STUDY OF HIGH SENSITIVE C-REACTIVEPROTEIN (HSCRP)AS PROGNOSTIC MARKER IN PULMONARY TUBERCULOSIS PATIENTS

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Abstract- Tuberculosisis an infectious disease caused by Mycobacterium tuberculosis. It is the major public health problem and ninth leading cause of death worldwide. TB is highest burden in India. Mycobacterium tuberculosisusually affects the lung and causes pulmonary tuberculosis but other organs are involved in up to one third of cases. hsCRPis an acute phase protein and inflammatory markers for both acute and chronic inflammation. hsCRP is a sensitive indicator of inflammation in pulmonary tuberculosis and proper evaluation of hsCRP in pre and post treatment indicates therapeutic response.
Aim- To estimate serum level of hsCRP in pre and post treatment of newly diagnosed pulmonary tuberculosis patients.
Material & methods:- The present study was conducted in Department of Biochemistry, Department of Pulmonary Medicine, SGT Medical College, Hospital & Research Institute, SGT University, Budhera, Gurugram and District TB Centre, Gurugram, Haryana, India. The 100 newly diagnosed pulmonary tuberculosis patients were included of age group more than 15 years from OPD, IPD and DOTS centre of SGT Medical College, Hospital & Research Institute, SGT University, Budhera, Gurugram and District TB Centre, Gurugram. The venous blood sample was collected as per guidelines of RNTCP (DOTS) in pre and post treatment. The level of serum hsCRPwas analyzed by ELISA method (Calbiotech ELISA KIT).
Result:- The increased level of serum hsCRP in pre-treatment (8.69±4.85 mg/L) compared to post treatment (3.86±2.04 mg/L) with $p<0.01$.
Conclusion:- The level of serum hsCRP was decreased in post-treatment in comparison of pre-treatment in pulmonary tuberculosis patients. Thus, it signifies the effect of anti-tubercular treatment and play role as prognostic marker in pulmonary tuberculosis patients.

Key words:- High sensitive C-reactive protein (hsCRP), Tuberculosis(TB), Pulmonary tuberculosis (PTB), Anti-tubercular treatment (ATT), Directly observed treatment short course (DOTS).

I. INTRODUCTION

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis, whicha rod is shaped acid-fast bacilli. Itis transmitted via aerosolized droplet nuclei by coughing, sneezing or speaking. Mycobacterium tuberculosis mainly affects the lungs but other organs are also involved in up to one-third of cases.[1] As per WHO global tuberculosis report 2017, tuberculosis is global burden and ninth leading cause of death ranking above HIV/AIDS. Globally, 10.4 million people were infected with tuberculosis in 2016.[2] The estimated incidence of tuberculosis in India was approximately 28,00,000 in 2016 which is a quarter of the world's TB cases.[3]

C-reactive protein (CRP) is an acute-phase protein and non-specific marker of systemic inflammation.[4]Itwas first discovered in 1930 by Tillet and Francisin patients infected with Streptococcus pneumonia who found that the somatic C polysaccharide of S. pneumonia formed a precipitate when added to the sera of patients with acute pneumococcal pneumonia. Therefore, it was named C-reactive protein.[5]Itis produced by hepatocytes within 4-6 hours after onset of tissue injury or inflammation.[6]

CRP is an established marker of inflammation and its serum concentration is useful in assessing grade of systemic inflammation.[7] It plays beneficial role in the clinical evaluation of respiratory tract infections and increased level of CRP is an indication to initiate antibiotic therapy.[8,9] Moreover, estimation of CRP can be useful in determining efficacy of anti-tubercular treatment.[10] Recently, the method has improved in analysis of serum concentration upto 0.1mg/Lby high-sensitive C-reactive protein (hsCRP) which enableto use hs-CRP concentration as a prognostic marker in chronic inflammatory diseases.[11]

As per Breen et al. (2008)[12] and and Chalmers et al.(2008)[13] CRP level was increased inconfirmed case of tuberculosis patients.Rao S et al. (2009)[14], Wilson D et al. (2011)[15] and Christina Y et al. (2013)[16] reported that CRP levels were higher in the patients before treatment. But in contrast to them Ito KM et al. (2004) described that no increase in level of CRP in active tuberculosis patients.[17]Huda SK et al. (2013) reported that hsCRP levels were significantly increased in pulmonary tuberculosis patients compared to healthy control.[18]

Thus, the above mentioned reports of various studies has drawn our attention to study the fact related to the

circulating level of hsCRP in pulmonary tuberculosis patients and efficacy of anti-tubercular treatment to serve as prognostic marker.

Material and methods:-

This study was conducted in 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 clinical features, positive sputum for acid-fast bacilli (AFB) and/or radiological abnormalities consistent with pulmonary tuberculosis (PTB) of age group more than 15 years and having normal blood sugar levels. Patients having already on ATT, age less than 15 years, high blood sugar level and suffering from HIV and hepatitis-B were excluded from this study.

After explaining purpose of the present study and taking written consent from the patients visiting OPD, IPD and DOTS centre of SGT Medical College Hospital and District TB Centre, Gurugram 5ml venous blood sample was 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 hsCRP was analyzed by ELISA method (Calbiotech ELISA KIT) in Central Laboratory, Department of Biochemistry, SGT Medical College Hospital, SGT University, Budhera, Gurugram.

Statistical Analysis:- Statistical Package for the Social Sciences (SPSS) version 21.0 was used for statistical analysis. Results were expressed in mean ± standard deviation. The comparison between serum hsCRP level in pre and post treatment was done by Paired Student's t-test. The variables were considered statistically significant with $p<0.05$.

Result:-

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

The serum level of hsCRP was increased in pre-treatment (8.69±4.85 mg/L) than post treatment (3.86±2.04 mg/L) with $p<0.01$ (Table 2; Figure 1). The correlation was positive between pre and post treatment hsCRP level (Figure 2).

Table 1: Demographic characteristics of patients

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

Table 2: Showing mean ± SD of serum hsCRP level in PTB patients

Parameters	Pre-Treatment (n=100)	Post-Treatment (n=100)	t-value	p-value
hsCRP (mg/dL)	8.69±4.85**	3.86±2.04**	16.40	0.00

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

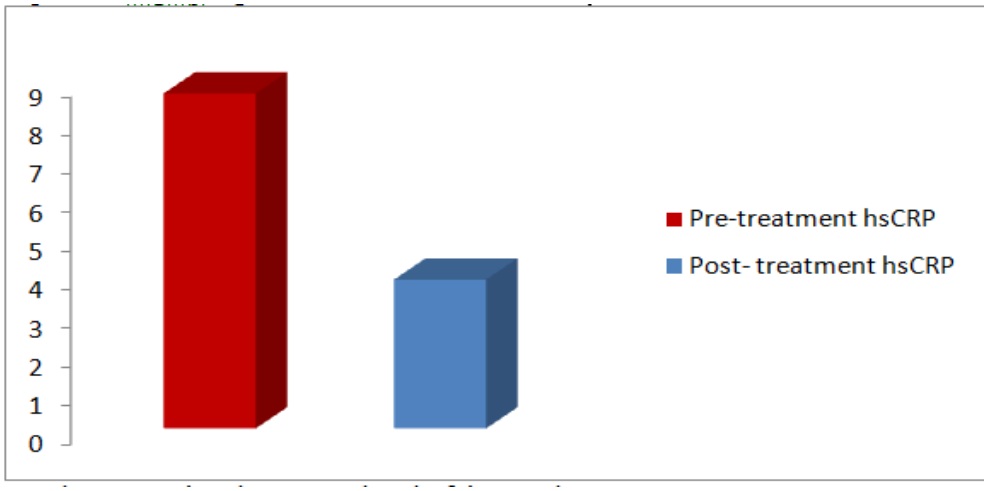


Figure 1:- Showing serum level of hsCRP in pre & post treatment.

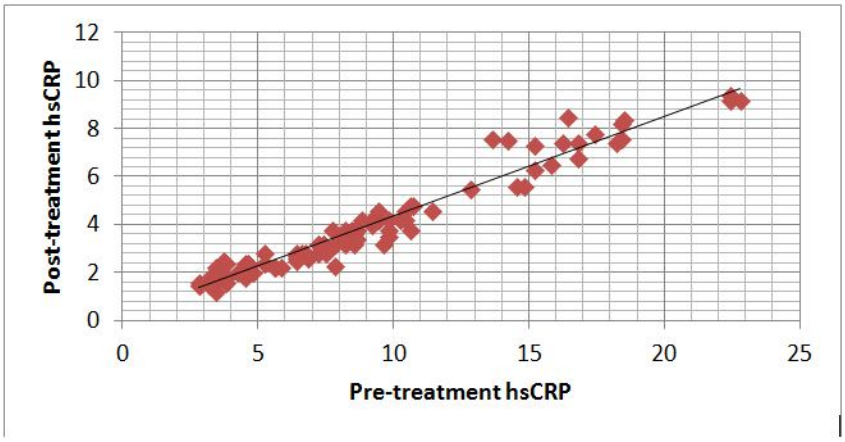


Figure 2:- Showing positive correlation between level of hsCRP in pre & post treatment.

DISCUSSION

In this study serum hsCRP level was increased in pre-treatment compared to post-treatment with $p<0.01$ in pulmonary tuberculosis patients. This result is in accordance to Breen et al. (2008)[12] , Chalmers et al.(2008)[13] , Rao S et al. (2009)[14], Wilson D et al. (2011)[15] , Christina Y et al. (2013)[16] and Huda SK et al. (2013)[18]. In contrast to Ito KM et al. (2004).[17] Huda SK et al. reported high level of hsCRP in pulmonary tuberculosis patients compared to healthy control.[18]

As de Beer FC et al. (1984) after initiation of anti-tubercular treatment level of C-reactive protein level decreased in pulmonary tuberculosis patients.[19] Similarly, Bajaj G et al. (1989) also reported that CRP levels decreased after anti-tubercular treatment.[20]Rao S et al. concluded that level of CRP play major role in identifying the severity of disease and indirectly helping the TB health workers to find delayed convertors and defaulters.[14]

CONCLUSION

In this present study, interesting changes in level of serum hsCRPwas found in pre and post anti-tubercular treatment. The post-treatment hsCRP level was significantly low compared to pre-treatment with $p<0.01$. Thus, it signifies the efficacy of anti-tubercular treatment and hsCRP serve as prognostic marker in pulmonary tuberculosis.

Conflict of interest:- None declared.

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