Can we consider erythrocyte sedimentation rate and C-reactive protein as a severity index in pemphigus vulgaris?

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Background: Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are 2 inflammatory indicators that increase in many pathologic and physiologic conditions. Pemphigus vulgaris (PV) is an autoimmune skin disease in which autoantibodies against desmogleins cause acantholysis. In this study we have measured ESR and CRP levels in patients with PV to evaluate the relationship between an increase in these markers and disease severity.

Methods: In this cross-sectional study, we selected patients with proven diagnosis of PV who referred to the Dermatology referral clinic, Faghihi hospital, Shiraz, Iran during a one year period. There were 30 patients enrolled in this study who provided blood samples to measure their ESR and CRP levels. We used the Mahajan scoring system to determine the disease severity.

Results: In 27 (90%) cases, ESR was normal and 20 (66.7%) cases had negative CRP. There was a significant correlation between CRP and PV severity (P=0.015); however, there was no correlation between ESR and disease severity (P=0.126).

Conclusion: A correlation existed between CRP and severity of PV. Further studies must be undertaken to prove the prognostic role of CRP in PV. The discovery of new prognostic factors can change the treatment strategy and protocol for PV.

Keywords: pemphigus vulgaris, C-reactive protein, erythrocyte sedimentation rate, desmoglein

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INTRODUCTION

Pemphigus, a potentially fatal disease, is part of a group of blistering mucocutaneous autoimmune disorders. This disease is classified into 2 main groups: pemphigus vulgaris (PV) and pemphigus foliaceus (PF) according to the level of blisters [1-5].

PV is the most common variant, which is characterized by IgG autoantibody against desmoglein 3 (Dsg 3) that results in acantholysis in the epidermis and emergence of intraepithelial flaccid blisters that affect both the skin and mucosal membranes. Although it has a low incidence, the disease is life-threatening, mainly due to dehydration or secondary systemic infection. Corticosteroid use dramatically decreases the mortality rate [1-9].

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are two acute phase reactant proteins that elevate in response to acute and chronic inflammation [10-15]. CRP is predominantly produced by the liver within 4-6 hours of inflammatory process initiation and reaches a peak after about 24-50 hours. It will reduce 5-7 hours after appropriate treatment and removal of the inflammatory stimulant [16-19].

ESR is a measurement of suspension stability of anticoagulated red blood cells (RBC) in plasma in one hour. Normally, negative charged erythrocytes repel each other. In an inflammatory condition, there is an increase in positively charged proteins such as fibrinogen that results in elevated ESR.

Hence, ESR indirectly indicates acute phase protein concentrations [12,20].

These acute phase reactants are markers of choice in diagnosis, prognostic prediction, and evaluation of response to treatment due to their rapid and excessive increase, and cost-effectiveness [12,19].

The aim of the present study was to investigate the diagnostic value of CRP and ESR in PV. We also sought to examine the relationship between serum levels of these two markers and the severity of PV.

MATERIALS AND METHODS

In this cross-sectional study, we enrolled 41 patients with biopsy proven PV who referred to Dermatology referral clinic between May 2014 and April 2015.

Exclusion criteria consisted of patients with elevated ESR and CRP who experienced recent infections, heart attacks, surgeries, malignancies, and rheumatologic diseases. Patients with positive gram stains were also excluded. Based on these criteria, we excluded 11 patients from study participation. From the remaining 30 participants, 13 (43.3%) were male. Patients' age ranged from 19 to 63 years with a mean age of 40.3±13.8 years. There were 2 patients admitted on 2 occasions during the course of the study. We considered the data from each of these admissions as individual data. Among these patients, 5 were newly diagnosed with PV. Blood samples were taken from the PV patients upon their arrival to the hospital and before initiation of any treatment. At least 0.6 cc of blood was obtained for the CRP test. These samples were maintained in clot tubes and measured by a semi-quantitative method. For the ESR test, 2 cc blood samples were collected in EDTA tubes and measured by an automated method (Electa Lab). All blood samples were sent to a specific laboratory. The cutoff point for CRP in this laboratory was 6, therefore patients with CRP levels less than 6 were considered to have normal results.

We chose the Mahajan scoring system because of its simplicity to assess disease severity. This index is based on the percentage of body surface area involvement and severity of mucosal involvement [21]. The Mahajan scoring system classifies severity into four groups: mild, moderate, severe, and extensive.

We prepared a data gathering sheet that contained information about patients' demographic data, their full medical history (diseases, drugs), laboratory test results (CBC, creatinine, ESR, CRP), and disease severity as determined by the Mahajan scoring system.

The results were analyzed by SPSS software version 20. Continuous variables were presented as mean±SD and qualitative variables were recorded as numbers (%). We used the chi-square test to evaluate the correlation of ESR and CRP with disease severity.

Informed consent was obtained from all selected patients. The Ethical Committee of Shiraz University of Medical Sciences approved this study. The Vice-Chancellery of Research and Technology of Shiraz University of Medical Sciences financially supported this study.

RESULTS

A total of 30 patients enrolled in the study, 13 (43.3%) males and 17 (56.6%) females, with an age range between 19 to 63 years (mean: 40.3±13.8 years). According to the Mahajan scoring system and Lund and Browder burn chart, 19 (63.3%) patients had mild disease and 7 (23.3%) had moderate disease. There were 2 (6.7%) patients with severe disease and 2 (6.7%) with extensive disease (Table 1).

In general, 27 (90%) patients had normal ESR levels, 2 (6.7%) had elevated ESR, and one case was missed to follow up. Assessment of CRP showed that 20 (66.7%) had negative CRP results and 10 (33.3%) had positive CRP results. Table 2 lists the patients' ESR and CRP results, and their correlation with disease severity. Although there was a significant correlation between CRP and disease severity (P=0.015), we observed no correlation between ESR and disease severity (P=0.126).

Table 1. Characteristics of patients with pemphigus vulgaris admitted to the Dermatology Ward of Faghihi Hospital, Shiraz, Iran.

Characteristics	Number (%) or mean±SD
Sex	
Male	13 (43.3)
Female	17 (56.6)
Age (years)	40.3±13.8
Severity	
Mild	19 (63.3)
Moderate	7 (23.3)
Severe	2 (6.6)
Extensive	2 (6.6)

Table 2. Correlation of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) with the severity of pemphigus vulgaris (PV).

Severity	ESR N (%)		*P*-value	CRP N (%)		*P*-value
	Normal	High		Negative	Positive	
Mild	18*	0	0.015	16	3	0.126
Not mild						
Moderate	5	2		2	5	
Severe	2	0		2	0	
Extensive	2	0		0	2	
Total	27	2		20	10	

* One missing data in this group.

Among the 5 new cases of PV, 3 (60%) had a positive CRP and all had normal ESR levels.

During the course of the study, 2 cases were hospitalized. We considered each admission as an individual admission. One of the admitted patients presented with the moderate form of disease at the first admission and severe form at the subsequent admission. In both admissions she had a normal ESR; however, her CRP was positive at the first admission and negative at her second admission. The other patient was admitted with the severe form of the disease at the first admission and the mild form at the second admission. In both admissions, she had a negative ESR, whereas her CRP was positive.

DISCUSSION

PV is a life threatening autoimmune disease. Although corticosteroids have revolutionized treatment and dramatically decreased the mortality rate, there is morbidity and a mortality rate of approximately 10%. Despite treatments, PV is not curable, although it can be controlled by appropriate medications [2,7-8,22-24].

ESR and CRP are both nonspecific tests that can increase in many diseases. The combination of both tests is very useful in diagnosis, determination of disease severity, and prediction of disease prognosis. Both ESR and CRP are superior inflammatory markers due to their rapid response and cost-effectiveness. Previous studies have mentioned CRP as a prognostic marker for future cardiovascular events, acute exacerbation of COPD, hospital admissions, and mortality. Other studies have mentioned the role of CRP in the pathogenesis of diseases such as cardiovascular and inflammatory bowel diseases. CRP can play a diagnostic role in infections [11,12,14,18,25-29]. ESR also has a diagnostic role in numerous diseases such as giant cell arthritis and polymyalgia rheumatica. ESR provides useful information to the physician after initiation of treatment [18].

To our knowledge, although no study has been performed to measure ESR and CRP in patients with PV, there was a study on patients with endemic PF. The results of that study revealed an increase in CRP in 60% of the patients and an increase in ESR in all of the patients [30]. Some studies showed that these two markers may correlate with other skin diseases. They reported elevated CRP levels in skin diseases with systemic inflammation such as psoriasis, urticaria, and acne rosacea. Psoriatic patients who do not have arthritis may also have increased CRP and ESR levels. Decreased levels of ESR and CRP have been shown after appropriate treatment. A number of studies have reported an association between the Psoriasis Area and Severity Index (PASI) and CRP levels. It has been suggested that the duration of remission in psoriasis can be correlated with the level of CRP at the end of treatment. The level of CRP is important in determining whether to continue or abandon treatment. On the other hand, studies of acne vulgaris have shown no correlation between disease and CRP elevation, even in the severe form of the disease. There is controversy regarding CRP levels in studies performed on acne rosacea [31-35].

Our study showed a significant correlation between the increase in CRP and severity of the disease, though we found no correlation between ESR and PV severity.

There were limitations in this study. Some of our patients had received medications before their admission that appeared to affect the results for ESR and CRP. However, after careful assessment of their medical histories, most stated that they had quit their treatments. Additional studies with

more participants would be needed to confirm the results of the current study. Since the present study was a cross-sectional study, we could only evaluate the correlation. Thus, in order to evaluate causalities, it would be necessary to design case control and clinical trial studies.

As long as no definite cure exists for PV, it is essential to control this disease. Finding new prognostic factors can enable appropriate, prompt changes in the drug regimens to prevent unpleasant consequences and mortality. In this study we have found a significant correlation between CRP and the severity of PV. There was no correlation between ESR and PV. Additional studies should be conducted to confirm this relationship. Future studies could assess the role of ESR and CRP during follow up care of PV patients and their response to treatment by measuring these two factors after initiation of treatment.

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Conflict of Interest: None declared.

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