 (78.4)	69 (63.3)	0.011*
Hemoptysis	6 (10.3)	14 (27.5)	20 (18.3)	0.021*
Chills	5(8.6)	7 (13.7)	12 (11.0)	0.396
Chest pain	7 (12.1)	10 (19.6)	17 (15.6)	0.279
Backache	0	2 (3.9)	2 (1.8)	0.128
Clubbing	7 (12.1)	12 (23.5)	19 (17.4)	0.116
Lethargy	3 (5.2)	2 (3.9)	5 (4.6)	0.755
Abdominal swelling	1 (1.7)	0	1 (0.9)	0.346

Data shown as number of patients with percentage in parentheses. * Significant by X^2 test.

Table III: Diagnostic procedure used

Procedure	Patients, n (%)
FNA	90 (90.8)
Chest radiograph	87 (79.8)
Erythrocyte sedimentation rate	86 (78.9)
Tuberculin skin test	79 (72.5)
Sputum culture	77 (70.6)
Acid-fast bacilli smear	51 (46.8)

Table IV: Therapeutic combination used

Drug regimen Patients, n (%)	
2EHRZ+6H2R2	22 (20.2)
2EHRZ	19 (17.4)
3EHRZ	15 (13.7)
3EHRZ+5HR	14 (12.8)
3EHRZ+4H2R2	13 (11.9)
2EHRZ+6HR	9 (8.3)
2SEHRZ+6H2R2	6 (5.5)
3EHR+4H2R2	5 (4.6)
3SEHR+6HR	2 (1.8)
3SEHR+9H2R2	2 (1.8)
3HRZ+9HR	1 (0.91)
4EHR+5EHR	1 (0.91)

E = Ethambutol; H = isoniazid; R = rifampicin; Z = pyrazin amide; S = streptomycin.

Discussion

TB lymphadenitis is the most common form of extra-pulmonary tuberculosis especially among young adult males.[7] Tuberculosis is responsible for 30–52% of diseases causing lymphadenopathy in developing countries, whereas in developed countries it is only 1.6%.[17] In terms of age, the incidence of TB lymphadenitis was significantly higher in the age group 21–30 years followed by 51–60, 31–40, and 41–50 years, confirming a previous report.[18] The reasons for this high incidence in the age group 21–30 years may be weakening of the immune system due to smoking, which may indirectly increase the susceptibility to opportunistic infections[19,20] and the environmental pollution.[18,21] The findings of the current study contradict the findings reported by Koffi et al.[19] and Gajalakshmi,[20] because a majority (19.3%) of the patients in this age group were nonsmokers.

The majority of patients in our study presented with typical symptoms and signs, which were similar to the findings reported in other studies.[24,25] However, there are other reports that suggest atypical symptoms and signs to be more common among TB lymphadenitis patients.[23] In agreement with the findings of other studies,[23,26] FNA of the lymph nodes was the most consistent method to identify the bacteriologic agent responsible for lymphadenopathy. In addition, tuberculin skin test was a basic tool in the diagnosis of tuberculosis infection among 72.5% of patients.[27] On the other hand, sputum culture was found to be the least reliable test for the diagnosis of TB lymphadenitis.

Conclusion

The incidence of TB lymphadenitis was slightly higher in males than in females. 2EHRZ (ethambutol, isonaiazid, rifampicin, pyrazinamide) + 6H2R2 (ethambutol, rifampicin) combination therapy showed a better treatment outcome than others. Diabetes mellitus and HIV were the risk factors. FNA was the most reliable diagnostic test

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