

**INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY,  
BIOLOGY AND CHEMISTRY****Research Article****High sensitive C-Reactive Protein in Patients with  
Pulmonary Tuberculosis in Tikrit City****Huda Saleh Khuder<sup>1\*</sup>, Ashwaaq Younis Norrei<sup>2</sup>, Yossra Saleh Khuder<sup>3</sup>**<sup>1</sup>Department of Pharmacognosy and Medical plant, College of Pharmacy, University of Tikrit, Iraq.<sup>2</sup> Department of biology, College of education, University of Samarra, Iraq.<sup>3</sup>Department of Obstetrics and Gynecology, College of Medicine, University of Tikrit, Iraq.**ABSTRACT**

The present study was conducted to evaluate the High sensitive C-reactive protein (Hs-CRP) in patients with pulmonary tuberculosis at pulmonary tuberculosis contention center in Tikrit city, Iraq from January to May (2013). All patients with pulmonary tuberculosis > 12 years of age, of either gender were evaluated for their serum Hs-CRP level. During four months study period, 20 patients with pulmonary tuberculosis were evaluated for Hs-CRP level, of which 14 (70 %) were females and 6 (30 %) were males, in addition to 20 apparently healthy subject as a control group, 3 (15 %) of them are males and 17 (85%) were females. The mean serum Hs-CRP levels were significantly higher in patients with pulmonary tuberculosis compared with control group of healthy subjects ( $6.29 \pm 2.84$  mg/l versus  $1.86 \pm 0.17$  mg/l,  $p < 0.000$ ). The present study detected elevation of Hs-CRP in patients with pulmonary tuberculosis.

**Key words:** Pulmonary tuberculosis, Lower respiratory tract infection, High sensitive C-Reactive Protein, Inflammatory marker.

**INTRODUCTION**

Pulmonary tuberculosis or tubercle bacillus (TB) is a contagious and air born disease, characterized by inflammation of lung parenchyma and caused by the intracellular bacterium *Mycobacterium tuberculosis* (1). One third of the world's population is thought to have been infected with *M. tuberculosis* (2), with new infections occurring in about 1% of the population each year (3). In 2007, there were an estimated 13.7 million chronic active cases globally (4), while in 2010, there were an estimated 8.8 million new cases and 1.5 million associated deaths, mostly occurring in developing countries (5). Pakistan alone accounts for 44% of total TB burden in the Eastern Mediterranean Region of the WHO comprising 23 countries (6). In India, approximately 4.8 million people are suffering from TB infection of which 2.2 million are smear positive; the annual risk of infection is 1 to 2% and the case fatality rate is 24% (7). It is also a major cause of illness and death worldwide especially in Africa and Asia, in Nigeria, a prevalence of 460,000 has been reported (8). Based on 2009 estimates in Iraq, the incidence of TB was

56 per 100,000 population per year for all forms of TB cases (9). The association between TB and malnutrition is well recognized; TB can lead to malnutrition and malnutrition may predispose to tuberculosis (10). CRP is an established marker of acute inflammation, and its serum concentration is frequently determined to assess the grade of systemic inflammation (11), e.g., in rheumatic (12) or intestinal (13) diseases, or to verify bacterial etiology of inflammation such as pneumonia in adults (14) and children (15) alike. Recently, the immunoturbidimetric method on latex particles has been used to determine very low CRP concentrations. The method has improved analytical sensitivity in determining serum concentration of high-sensitive CRP (hsCRP) to 0.1 mg/L, thus enabling the use of hs-CRP concentration as a prognostic marker of chronic inflammation in patients with cardiovascular disease (16), diabetes mellitus (17,18) and asthma (19, 20). The objective of the present study was to assess changes in the concentration of hs-CRP in patients with pulmonary tuberculosis infection. The

hs-CRP can serve as a sensitive indicator of activity of the disease and its proper evaluation indicates a good therapeutic response.

#### MATERIAL AND METHODS

This study was conducted at pulmonary tuberculosis contention center in Tikrit city, Iraq, from January till May (2013). All patients of > 12 years of age, of either gender with cough and expectoration for more than 15 days, weakness and constant fatigue, weight loss, fever, night sweats, chest pain, coughing up blood and loss of appetite were enrolled and evaluated with detail history, relevant examination and specific investigations i.e. chest radiograph and early morning sputum for acid fast bacilli (AFB) for three consecutive days. The evidence of any one positive smear of sputum for AFB were considered as cases of pulmonary tuberculosis. Pleural fluid (if present) were also evaluated as having pulmonary tuberculosis. All the patients were taken consecutively and an informed consent was taken from each patient. 3 ml sample of venous blood in a disposable syringe was taken and Serum was separated from venous blood clotted at room temperature, stored at - 20°C and Serum was taken for the evaluation of Hs-CRP level. Patients with rheumatic fever, myocardial infarction, leprosy, congestive heart failure, different infectious diseases (meningitis, poliomyelitis, infectious mononucleosis and syphilis), malignancy, rheumatoid and septic arthritis and the postoperative and puerperal periods and on antibiotic therapy were considered in exclusion criteria.

The laboratory tests consisted of measurement of CRP using high sensitive ELISA kit (DRG International, INC., USA). It is based on the principle of a solid phase enzymelinked immune sorbent assay. The assay system utilizes a unique monoclonal antibody directed against a distinct antigenic determinant on the CRP molecules. The test sample is allowed to react simultaneously with the two antibodies, resulting in the CRP molecules being sandwiched between the solid phase and enzyme-linked antibodies. Statistical analysis was performed using SPSS software version 19. The frequency and percentage (%) was calculated for gender distribution. The mean and standard deviation (SD) was calculated for hs-CRP. The independent - samples t-test was applied between categorical variables and the p-value 0.05 was considered as statistically significant.

#### RESULTS

During the study period, 20 patients with pulmonary tuberculosis were studied for Hs-CRP, of which 14 (70 %) were females and 6 (30 %) were males, in addition to 20 apparently healthy subject as a control group, 3(15 %) of them are males and 17(85%) was females (Table 1). Very

highly significant ( $p=0.000$ ) increase was observed in the level of high sensitive C-Reactive protein in patient with pulmonary tuberculosis as compared to control subject (Table 2),(figure1).

#### DISCUSSION

Serum-CRP is an acute phase reactant proteins synthesized by hepatocytes under the influence of interleukin-1 arising at sites of infection, inflammation and trauma (21). It has been shown to be beneficial in the clinical evaluation of respiratory tract infections in adults (22). Additionally, an elevated CRP has been used as an indication to initiate antibiotic therapy (23). Now it has attracted the attention of various researchers, as an indicator to differentiate tubercular from non-tubercular infections or diagnose extra pulmonary tuberculosis. However, reports have been conflicting. One study found out that elevated serum levels of serum-CRP can be useful in differentiating tuberculosis from non-tubercular diseases (24), whereas another study found it to be of not much value (25). Moreover, few studies which have found it to be useful were in patients of pleural effusion(26).

In the present study, the mean age of patients was  $42.3 \pm 20.64$  (15-80 years) and majority of the subjects were from rural population, these findings are consistent with the study by Shaikhet *al.*(27).also in this study, we found that females showed high risk levels of hs-CRP than males, which may be resulted by chance in such small sample size, dissimilar to Breyer's study (2005-2007)(28)which showed an increased likelihood for highly elevated CRP in males.

Standard assays for CRP lack the sensitivity needed to determine the levels of inflammation, and thus, clinical utility of standard CRP evaluation is extremely limited. Recent improvements have resulted in a new generation of highly sensitive assays that can detect the CRP at levels 100-fold lower than the earlier assays(29). Using hs-CRP, assessment of conditions indicative of chronic, low-grade inflammation is now possible.

In our study, the results indicate that Serum hs-CRP levels were found to be significantly higher in Patient with tuberculosis (pre-therapeutically) as compared with the control group of healthy subjects and the values were  $6.29 \pm 2.84$  mg/L and  $1.86 \pm 0.17$  mg/L respectively ( $P < 0.000$ ). this results were consistent with the previous studies performed by Maasilta and Kostiala in which the patients with Tuberculous had significantly higher levels of CRP than healthy volunteers (30). Breen *et al.* found that an elevated CRP detected 85% of proven tuberculosis cases in London (31). Chalmers *et al.* showed elevated CRP in patients with TB as high as 44 mg/L (32). While inconsistent with the study of Ito *et al.* which

describe patients with active tuberculosis without increase in CRP concentration (33).

The reasons for the inverse association between systemic inflammation and reduced pulmonary function are unclear but several mechanisms maybe involved. First, reduced lung function may be responsible for systemic inflammation. Like hepatocytes, inflammatory lung or pulmonary epithelial cells, have been shown to express CRP and IL-6. An alternative mechanism—reverse causation—cannot be excluded. High levels of cytokines and acute phase reactants in peripheral circulation maybe a cause rather than a consequence of poor lung function (34).

Limitations of the present study were small number of study subjects, and not analyzing drugs. However, may the results of this study be

confirmed in an independent study including a greater number of subjects.

It is concluded that hs-CRP can serve as a sensitive indicator of activity of the disease and the return to normal values of initially elevated CRP levels may indicate a good therapeutic response.

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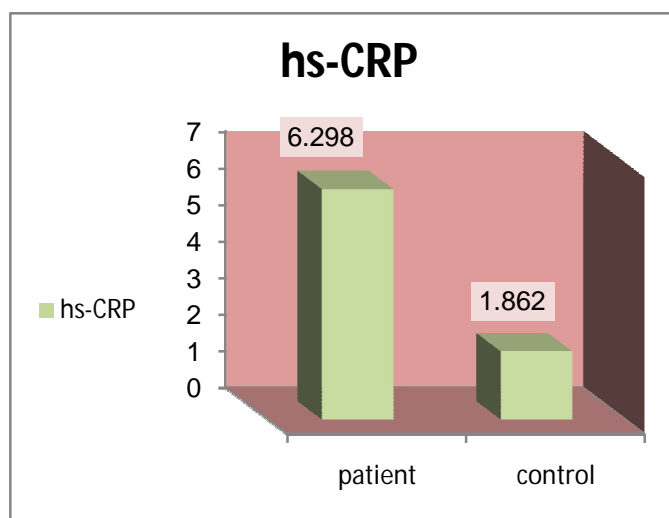
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**Table (1):Distribution of groups according to gender.**

Groups	Female	Male	Total
Patient	14(70 %)	6(30 %)	20(50%)
Control	17(85%)	3(15 %)	20(50%)
Total	31(100%)	9(100%)	40(100%)

**Table (2): Comparison between high sensitive C-Reactive protein in patient with pulmonary tuberculosis and control subject.**

Parameter	Control subject (n=20)	Patient (n=20)	P-value
Hs-CRP (mg/dl)	1.86±0.17	6.29±2.84	0.000



**Figure (1):Comparison between high sensitive C-Reactive protein in patient with pulmonary tuberculosis and normal subjects.**

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