

Evaluation of Serum Zinc Concentration in Patients with Tuberculous Lymphadenitis

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Abstract

Original Research Article

Background: Tuberculosis which is a severe bacterial infection caused by Mycobacterium tuberculosis, compromises the immune system. Inadequate intake of micronutrients alters the immune response of the host predisposing to infection. Zinc plays vital role in the immune status. So serum zinc concentration in patients with tuberculous lymphadenitis is a very potential thing in treating the respective patients. **Aim of the study:** The aim of this study was to evaluate the serum zinc concentrations in patients with tuberculous lymphadenitis. **Methods:** The study was conducted in the Department of Internal Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from January 2016 to March 2017. The study included 25 freshly diagnosed tuberculous lymphadenitis patients as case and 25 tuberculosis negative normal healthy subjects as control as per inclusion and exclusion criteria. Serum zinc concentrations were estimated by using atomic absorption spectrophotometry before initiating antituberculosis chemotherapy. **Result:** In analyzing serum zinc level of the study patients, it was observed that, 17 (68.0%) patients had <70 µg/dl (low) in Case Group and 10 (40.0%) in Control Group. The mean serum zinc was 66.3±14.2 µg/dl in Case Group and 74.9.0±13.8 µg/dl in Control Group. The difference was statistically significant (p<0.05) between two Groups. **Conclusion:** This study indicates that tuberculous lymphadenitis patients have lower level of serum zinc concentrations. This demands the need for further investigations so that strategies for zinc supplementation can be planned in monitoring responses to antituberculous chemotherapy in addition to its potential as diagnostic parameter.

Keywords: Tuberculosis, Micronutrient, Zinc, Chemotherapy.

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INTRODUCTION

Tuberculosis is a global disease and the second leading cause of death from an infectious disease worldwide. In 2015 an estimated 10.4 million new cases occurred globally and 1.4 million people died of TB. Bangladesh is the sixth highest TB-burden country in the world [1]. Despite effective treatment regimen for tuberculosis (TB), it remains a major source of morbidity and mortality throughout the world in developing countries, including Bangladesh. In Bangladesh, the prevalence of reported active TB in 2015 was 362 (Range: 234-517) per 100,000 population with a mortality of 45(range: 27-68) per 100,000 population (WHO 2015). TB-lymphadenitis is the most common comprises 68% [2] of all extra-pulmonary tuberculosis patients. The association between poverty and TB is well-recognized, and the highest rates of TB

were found in the poorest section of the community [3]. TB occurs more frequently among low-income people living in overcrowded areas and persons with little schooling [4]. Poverty may result in poor nutrition which may be associated with alterations in immune function (WHO int. publications). Nutritional status is one of the most important determinants of resistance to infection, and it is well-established that nutritional deficiency is associated with impaired immune functions⁵. Undernutrition increases the risk of tuberculosis and in turn tuberculosis can lead to malnutrition. Undernutrition is therefore highly prevalent among people with tuberculosis. It has been demonstrated that undernutrition is a risk factor for progression from tuberculosis infection to active tuberculosis disease and that undernutrition at the time of diagnosis of active tuberculosis is a predictor of

increased risk of death and tuberculosis relapse. However, the evidence concerning the effect of nutritional supplementation on tuberculosis prevention and health outcomes among people with tuberculosis had not previously been systematically reviewed (WHO int. nutrition). Recent reviews have shown that deficiency in the micronutrients and trace elements may have adverse effects on the immune status [5] and micronutrient supplementation can lead to boosting of the immune system, which may help improve the response to TB treatment. A great deal of research supports the fact that the impairment of the immune system due to trace element deficiency can be sufficient to increase the risk of mortality and morbidity due to infections. It is also stated that the supplementation of trace elements restores immune competence [6]. Zinc (Zn) is referred to as a trace element. It plays a vital role over immune system in various ways. Both innate and acquired immunity are impaired by zinc deficiency. Deficiency affects host defense by reducing the number of circulating T cells and phagocytosis activity of other cells which ultimately impair cell mediated immunity. The cell-mediated immunity plays a major role in the causation of tuberculosis. The low concentrations of serum zinc in tuberculous lymphadenitis patients may be from preexisting deficiencies due to nutritional deficiency that enhanced susceptibility to infection, and/or for consumption of serum zinc in TB lymphadenitis due to redistribution. A case control study from Indonesia reported that the prevalence of low serum zinc concentrations among pulmonary tuberculosis (PTB) patients and control subjects were 21% and 5% respectively [7]. Ghulam and co-authors from Pakistan found significantly low serum zinc levels in PTB patients compared to controls [8]. A systematic review of relevant epidemiological research involved meta-analysis from 11 intervention trials revealed that the global risk of zinc deficiency was estimated at 31%, ranging from 4-73% across WHO sub-regions. Research conducted recently suggests that prevalence of zinc deficiency in developing countries is very common and 61% of the population is at increased risk of low dietary zinc intake [9]. Studies demonstrated that 49.4% of adolescent girls in Delhi [10] and 52% non-pregnant women of central India suffered from zinc deficiency [11]. There is a lack of literature to reflect zinc deficiency in Bangladesh. Malnutrition and poverty in Bangladesh are the leading cause of high rate of zinc deficiency, especially in early pregnancies [12]. Randomized trial reports have shown that vitamin A and micronutrient supplementation resulted in improved prognosis in pulmonary tuberculosis. Since there are a lot of studies reporting malnutrition and beneficial effects of micronutrient supplementation but very few studies on the deficiency status of these micronutrients per se in tuberculosis patients, the present study was carried out to compare the plasma level of zinc in tuberculous lymphadenitis. The aim of this study was to evaluate the serum zinc concentrations in patients with tuberculous lymphadenitis.

OBJECTIVE

The general objective of this study was to evaluate the serum zinc concentrations in patients with tuberculous lymphadenitis.

METHODOLOGY & MATERIALS

The study was conducted in the Department of Internal Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from January 2016 to March 2017. The study included 25 freshly diagnosed tuberculous lymphadenitis patients as case and 25 tuberculosis negative normal healthy subjects as control as per inclusion and exclusion criteria. Data were collected by using pre-designed data sheet prepared for the study with face to face interview, relevant clinical examinations and investigations. The data sheet was pre-tested and face validated by consulting with experts. According to the inclusion criteria patients with newly diagnosed Tuberculous lymphadenitis, and patients of any gender aged between 15-60 years were included in the study. On the other hand, according to the exclusion criteria of this study, patients already on anti-tuberculous therapy, disseminated tuberculosis, diabetic, women with pregnancy or taking oral contraceptives, patients with chronic liver disease or renal failure, cases with myocardial infarction, carcinoma or nephritic syndrome and/or zinc receiving patients were excluded from this study. Patients with FNAC or Biopsy proven newly diagnosed untreated tuberculous lymphadenitis patients were selected as cases. For collecting of patients I used to go to OPD of internal Medicine and ENT and also to DOTS (directly observed treatment, short course) Centre, BSMMU. I also used to search newly diagnosed patients with tubercular lymphadenitis admitted in IPD, internal Medicine, BSMMU. I requested my colleagues to inform me or to send the patient with newly diagnosed tuberculous lymphadenitis to me at an allocated place and time if they found in OPD or admitted in IPD. At first Study purpose was explained to the patient and informed written consent was taken, then history was taken and examination was performed to exclude contributory and co-morbid conditions that may alter the serum zinc concentration. BMI of the patients was calculated; MT was done. CBC, SGPT, S. Creatinine and random blood sugar was done in all cases. Chest-X-ray and Ultrasonography of abdomen were done to exclude disseminated tuberculosis or other diagnosis. Age, sex matched healthy control who were fulfill the inclusion and exclusion criteria were collected from patient's attendance, hospital staff and patients with other diagnosis that did not alter the serum biochemistry from IPD and OPD of BSMMU. Controls were selected on the basis of only history and clinical examination. Three milliliter of Venous blood was collected by a trained technician who has proper knowledge about the procedure and safety of venipuncture. This study has minimum chance of physical risks during three ml of

blood sample collection. If any complication arises during blood collection that were managed properly. The blood specimens for zinc assay was collected in zinc-free tubes supplied from Atomic Energy Centre, Dhaka. Venous blood specimens were placed immediately after collection in a cold box, protected from light exposure and transported on ice packs to Atomic energy center, Dhaka. The serum was separated within six hours of collection and stored at -20°C until processing. Serum zinc levels were measured by atomic absorption spectrophotometry to determine the serum zinc concentration. Investigator will use a code number for each subject and code number was decoded by investigator. Thus confidentiality and anonymity was maintained. As it is an observational and case control study, no experimental drugs was used in this study. About 3 ml venous blood was collected from every cases (prior to initiation of anti-TB treatment) and controls in trace element free tube. These test tubes were made zinc free from Atomic Energy Centre laboratory prior to use. Venous blood specimens were collected by a trained technician. Powder free gloves were used during blood collection. Serum was separated by centrifugation within 2 hour of collection and kept at -20°C until analyzed within 4 days. Concentration of zinc in serum was determined using an atomic absorption spectrophotometry at Analytical chemistry laboratory of Atomic Energy Centre, Dhaka, Bangladesh.

RESULT

In this study finally 50 subjects were included in this study, 25 were newly diagnosed tuberculous lymphadenitis patients before starting anti tubercular therapy as case and 25 were tuberculosis negative control. In analyzing age and gender of the total participants, it was observed that, more than half (52.0%) of the patients belonged to age ≤ 30 years in Case Group and 15 (60.0%) in Control Group. The mean age was 32.1 ± 12.0 years in Case and 30.1 ± 12.0 years in Control Group. More than half (52.0%) patients were female in Case and 14 (56.0%) in Control Group. On the other hand, in local examination of the study patients, it was observed that, more than three fourth (80.0%) patients had neck gland. Single LN had 6 (24.0%). The mean length was 3.4 ± 0.8 cm with ranged from 2 to 5 cm. Mean wide was 2.8 ± 0.6 cm with ranged from 2 to 5 cm. Tenderness had 3 (12.0%). Twenty three (92.0%) patients had firm. Smooth surface had 15 (60.0%), relation with surrounding structures 19 (76.0%) patients had mobile. Almost three fourth (72.0%) patients had matted nature. In analyzing serum zinc level of the study patients, it was observed that, 17 (68.0%) patients had <70 $\mu\text{g/dl}$ (low) in Case Group and 10 (40.0%) in Control Group. The mean serum zinc was 66.3 ± 14.2 $\mu\text{g/dl}$ in Case Group and 74.9 ± 13.8 $\mu\text{g/dl}$ in Control Group. The difference was statistically significant ($p < 0.05$) between two groups.

Table-1: Age and gender distribution of participants (N=50)

Particulars	Case (n=25)		Control (n=25)	
	n	%	n	%
Age (Years)				
≤ 30	13	52	15	60
31-40	5	20	5	20
41-50	5	20	3	12
> 50	2	8	2	8
Mean \pm SD	32.1 \pm 12.0		30.1 \pm 12.0	
Range (min, max)	17, 60		17, 61	
Gender				
Male	12	48	11	44
Female	13	52	14	56

Table-2: Distribution of cases by examination of Lymphnodes (n = 25)

Particulars	n	%
Site		
Neck gland	20	80
Unilateral	15	75
Bilateral	5	25
Axillary	3	12
Others	2	8
Number of LN		
Single	6	24
Multiple	19	76
Tenderness	3	12
Consistency		
Soft	1	4
Firm	23	92
Hard	1	4
Surface		
Irregular	10	40
Smooth	15	60
Type		
Mobile	19	76
Fixed	6	24
Nature		
Matted	18	72
Discrete	7	28

Table-3: Distribution of the study patients by serum zinc level (n=50)

Serum zinc ($\mu\text{g/dl}$)	Case (n=25)		Control (n=25)		p value
	n	%	n	%	
<70 (low)	17	68	10	40	
70-120 (normal)	8	32	15	60	
>120 (high)	0	0	0	0	
Mean \pm SD	66.3 \pm 14.2		74.9 \pm 13.8		0.034 ^s
Range (min, max)	38.6, 102.9		52.5, 120		

s= significant p value reached from unpaired t-test

DISCUSSION

The aim of this study was to evaluate the serum zinc concentrations in patients with tuberculous lymphadenitis. In this study, we observed a significant amount of low serum zinc concentrations in patients with tuberculous lymphadenitis than tuberculous negative controls. These observations are in agreement with the reports from in this country [13], India [14], Indonesia [7], Ethiopia [15] and Ecuador [16]. In contrary to the previous studies and the current one [17], from Turkey studied 22 pulmonary TB patients and 18 healthy subjects and found an increase in the levels of serum zinc in PTB but the mechanism of this increase was not explained. In our study, the serum zinc concentrations revealed an inverse relationship with increasing age in both TB lymphadenitis patients and controls and the difference is not significant. This finding validates the observation of a previous study [8]. In this study, the mean serum zinc concentrations differences between male and female were not significant in both TB cases and controls. It is in agreement with a study in Indonesia⁷ and in Ethiopia [15] but inconsistent with a previous study in India where they found 11% low serum zinc in female than male and in Lisbon, Portugal; where [18] found significantly high serum zinc concentration in male than female. The comparisons between BMI categories and mean serum zinc concentrations were not statistically significant between cases and controls in this study. Association of age, Gender and BMI with serum zinc level in patients with tuberculous lymphadenitis was evaluated in the present study. Any significant association was not observed among them. A study published in 2006¹⁵ observed that there was no significant association between age and serum zinc level in patients of tuberculosis. In another study from Lucknow, India, it was reported that there was no association of age with serum zinc level in patients with tuberculosis [19]. A study in Ethiopia [15] found no association of BMI with serum zinc concentrations in tuberculosis patient. We enrolled a small sample size of 50 subjects. Among them, females were more than males. These data corroborate with a previous study in Ethiopia [15] where more than half (58%) of the study subjects were female but incongruent with a recent study in India [20] where more than half (54.3%) of the study subjects were male. This finding may be due to convenient sampling design or due to male dominance of the society like Bangladesh, where males are mostly responsible for bread and butter of his family. In this present study the highest numbers of patients were in the young age group. It is congruent with the study done by [20] but incongruent with the study done by Choudhury N *et al.*, where mean age group was little higher than the current study. In this current study, it was observed that the frequency of low BMI status was more in TB patients than control. The difference were statistically not significant ($p>0.05$) between two groups. It is consistent with an Indonesian study [7], where they observed low BMI in tuberculosis than

control. Most of respondents for both case and control were in normal BMI. These findings are congruent with the observation of a previous study [15]. Investigation profile showed, TB patients observed relatively low hemoglobin with high WBC total count, ESR and MT reaction in this study. These findings are in agreement with the reports from Indonesia⁷ and India [20].

Limitations of the study

This was a single centered study with a small sized of sample. So the findings of this may not reflect the exact scenario of the whole country.

CONCLUSION AND RECOMMENDATIONS

For getting more specific findings we would like to recommend for conducting more studies regarding the same issue with larger sized sample.

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