

## A Study of Serum Magnesium levels in Pulmonary Tuberculosis

Manjunath M<sup>1</sup>, Krupashree G<sup>2\*</sup>, Sushma S Biradar<sup>3</sup>, Mohammed Nizamuddin Attar<sup>4</sup>

<sup>1,2</sup> Senior Resident, Senior Resident, Dept of General Medicine, KoIMS Madikeri

<sup>3,4</sup> Senior Resident, Senior Resident, Dept of General Medicine, KIMS Hubli

\*Corresponding Author and reprint request to: Krupashree G, # 1860, Devrajnagar  
Doddballapur Bengaluru rural-561203

### ABSTRACT

**Background:** Tuberculosis, a public health emergency, has continued to be burden for society both in terms of mortality and morbidity. Once diagnosed, the follow up for assessment is usually done clinically or methods which are not very effective or require expertise.

**Objective:** To estimate Serum Magnesium levels in Pulmonary Tuberculosis.

**METHODS:** This prospective study was conducted from inpatient and outpatient attached to Bapuji Hospital and Chigateri General Hospital attached to J.J.M. Medical College, Davangere attending the RNTCP clinics and inpatients. In the present study, 50 patients and 50 controls were included after fulfilling the inclusion and exclusion criteria. Appropriate investigations were done and patients were followed up for 2 months. Serum Magnesium levels were estimated at the start of treatment and 2 months after the treatment.

**RESULTS:** The mean age in study group was  $39 \pm 14.4$  years with male predominance. ESR was elevated in all patients and significant biochemical abnormality detected was raised globulin levels. The Mean serum magnesium levels pre-treatment was  $1.76 \pm 0.24$  mg/dL and post treatment were  $2.00 \pm 0.13$  mg/dL. Magnesium levels were lower with more severe disease and with prolonged duration of illness.

**CONCLUSION:** A significant inverse relationship was observed with duration of illness and severity of disease with serum magnesium levels.

**KEYWORDS:** Serum Magnesium, Pulmonary Tuberculosis, illness, duration

**INTRODUCTION:** Tuberculosis is an infectious disease caused by bacteria *Mycobacterium tuberculosis* is considered to be one of the deadliest infectious diseases worldwide. Most commonly *M. tuberculosis* is spread from person to person by airborne transmission of droplet nuclei.

TB remains one of the biggest global human killers accounting for 10 million new cases of active TB and 1.4 million TB-related deaths with an incidence of cases per 100,000 inhabitants. Tuberculosis remains a major global public health problem despite an effective chemotherapy and relatively low transmission rate compared with other contagious diseases. The observed decline in the global TB pandemic during the last century is considered to be largely due to improved living standards and the use of antibiotics in the 20<sup>th</sup> Century. TB today is a disease of poverty, with more than 95% of total TB cases occurring in developing countries and more than half of all deaths occurring in Asia. [1,2] In 1993, TB was declared by the World Health Organization (WHO) a global public health emergency. But while TB has gradually disappeared from the health agenda of countries in the developed world, TB has increased in the developing nations and has become the most important cause of death. [3]

Lately serum magnesium has gained importance in various bodily functions especially in diabetes, critical care setup wherein a few studies, advocating its role in immune regulation, as

a supplementing the same to improve the outcomes. But the literature in Indian setup in this regard is sparse. [4,5] Therefore, this study was planned to estimate Serum Magnesium levels in Pulmonary Tuberculosis.

**MATERIALS AND METHODS:** This prospective study was conducted from inpatient and outpatient attached to Bapuji Hospital and Chigateri General Hospital attached to J.J.M. Medical College, Davangere attending the RNTCP clinics. In the present study, 50 patients and 50 controls were included and following observations were made with respect to various parameters. Controls were recruited from nursing staff, teaching staff, students, postgraduates. 50 newly detected cases of pulmonary tuberculosis, who met the inclusion and exclusion criteria were selected.

**Inclusion criteria:** Sputum positive TB

**Exclusion criteria:** Old pulmonary TB, Immunosuppressive states such as HIV, DM, Sepsis, Chronic renal failure, Patients on diuretic therapy, COPD, Asthma, Malnutrition

Detailed history regarding duration of illness, complains, drug history, family history of diabetes and TB smoking, alcohol were recorded. Detailed general physical examination and systemic examination was carried out in all cases.

Respiratory signs suggestive of TB were

- Signs of fibrosis
- Signs of cavity
- Signs of consolidation especially in apical regions
- Apical crepitations or post tussive crepitations

This history and examination was recorded in the form of questionnaire as per proforma.

The radiographs taken were evaluated and the severity of disease was graded radiologically as:

**GRADE I:** Minimal disease- infiltration confined to a small part of lung, no cavitation

**GRADE II:** moderately advanced disease- disseminated infiltrative lesions occupying large areas but total area of involvement being less than that of one lung, or cavitary lesions with adjacent consolidation where cavities are less than 3cm in diameter and or/ occupy less than 1/3<sup>rd</sup> area of lung

**GRADE III:** Far advanced disease- disseminated infiltrative lesions occupying an area equivalent to more than one lung, or cavitary lesions of more than 3cm in diameter and or / total area of involvement with cavitary lesions being more than 1/3<sup>rd</sup> of lung volume

All patients with features suggestive of PTB were investigated according to RNTCP protocol and sputum positivity was determined.

Patients who were sputum positive and fulfilling the criteria were further investigated with Blood investigations including Complete blood count, Renal function test, liver function tests, serum electrolytes, ESR and serum magnesium levels.

They were started on DOTS regimen with (HRZE)<sub>7</sub> for 2 months and (HRE)<sub>7</sub> for 4 months. Serum magnesium levels were repeated at 2 months of treatment and recorded.

The controls were selected from students, doctors and nursing staff attached to J.J.M.M.C Estimation of serum magnesium was done using VITROS Mg slide method.

**Statistical analysis:** Results are presented as Mean, SD and range values for continuous measurements and frequencies as number and percentages. Intergroup comparisons are done by unpaired t test and Paired t test for intra group comparisons. Categorical data was analysed by chi-square test. Simultaneous multiple group comparisons are done by One-way ANOVA. A P- value of 0.05 or less was considered to be statistically significant. Data was analysed by SPSS (Version,17) Software.

**RESULTS:** The average age in control group was  $30.9 \pm 7.8$  years and in study group was  $39 \pm 14.4$  years. Majority of patients 56% (29) were below 40 years and 44% were above 40 years. In study group, majority were males with 21 females and 29 males. In control group, there were 31 males and 19 were females.

**TABLE 1: AGE DISTRIBUTION IN CASES & CONTROLS**

	Cases		Controls	
	Mean	SD	Mean	SD
Age (Yrs)	39.4	14.4	30.9	7.8
Range	18 - 80 yrs		18 - 46 yrs	

In our study, 30 (60 %) cases presented within 2 months of illness and remaining 20 (40 %) had illness for more than 3 months.

In our study, Anaemia was seen in 20 (40%) patients with mean HB of  $11 \pm 2.79$  g/dL. Thrombocytosis was observed in 6 (12 %) patients with mean platelet counts of 2.9lakhs/millimetre. Mean Total leucocyte counts were 7342 per millilitre.

Mean albumin levels was  $3.95 \pm 0.589$  g/dL and Hypoalbuminemia was observed in 9(18%) patients with min value of 2.8g/dL. Mean globulin levels were  $3.65 \pm 1.042$  g/dL and they were elevated in 12 (24%) patients. A:G ratio was altered in most cases 46 (92%) cases with reversal in 10 (20%) patients.

ESR was elevated in all the cases with mean ESR of  $64.72 \pm 18.350$  mm/hr. the lowest being 30 mm/hr and highest being 100 mm/hr.

<b>TABLE 2: DISTRIBUTION OF VARIOUS BLOOD PARAMETERS IN STUDY GROUP</b>				
	MEAN	SD	MIN	MAX
HEMOGLOBIN (g/dL)	11	2.79	6	15
TOTAL LEUCOCYTE COUNT (thousands/mm <sup>3</sup> )	7342	1997.2	3800	11300
PLATELETS (lakhs/mm <sup>3</sup> )	2.9	1.090	1	5.2
UREA (mg/dL)	25	0.890	15	40
CREATNINE (mg/dL)	1	0.340	0.60	1.5
SODIUM (mmol/L)	137.4	3.275	129	145
POTASSIUM (mmol/L)	3.9	0.340	3.3	4.6
CHLORIDE (mmol/l)	99.8	4.209	92	107
TOTAL PROTEIN(g/dL)	7.6	1.127	5.1	11.7
ALBUMIN(g/dL)	3.95	0.589	2.8	5
GLOBULIN(g/dL)	3.65	1.042	2.2	7.8
A: G	1.16	0.309	0.5	1.7
ESR (mm/hr)	64.72	18.350	30	100

In our study it was observed that Grade II lesions were more frequent (48 %) followed by Grade I (30 %) and then Grade III (22%).

Non cavitary lesions were found in 62 % patients and Cavitary lesions were found in 38 %.

Bilateral lesions were observed in 44 % patients and right sided in 36 % patients and left sided in 20 % patients.

The mean serum levels in control population was  $1.97 \pm 0.14$  mg/dL and in the study population was  $1.76 \pm 0.24$ . Study population had lower serum magnesium levels, which was statistically significant, when compared to control population .

TABLE 3: SERUM MAGNESIUM LEVELS IN CASES AND CONTROLS							
	No.	Mean	SD	Minimum	Maximum	t value	P value
Cases	50	1.76	0.24	1.23	2.14	5.47	< 0.001, HS
Controls	50	1.97	0.14	1.69	2.3		
Unpaired t test							

The mean serum magnesium levels in study population were  $1.76 \pm 0.23$  mg/dL in males and  $1.75 \pm 0.25$  mg/dL in females. The mean serum magnesium levels in control groups were  $1.96 \pm 0.12$  mg/dL and in females were  $1.98 \pm 0.17$ mg/dL. No statistical significance was found between the two.

TABLE 4: MAGNESIUM LEVELS IN RELATION TO GENDER						
Group	Sex	No.	S. MAGNESIUM (mg/dL)		M vs F	
			Mean	SD	T	P
Cases	Male	29	1.76	0.23	0.04	0.97, NS
	Female	21	1.75	0.25		
Controls	Male	31	1.96	0.12	0.59	0.56, NS
	Female	19	1.98	0.17		
Unpaired t test						
* P > 0.05, NS						

**DISCUSSION:** In this prospective study, 50 sputum positive patients and 50 healthy patients were included and data was collected and characteristics were compared.

Incidence of pulmonary TB was seen in young adults and had male predominance. The mean age in study group was  $39 \pm 14.4$  years with male predominance. Majority of patients 56% (29) were below 40 years and 44% were above 40 years. This is in accordance with national statistics which shows adolescent and young adult age was affected more than elderly. In our study most of patients presented within 2 months of illness and prolonged duration of illness was associated with lower of serum magnesium. In a study conducted by Irfan et al at Yenepoya medical college also had similar observations.[6]

In study population cough (64 %) was the most common symptom followed by fever (60 %), weight loss (44%), hemoptysis (22%), chest pain (24%). Pallor (44 %) and clubbing (40 %) were significant clinical signs found in this study population. In this study as only naïve TB patients were included, clinical stigmata of old PTB such as signs of volume loss were not found.

Haematological parameters which correlate with detection of TB or disease severity or cure rate have been of particular interest. In one of pioneering studies on electrophoresis study of protein levels in TB patients it was observed that before treatment of the tuberculous process the albumin/alpha-2 globulin ratios were low and the gamma globulin levels were increased. As improvement occurred, albumin/alpha-2 globulin ratios increased and gamma globulin values decreased. [7] In study by Ekwempu et al, where serum albumin, globulin and A: G ratio were studied and compared with control group. The albumin was significantly higher in study group compared to control ( $2.95 \pm 0.86$  and  $2.75 \pm 0.65$  g/dl) while total protein and globulin was significantly lower ( $6.17 \pm 1.66$  and  $6.76 \pm 0.86$  g/dl,  $p = 0.011$  and  $3.22 \pm 1.9$  and  $3.97 \pm 0.86$  g/dl with  $p = 0.016$ ). Patients seropositive for HIV antibody had a decrease in serum total protein, albumin and globulin but high albumin/globulin ratio. [8] In a study for screening and evaluation of proteins for novel potential biomarkers serum albumin was also validated as one of the potent candidate for prognostic estimator. [9] In a study done by R.K.Vyas et al [10], there was significant difference in the mean value of serum Albumin/Globulin ratio ( $1.790 \pm 0.2512$ ) in control group & mean  $\pm$  SD value in study group is ( $1.158 \pm 0.4871$ ). [11] Similar observations were seen in our study with Mean albumin levels was  $3.95 \pm 0.589$  g/dL, Mean globulin levels were  $3.65 \pm 1.042$  g/dL and alteration of A:G ratio in majority of cases. Statistically significant association with extent and serum magnesium levels were found with total protein, globulin. The A:G ratio was also altered However no statistically significant association was found with severity of disease or magnesium levels.

Anaemia is a common hematologic complication among TB patients and is a strong risk factor for mortality. It is due to cytokines released by activated macrophages which causes diversion of iron into iron stores in the reticulo-endothelial system resulting in decreased iron concentration in the plasma, inhibition of erythroid progenitor cell proliferation and in appropriate production and activity of erythropoietin. In our study anaemia was seen in 40% patients, thrombocytosis in 12% patients, ESR was elevated in all the cases. Raised ESR is a sensitive marker for TB but not specific. Thrombocytosis and Raised ESR are due to chronic inflammatory process seen with TB. This is in accordance with a Canadian study done by Ajibola Alabi et al [12] in which among children and adolescent were taken into consideration but the found no utility of CBC panel with respect to the treatment and also with an Ethiopian study by Feven Abay et al [13]. In a case-control study by Yutika et al, 60% of anaemia in sputum positive cases was iron deficiency anaemia, While 22% of anaemic sputum negative cases had iron deficiency anaemia and there was significant delay in sputum conversion associated in anaemic patients. [14] Also in another study of 21,946 IDA patients in Taiwan, it was noted that incidence of TB and IDA association was significantly stronger within the 5 years after new IDA diagnosis for both genders and all age groups hence showing anemia to be a risk factor for acquiring the illness. [15]

The mean serum magnesium levels in control population was  $1.97 \pm 0.14$  mg/dL and in the study population was  $1.76 \pm 0.24$  and levels were lower in patient with severe form of illness and also with longer duration of disease. The Mean serum magnesium levels pre-treatment was  $1.76 \pm 0.24$  mg/dL and post treatment was  $2.00 \pm 0.13$  mg/dL. This is similar to studies by Irfan et al [6], Ali Raza Memon et al. [11] Most of these studies attribute the variation in serum magnesium levels to associated malnutrition either due to socioeconomic status or due to anorexia associated with disease.

**Conclusion:** Serum magnesium levels were studied in 50 newly detected pulmonary tuberculosis cases and compared with controls and after start of Antitubercular treatment. A

significant inverse relationship was observed with duration of illness and severity of disease with serum magnesium levels.

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## **DECLARATIONS**

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*Conflict of interest:* None

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