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Original Research Article

Biochemical abnormalities and Vitamin D levels in sputum positive pulmonary tuberculosis

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Abstract

Background: Tuberculosis has been associated with various biochemical abnormalities including low hyponatremia, serum albumin, hypocalcaemia, low vitamin D levels.
Methods: 50 patients aged ≥ 18years of age with of sputum positive pulmonary tuberculosis were included in the study. Renal function, liver function, electrolytes and Vitamin D levels were measured at 0, 2 and 6 months of anti-tuberculosis treatment. The qualitative variables were analysed by chi-square tests. The quantitative variables were analysed by using paired t test. Five percent probability level was considered as statistically significant i.e., $p<0.05$.
Results: The mean age was 38.5 years with a male to female ratio of 1.08:1. Hyponatremia was present in 24% of the patients. The mean total serum protein value were 6.72±0.89,7.42±0.74 and 8.15±0.68 g/dl and serum albumin of 2.97±0.50, 3.37±0.39 and 3.75±0.37 g/dl respectively at 0, 2 and 6 months. The mean serum calcium values observed were 8.2±0.63, 8.82±0.68 and 9.45±0.63 mg/dl at 0, 2 and 6 months respectively. The mean values for vitamin D at 0, 2 and 6 months were 9.14±6.94, 15.33±6.42 and 23.17±6.86 ng/ml respectively. 92% of the patients had low serum levels of vitamin D and 66% of the patients had serum vitamin D levels less than 10 ng/ml at presentation.
Conclusion: Various biochemical abnormalities including hyponatraemia, low serum albumin and protein levels and low serum calcium levels are seen in pulmonary tuberculosis. Vitamin D levels are significantly lower in patients with TB and there is a significant improvement in the vitamin D levels with treatment of TB.
Keywords: Biochemical derangements, calcium metabolism, tuberculosis.

1. Introduction

Tuberculosis (TB) is a global health problem with about 8.6 million people having TB in 2012 and a mortality rate reaching up to 1.3 million [1]. India contributes to the maximum burden of TB in the world with approximately 40% of the populace being infected with TB [1]. There are various typical and atypical clinical presentations of tuberculosis which poses a diagnostic and therapeutic challenge to the physicians. Various biochemical abnormalities have been associated with TB which may range from minimal to profound depending on factors like immune status and a type of disease whether pulmonary or extra pulmonary [2]. Previous studies have reported biochemical laboratory abnormalities such low serum albumin, hyponatraemia, hypocalcaemia, low vitamin D levels, and abnormal liver functions of varying severity in TB [2, 3]. Furthermore observations from meta-analysis suggest that low serum vitamin D levels are associated with higher risk of active tuberculosis [4].

In this background the current study was undertaken to assess the various biochemical abnormalities in TV with specific reference to levels of vitamin D in patients with pulmonary tuberculosis.

2. Materials and Methods

This was a prospective observational study conducted between July 2013 to February 2014 in adult patients aged ≥ 18years of age diagnosed to have sputum positive pulmonary tuberculosis with conventional Ziehl-Neelsen in a tertiary care centre.

2.1 Inclusion Criteria:

1. All patients aged ≥ 18years with sputum positive pulmonary tuberculosis

2.2 Exclusion Criteria:

1. Patients with extrapulmonary or disseminated TB
2. Patients with co-existing co-morbidities like chronic liver disease, chronic kidney disease
3. Patients lost to follow up

Informed consent was obtained from all patients prior to undertaking the study. Demographic data was collected and entered in pre-structured questionnaire. A peripheral venous sample was collected in 2 plain vials using disposable syringe from each subject for, biochemical parameters and Vitamin D respectively levels at the entry of study, after completion of intensive phase (2 months) and at end of treatment (6 months). Serum levels of liver function parameters such as bilirubin, alkaline phosphatase, aspartate transaminase, alanine transaminase, calcium, phosphorus and alkaline phosphatase were conducted by Random access clinical chemistry analyser synchron CX5 (USA).

2.3 Statistical analysis

The statistical analysis was performed using SPSS version 20. The qualitative variables were analysed by chi-square tests. The quantitative variables were analysed by using paired t test (Repeated measure analysis). Five percent probability level was considered as statistically significant i.e., $p<0.05$.

3. Results

The mean age of the patients was 38.5 years. Our study consisted of 50 patients of which 26 (52%) were males and 24(48%) were with a male to female ratio of 1.08:1. The most common age group was 26-35 years followed by 18-25 years. The age distribution of the patients is shown in Table 1. Fever and cough were the most common symptoms followed by anorexia and weight loss (Table 2).

The renal function tests were within normal range for all the patients. The serum sodium values ranged from 121 to 148 meq/L at 0 months. Hyponatremia was present in 24% of the patients at presentation. The sodium levels returned to normal on follow up. The renal function parameters on presentation and follow up have been shown in Table 3.

The liver function tests showed levels within physiological limits. The mean total serum protein value were 6.72±0.89, 7.42±0.74 and 8.15±0.68 g/dl and serum albumin of 2.97±0.50, 3.37±0.39 and 3.75±0.37 g/dl respectively at 0, 2 and 6 months. There was a statistically significant increment in the levels of serum protein and serum albumin when compared between 0, 2 and 6 months of treatment. The liver function parameters on presentation and follow up have been shown in Table 4.

The mean serum Calcium values observed were 8.2±0.63, 8.82±0.68 and 9.45±0.63 mg/dl at 0, 2 and 6 months respectively. A statistically significant increase in serum calcium levels was found at 0, 2 and 6 months. The mean values for vitamin D at 0, 2 and 6 months were 9.14±6.94, 15.33±6.42 and 23.17±6.86 respectively. 92% of the patients had low serum levels of vitamin D and 66% of the patients had serum vitamin D levels less than 10 ng/ml at presentation. There is a significant improvement in the vitamin D levels with treatment at 2 and 6 months with 28% and 68% of the patients having normal levels of serum vitamin D. The serum calcium phosphorous and vitamin D levels in the patients with pulmonary tuberculosis is shown in Table 5.

Table 1: Age Distribution of patients with pulmonary tuberculos

Age Group (years)	Number of patients (%)
18-25	11(22)
26-35	15(30)
36-45	9(18)
46-55	6(12)
56-65	7(14)
66-75	0(00
76-85	2(4)

Table 2: Presenting symptoms of patients with pulmonary tuberculosis

Parameters	Frequency	Percent
Fever	49	98.0
Cough	48	96.0
Dyspnoea	11	22.0
Chest pain	4	8.0
Anorexia	46	92.0
Hemoptysis	5	10.0
Weight Loss	42	84.0

Table 3: Mean and Standard Deviation (SD) of renal function tests at 0, 2 and 6 months of treatment in study group

Parameter	0 month	2 months	6 months	P-value (Overall)*	P-value** (0 months & 2 months	P-value** (0 months & 6 months	P-value** (2 months & 6 months
	(mean±SD)	(mean±SD)	(mean± SD)				
Serum Urea (mg/dl)	26.00±8.93	25.28±9.19	24.48±8.99	0.27	0.29	0.11	0.24
Serum Creatinine (mg/dl)	0.64±0.27	0.62±0.21	0.55±0.22	0.01	0.45	0.01	0.02
Serum Na^+ (mEq/L)	137.86±5.68	139.54±3.36	140.78±2.60	<.001	0.01	<.001	0.00
Serum K^+ (mEq/L)	4.14±0.43	4.18±0.31	4.19±0.24	0.58	0.48	0.30	0.59

*p value calculated by repeated measure analysis

**p value calculated by post hoc analysis

Table 4: Mean and Standard Deviation(SD) of liver function tests at 0, 2 and 6 months of treatment in study group

Parameter	0 month	2 months	6 months	P-value* (Overall)	P-value** (0 months & 2 months	P-value** (0 months & 6 months	P-value** (2 months & 6 months
	(mean±SD)	(mean±SD)	(mean±SD)				
T.bil/D.bil (mg/dl)	0.47±0.14	0.45±0.11	0.46±0.09	0.57	0.32	0.71	0.55
ALT(IU/L)	30.12±13.31	26.62±9.67	27.18±9.80	0.03	0.01	0.04	0.49
AST(IU/L)	38.88±18.22	32.70±12.42	30.32±10.44	<.06	0.07	<.06	0.07
T. Protein(g/dl)	6.72±0.89	7.42±0.74	8.15±0.68	<.001	<.001	<.001	<.001
Albumin(g/dl)	2.97±0.50	3.37±0.39	3.75±0.37	<.001	<.001	<.001	<.001

*p value calculated by repeated measure analysis

**p value calculated by post hoc analysis

Table 5: Mean and Standard Deviation of Calcium, phospate and vitamin D levels at 0, 2 and 6 months of treatment in study group

Parameter	0 month	2 months	6 months	P-value* (Overall)	P-value** (0 months & 2 months	P-value** (0 months & 6 months	P-value** (2 months & 6 months
	(mean±SD)	(mean±SD)	(mean±SD)				
Serum Ca^{2+}(mg/dl)	8.20±0.63	8.82±0.68	9.45±0.63	0.04	<.001	<.001	<.001
Serum $Po4^{2-}$(mg/dl)	4.61±0.88	4.39±0.61	4.43±0.75	0.10	0.04	0.16	0.66
Vitamin D (ng/dl)	9.14±6.94	15.33±6.42	23.17±6.86	<.001	<.001	<.001	<.001

*p value calculated by repeated measure analysis

**p value calculated by post hoc analysis

4. Discussion

Majority of the patients were in the young age group (16-35 years). Previous studies have noted that 10% of tuberculosis cases are in the under twenties, with the most affected age group being the 20–49-year-old, accounting for 70% of all those affected [5]. Fever and cough were the most common symptoms followed by anorexia and weight loss which is similar to observations made in previous studies [6].

The renal function parameters were relatively within normal range for all the patients. Previous studies have also documented the relatively safety of 1st line anti-tubercular therapy with nephrotoxicity being primarily seen with Streptomycin and second line anti tubercular drugs [7]. Hyponatraemia was present in 12 patients at presentation in this study. The patients were however asymptomatic and their sodium levels returned to normal on follow up. This observation supports the findings of previous studies which show up-to 51% of the patients may have hyponatraemia [8].

There was a significant increase in total protein and albumin levels during the course of treatment. These changes could be attributed to improvement in nutritional status and reversal of albumin to globulin ratio is common in tuberculosis with normalization of this ratio with treatment. These observations are in agreement with previous studies [9,10]

There was statistically significant increase over time in serum calcium levels in the study. Earlier studies have also reported hypercalcemia with in patients with tuberculosis [11]. An association between 25 hydroxyvitamin D (25[OH] D) levels and TB has been described in few studies and Vitamin D deficiency has been implicated as a risk factor for tuberculosis [12]. Vitamin D is postulated to reduce the viability of *M. tuberculosis* by enhancing the fusion of the phagosome and lysosome in

infected macrophages and promoting autophagy in monocytes as well as playing an important role in the expression of cathelicidin and defensin-2 which are antimicrobial peptides against Mycobacterium tuberculosis [13,14]. In our study, 92% of the patients had low levels of serum vitamin D and almost two-third of the patients had vitamin D levels less than 10 ng/dl at presentation. There was a significant improvement in the Vitamin D levels with treatment at 2 and 6 months. Previous studies have drawn attention towards widespread prevalence of Vitamin D deficiency and have also results suggested a possible therapeutic role for vitamin D in the treatment of TB [15,16].

5. Conclusion

Various biochemical abnormalities including hyponatraemia, low serum albumin and protein levels and low serum calcium levels are seen in patients with pulmonary tuberculosis. Vitamin D levels are significantly lower in patients with TB and there is a significant improvement in the vitamin D levels with treatment of TB.

Conflict of Interest: Nil

Acknowledgment: Nil

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