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ORIGINAL ARTICLE

Association of Serum Magnesium with Sputum Smear Conversion at the end of 2nd month among Smear Positive Pulmonary Tuberculosis Patients

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Abstract

Background: *The progress of an infectious condition is partly affected by the overall nutrition of the host. Many of the essential trace elements like zinc, copper, magnesium influence the function of the immune system. Magnesium levels also influence tuberculosis. Tuberculosis and malnutrition is well recognized to go hand in hand as one can lead to the other.*

Methods: *This prospective observational study was conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from July 2018 to June 2020. A total of 85 new smear positive pulmonary tuberculosis cases were enrolled in this study. Serum Magnesium was measured by the colorimetric method using Xylidyl Blue-I. Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-23).*

Results: *In this study 74(87.1%) patients had sputum smear conversion and 11(12.9%) had delayed sputum smear conversion at the end of intensive phase of treatment. Mean initial serum magnesium was 1.95±0.26 mg/dl and mean serum magnesium at the end of 2nd month was 2.07±0.24 mg/dl. Significant association was found in sputum smear conversion with smoking, initial serum magnesium level and serum magnesium level at the end of 2nd month. There was no significant association of sputum smear conversion with diabetes mellitus and BMI. In multivariate logistic regression analysis, initial low serum magnesium level and smoking were found to be independent predictors for sputum smear non-conversion at the end of 2nd month but low serum magnesium at the end of 2nd month was not found to be independent predictor for sputum smear non-conversion.*

Conclusion: *Hypomagnesaemia at the initiation of anti-tubercular therapy was significantly associated with sputum smear non-conversion at the end of intensive phase of treatment.*

Key words: *Smear positive pulmonary tuberculosis, Smear conversion, Serum magnesium*

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Introduction:

Worldwide, tuberculosis is the leading cause of death from a single infectious agent. Millions of people continue to fall sick with TB each year. In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million) among HIV-negative people and there were an additional 300000 deaths from TB (range, 266000–335000) among HIV-positive people.[1] Tuberculosis is a curable and preventable disease caused by infection with mycobacteria from the Mycobacterium tuberculosis complex.[2] Magnesium is the eight common element in the crust of earth, fourth most abundant cation in human body and second abundant intracellular cation. It may exist as protein bound, complexed or in free form. It is primarily found within the cell, where it acts as a counter ion for the energy-rich ATP and nuclear acids. It is a cofactor in more than 300 enzymatic reactions. Magnesium critically stabilizes enzymes, including many ATP generating reactions.[3] It is also key component in various reactions that require kinases and important factor in both cellular and humoral immune reactions .[4,5] Magnesium participates in immune responses in numerous ways: as a cofactor for immunoglobulin synthesis, C'3 convertase, immune cell adherence, antibody-dependent cytolysis, IgM lymphocyte binding, macrophage response to lymphokines, T helper-B cell adherence, binding of substance P to lymphoblasts and antigen binding to macrophage RNA.[6]

The development of tuberculosis passes through several distinct stages-initial infection, entry of the pathogen into tissues and cells, survival and replication within macrophages, subversion of immune defense mechanisms, establishment of dormancy, reactivation from the latent state and induction of gross tissue necrosis that is responsible for cavitary formation, entry of bacilli into the sputum and transmissibility of infection. The progression of the disease process to resolution and healing or to progression with extensive necrosis is determined by the nature of the host immune system.[7]

Hypomagnesaemia promotes low-grade inflammation as demonstrated by elevated concentrations of C-Reactive Protein (CRP) and TNF-alpha.[8,9] Mg improves markers of inflammation and oxidative stress.[10] Irfan et al. observed that, a significant inverse relationship was observed between the level of serum magnesium with duration of illness and extent of the disease.[11] Memon et al. concluded that decreased serum magnesium is an important finding in pulmonary tuberculosis patient.[12] Agrawal et al. showed that lower serum magnesium level at the initiation of tuberculosis therapy was significantly associated with delayed sputum conversion among smear positive pulmonary tuberculosis patients.[13] That's why one needs to find out the association of serum magnesium level with delaying the sputum conversion in order to lay the foundation of effective intervention in our country. The main objective of this study is to find out the association of serum magnesium with sputum smear conversion at the end of 2nd month among smear positive pulmonary tuberculosis patients.

Methods:

This prospective observational study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period from July 2018 to June 2020. New cases of sputum smear positive pulmonary tuberculosis patient aged e" 18 years who attended in NIDCH both indoor & outdoor and who gave informed consent were enrolled in this study. MDR TB, XDR TB, CAT -1 failure, retreatment case, pregnancy, chronic renal failure and patient with long term corticosteroid therapy were excluded from the study. A total of 95 new smear positive pulmonary tuberculosis patients attending in the above hospital were included in this study. Among them 10 (7 patients were lost to follow up and 3 were died) patients were excluded from this study. Finally 85 patients were enrolled in the study. Having obtained ethical clearance from the Ethical Committee and informed written consent from the patients, the data collection was commenced. All patients were subjected to detailed history taking, physical examination and necessary investigations. Investigations included complete blood count, random blood sugar, sputum for AFB, chest x-ray, s. creatinine, SGPT, Sputum for Gene Xpert and serum magnesium level. Patients were treated by Cat-1 anti TB treatment. At the end of 2nd month of treatment all patients were followed up clinically and sputum for AFB and serum magnesium were done. Serum Mg levels were measured by the colorimetric method using Xylidyl Blue - I. The collected data of each patient was recorded systematically. All data were analyzed by using computer based SPSS -23 (statistical package for social sciences). Data were presented in frequency, percentage and mean and standard deviation as

applicable. Chi square test was used for categorical variables. Unpaired t-test was used for continuous variables as shown cross tabulation. Multivariate logistic regression analysis was used for sputum smear non-conversion and the results were expressed as odds ratios with 95% confidence intervals (CI). P value of less than 0.05 was considered as statistically significant.

Results:

Table-I

Demographic characteristics of the study patients (n=85)

Demographic characteristics	Number of patients	Percentage
Age (years)		
≤20	2	2.4
21-40	42	49.4
41-60	40	47.1
>60	1	1.2
Mean age (years)	40.0±12.5	
Range (min-max)	19.0-70.0	
Sex		
Male	72	84.7
Female	13	15.3

Table II

Distribution of serum magnesium among the study patients (n=85)

Serum magnesium (mg/dl)	Mean±SD
Initial	1.95±0.26
Range (min-max)	1.1-2.55
At the end of 2nd month	2.07±0.24
Range (min-max)	1.35-2.6

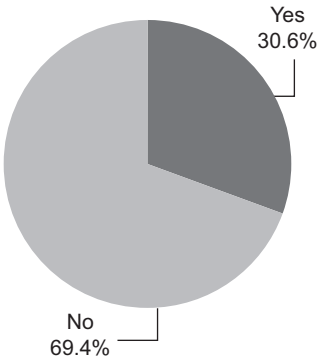

Fig.-1: *Pie chart showing smoker among the study patients*

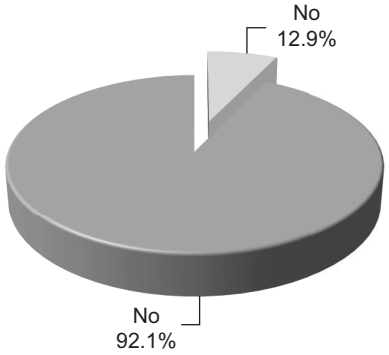

Fig.-2: *Pie chart showing diabetes mellitus among the participants*

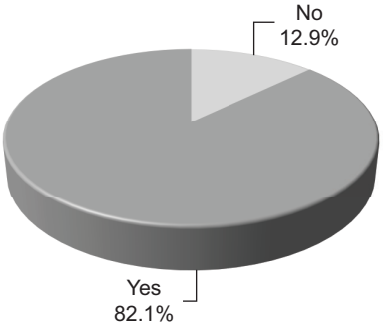

Fig.-3: *Pie chart showing sputum smear conversion at the end of 2nd month*

Table-III

Association between diabetes mellitus and sputum smear conversion (n=85)

Diabetes mellitus	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
Yes	2	18.2	4	5.4	0.123ns
No	9	81.8	70	94.6	

(ns= not significant; p value reached from chi square test)

Table-IV

Association between smoking and sputum smear conversion (n=85)

Smoker	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
Yes	7	63.6	19	25.7	0.017[s]
No	4	36.4	55	74.3	

(s= significant; p value reached from chi square test)

Table-V

Association between initial BMI and sputum smear conversion (n=85)

BMI (kg/m^2)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<18.5	6	54.5	18	24.3	
18.5-24.9	5	45.5	53	71.6	0.105[ns]
≥25.0	0	0.0	3	4.1	

(ns= not significant; p value reached from chi square test)

Table-VI

Association between BMI at the end of 2nd month and sputum smear conversion (n=85)

BMI (kg/m^2)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<18.5	4	36.4	16	21.6	
18.5-24.9	7	63.6	54	73.0	0.450[ns]
≥25.0	0	0.0	4	5.4	

(ns= not significant; p value reached from chi square test)

Table-VII

Association between initial serum magnesium level and sputum smear conversion (n=85)

Initial serum magnesium (mg/dl)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<1.82	10	90.9	12	16.2	
1.82-2.43	1	9.1	60	81.1	
>2.43	0	0.0	2	2.7	
Mean±SD	1.53	±0.24	2.01	±0.19	0.001[s]

(s= significant; p value reached from unpaired t-test)

Table-VIII

Association between serum magnesium level at the end of 2nd month and sputum smear conversion (n=85)

Serum magnesium at the end of 2nd month (mg/dl)	Sputum non conversion(n=11)		Sputum conversion (n=74)		p value
	n	%	n	%	
<1.82	8	72.7	7	9.4	
1.82-2.43	3	27.3	64	86.5	
>2.43	0	0.0	3	4.1	
Mean±SD	1.69	±0.19	2.13	±0.20	0.001[s]

(s= significant; p value reached from unpaired t-test)

Table-IX

Multivariate regression analysis for sputum smear non-conversion (n=85)

Variable	Adjusted OR	95% CI		P value
		Lower	Upper	
Smoking	7.377	1.038	52.451	0.046[s]
Initial low serum magnesium level	37.648	3.081	99.087	0.004[s]
Low serum magnesium level at the end of 2nd month	4.517	0.682	29.894	0.118[ns]

(s= significant, ns= not significant, OR=Odd's Ratio; p value reached from multivariate logistic regression analysis)

Discussion:

Early diagnosis and effective treatment of TB remains the key to success for infection control. For assessment of outcome of TB treatment, sputum smear microscopy at two month of DOTS treatment is a very important parameter.[13]

This prospective observational study was carried out with an aim to determine the serum magnesium level in smear positive pulmonary tuberculosis patients and to observe the smear conversion at the end of 2nd month of anti-tubercular therapy. This study also finds out find out any association of serum magnesium status in non-converter patients. In this study it was observed that almost half (49.4%) of the patients belonged to age 21-40 years. The mean age was found 40.0±12.5 years with range from 19 to 70 years. Almost similar study conducted by Guler et al. which showed the mean age was found 42.8±16.4 years.[14] In the present study it was observed that majority 72(84.7%) patients were male and 13(15.3%) were female. Male to female ratio was 5.5:1. In a study Agrawal et al. which showed most participants (67%) were male and 33.0% were female.[13] This study showed more than two third (68.2%) patients had initial BMI 18.5-24.9 kg/m^2, 24(28.2%) had <18.5 kg/m^2 and 3(3.5%) had e"25.0 kg/m^2. Almost three fourth (71.8%) patients had BMI 18.5-24.9 kg/m^2, 20(23.5%) had <18.5 kg/m^2 and 4(4.7%) had e"25.0 kg/m^2 at the end of 2nd month.

In this current study it was observed that 26(30.6%) patients were smoker and 59(69.4%) were non-smoker. Bouti et al. documented that smoker was 36.1%.[15] Another study reported by Azarkar et al. which showed smoker was 14(16.5%).[16] In this study it was observed that only 6(7.1%) patients had diabetes mellitus.

In this study it was observed that 74(87.1%) patients had sputum conversion at the end of 2nd month. Ndubuisi et al. found sputum conversion rate among new smear positive pulmonary tuberculosis patients at the end of 2nd month post therapy was 86.9%.[17] Kuaban et al. also showed similar results.[18]

In this study it was observed that mean initial serum magnesium was found 1.95±0.26 mg/dl with range from 1.1 to 2.55 mg/dl. The mean serum magnesium at the end of 2nd month was found 2.07±0.24 mg/dl with range from 1.35 to 2.6 mg/dl.

Irfan et al. reported that serum magnesium was 1.633±0.065 mg/dl.[11] Another study documented by Memon et al. where they found serum magnesium was 1.21±0.083 mg/dl.[12]

In this present study it was observed that 2(18.2%) patients had diabetes mellitus in sputum non-conversion and 4(5.4%) in sputum conversion group. The difference were not statistically significant ($p>0.05$) between two group. In my study it was observed that 7(63.6%) patients were smoker in sputum delayed conversion group and 19(25.7%) in sputum conversion group. The difference were statistically significant ($p<0.05$) between two group. Metanat et al. narrated that there was a significant delay in sputum conversion time between smoker and non-smoker.[19] Anandaraj et al. described smoking was significantly associated with delayed sputum smear conversion at the end of intensive phase.[20]

In this current study it was observed that initial BMI <18.5 kg/m^2 was found 6(54.5%) patients in sputum not conversion and 18(24.3%) in sputum conversion group. The difference was not statistically significant ($p>0.05$) between two group. At the end of 2nd month, BMI 18.5-24.9 kg/m^2 was found 7(63.6%) patients in sputum non-conversion and 54(73.0%) in sputum conversion group. The difference was not statistically significant ($p>0.05$) between two group.

Our study showed that mean initial serum magnesium was found 1.53±0.24 mg/dl in sputum non-conversion and 2.01±0.19 mg/dl in sputum conversion group. The difference were statistically significant ($p<0.05$) between two group. The mean serum magnesium at the end of 2nd month was found 1.69±0.19 mg/dl in sputum non- conversion and 2.13±0.20 mg/dl in sputum conversion group. The difference was statistically significant ($p<0.05$) between two group. Delayed sputum smear conversion occurred in 11(12.94%) sputum smear positive PTB patients. Among them 10 delayed sputum smear conversion patient had initial serum magnesium levels <1.8 mg/dl and 8 had serum magnesium levels < 1.8 mg/dl at the end of 2nd month. In the study Memon et al. (2014) described that serum magnesium was found significantly lower in patients as compared with the controls.[12] In the study Agrawal et al. showed that lower serum magnesium level at the initiation of tuberculosis therapy was significantly associated with delayed sputum conversion among smear positive pulmonary tuberculosis patients.[13]

In multivariate logistic regression analysis, initial low serum magnesium level and smoking were found to be independent predictors for sputum smear non-conversion at the end of 2nd month. Among the predictors, initial low serum magnesium level was the strongest predictor of sputum smear non-conversion. However, low serum magnesium level at the end of 2nd month was not found to be independent predictor for sputum smear non-conversion at the end of intensive phase of the treatment.

Conclusion

Initial low serum magnesium level was significantly associated with sputum smear non-conversion at the end of 2nd month. The underlying mechanism responsible for the association of initial low magnesium level with significant delay in the sputum smear conversion yet to be discovered.

Conflict of Interest: The authors of this paper have declared that there is no conflict of interest to any of the authors.

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