



PARATHYROID HORMONE LEVEL IN PULMONARY TUBERCULOSIS PATIENTS

Biochemistry

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ABSTRACT

BACKGROUND: Pulmonary tuberculosis is a deadly infectious disease caused by acid fast bacilli Mycobacterium Tuberculosis and is responsible for more than 1.5 million deaths every year, hence is a major global health problem specially in developing countries. Interrelation between Tuberculosis and malnutrition is as old as the disease itself. Disease outcome and mortality in PTB depends on strength of immune system which in turn influenced by the nutritional status of an individual. Calcium is an essential macro mineral is altered in various infection including granulomatous diseases.

MATERIAL AND METHOD : The study was conducted on 100 adults (both males and females) from low socioeconomic status out of which 40 were newly diagnosed (Group A), 30 were relapsed PTB cases (Group B) and 30 were healthy age and gender matched non family member of patients that served as controls (Group C). After an informed consent, all were subjected to anthropometric measurements and biochemical investigations i.e Total protein (Biuret Method, Accurex), Albumin (BCG dye binding method Accurex). Total Calcium (Arsenozo III Method, Accurex), Phosphorus (Phosphomolybdate UV Method, Accurex) and ALP (Kinetic Method).

RESULT AND DISCUSSION : No significant difference was seen in ages among all the groups. BMI, Total protein and Albumin were significantly ($P < 0.05$) low in Pulmonary Tuberculosis (PTB) than controls. Since TB is associated with severe cachexia, wasting and low albumin, ionic and corrected TCa was calculated and were significantly high ($p < 0.05$).

CONCLUSION : Poor nutrition (Low protein) may be a risk factor for the tuberculosis. And studies indicating that incidence of tuberculosis is unusually high among malnourished people. The host protective immune mechanism of TB infection depends critically on the interaction and cooperation between monocyte-macrophages and t-lymphocytes.

KEYWORDS

INTRODUCTION:

Pulmonary Tuberculosis (PTB) is a deadly infectious disease caused by different strains of Mycobacterium Tuberculosis (MTB) that usually affects apices of lungs. One-third of the world's population is thought to have been infected with MTB with new infection occurring in about 1% of the population each year. (1) Making PTB a global health issue. The disease is called by some. The Mother of Diseases" and is as much a social disease as an infectious disease. TB is associated with poverty overcrowding, alcoholism, stress, drug addiction and malnutrition found commonly in developing countries like India. (2) India is the highest TB burden country with WHO statistic for 2011 giving an estimated figure of 2.2 million cases in India out of a global incidence of 8.7 million cases (2). Although the causative agent is MTB, among various risk factor for TB, undernutrition is the most significant accounting for the highest population attributable risk (PAR) for TB in India. (3) On one hand malnourished are highly vulnerable to TB can lead to or worsen Preexisting undernutrition by decreasing appetite and by increasing catabolism (3). It is a Known that both TB and malnutrition are synergistically associated to each other. Among Various methods of nutritional assessment, apart from anthropometric, macronutrient level in blood is important indicator of nutritional status of an individuals. Calcium and Phosphorus are essential macronutrients whose level is altered to a significant extent in various diseased states causing clinical manifestation.

Calcium is an essential macro mineral, the 5th most common metallic element found in three body compartments. The skeleton, soft tissue and the Extra Cellular fluid (ECF) and is altered in various granulomatous disease and simultaneously causing a spectrum of clinical features (4). Phosphorus is an important and widely distributed element of the body present both extracellularly and intracellularly. An acute decline in serum phosphate level may result in rapid complication and altered RBC function specially in immune compromised individuals (5). Since MTB infection is associated with compromised cell mediated immunity, assessment of Ca and Phosphorus (P) status will provide additional information for effective management of the disease. Evaluation of serum ALP in degenerative disease like PTB will not only provide information on liver dissemination of Tuberculosis but also will help in understanding the systemic manifestation of the disease.

AIM : The present study aims to determine the level of Protein in newly diagnosed and relapse cases of Pulmonary Tuberculosis. Another objective is to characterize level of protein in various categories of PTB patients and compare them with healthy controls.

MATERIAL AND METHOD :

The study was conducted in the Institute of Respiratory diseases (IRD) in association with Department of Biochemistry, SMS Medical college, Jaipur. 100 Adult patients (both male and female) from low socio-economic status diagnosed with pulmonary Tuberculosis (PTB) of which 40 (M=30;F=10) were newly diagnosed (Group A) and 30 (M=20;F=10) relapse cases (Group B) were recruited for the study. 30 (M=22; F=8) healthy, age matched individuals tested free of MTB without any previous or present symptoms of Tuberculosis or any other pulmonary disease and non family member of patients served as controls (Group C). Following diagnostic criteria was used for PTB. 1. Positive culture for MTB. (2 consecutive samples) smear for AFB. 3. Typical chest X-ray showing bilateral upper zone involvement with or without cavitations & with/without +ve sputum smear but with typical PT symptoms. 4. Patients with 2 or 3 criteria had to show clinical and radiological improvements with anti tuberculosis therapy. Relapse cases are patients who have completed treatment and declared cured, however they came up with typical PTB symptoms with +AFB smear or radiological deterioration. Patients suffering from drug resistant TB (MDR), extrapulmonary TB, those with significant renal, cardiac neoplasm or respiratory disease (other than PTB like lung cancer) etc. diabetes, endocrine or genetic disorder were excluded from the study. HIV positive cases, Pregnant or lactating women and those on oral nutritional supplements were also excluded. None of the patients or control subjects were on calcium supplements. All subjects gave their written consent to participate in the study.

Sample collection and bacteriological examination

Two consecutive sputum sample of each patient were collected and subjected to Acid fast Staining. In order to determine smear Positivity index, number of Acid fast Bacilli (AFB) were counted and analysed as follows : No AFB in 100 fields-negative 1-9 AFB in 100 fields-scanty ; 10-99 AFB in 100 fields-+ 1 ; 1-10 AFB per field +2 and more than 10 AFB per field-+3.

Measurement of biochemical parameters

After an overnight fast (12 hrs), venous blood was drawn from antecubital vein of each subjects by using aseptic technique in plain vial. Total protein (Biuret Method, Accurex), Total calcium (Arsenozo III Method, Accurex) Phosphorus (Phosphomolybdate UV Method Accurex) and ALP (Kinetic Method) were estimated routinely on Clinical Chemistry RANDOX IMOLA 3 Autoanalyzer.

Statistical Analysis : Quantitative data were expressed as mean SD Comparison was made using student-t test (independent sample t-test). P value less than 0.05 was considered significant. Correlation

between various parameters was studied by Pearson Correlation.

RESULTS AND DISCUSSION

Tuberculosis is commonly a disease of lungs where it forms localized infection after inhalation. Almost one third of the world's population is infected with Mycobacterium tuberculosis and the majority of these individuals live in less developed

countries (Swaminathan et al 2008). Therefore, despite recent progress TB remains an important global public health problem (WHO 2009). Nutrition and infection interact with each other synergistically. Recurrent infection leads to loss of body nitrogen and worsen nutritional status and malnutrition produces greater susceptibility to infection. The study deals with status of calcium and its metabolites in Tuberculosis infection.

Table : 1 General characteristics of study subjects :

Characteristics	Group A (Newly Diagnosed cases)	Group B (Relapsed cases)	Group C (Controls)	P- value
No. of cases	40	30	30	
No. of males	30 (75)	20 (66.67)	22 (73.33)	0.063 NS
No. of females	10 (25)	10 (33.33)	8 (26.66)	
Average Age (mean +SD) in years	48.53 +- 19.58	43.07 +- 18.7	45.13 +- 14.08	0.44 NS
Average BMI (mean+SD) Kg/m ²	14.6 +- 2.2	17.1 +- 2.8	26.8 +- 3.01	< 0.001 S
SPUTUM STATUS				
Negative	10 (25)	15 (50.0)	30 (100)	
+1	10 (25)	11 (36.67)	0 (0.00)	<0.001 S
+2	13 (32.5)	3 (10.00)	0 (0.00)	
+3	7 (17.5)	1 (3.33)	0 (0.00)	
Smoking status				
No. smoking	32 (80.0)	20 (66.67)	8 (26.66)	
No. Non-smoking	8 (20.0)	10 (33.33)	22 (73.33)	<0.001 S
Alcohol Intake				
No. of Alcoholics	21 (52.57)	15 (50.00)	3 (10)	
No. Non Alcoholics	19 (47.5)	15 (50.00)	27 (90)	<0.001 S
No. of Rural cases	35 (87.5)	23 (76.67)	10 (33.33)	
No. of urban cases	5 (12.5)	7 (23.33)	20 (66.67)	<0.001 S

General characteristics of study population is depicted in **Table 1**. Newly diagnosed PTB cases (Group A) studied were 40 out of which 75% were males and 25% were females and in Group B i.e relapsed cases, 66.67% were males and 33.33% females. Patients group was compared with healthy controls that were 30 in number (22 males and 8 female) and constitute Group C. Difference was non significant with regard to male female ratio among all groups. Average age of Group A (Newly diagnosed) was 48.53=19.58 years, Group B (relapse cases) was 43.07+18.7 and controls were of 45.13+14.08 years. NO significant difference was seen in the ages among all groups. Mean body Mass Index (BMI) of Pulmonary Tuberculosis patients (both Group A and B) was 14.6+2.2 and 17.1+2.8 kg/m² respectively and was significantly lower than controls i.e 26.8+3.0 (p<0.001) Nutrition is the most important factor affecting susceptibility to any infection and disease outcome. BMI is much better indicator of

nutritional status than weight alone because it takes height into account (9). It has been well documented that PTB is associated with severe cachexia, weight loss and generalized weakness. All these factors beside low economic status of our study population causing nutritional depletion are all responsible for low BMI in cases than in controls significant difference was observed in smoking and alcoholic habits of Group A and B patients when compared to controls (p<0.001). As seen in **table 1** Nonsignificant difference was seen among all the Groups with regard to their smoking and alcoholic habits (p<0.001). Since smoking adversely affects lung function and reduces its vital capacity cases of PTB disease and relapse are more common in smokers than non smokers. Significant difference was seen with regard to the locality of study population. 87.5% of Group A and 76.67% of Group B patients belong to rural areas. Only 33.3% of control subjects belonged to rural areas.

Table : 2 - Parathyroid Hormone & Other Biochemical parameters profile of study population.

S.no	Biochemical parameter	Group A (Newly) diagnosed	Group B (Relapsed)	Group C (Control)	Significance (P VALUE)		
					I vs III	II vs III	I vs II
1	Total Protein (g/l)	6.679 +- 0.53	7.363 +- 0.89	7.908 +- 0.75	S	NS	S
2	Albumin (g/l)	3.076 +- 0.64	4.020 +- 1.03	4.523 +- 0.56	S	NS	S
3	SGOT (U/L)	38.76 +- 14.6	36.00 +- 18.7	28.31 +- 13.0	NS	NS	NS
4	SGOT (U/L)	22.3 +- 10.1	27.14 +- 15.5	25.36 +- 14.4	NS	NS	NS
5	Serum Phosphate (mg/dl)	4.632 +- 1.21	4.560 +- 0.671	4.360 +- 0.54	NS	NS	NS
6	Total calcium (mg/dl)	8.640 +- 0.882	8.100 +- 0.51	8.154 +- 0.54	NS	NS	S
7	Ionic calcium (mg/dl)	4.729 +- 0.52	4.149 +- 0.44	4.028 +- 0.24	NS	NS	S
8	Corrected TCa (mg/dl)	8.869 +- 0.98	7.662 +- 0.93	7.100 +- 0.45	S	S	S
9	Alk. Phosphatase U/L	261.4 +- 105.5	190.2 +- 57.0	185.6 +- 31.8	S	NS	S
10	Vitamin D (ng/ml)	16.1 +- 7.2	23.8 +- 11.0	30.02 +- 6.7	S	NS	S
11	Parathyroid Hormone (pg/ml)	27.8 +- 15.7	38.6 +- 16.3	42.0 +- 7.7	S	S	S

Table: 2 Indicates the mean level of parathyroid hormone profile of all Group. The present study shows significantly low level of parathyroid hormone (27.8 +- 15.7 38.6 +- 16.3 42.0 +- 7.7) in Newly Diagnosed PTB patients than that of controls (7.908+0.75 g/l and 4.523+0.569 g/l respectively (p<0.001) Mean were (27.8 +- 15.7 38.6 +- 16.3 42.0 +- 7.7) respectively which significantly less than control.

Difference in Total protein and albumin level between Group A and Group B was not significant. Reduced Total protein found in our study might be due to pre-existing undernutrition, malabsorption in Tb infection, increased catabolism and anorexia in PTB cases. Further, low albumin and high globulin level are known complications of PTB observed in various studies (10). Albumin is an important component of plasma antioxidant activity and is a negative acute phase protein which decreases during any inflammatory condition. Injury or in stress as a result of increased metabolic need for tissue repair and free and radical utilization (II) Further leakage of albumin through vascular

endothelium and reduced hepatic synthesis is are the factors combined with undernutrition and loss of appetite associated with PTB results in low albumin level in patients (both newly diagnosed and relapse) than in controls (12).

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