

Original Article

Correlation between the disease severity and serum levels of c reactive protein, erythrocyte sedimentation rate and ferritin in patients with chronic spontaneous urticaria: A cross-sectional study

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Abstract

Background Chronic spontaneous urticaria, or CSU, is the recurrence of persistent, recurrent wheals, angioedema, or both for more than six weeks due to known or unidentified causes. C reactive protein (CRP) levels can be measured to assess disease activity, prognosis, and therapy effectiveness. CRP testing is advised for all patients with chronic urticaria, according to the most recent EAACI/GA2LEN/EDF/WAO guidelines.

Methods For this study, 76 patients with a clinical diagnosis of persistent spontaneous urticaria were enrolled. The levels of serum ferritin, ESR, and CRP were calculated. The urticaria activity score (UAS 7) was used to gauge the severity of the disease. The Dermatology Life Quality Index was used to evaluate quality of life at the time of blood sample.

Results The mean CRP level was 0.8 mg/L, and 36.84% of patients had increased CRP levels. Of the patients, 34.21% had elevated ESR. When comparing CRP and UAS7, the Pearson correlation value was 0.5, showing a moderately positive association. When comparing ESR and UAS7, it was 0.1, showing a very weak positive correlation. DLQI on average was 7.5.

Conclusion Elevated CRP is linked to increased disease activity, and measuring this activity can help manage patients with CSU more effectively.

Key words

Chronic spontaneous urticaria; CRP; ESR; Ferritin.

Introduction

Chronic urticaria, which can be either chronic spontaneous or chronic inducible, is defined as the formation of recurrent wheals for longer than six weeks.¹ The most typical form of chronic urticaria is CSU.²

Patients with CSU have often reported having elevated CRP. CRP levels can be measured to assess disease activity, prognosis, and therapy effectiveness. Elevated ferritin and ESR levels are also linked to elevated CRP.³

This study aims to link the levels of C reactive protein, ESR, and ferritin with the severity of the disease in chronic spontaneous urticaria.

Methods

With ethical committee approval, this study was

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an observational study carried out in the Department of Dermatology's outpatient block. The study was conducted over the course of five months. Consecutive sampling was used to enlist 76 patients who met the study's inclusion and exclusion requirements.

Inclusion criteria Patients with clinical evidence of chronic spontaneous urticaria.

Exclusion criteria Patients with other types of chronic inducible urticaria and urticarial vasculitis; patients with other autoimmune, allergic, malignant, infections and inflammatory disorders; patients with chronic debilitating diseases; patients on NSAIDs, systemic steroids, OCPs and other immunosuppressive and anti-inflammatory agents in the last 4 weeks or at present (which may alter CRP, ESR and ferritin levels); patients who are pregnant or lactating; patients who are alcoholics, smokers or drug abusers.

The study included 76 participants who met the inclusion and exclusion criteria and had been clinically diagnosed with chronic spontaneous urticaria. Each patient's demographic information and a thorough case history, (including the duration of CSU, the occurrence of concurrent angioedema, comorbidities, family history, and treatments received) were collected. All CSU patients had testing in the lab, including CRP, ESR, and ferritin. The institution's laboratory defined an increased CRP level as one greater than 0.5 mg/dl. ESR levels more than 22 mm/hr and greater than 29 mm/hr in males and females, respectively, were deemed high. 4.63 to 204 ng/ml of ferritin was seen as normal. For these examinations, five milliliters of venous blood were taken. Using the urticaria activity score (UAS 7), the disease's activity was assessed. This was computed using the itch and hive scores over a period of seven days (lowest score=0; highest score=42). The Dermatology

Life Quality Index (DLQI) was used to evaluate quality of life at the time of blood sample.

The data were statistically analysed.

Evaluation of DLQI and UAS7

1) DLQI assessment includes ten items in the following six subsections:^[4]

- Symptoms and feelings
- Daily activities
- Leisure
- Work and school
- Personal relationships
- Treatment

Giving each a score: "Not at all"=0, "A little"=1, "A lot"=2, and "Very much"=3.

Total Points: 0-1: No effect at all on patient's life, 2-5: Small effect on patient's life, 6-10: Moderate effect on patient's life, 11-20: Very large effect on patient's life, 21-30: Extremely large effect on patient's life

2) Assessment of UAS7:^[5]

Hive rating: No wheals equals 0, <20 wheals per 24 hours=1, 20–50 wheals per 24 hours=2, >50 wheals per 24 hours=3.

Pruritus intensity: No = 0, Mild=1, Moderate=2, Intense=3.

UAS₇: ≤ 6: Well controlled, 7-15: Mild, 16-27: Moderate, 28-42: Severe

Data collection and analysis were done using an excel spreadsheet and the statistical analysis programme SPSS, which was released in 2016 by IBM Corp. Version 24.0 of IBM SPSS Statistics for Windows. IBM Corp; Armonk, New York. Absolute numbers (percentages)

served as a representation for qualitative factors. For quantitative continuous variables, parameters such as mean, median, and standard deviation were used. The correlation between UAS and both normal and elevated CRP and ESR was determined using the chi-square test and Fisher's exact test. The correlation coefficient of Pearson was utilised to determine the degree to which CRP, ESR, DLQI, and UAS are associated. A p-value of 0.05 was regarded as statistically significant after taking into account all the rules of statistical tests.

Results

The study included 76 patients in total. 24 out of 76 (or 31.6%) were men and 52 out of 76 (or 68.4%) were women. The mean age of patients was 33.26 (standard deviation 9.33), the patients' ages varied from 16 to 50. The mean disease duration was 22.39 weeks, with a standard deviation of 13.29 and a range of 7 to 51 weeks. Homemakers made up the majority of the study's participants (39.47%), followed by farmers (28.94%) and students (18.42%). 18 out of 76 people (23.68%) had angioedema. In (20 out of 76)26.31% of the patients, there was a history of the lesions getting worse when they ate a certain food.

The patients' CRP levels varied from 0.2 to 3.4 mg/L, with a mean CRP of 0.8 and a standard deviation of 0.8. 36.84% of patients (28 out of 76) had elevated CRP levels (**Table 1**). The patients' mean ESR was 24.43 mm/hr, with a standard deviation of 13.14, and their ESR values varied from 7 to 53 mm/hr. Out of 76 individuals, 26 (34.21%), had elevated ESR (**Table 2**). With a mean value of 30 and a standard deviation of 24.11, the patients' ferritin levels ranged from 5.7 to 82.4 ng/ml. Each and every patient had ferritin values inside the acceptable limit (**Table 3**).

The patients' mean UAS7 values varied from 5

Table 1 CRP among patients with chronic spontaneous urticaria.

CRP (mg/dl)	Frequency	Percentage
≤ 0.5	48	63.15
0.6–1	4	5.3
1.1–1.5	8	10.5
1.6–2	10	13.15
2.1–2.5	2	2.6
2.6–3	0	0
3.1–3.5	4	5.3
Total	76	100

Table 2 ESR among patients with chronic spontaneous urticaria.

ESR (mm/hr)	Frequency	Percentage
≤ 10	12	15.8
11 – 20	28	36.9
21 – 30	16	21
31 – 40	8	10.5
41 – 50	6	7.9
>50	6	7.9
Total	76	100

Table 3 Serum ferritin among patients with chronic spontaneous urticaria.

Ferritin (ng/ml)	Frequency	Percentage
≤ 10	18	23.68
10.1 – 20	16	21
20.1 – 30	10	13.15
30.1 – 40	10	13.15
40.1 – 50	4	5.26
50.1 – 60	2	2.63
60.1 – 70	8	10.52
70.1 – 80	6	7.89
>80	2	2.63
Total	76	100

to 38, with a standard deviation of 9.7 and a mean value of 20.32. 13.15% (10 out of 76) of the patients had the disease under good management. 17.1% (13 out of 76) of the patients had mild disease activity, 40.78% (31 out of 76) had moderate disease activity, and 28.94% (22 out of 76) had severe disease activity (**Figure 1**).

A total of 16 (72.72%) and 6 (27.27%) of the 22 patients with significant disease activity showed increased and normal CRP, respectively. Eight (36.3%) patients had elevated ESR, while 14 (63.63%) patients had normal ESR. Among them, eight individuals had both high ESR and

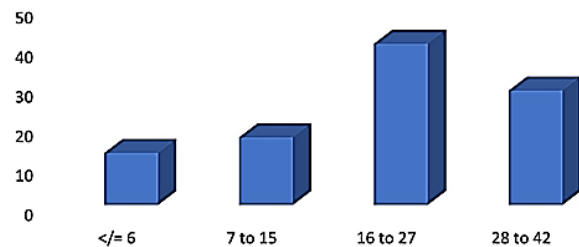


Figure 1 UAS 7 score among patients with chronic spontaneous urticaria (n=76).

Table 4 Comparison between ESR, CRP levels and the disease activity.

	Severe disease activity	Moderate disease activity
Elevated CRP only	8	8
Elevated ESR only	0	11
Elevated CRP and ESR	8	0
Normal CRP and ESR	6	12
Total	22	31

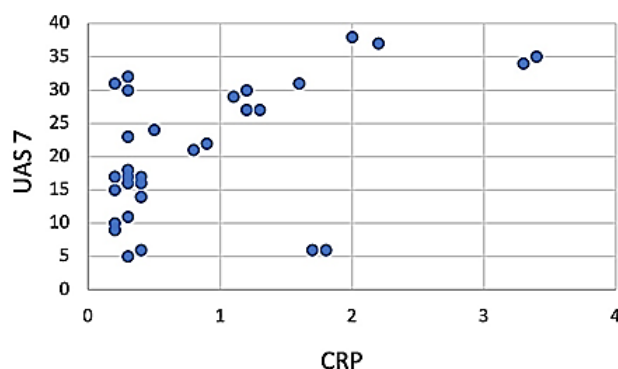


Figure 2 Pearson correlation between UAS 7 and CRP showing a moderately positive correlation ($r = 0.5$).

CRP, six had both normal ESR and CRP, six had only elevated CRP, and none had only elevated ESR (**Table 4**).

Eight patients (25.8%) had increased and 23 (74.19%) had normal CRP of the 31 patients with moderate disease activity. A total of 11 (35.48%) had elevated and 20 (64.51%) had normal ESR. Only CRP was elevated in eight individuals, only ESR in 11, and both were elevated in none of the 12 cases (**Table 4**).

Patients with elevated CRP had a mean UAS7 of 26.5 while those with normal CRP had a mean UAS7 of 16.3, and this difference was

statistically significant (P value = 0.004) (**Table 5**). A somewhat positive connection between CRP and UAS7 was indicated by a Pearson correlation coefficient of 0.5 (**Figure 2**). Patients with elevated ESR had a mean UAS7 of 21.8, while those with normal ESR had a mean UAS7 of 20.8; however, this difference was not statistically significant (P value = 0.8) (**Table 5**). The ESR and UAS7 comparison's Pearson correlation coefficient is 0.1, which denotes a very weakly positive correlation (**Figure 3**).

The patients' DLQIs ranged from 3 to 19. The mean DLQI was 7.5. The majority of the patients (40, 52.6%) had DLQIs between six and ten (**Table 6**). The DLQI and UAS7 comparison's Pearson correlation coefficient was 0.6, showing a substantially favourable link (**Figure 4**).

Discussion

Mast cell dependence characterises the multifactorial inflammatory condition known as chronic spontaneous urticaria.³ Compared to men, women get chronic urticaria more frequently.⁶ In our study, the majority (68.4%) of the patients were women, which was similar to a study by A. Grzanka *et al.* in which 73% of the patients were women.⁷

Table 5 P value comparing CRP, ESR and mean UAS 7.

Ferritin (ng/ml)	Frequency	Percentage
Elevated CRP	26.5	0.004
Normal CRP	16.3	
Elevated ESR	21.8	0.8
Normal ESR	20.8	

Table 6 DLQI among patients with chronic spontaneous urticaria.

DLQI	Frequency	Percentage
0 – 1	0	0
2 – 5	20	26.3
6 – 10	40	52.7
11 – 20	16	21
21 – 30	0	0
Total	76	100

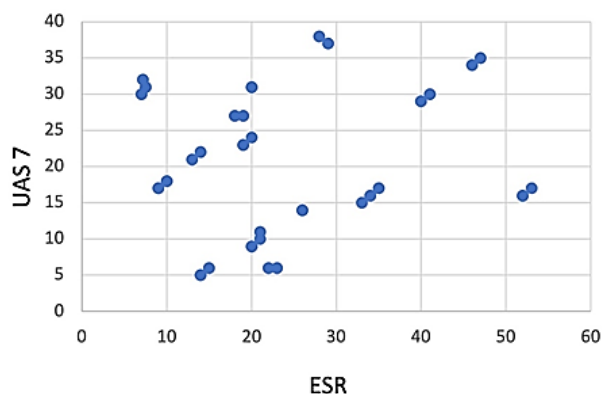


Figure 3 Pearson correlation between UAS 7 and ESR showing a very weak positive correlation ($r = 0.1$).

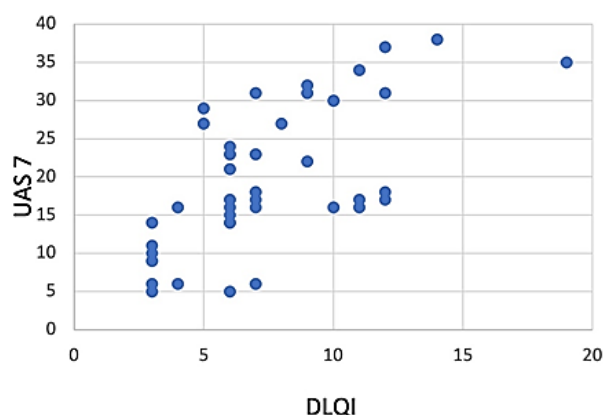


Figure 4 Pearson correlation between UAS 7 and DLQI showing a strongly positive correlation ($r = 0.6$).

The average duration of the illness in this study was 22.39 weeks, with a standard deviation of 13.29. The median disease duration in the study by A. Grzanka *et al.* was 2.5 years.⁷

Angioedema was observed in 23.68% of the individuals in this study. 48.7% of patients in a research by Pavel Kolchir *et al.* had concomitant angioedema.³ In a study by Czarnecka Operacz M *et al.*; 37.5% of individuals with chronic urticaria also developed angioedema.⁸

The urticaria activity score (UAS), used on 7 consecutive days (UAS7), is a well-known and highly approved outcome tool that is used to assess CSU activity and is reported by the patients themselves.⁹

The mean UAS7 for the patients in this study was 20.32. In 13.15 percent of patients, the illness was under good control. 17.1% of patients had mild disease activity, 40.78% had moderate disease activity, and 28.94% had severe disease activity. Criado RF *et al.* did a study in which Patient UAS scores ranged from low (45%) to high (55%) in patients.¹⁰

Hepatocytes produce the acute-phase protein C-reactive protein (CRP) in response to an increase in pro-inflammatory cytokines. In 24-72 hours following any tissue damage or infection, CRP can increase. CRP can be increased in diseases such as autoimmune disorders, cardiovascular disorders, cancers, and digestive issues.^{11,12} It has been suggested that CRP may serve as a biomarker of treatment responsiveness because several studies have found an increase in CRP in CSU patients. Recent research suggests that elevated CRP levels may indicate both a poor response to antihistamines and a favourable response to oral cyclosporine.¹³ As an acute phase reactant, CRP may make chronic urticaria more inflammatory, which would make the condition more active.¹⁴

In our study, the mean CRP value was 0.8 mg/L, and 36.84% of patients had increased CRP levels. Patients with elevated CRP had a mean UAS7 of 26.5 while those with normal CRP had a mean UAS7 of 16.3, and this difference was statistically significant (P value=0.004). The CRP and UAS7 comparison's Pearson correlation coefficient was 0.5, showing a moderately positive association.

In a research by Pavel Kolchir *et al.*; 313 out of 1019 patients had elevated CRP levels, with a mean CRP of 10.6 mg/L among those who had elevated CRP. When compared to patients with normal CRP levels, those with raised CRP levels had higher disease activity (UAS7).³ CRP level and disease activity were observed to positively

correlate in a study by Czarnecka Operacz M *et al.*⁸

This suggests that patients with greater CRP levels than those with normal CRP levels had more severe disease activity.

In this study, the average ESR value was 24.43 mm/hr, and 34.21% of patients had elevated ESR levels. Patients with elevated ESR had a mean UAS7 of 21.8, while those with normal ESR had a mean UAS7 of 20.8; however, this difference was not statistically significant (P value=0.8). ESR and UAS7 have a 0.1 Pearson correlation coefficient, which indicates a very weakly positive association.

In a research by Pavel Kolkhir *et al*; 11% of the 768 CSU patients and 19% of the 825 CSU patients showed increased CRP and ESR, respectively. One-third of the patients with elevated CRP had elevated ESR, although there was no discussion of the relationship between ESR and illness severity.³

The participants in this study had a mean ferritin level of 30 ng/ml. Ferritin levels for all of the patients were within normal limits.

In a study by Pavel Kolkhir *et al*; ferritin levels were noticeably higher in people with elevated CRP levels.³

The individuals in this study had a mean DLQI of 7.5 and a standard deviation of 3.5. The majority of the patients (40, 52.6%) had DLQIs between 6 and 10, indicating that the condition has a moderate impact on the patients' quality of life. The DLQI and UAS7 comparison's Pearson correlation coefficient was 0.6, showing a substantially positive link.

In a study conducted by Pavel Kolkhir *et al*, those with elevated CRP levels had significantly

higher rates of ferritin.³

The mean DLQI of the patients in this study was 7.5 with a standard deviation of 3.5. Majority (40, 52.6%) of the patients were having DLQI of six to ten indicating that the disease has a moderate effect on patient's life. Pearson correlation coefficient comparing DLQI and UAS7 was 0.6 indicating a strongly positive correlation.

According to a study by Pavel Kolkhir *et al*; patients with higher levels of CRP had a considerably higher quality of life impairment than those with normal levels of CRP.³

Key Message Higher disease activity is linked to elevated CRP levels. Its evaluation may be useful in determining how to handle patients with CSU. Conversely, there is no direct correlation between serum ferritin and ESR levels and disease activity.

Conclusion

Elevated CRP values are frequent and more important in CSU patients than elevated ESR. Additionally, increased disease activity is linked to elevated CRP. Optimising the treatment of patients with CSU may benefit from the evaluation of CRP levels.

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