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Original Research Article

Role of Micronutrient Zinc in Pulmonary Tuberculosis

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Abstract: Addressing malnutrition is among the many challenges in the effective control of tuberculosis. The nutritional status of micronutrients is poorly standardized. Zinc being one of the most vital micronutrients, it is taken up for study.This study is to analyze the status of Zinc in the serum of pulmonary tuberculosis patients. The levels of serum Zinc is measured and documented in freshly diagnosed and completely treated cases of pulmonary tuberculosis and compared with the levels of apparently healthy individuals in this study. Group I-50 Newly diagnosed tuberculosis patients. Group II-50 Known Tuberculosis patients who have completed Anti-Tuberculosis Treatment. Group III-50 healthy individuals. Serum levels of zinc were measured by Atomic Absorption Spectrophotometry. Group I showed a significant decrease in the mean level of serum zinc (39.76±20.27) as compared to controls (86.42±16.51, p=0.001). There was no significant difference in the mean Zinc (p=0.415) levels between group II and group III. Zinc deficiency status observed in tuberculosis patients may be an aggravating factor for detrimental consequences. Therefore nutritional assessment and Zinc supplementation may represent a novel approach for fast recovery in tuberculosis patients.
Keywords: Zinc, pulmonary tuberculosis, prognosis, malnutrition, MDR

INTRODUCTION

Tuberculosis is a curable infectious disease causing significant morbidity and preventable deaths worldwide. India tops the first five countries ranked in terms of absolute number of cases. TB and HIV are lethal partners and thereby they have made the situation worse, which has been further complicated by the emergence of strains of multidrug resistant tuberculosis. These challenges can be better controlled by measures initiated by the Govt. which includes effective surveillance system, accelerated identification of cases, expansion of DOTS program in hard to reach areas, laboratory facilities and monitoring of micronutrient status. Malnutrition is one among the many challenges facing the effective control of Tuberculosis. The nutritional status, especially of micronutrients is still poorly documented[1].

Micro nutrient study is related to addressing malnutrition which needs to be part of the efforts directed towards control of tuberculosis as PTB can result in malnutrition. Moreover malnutrition may account for a greater population attributable to risk of TB than HIV infection and certainly a much more correctable one[2]. Malnutrition can predispose PTB. Zinc is one of the micronutrient necessary for the normal functioning of the immune system[3]. Plasma zinc levels drop by 50% in the acute phase response to injury, due to sequestration of zinc by liver[4] Zinc deficiency leads to increased susceptibility to infection. Therefore in this study the micronutrient Zinc is taken for its role in the management of tuberculosis.

MATERIALS AND METHODS

It is an age and sex matched Case Control study conducted in Stanley Medical College, Chennai. The present study was conducted after getting the approval from the ethical committee of Stanley Medical College and Hospital.

Group I population includes 50 cases of PTB patients freshly diagnosed by sputum AFB including both males and females who are between 18 and 60 years.

Group II includes 50 known Tuberculosis patients who have completed Anti-Tuberculosis treatment. The cases were selected from those attending the TB clinic at Guduvanchery GPHC and chest clinic at Govt. Stanley Medical College from March 2010 to September 2010. The study subjects were clearly informed of the nature of the study and the serum

samples were collected after getting written informed consent from them.

Group III control population includes 50 healthy subjects without any history of PTB. The control subjects were volunteers with sound health as evidenced by medical history, complete physical examination and routine laboratory tests performed before the commencement of the study.

Patients with Multidrug resistant (MDR) tuberculosis, extra pulmonary tuberculosis, Children with primary pulmonary TB, Pregnant PTB patients, PTB patients with impaired hepato renal function and malignancies were excluded from this study.

5 ml of venous blood was drawn from the subjects. After collection, blood samples were allowed to clot and then were centrifuged to separate serum. Serum samples were stored at 4°C for 1 month. The samples were analyzed for Serum zinc and the results were analyzed based on the data collected.Serum levels of zinc were measured by atomic absorption spectrophotometry (Perkin Elmer (3110)).

RESULTS AND STATISTICAL ANALYSIS

Mean and standard deviation of variables – Serum Zinc was estimated for subjects in Group I, Group II and controls (as shown in Table No.). Anova was employed to find out the level of significance between the three groups. Tukey HSD test was used to find the P value and comparison between control and study group.

Statistical Results

- Serum Zinc level ranges between (51.90 – 120.00 µg/dl) in control, (23.60 -115.20 µg /dl) in Group I, (50.50 – 115.20 µg/dl) in Group II estimated by Atomic Absorption Spectrophotometry.
- Serum Albumin level ranges between (3.5 – 4.8 g/dl) in Control, (2.5 – 4.1 g /dl) in Group I, (3.1 – 4.5 g/dl) in Group II, estimated by Bromocresol green dye binding method.
- Serum total protein ranges between (6.0 – 7.8 g/dl) in control, (7.0 – 9.1 g/dl) in Group I, (6.6 – 8.2 g/dl) in Group II estimated by Biuret method.
- Serum total Bilirubin ranges between (0.4 – 1.1 mg/dl) in control, (0.3 – 1.2 mg/dl) in Group I, (0.2 – 1.0 mg/dl) in Group II estimated by Jendrassik and Grof method.
- Serum AST level ranges between (15 – 40 IU/L) in control, (15 – 40 IU/L) in Group I, (16 – 40 IU/L) in Group II estimated by UV Kinetic method.
- Serum ALT level ranges between (12 – 40 IU/L) in control, (10 – 40 IU/L) in Group I, (10 -40 IU/L) in Group II estimated by UV Kinetic method.
- Serum Alkaline phosphatase ranges between (60 – 130 U/L) in control, (51 – 132 U/L) in Group I, (62-143 U/L) in Group II, estimated by P – Nitrophenyl phosphate method.
- Blood urea level ranges between (15-37 mg/dl) in control, (15 - 39 mg/dl) in Group I, (15-39 mg/dl) in Group II, estimated by UV Kinetic method.
- Serum creatinine level ranges between (0.8 – 1.2 mg/dl) in control, (0.7 – 1.2 mg/dl) in Group I, (0.7 – 1.1 mg/dl) in Group II, estimated by modified Jaffe's method.

Table 1: Mean values of variables in groups

S.No	Variable	Group					
		Control(Group III)		Freshly Diagnosed (Group I)		Completely Treated (Group II)	
		Mean	SD	Mean	SD	Mean	SD
1.	Zinc (µg/dl)	86.42	16.51	39.76	20.27	80.48	11.78
2.	Albumin (g/dl)	37.82	0.34	31.24	2.69	37.64	3.13
3.	T.Protein (g/dl)	6.65	0.43	8.35	0.58	7.43	0.43
4.	Bilirubin (mg/dl)	0.79	0.15	0.73	0.26	0.69	0.19
5.	AST (IU/L)	24.06	6.83	22.00	6.26	24.60	6.98
6.	ALT (IU/L)	27.26	7.16	24.90	8.35	25.50	7.80
7.	ALP(U/L)	89.26	20.15	89.06	20.84	91.92	23.11
8.	Urea (mg/dl)	22.86	6.12	24.58	5.59	24.48	5.68
9.	Creatinine (mg/dl)	0.97	0.13	0.98	0.14	0.95	0.16

Table 2: ANOVA – Comparison between and within groups

Sl.No	Variable	Group	Mean Square	F	P value
1.	Zinc (µg/dl)	Between groups within groups	32248.822 274.042	117.678	0.001
2.	Albumin (g/dl)	Between groups within groups	16.177 5.716	2.830	0.001
4.	T.Protein (g/dl)	Between groups within groups	35.950 0.235	153.02	0.001
5.	Bilirubin (mg/dl)	Between groups within groups	0.121 0.042	2.910	0.058
6.	AST (IU/L)	Between groups within groups	94.127 44.958	2.094	0.127
7.	ALT (IU/L)	Between groups within groups	75.227 60.725	1.239	0.293
8.	ALP (U/L)	Between groups within groups	127.460 458.028	0.278	0.757
9.	Urea (mg/dl)	Between groups within groups	46.607 33.692	1.383	0.254
10.	Creatinine mg/dl)	Between groups within groups	0.011 0.022	0.506	0.604

Comparison of Age within Groups
One way

Table 3: Age in years Mean and Standard Deviation

	N	Mean	Std. deviation
Control	50	42.90	11.777
Freshly diagnosed	50	42.98	13.484
Completely treated	50	44.58	9.433
Total	**150**	**43.49**	**11.631**

Table 4: Anova – Age in years

	Mean square	F	P value
Between groups	44.907	.329	0.720
Within groups **Total**	136.501		

P > 0.05 – Not significant

Age wise Comparison of Zinc within Groups
One way

Table 5: Upto 40 years

Variable	Group	N	Mean	SD
Zinc(µg/dl)	Control	18	89.93	11.80
	Freshly diagnosed	21	42.34	22.43
	Completely treated	12	81.49	15.65

Table 6: Tukey HSD – Multiple Comparisons

Dependent variable	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	P Value
Zinc (µg/dl)	Control	Freshly diagnosed	47.4905	5.702	0.001
	Control	Completely Treated	8.441	6.61	0.415
	Freshly diagnosed	Completely treated	-39.148	6.424	0.001

One way

Table 7: Above 40 years

Variable	Group	N	Mean	Std Deviation
Zinc (µg/dl)	Control	32	84.437	18.53
	Freshly diagnosed	29	37.88	18.72
	Completely treated	38	82.92	11.05

Table 8: Tukey HSD- Multiple comparisons

Dependent variable	(I) Group	(J) Group	Mean Difference (I-J)	Std.Error	P Value
Zinc (µg/dl)	Control	Freshly diagnosed	46.547	4.136	0.001
		Completely Treated	1.513	3.871	0.919
	Freshly diagnosed	Completely treated	-45.034	3.978	0.001

Mean values of Variables in Groups

Variables	GROUP-I	GROUP-II	CONTROL
Zinc(µg/dL)	39.76±20.27	80.48±11.78	86.42±16.51

- Group I showed a significant decrease in the mean level of serum zinc (39.76±20.27) as compared to controls (86.42±16.51,p=0.001)
- There was no significant difference in the mean Zinc (p=0.415) levels between group II and group III

DISCUSSION

Pulmonary tuberculosis is a global disease affecting about 1/3 rd of the world's population with its attendant mortality and morbidity. In India tuberculosis kills more adults in the productive age group (15 – 54 Years) than any other infectious disease[5].PTB can be diagnosed by a thorough evaluation of history, clinical symptoms and signs, bacteriological and radiological features. It results in changes in the serum levels of many micronutrients.

Zinc induces the production of metallothionein which is an excellent scavenger of hydroxyl radical and also inhibits NADPH oxidases which catalyze the production of superoxide from oxygen[6]. Zinc acts by stopping the body to grow and repair tissues in order to conserve the nutrient or it may even break down its own tissues to make the nutrient available[7]. Zinc is closely associated with many enzymes and has an important role in the immune system and metabolism.

Zinc is closely associated with many enzymes and has an important role in the immune system and metabolism.

There is limited data available on the micronutrient status and the relationship between nutritional status and TB. Increased incidence of TB in the recent era is also one of the factors for evaluating the status of zinc.This study on the role of zinc along with serum albumin and total protein in PTB may help us to assess the nutritional status of PTB patients.

One way ANOVA F – test was used to analyze whether the three groups were age matched.

Mean age of the control group was 42.90 ± 11.77, for the group composed of freshly diagnosed patients mean age was 42.98 ± 13.48 and for the group composed of completely treated patients the mean age was 44.58 ± 9.43.All the three groups were found to be age matched (P = 0.720).

Similarly chi-square test was performed to find out any difference in the male female composition among the three groups. It was found that the three groups were sex matched (p = 0.076).One way Anova F test and multiple comparisons Tukey HSD test were used to analyze the variables among the three groups.

In the present study, age wise comparison of Group I, Group II with controls was made and tabulated in tables 3, 4, 5, 6, 7 and 8. Based on the age, subjects were divided into two age groups – upto 40 years and above 40 years.

The following results were obtained.

- In both age groups there was significant P value on comparison of mean levels of serum zinc (p=0.001) between Group I and controls.
- In both age groups on comparison of mean levels of serum zinc
  P = 0.919 - Above 40 years; P = 0.415 - Upto 40 yearswas obtained between Group II and control, P value was not significant.

In the present study, sex wise comparison was done between male and female subjects selected in Group I, Group II and controls.

- In both male and female there was significant P value on comparison of the mean levels of serum zinc (0 = 0.001) between Group I and control.
- In both male and female, when comparison was done between Group II and control, P value was not significant.

Serum Zinc - (P = 0.135) in males; (P = 0.312) in females

In the present study, the mean levels of Serum zinc, Serum albumin, Serum total protein, Serum total bilirubin, Serum AST, Serum ALT, Serum Alkaline phosphatase was found to be normal in the control subjects.

In the present study, Group I patient showed significant decrease in the mean level of serum zinc as compared to controls.

The low serum zinc level in these patients is due to several reasons, mainly redistribution of zinc to the liver, mediated by increased hepatic synthesis of metallothionein. Infection may lead to inflammation triggered by certain cytokines (eg. IL/1β and TNF α). So this process may activate the synthesis of metallothionein, the intra cellular binding protein which results in sequestration of zinc within cells [8]. In chronic infections there may be a change in distribution of zinc in the body tissues with a net flow of zinc to the liver for the synthesis of acute phase reactants including metallo enzymes. Zinc may be utilized by MTB for growth and multiplication[9].

The present study in Group I showed significant decrease in the mean level of serum albumin as compared to controls. Albumin being a negative acute phase reactant, its level in the serum decreases with increase in severity. This is because of hemodynamic changes that occur in response to T cell reaction and decreased synthesis as a result of direct inhibition by cytokines. Decrease in the albumin level supports the induction of malnutrition and loss of weight by MTB infection[10].

In the present study, the mean level of total serum protein was increased in Group I compared to controls. This has been solely due to increase in the globulin fractions[11] as the albumin fraction has been decreased in these patients. Serum ceruloplasmin is one of the globulin fractions that contribute to the increase in total protein level. Regarding Albumin – Globulin ratio, the ratio decreases in direct proportion to the severity of the lesion.

In the present study, Group II patients showed that the mean serum zinc levels were nearer to the normal serum zinc levels. The lower levels of serum zinc in PTB patients and the nearer to normal levels of serum zinc in treated patients reveal that ATT treatment may have some influence on serum zinc levels[12]. Early restoration of nutrition could also lead to immunological changes that could enhance the clearance of mycobacteria and reduce infectiousness of the patient[13].

The present study showed that the mean level of serum albumin was increased to near normal in completely treated Group II cases compared to freshly diagnosed PTB patients. The elevation of serum albumin level in completely treated cases suggest the cessation of acute hemodynamic changes that occurred previously in PTB freshly diagnosed cases in response to tissue damage.

Study on Group II showed that the mean level of serum total protein was near normal as compared to Group I. It might be due to increased synthesis of albumin and reduction in globulin level i.e. serum ferroxidase (Ceruloplasmin α2 globulin) [14].

In the present study, there was no significant change in the mean levels of other parameters in Group I and Group II as compared to controls, suggesting that liver function are not entirely affected and renal function is normal.

CONCLUSION

The present study on PTB patients (both freshly diagnosed and treated cases) showed that there was highly significant decrease in the serum zinc levels in freshly diagnosed cases. In treated cases serum zinc levels were assessed and they ranged closer to normal levels on comparison with apparently healthy individuals. Serum albumin levels were also decreased in freshly diagnosed cases. In treated cases, serum Albumin levels were near to normal.

Therefore nutritional assessment in PTB patients should be carried out and balanced dietary regime is recommended in management and favourable outcome. This study strengthens the need for zinc supplementation in freshly diagnosed cases for preventing malnutrition and thereby bringing about speedy recovery and reduces the incidence of relapse.

REFERENCES

1. Karyadi E, Schultink W, Nelwan RH, Gross R, Amin Z, Dolmans WM, van der Meer JW, Hautvast JG, West CE; Poor micronutrient status of active pulmonary tuberculosis patients in

Indonesia. The Journal of nutrition, 2000; 130(12):2953-8.
2. Cegielski JP, McMurray DN; The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. The International Journal of Tuberculosis and Lung Disease, 2004; 8(3):286-98.
3. Ibs KH, Rink L; Zinc-altered immune function. The Journal of nutrition, 2003; 133(5):1452S-6S.
4. Shenkin A, Baines M; Vitamins and trace elements chapter 27 Tietz fundamentals of clinical chemistry edited by Carl A. Burtis, Edward R. Ashwood 6th edition,Saunders publications, 2008; 505-507.
5. Epidemiology of communicable diseases. Park's text book of preventive and social medicine, 19th edition, edited by K.Park, Banarsidas Bhanot publishers, 2007; 150.
6. Prasad AS; Zinc in human health: effect of zinc on immune cells. Molecular Medicine-Cambridge Ma Then New York. 2008; 14(5/6):353.
7. Prentice AM, Gershwin ME, Schaible UE, Keusch GT, Victora CG, Gordon JI; New challenges in studying nutrition-disease interactions in the developing world. The Journal of clinical investigation, 2008; 118(4):1322-9.
8. Opal SM, Keusch GT; Host responses to infection, Infectious diseases 2nd edition, edited by Jonathen Cohen, William, G. Powderly Mosby publishers, 2004; 37.
9. Boloorsaz MR, Khalilzadeh S, Milanifar AR, Safavi A, Velayati AA; Impact of anti-tuberculosis therapy on plasma zinc status in childhood tuberculosis. Eastern Mediterranean Health Journal, 2007; 13(5):1078-84.
10. Ramakrishnan K, Shenbagarathai R, Kavitha K, Uma A, Balasubramaniam R, Thirumalaikolundusubramanian P; Serum zinc and albumin levels in pulmonary tuberculosis patients with and without HIV. Japanese journal of infectious diseases, 2008; 61(3):202.
11. Poh SC, Seet AM; Alpha1 antitrypsin levels in chronic obstructive lung disease and pulmonary tuberculosis in Singapore. Singapore medical journal, 1975; 16(2):89.
12. Khanna BK, Kumar R, Mukerji PK, Chowdhury AR, Kamboj P. Plasma copper and zinc levels in pulmonary tuberculosis. Ind.T.Tub., 1982; 29(3):179-184.
13. Gupta KB, Gupta R, Atreja A, Verma M, Vishvkarma S; Tuberculosis and nutrition. Lung India, 2009; 26(1):9.
14. Batra HS, Singh P, Somani BL, Gupta A, Sampath S, Ambade V; Serum ferroxidase albumin ratio as a marken in pulmonary tuberculosis. Indian Journal of Clinical Biochemistry, 2007; 22(2):106-8.