Original Research Article

Comparative study of serum zinc and insulin levels in pulmonary tuberculosis patients with normal subjects

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Abstract

Background: Tuberculosis (TB), one of the oldest diseases known to affect humans, is major cause of death worldwide. Throughout history, tuberculosis (TB) has been identified by its most prominent constitutional symptom – wasting (i.e., "phthisis" or consumption). In India, tuberculosis is more prevalent in lower socioeconomic strata, and about 30% of the world population of tuberculosis resides in India. The estimated incidence and prevalence of TB in India are 1.9% and Between 2% and 7% respectively. Every year, 8 million people contract tuberculosis, of which 95% are in the developing world.[1] **Aim:** To estimate and compare serum Zinc levels, and serum Insulin in pulmonary tuberculosis patients with healthy volunteers. To estimate Total Protein and Albumin levels to rule out hypoproteinemia. To estimate Fasting Blood Sugar to rule out Diabetes mellitus **Materials and Method:** the study included 40 newly detected sputum smear positive, pulmonary tuberculosis patients and 40 healthy volunteers. Serum zinc was estimated by colorimetric method using RA-50 semi autoanalyser. Serum Insulin was estimated by solid phase enzyme linked immunosorbant assay (ELISA). Total protein was estimated by biuret method. Albumin was estimated by bromocresol green method. Blood Glucose was estimated by GOD-PAP. **Results and Conclusion:** There was a statistically significant decrease in the mean Zinc values in tuberculosis patients when compared to the control group (P<0.0001). The mean Zinc levels in tuberculosis patients was 170.97±34.99µg/dl and in the controls it was 207.71±38.37µg/dl. The serum Insulin level in pulmonary tuberculosis patients is 9.27±7.86µIU/ml and in the control's it is 9.48±5.07µIU/ml. There was no statistical significance in insulin levels in the study groups. Total protein, albumin and Fasting Blood Sugar were normal in both Patients and Control without any statistical significance between two group and the exclusion criteria's were met.
Key Words: Pulmonary Tuberculosis, Zinc, Insulin, Total Protein, Albumin, Fasting Blood Sugar.

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INTRODUCTION

Tuberculosis (TB) is an important global health problem. It has more impact on developing and under developing countries. The Impact of tuberculosis can be seen by the fact that in 1993, The World Health Organization (WHO) declared tuberculosis is a global emergency. WHO estimated that tuberculosis infects about 1/3rd of world's population. Every year, 8 million people contact tuberculosis of which 95% are in the developing world[1]. It is estimated that between 2002 and 2020, tuberculosis will be affect nearly 1 million people and 35 million will be die of tuberculosis, if it is not controlled[2]. In Zinc deficiency, there is a reduction in the activity of serum thymulin, the thymus-specific hormone that is involved in T-cell function, and an imbalance develops between Th1 and Th2 helper cells. The lytic activity of natural killer cells also decreases. Moreover, Zinc is also necessary for

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intracellular binding of tyrosine kinase to the T-cell receptors CD-4 and CD-8, which are required for T-lymphocyte activation. These complex changes result in an impairment of cell-mediated immunity and may be the basis for increased infection rates seen in marginal Zinc depletion.[33] Moreover low concentration of micronutrients such as Zinc in patients with pulmonary tuberculosis may be the result of anorexia and impaired absorption of nutrients and increased catabolism.[3,5] Insulin is a hormone of universal action and main growth factor in the human body. Borderline diabetes has been reported in TB cases and Diabetes has also been considered a risk factor for TB. The relationship between impaired cellular immunity and impaired insulin function has also been reported. The question is whether the metabolic derangements are part of the clinical course of the disease, or whether people with these types of metabolic derangements are prone to tuberculosis[4] It is anabolic hormone that stimulates the uptake of glucose into fat and muscle, promotes the conversion of glucose to glycogen or fat for storage, inhibits glucose production by the liver, stimulates protein synthesis and inhibits protein breakdown[7] The relation between insulin action and the immunological mechanism of macrophages and lymphocytes has been well documented. It has been reported that insulin exerts a very strong effect on macrophage action by increasing pyruvate dehydrogenase (PDH) complex activity and some other enzymes that play an important role in their phagocyte capacity. The difference between being susceptible to TB or not probably depends on proper lymphocytes sensitization / macrophage activation.[4]

MATERIALS AND METHODS

The study included 40 pulmonary tuberculosis patients. Patients were selected from the outpatient and inpatient departments of pulmonology and Medicine of JSS Medical College Hospital, Mysore. Clinical Diagnosis was based on history and Sputum Microscopy for AFB (acid fast Bacilli). The age of patients varied from 20-40 years. The cases were selected on the basis of simple random sampling method. The study protocol was approved by the Institutional Ethical Committee and Informed consent was obtained from the subjects under study. Metabolic diseases altering the levels of Zinc and Insulin like Hypoprotenemia and Diabetes mellitus were ruled out. Other pre-existing illness likely to affect the levels of Zinc and Insulin were excluded. The results were compared with 40 randomly selected normal healthy individuals after obtaining due consent. The controls were age and sex matched. The Investigations included serum Zinc, insulin, total protein and albumin and Fasting Blood Sugar. The same were compared with controls. Under all aseptic precautions, about 3ml of venous blood was collected in gel tubes, allowed to clot and it was centrifuged at 4000 rpm for 5 minutes. The serum separated was then used for the estimation of Zinc, Insulin, Total protein and albumin and Fasting Blood Sugar. Zinc present in the sample is chelated by 5-Br-PAPS (2-(5-Bromo-2-pyridylazo) -5-(N- propyl- N-sulpho propyl amino) – phenol in the reagent. The formation of this complex is measured at the wavelength of 560 nm[6]. Insulin was estimated by solid phase enzyme linked immunosorbant assay (ELISA).[8] Blood Glucose was estimated by GOD-PAP method using RANDOX KIT-GL 3815 in the Randox, Daytona auto analyser[9].T Protein and Albumin was estimated using the Randox, Daytona auto analyzer. T protein was estimated by Biuret method, end point using Erba Mannheim kit FBCER0057[10]. Albumin was estimated by Bromocresol green method using Randox kit AB380012.[11] statistical methods applied in the study are Descriptive Statistics, 't' test independent samples, F test (ANOVA test), Product movement correlation.

OBSERVATIONS AND RESULTS

The present study was conducted on 40 untreated adult pulmonary tuberculosis patients and 40 healthy controls. The cases and controls were age and sex matched. The age group was between 20-40 years. The mean age in tuberculosis patients was 34.4 ± 5.85 years and in controls, it was 34 ± 5.48. Among 40 patients 28 were men and 12 were women. The total protein, albumin A/G ratio in patients was 7.27±0.92 g/dl, 3.61±0.17 g/dl and 1.04±0.26 g/dl respectively. In controls, it was 8.47±0.43 g/dl, 4.43±0.42 g/dl and 1.12±0.21 g/dl respectively and were within normal limits in both group and hence met our exclusion criteria.

The mean FBS level in pulmonary tuberculosis patients was 88.9 ± 10.01 mg/dl, in control it was 90.15 ± 9.02 mg/dl. There was no significant increase or decrease in the mean FBS values compared between patients and controls. FBS was used to exclude diabetes in patients and controls. There was significant decrease in Zn in pulmonary tuberculosis patients when compared to controls, (170.97 ± 34.99µg/dl and 207.7 ± 38.37 µg/dl respectively). P< 0.0001 The serum Insulin level in pulmonary tuberculosis patients is 9.27 ± 7.86 µIU/ml and in the controls it is 9.48 ± 5.07 µIU/ml. There was no statistical significance in insulin levels in the study groups. P> 0.05

Table 1: Mean and SD of Serum Zn and Insulin in the study group

	Mean ± SD		p-value
	Tuberculosis patients	Controls	
Zinc	170.97± 34.99	207.71 ± 38.37	<0.0001
Insulin	9.27 ± 7.86	9.48 ± 5.07	>0.05

Table 2: Correlation between the various parameters

	Zn	INSULIN
Zn	1.000	-0.398*
INSULIN		1.000

* 'p' value <0.05 (Statistically significant),Zinc is negatively correlated with Insulin('p'<0.05)

DISCUSSION

The present study was conducted on 40 untreated adult pulmonary tuberculosis patients and 40 healthy controls. Among 40 patients 28 were men and 12 were women. Total protein, albumin was done to rule out hypoproteinemia so that apparent. Both in patients and controls, the total protein level and albumin levels was within normal range and the criteria to rule out hypoproteinemia was met. In the present study, there was significant decrease in Serum Zinc levels in the patients than in controls groups. The mean serum zinc levels in patients and controls was 170.97±34.99 and 207.71±38.37 respectively ($p<0.0001$). Low Zinc Status in patients with inflammatory disease has been attributed to loss of Zinc from catabolised tissue and increased urinary excretion of Zn subsequent to its mobilization by IL-1. Low Zinc are likely the result of redistribution of Zinc from plasma to other or reduction of hepatic production of the Zinc carrier protein α-2 macroglobulin and of a rise in the production of metallothionein.[5] Khanna BK *et al.*, in their study have pointed that pulmonary TB affects metabolism of trace elements like any other infectious disease. In their study there was fall in plasma Zinc level in the cases and was found to be statistically significant.[12] Muthuraj M *et.al.*, in their study found significant decrease in serum Zinc in patients with PTB Pulmonary tuberculosis, irrespective of their HIV status. The possible causes for the low serum Zinc were considered to be nutritional factors, Enteropathy and acute phase reactant proteins.[13,14] Decreased Zinc was likely due to the redistribution of Zinc from plasma to other tissue, or a reduction of the hepatic production of the Zinc-carrier proteins macroglobulin and to a rise in the productions of metallothionins a protein that transports Zinc to the liver.[14] In our study the mean serum Insulin levels in patients and controls was 9.27 ± 7.86 µIU/L and 9.48 ± 5.07 µIU/L. There was no statistical significance in Insulin level between the patients and controls ($p>0.05$). Within group comparison between Zinc and Insulin shows significant negative correlation ($p<0.05$). Bell L *et al.*, in their study, the results obtained showed a sluggish OGTT for both glucose and insulin suggesting a partial glucose intolerance and also the possibility of a certain insulin dysfunction in the patient group compared with the control group and concluded saying that the study strongly suggest that insulin-glucose metabolism is altered in TB Patients.[4] Guptan A *et al.*, in their study quoted that, in Philadelphia survey there was 8.4% of 3,106 diabetes had pulmonary tuberculosis against only 4.3% of 71,767 healthy population. Tuberculosis was present in 17% of the diabetics who had the disease for more than 10 years completed to 5% in the diabetics with less than 10 years of the disease. A higher prevalence of tuberculosis was found in diabetics requirement more than 40 units of insulin per day.[15]

In the Tanzanian study, done as per WHO criteria, in 506 consecutive patients with sputum positive pulmonary Tuberculosis, diabetes was present in 11 patients (4% prevalence) and Impaired glucose tolerance in 82 patients (16.2%).[16] The Nigerian study, done on 54 patients with active pulmonary tuberculosis found that 3 patients had OGTT values in diabetic range and 20 had IGI.[17] An 8 year study, done in Japan revealed the prevalence of diabetes in case of active Tuberculosis was 13.2% and was higher in males than in females (7/30) Impaired glucose tolerance in tuberculosis in much higher than overt diabetes.[18]

CONCLUSION

From our study it is clear that there is significant decrease in serum zinc levels of tuberculosis patients. We in our study did not find any significant difference correlation of insulin between the groups. However coincidental finding in within group comparison shows significant negative correlation between serum Zinc and Insulin levels in the Patients, the exact mechanism is unclear and requires further study.

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