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RESEARCH ARTICLE

EFFECT OF SERUM CALCIUM AND PHOSPHORUS IN ANTI-TUBERCULAR TREATMENT

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ABSTRACT

Tuberculosis is the major public health problem and ninth leading cause of death globally. Calcium and phosphorus are important macro-minerals required for various physiological functions and changes may cause detrimental effect as it has role in patho-physiology of pulmonary tuberculosis. **Aim:** Estimation of serum calcium and phosphorus in pre and post-treatment of newly diagnosed pulmonary tuberculosis patients. **Method:** This study was conducted in the Departments of Biochemistry and Pulmonary Medicine, FMHS, SGT University and District TB Centre, Gurugram, Haryana. 100 newly diagnosed pulmonary tuberculosis patients above 15 years of age were included in the study. The venous blood samples were collected from patients of pre and post treatment. The level of serum calcium and phosphorus was analyzed by fully auto-analyzer. **Result:** The serum calcium level was significantly low in pre-treatment (8.22 ± 0.69 mg/dL) as compared to post treatment (9.30 ± 0.75 mg/dL) with $p < 0.01$. Similarly, the level of serum phosphorus was significantly higher in pre-treatment (4.86 ± 0.97 mg/dL) as compared to post-treatment (3.84 ± 0.87 mg/dL) with $p < 0.01$. **Conclusion:-** The level of serum calcium was increased and level of serum phosphorus was decreased in post-treatment compared to pre-treatment in pulmonary tuberculosis patients, which signifies the effect of anti-tubercular treatment and need of calcium supplementation with regular monitoring during the treatment.

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INTRODUCTION

Tuberculosis is an infectious diseases caused by *Mycobacterium tuberculosis* (MTB). It is transmitted by droplet nuclei, which are aerosolized by coughing, sneezing, or speaking. MTB mainly affects the lungs but other organs are also involved in up to one-third of cases (Kasper et al., 2015). As per WHO global tuberculosis report 2017, tuberculosis is global burden and ninth leading cause of death. In 2016, 10.4 million people were infected with tuberculosis worldwide (World Health Organization, Global TB Report-2017). In India, the estimated incidence of TB was 27, 90,000 in 2016 which is a quarter of the world's TB cases (India TB report 2018).

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Calcium and phosphorus are important macro-minerals required for the growth and development of bones and teeth, blood coagulation, action of enzymes, muscle contractility, neuromuscular irritability, synthesis of nucleoside co-enzymes like (NAD⁺ and NADP⁺) and production of high energy phosphate compounds (ATP, GTP and creatine phosphate) (Thomas, 2010; Vasudevan et al., 2016). Tuberculosis is granulomatous disease which changes the level of circulating calcium concentration (Baig et al., 2006). The tendency for the phosphorus level to be higher in those with elevated polymorphonuclear leucocyte counts but not significant in more extensive active disease suggesting an association with tissue destruction. Thus, it is more relevant to study the level of this element in pulmonary tuberculosis (Kardjito, 1984). The calcium and phosphorus abnormalities in pulmonary tuberculosis have been variedly reported in several studies carried out on the subject globally.

In Swedish study carried by Pruitt B *et al.* (1995) hypercalcaemia was found in 25% pulmonary tuberculosis patients (Pruitt *et al.*, 1995). Liam CK *et al.* (1998) reported that 27.5% Malaysian patients were detected hypercalcaemia out of which 12% patients had symptoms of hypercalcaemia with pulmonary tuberculosis (Liam *et al.*, 1998). Similar study was conducted by Roussos A *et al.* (2001) and reported that 25% Greek patients were detected hypercalcaemia with pulmonary tuberculosis but among them only 5% patients had symptoms of hypercalcaemia (Roussos *et al.*, 2001). In contrary to the above studies Shirai M *et al.* (1990), Hafiez AA *et al.* (1990), Ali Gombe A *et al.* (1997) and Ilaz A *et al.* (2004) reported that hypocalcaemia is associated with pulmonary tuberculosis.

Similar variation in serum phosphorus levels have been reported in pulmonary tuberculosis. Wells *et al.* (1923) observed phosphorus retention and reduced excretion thus increased urinary levels of lipid bound phosphorus in patients with tuberculosis (Wells *et al.*, 1923). But as per Sweany *et al.* (1923) phosphorus level varied from patient to patient and concluded that phosphorus might be associated lipoproteins liberated by the denaturation of cell membrane (Sweany, 1923). The study conducted by Sharma *et al.* (1981) found high level of phosphorus in patients with hypercalcaemia but not in normocalcaemic patients (Sharma, 1981). Meuthen *et al.* (1991) reported that hypercalcaemia and hyperphosphataemia in pulmonary tuberculosis (Meuthen *et al.*, 1991). Goldwin AO *et al.* (2010) reported that in pulmonary tuberculosis hypocalcaemia and hypophosphatemia is common (Godwin *et al.*, 2010).

There are some studies, which were focused on efficacy of anti-tubercular treatment in calcium and phosphorus level. Rohini K *et al.* (2013) reported low level of serum calcium and phosphorus in pulmonary tuberculosis patients before treatment compared to normal controls but during and after end of the treatment both ions have progressively increased in levels (Rohini *et al.*, 2014). In contrast to Rohini *et al.* the study conducted by Bhandari S *et al.* (2014) found decreased calcium level and increased phosphorus level at diagnosis and during the antitubercular treatment compare to healthy controls. However, both the levels became normal on completion of anti-tubercular treatment (Bhandari *et al.*, 2014). Godara S *et al.* (2017) reported raised level of serum calcium and phosphorus after anti-tubercular treatment compared to before treatment (Godara *et al.*, 2017). Thus, the above-mentioned reports of various studies in past drove our attention to study the fact related to the circulating level of calcium and phosphorus in pulmonary tuberculosis and efficacy of anti-tubercular treatment.

MATERIAL AND METHODS

This study was conducted in the Departments of Biochemistry and Pulmonary Medicine, FMHS, SGT University, Budhera, Gurugram and District TB Centre, Gurugram, Haryana, India. 100 newly diagnosed pulmonary tuberculosis patients were included in this study based on the clinical features, positive sputum for acid-fast bacilli (AFB) and/or presence of radiological abnormalities consistent with PTB with normal blood sugar levels in the age group more than 15 years. Patients on anti-tubercular treatment, age less than 15 years, high blood sugar level and suffering from HIV and hepatitis-B were excluded from this study. After explaining the purpose of

the present study and taking written informed consent from the patients visiting OPD, IPD and DOTS centre of SGT Medical College, Hospital and Research Institute and District TB Centre, Gurugram, 5ml venous blood samples were collected first after confirmation of diagnosis and secondly after completion of anti-tubercular treatment (ATT). The serum was separated from the collected blood samples by centrifugation and level of calcium and phosphorus was analyzed in fully auto-analyzer (Erba, EM-200) in the Central Clinical Laboratory of Biochemistry, SGT Medical College, Hospital and Research Institute, SGT University, Budhera, Gurugram.

Statistical Analysis: Statistical Analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 24.0, for windows (SPSS, Inc., Chicago). The data were expressed as mean \pm standard deviation (SD). Paired Student's t-test was used to compare the values between serum calcium and phosphorus (pre vs. post treatment) and Pearson's correlation coefficient was used to elucidate the association between the variables. $p < 0.05$ was considered statistically significant.

RESULTS

In this study, out of 100 newly diagnosed pulmonary tuberculosis patients 71 were males and 29 females with the mean age of 42.2 ± 16.9 (Table 1).

Table 1. Anthropometric parameters of the study population

Parameters	Mean \pm standard deviation (n=100)
Sex	Male=71 Female=29
Age	42.2 \pm 16.9
BMI (Kg/m ²) before treatment	16.90 \pm 3.18
BMI (Kg/m ²) after treatment	18.44 \pm 3.15

Table 2. Mean \pm SD of serum calcium & phosphorus levels in PTB patients

Parameters	Pre-Treatment (n=100)	Post-Treatment (n=100)
Calcium (mg/dL)	8.22 \pm 0.69**	9.30 \pm 0.75**
Phosphorus (mg/dL)	4.86 \pm 0.97**	3.84 \pm 0.87**

$p < 0.05$ Significant*, $p < 0.01$ Highly significant**

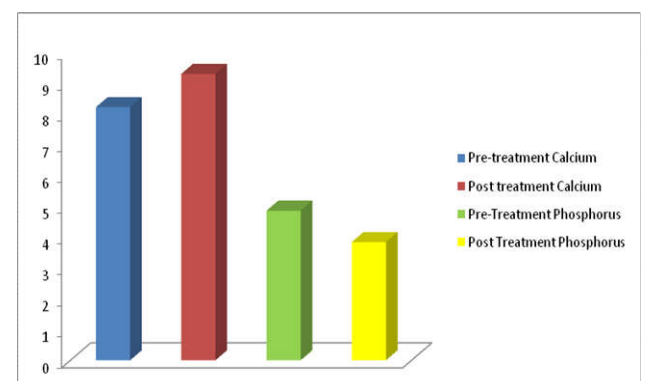


Figure 1. Serum levels of calcium & phosphorus in pre & post treatment

The body mass index (BMI) of the study population in pre and post anti-tubercular treatment was 16.90 ± 3.18 and 18.44 ± 3.15 respectively. The BMI of the study population was increased in post anti-tubercular treatment (Table 1).

Table 3. Correlation between serum calcium & phosphorus levels in PTB patients

Parameters	Calcium Pre Treatment	Calcium Post treatment	Phosphorus Pre Treatment	Phosphorus Post treatment	p-value
Calcium Pre Treatment	1	0.83**	-0.49**	-0.44**	0.000
Calcium Post treatment	0.83**	1	-0.55**	-0.52**	0.000
Phosphorus Pre Treatment	-0.49**	-0.55**	1	0.85**	0.000
Phosphorus Post treatment	-0.44**	-0.52**	0.85**	1	0.000

**Correlation is significant at the 0.01 level (2-tailed).

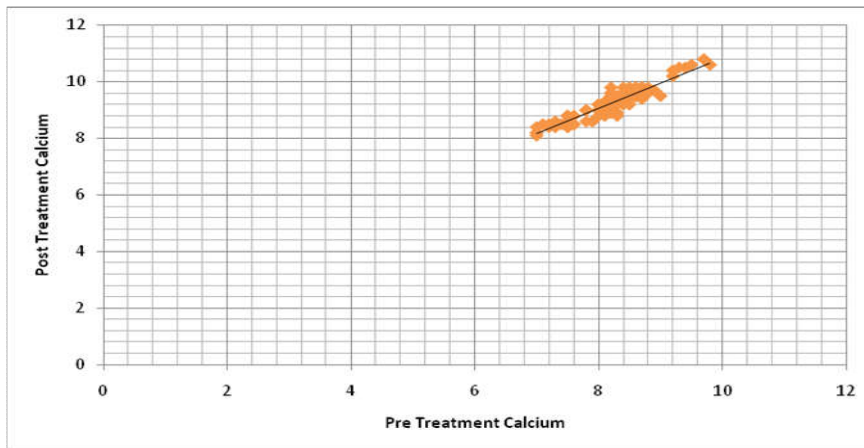


Figure 2. Positive correlation between the level of calcium in pre & post treatment

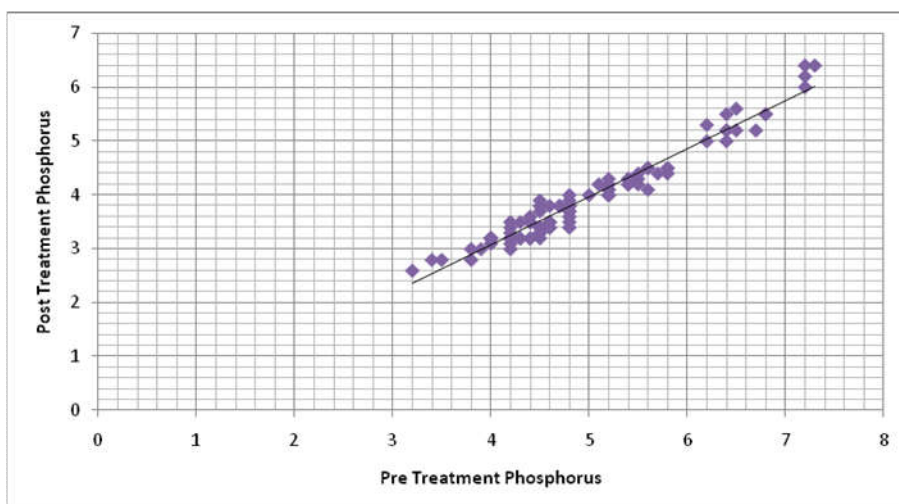


Figure 3. Positive correlation between levels of phosphorus in pre & post treatment

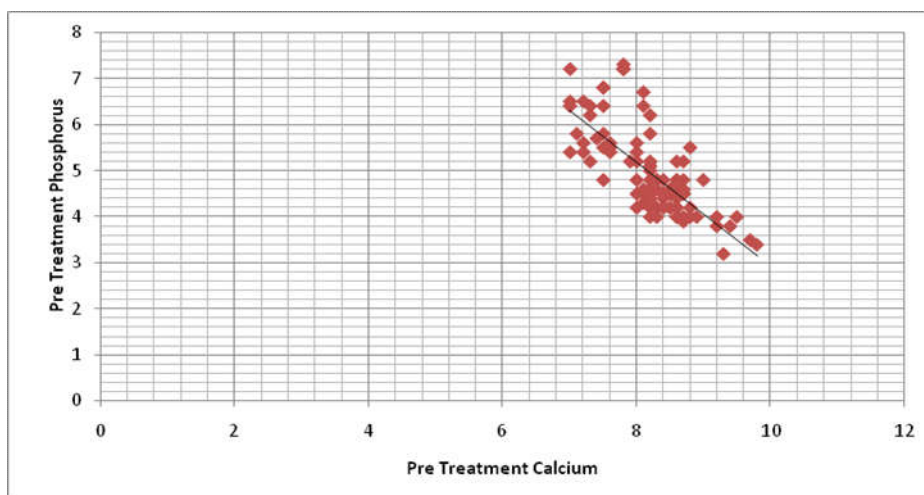


Figure 4. Negative correlation between serum calcium & phosphorus levels (pre-treatment)

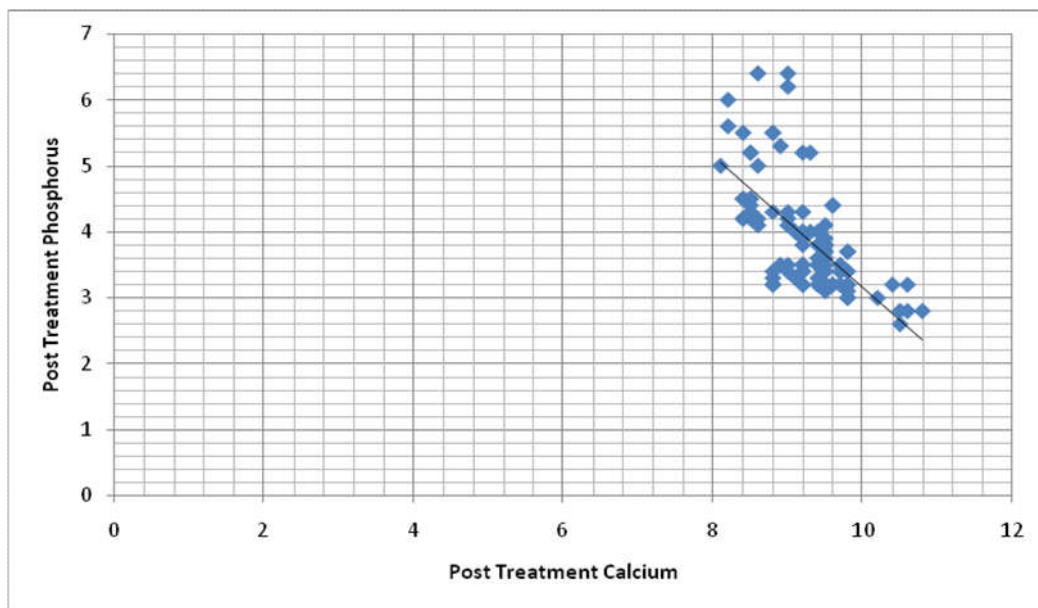


Figure 5. Negative correlation between serum calcium & phosphorus levels (post-treatment)

The serum calcium level was low in pre-treatment ($8.22 \pm 0.69 \text{ mg/dL}$) than post treatment ($9.30 \pm 0.75 \text{ mg/dL}$) with $p < 0.01$ (Table 2; Figure 1). Significant positive correlation was found between the serum calcium levels of pre and post treatment (Table 3; Figure 2). Similarly, the level of serum phosphorus in pre-treatment was higher ($4.86 \pm 0.975 \text{ mg/dL}$) than post-treatment ($3.84 \pm 0.873 \text{ mg/dL}$) with $p < 0.01$ (Table 2, Figure 1). Significant positive correlation was found between the serum phosphorus levels of pre and post treatment (Table 3; Figure 3). However, significant negative correlation was found between serum calcium and phosphorus levels of pre-treatment (Table 3; Figure 4). Similarly, significant negative correlation was found between serum calcium and phosphorus levels of post treatment (Table 3; Figure 5).

DISCUSSION

In this study serum calcium level was increased in post treatment compared to pre-treatment with $p < 0.01$. This result is in accordance with Shirai M *et al.* (1990), Hafiez *et al.* (1990), Ali *et al.* (1997) and Ijaz *et al.* (2004) who reported hypocalcaemia in tuberculosis. However, contradictory to Lind L *et al.* (1990), Meuthen *et al.* (1991), Chan *et al.* (1994), Pruitt *et al.* (1995), Liam *et al.* (1998) and Roussos *et al.* (2001) who reported hypercalcaemia in tuberculosis. Pulmonary tuberculosis is infectious granulomatous disease that alters the level of circulating calcium concentration (Baig, 2006). Hafiez *et al.* reported hypocalcaemia in pulmonary tuberculosis was due to anorexia and inhibition of active metabolites of vitamin-D (Hafiez *et al.*, 1990).

Similarly, Ijaz *et al.* concluded that hypocalcaemia in pulmonary tuberculosis patients was due to malnutrition and malabsorption (Ijaz *et al.*, 2004). The study of Rohini *et al.* (2013), Bhandari S *et al.* (2014) and Godara S *et al.* (2017) have strengthened the finding of present study who has reported low calcium level in pre-treatment and significantly raised level of calcium in post-treatment. Thus, the effect of anti-tubercular treatment has role in calcium metabolism in pulmonary tuberculosis patients. The circulating level of phosphorus was significantly decreased ($p < 0.01$) in post treatment compared to pretreatment in patients with PTB.

This finding is similar to the observations reported by Well HG *et al.* (1923), Sweany *et al.* (1923), Sharma *et al.* (1981) and Meuthen *et al.* (1991) who has reported hyperphosphataemia in tuberculosis. However, contradictory to Goldwin AO *et al.* (2010) who reported hypocalcaemia and hypophosphatemia in pulmonary tuberculosis.¹⁹ Similarly, the result of the present study was also in contrast to Rohini *et al.* (2013)²⁰ and Godara *et al.* (2017) who has reported that the level of serum phosphorus was decreased in pre-treatment and increased in post anti-tubercular treatment. Nevertheless, the result of present study is similar to Bhandari S *et al.* (2014)²¹ who concluded that serum phosphorus level was higher at pre anti-tubercular treatment and decreased to normal level after treatment. This could be due to the destruction of the cells, which liberate intracellular phosphate into the circulation.

Conclusion

In the present study, interesting changes in the levels of serum calcium and phosphorus was found in pre and post anti-tubercular treatment. The serum calcium level of post treatment was significantly increased compared to pre-treatment ($p < 0.01$). However, the post-treatment serum phosphorus level was significantly low compared to pre-treatment ($p < 0.01$). Thus, it signifies the efficacy of anti-tubercular treatment in pulmonary tuberculosis patients to maintain the level of calcium and phosphorus for normal functioning of the vital activities. Moreover, this finding indicates the need of calcium supplements and monitoring of serum calcium and phosphorus levels in PTB patients during anti-tubercular treatment.

Conflict of interest:- None declared.

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