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Original Research Article

Assessment of the Clinicoepidemiological Profile of Patients with Chronic Urticaria and Its Correlation with D-dimer Levels: A Prospective Cohort Study

Barunesh Kishore[1], Riya Upendra Rai[2]

[1]Associate Professor, Department of Skin & V.D (Dermatology), Narayan Medical College and Hospital (NMCH), Jamuhar, Rohtas, Bihar, India

[2]Assistant Professor, Department of Skin & V.D (Dermatology), Narayan Medical College and Hospital (NMCH), Jamuhar, Rohtas, Bihar, India

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Corresponding Author: Dr. Riya Upendra Rai

Conflict of interest: Nil

Abstract

Background: Chronic urticaria (CU) is a common dermatological disorder characterized by recurrent wheals and/or angioedema persisting for more than six weeks, significantly impairing quality of life. Recent evidence suggests a role of the coagulation pathway in its pathogenesis, with serum D-dimer emerging as a potential biomarker of disease activity.

Aim: To assess the clinicoepidemiological profile of patients with chronic urticaria and to evaluate its correlation with serum D-dimer levels.

Materials and Methods: This hospital-based prospective cohort study was conducted in the Department of Dermatology at a tertiary care centre. A total of 110 patients with chronic urticaria were enrolled after applying inclusion and exclusion criteria. Detailed clinical evaluation was performed, and disease severity was assessed using the Urticaria Activity Score over 7 days (UAS7). Serum D-dimer levels were measured using a quantitative immunoassay and categorized as normal (<0.5 µg/mL) or elevated (≥0.5 µg/mL). Patients were followed up at baseline, 4 weeks, and 8 weeks. Data were analyzed using SPSS version 27.0. Appropriate statistical tests, including Chi-square test, t-test, ANOVA, and correlation analysis, were applied. A p-value <0.05 was considered statistically significant.

Results: The majority of patients belonged to the 31–45 years age group (40.0%), with a female predominance (63.6%). Chronic spontaneous urticaria was the most common subtype (78.2%), and angioedema was present in 38.2% of patients. Elevated D-dimer levels were observed in 68 patients (61.8%) and showed a significant association with disease severity. Among patients with mild urticaria, 80% had normal D-dimer levels, whereas elevated levels were found in 66.7% of moderate and 89.5% of severe cases ($p < 0.001$). A strong positive correlation was observed between D-dimer levels and UAS7 score ($r = 0.68$, $p < 0.001$). Moderate correlation was noted with the presence of angioedema ($r = 0.41$, $p = 0.001$), while a weak but significant correlation was found with disease duration ($r = 0.29$, $p = 0.02$).

Conclusion: Chronic urticaria predominantly affects young to middle-aged females and is most commonly of the spontaneous subtype. Serum D-dimer levels show a significant association with disease severity and correlate strongly with UAS7 scores. D-dimer may serve as a useful adjunctive biomarker for assessing disease activity, aiding in risk stratification and guiding management in patients with chronic urticaria.

Keywords: Chronic Urticaria, D-dimer, Coagulation, UAS7, Epidemiology.

Introduction

Chronic urticaria (CU) is a common dermatological disorder characterized by the recurrent appearance of transient wheals, angioedema, or both for a duration exceeding six weeks. It significantly impairs quality of life due to persistent pruritus, sleep disturbances, and psychological stress. Epidemiological studies suggest that urticaria affects approximately 15–20% of individuals at least once in their lifetime, while chronic urticaria has a prevalence of about 0.5–1% in the general population (Zuberbier et al., 2018; Chauhan et al., 2019) [1, 2]. Chronic urticaria is broadly classified into chronic spontaneous urticaria (CSU) and inducible urticaria, with CSU being the more prevalent form. The etiopathogenesis of CU is complex and multifactorial, involving immunological, inflammatory, and autoimmune mechanisms. Autoantibodies directed against IgE

or its high-affinity receptor (FcεRI) have been implicated in a substantial proportion of patients, supporting an autoimmune basis in many cases (Kulthanan et al., 2013; Dabas et al., 2021) [3, 4].

In recent years, increasing attention has been directed toward the role of the coagulation and fibrinolytic systems in the pathophysiology of chronic urticaria. Activation of the extrinsic coagulation pathway leads to thrombin generation, which in turn enhances vascular permeability and mast cell activation, thereby contributing to wheal formation (Asero et al., 2007; Cugno et al., 2014) [5, 6].

D-dimer, a fibrin degradation product, has emerged as a potential biomarker reflecting activation of the coagulation and fibrinolysis pathways. Elevated plasma D-dimer levels have been consistently observed in patients with chronic urticaria, particularly during disease exacerbations. Several studies have demonstrated a positive correlation between D-dimer levels and disease severity, as measured by the urticaria activity score (UAS), suggesting its role as an indicator of disease activity (Takahagi et al., 2010; Kulthanan et al., 2013) [7, 3].

Furthermore, elevated D-dimer levels have been associated with more severe clinical manifestations, systemic symptoms, and resistance to conventional antihistamine therapy (Chauhan et al., 2019; Kaur et al., 2024).[2,8] Recent evidence also highlights that D-dimer levels tend to decrease with clinical remission, reinforcing their potential utility as a biomarker for monitoring disease progression and therapeutic response (Dabas et al., 2021; Chen et al., 2024) [4,9].

Aim & Objectives

Aim: To assess the clinicoepidemiological profile of patients with chronic urticaria and to evaluate its correlation with serum D-dimer levels.

Objectives

Primary Objective: To determine the association between serum D-dimer levels and disease severity as assessed by the Urticaria Activity Score over 7 days (UAS7).

Secondary Objectives

- To study the clinicoepidemiological characteristics (age, gender, subtype, duration) of patients with chronic urticaria.
- To evaluate the distribution of urticaria subtypes (chronic spontaneous vs inducible).
- To assess the relationship between D-dimer levels and presence of angioedema.
- To analyze the correlation between D-dimer levels and duration of disease.

Materials & Methods

Study Design: This study was designed as a hospital-based prospective cohort study aimed at evaluating the clinicoepidemiological profile of patients with chronic urticaria and its association with serum D-dimer levels. The prospective design enabled systematic follow-up and assessment of disease progression and biochemical correlations over time.

Study Setting: The study was conducted in the Department of Skin & V.D (Dermatology) at Narayan Medical College and Hospital (NMCH), Jamuhar, Rohtas, Bihar, India, which caters to a large and diverse patient population, ensuring adequate representation of chronic urticaria cases.

Study Period: The study was carried out over a period of 12 months, from November 2023 to October 2024.

Study Population: A total of 110 patients clinically diagnosed with chronic urticaria were enrolled consecutively from the outpatient and inpatient departments after fulfilling the eligibility criteria and providing informed consent.

Ethical Considerations: The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) prior to commencement of the study. Written informed consent was obtained from all participants after explaining the nature, purpose, and potential risks of the study. Confidentiality and anonymity of patient data were strictly maintained throughout the study.

Inclusion Criteria

- Patients aged ≥18 years
- Clinical diagnosis of chronic urticaria (presence of wheals and/or angioedema persisting for more than 6 weeks)
- Patients willing to participate and provide informed consent

Exclusion Criteria

- Patients with acute urticaria (<6 weeks duration)
- Patients with known coagulation disorders
- Patients on anticoagulant therapy
- Pregnant and lactating women
- Patients with systemic inflammatory or autoimmune diseases
- Patients unwilling to participate

Methodology

Clinical Assessment: All enrolled patients underwent a detailed clinical evaluation. A structured proforma was used to collect relevant data, including:

- Demographic details: age, gender, occupation

- Clinical history: duration, frequency, and pattern of urticaria
- Presence or absence of angioedema
- Identification of potential triggering factors (e.g., food, drugs, physical stimuli)
- Past medical history and drug intake
- A comprehensive dermatological examination was performed in all patients.

Disease Severity Assessment: Disease activity was assessed using the Urticaria Activity Score over 7 days (UAS7). Based on the total score, disease severity was categorized as:

- **Mild:** 0–15
- **Moderate:** 16–27
- **Severe:** 28–42

Laboratory Investigations

All patients underwent the following baseline investigations:

- Complete Blood Count (CBC)
- Erythrocyte Sedimentation Rate (ESR)
- Thyroid Function Tests (TFTs)
- Serum Immunoglobulin E (IgE) levels
- Serum D-dimer levels

Serum D-dimer levels were measured using a quantitative immunoassay method. Based on values, patients were categorized into:

- **Normal:**<0.5 µg/mL
- **Elevated:** ≥0.5 µg/mL
- **Follow-up Protocol**

Patients were followed up at:

- Baseline (0 weeks)
- 4 weeks
- 8 weeks

At each visit, clinical assessment and UAS7 scoring were repeated to monitor disease progression and treatment response.

Outcome Measures

Primary Outcome: To assess the association between serum D-dimer levels and disease severity (UAS7 score)

Secondary Outcomes

- To evaluate the clinicoepidemiological profile of chronic urticaria patients
- To determine the distribution of urticaria subtypes
- To assess the correlation between D-dimer levels and disease duration

Statistical Analysis

- Data were entered into Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.
- The Chi-square test (or Fisher's exact test, where applicable) was used for comparison of categorical variables. The association between serum D-dimer levels, UAS7 score, and disease duration was assessed using the Pearson correlation coefficient or Spearman's rank correlation, as appropriate.
- Comparisons of means were performed using the independent sample t-test for two groups and one-way ANOVA for multiple groups. A p-value <0.05 was considered statistically significant.

Results

A total of 110 patients diagnosed with chronic urticaria were included in the present prospective cohort study. All patients completed baseline evaluation, and follow-up data were available for analysis.

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 110)

Parameters	Variables	Frequency (n)	Percentage (%)
Age Group (years)	18–30	38	34.5%
	31–45	44	40.0%
	46–60	20	18.2%
	>60	8	7.3%
Gender	Male	40	36.4%
	Female	70	63.6%
Type of Urticaria	Chronic spontaneous urticaria (CSU)	86	78.2%
	Chronic inducible urticaria (CIndU)	24	21.8%
Presence of Angioedema	Yes	42	38.2%
	No	68	61.8%
Duration of Disease	6 weeks–6 months	48	43.6%
	6 months–1 year	34	30.9%
	>1 year	28	25.5%

Table 1and figure 1, presents the majority of patients belonged to the 31–45 years age group (40.0%), followed by 18–30 years (34.5%), indicating that chronic urticaria predominantly affects young to middle-aged adults. A smaller proportion of patients were in the 46–60 years (18.2%) and >60 years (7.3%) age groups.

There was a clear female predominance, with females constituting 63.6% of the study population compared to 36.4% males, suggesting a higher susceptibility among women.

Regarding the type of urticaria, chronic spontaneous urticaria (CSU) was the most common subtype, observed in 78.2% of patients, whereas chronic inducible urticaria (CIndU) accounted for 21.8%. This indicates that CSU represents the predominant clinical form in the study population.

The presence of angioedema was noted in 38.2% of patients, while 61.8% did not exhibit angioedema, highlighting that a considerable proportion of patients experience deeper tissue involvement. In terms of disease duration, the largest group of patients (43.6%) had symptoms lasting between 6 weeks and 6 months, followed by 30.9% with a duration of 6 months to 1 year, and 25.5% with disease persisting for more than 1 year. This distribution suggests that a significant number of patients present in the earlier phases of chronicity, although a notable proportion experience prolonged disease.

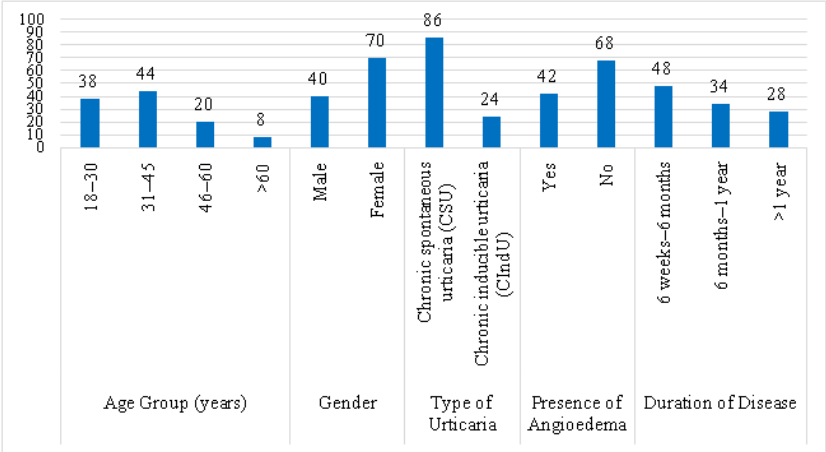

Figure 1: Demographic and Clinical Characteristics of Study Participants

Table 2: Distribution of Urticaria Severity (UAS7) and D-dimer Levels

Parameter	Mild (n=30)	Moderate (n=42)	Severe (n=38)	Total	p-value
Normal D-dimer (<0.5 µg/mL)	24 (80%)	14 (33.3%)	4 (10.5%)	42	<0.001
Elevated D-dimer (≥0.5 µg/mL)	6 (20%)	28 (66.7%)	34 (89.5%)	68	

Table 2 and figure 2 show that among patients with mild urticaria, 80% had normal D-dimer levels, whereas only 20% showed elevation. In contrast, elevated D-dimer levels were observed in 66.7% of moderate cases and 89.5% of severe cases. This demonstrates a strong positive association between disease severity and D-dimer levels. The difference was statistically highly significant ($p < 0.001$), indicating that elevated D-dimer is closely linked with increased disease activity.

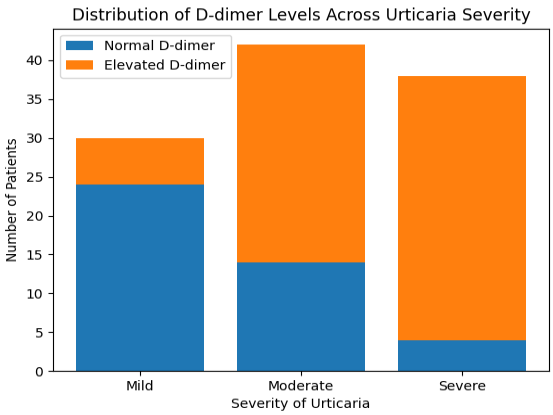

Figure 2: Distribution of Urticaria Severity (UAS7) and D-dimer Levels

Table 3: Correlation between D-dimer Levels and Clinical Parameters

Parameter	Mean D-dimer (µg/mL) ± SD	Correlation (r)	p-value
UAS7 Score	0.78 ± 0.34	0.68	<0.001
Duration of Disease	0.62 ± 0.28	0.29	0.02
Presence of Angioedema	0.81 ± 0.36	0.41	0.001

Table 3 show that A statistically significant positive correlation was observed between D-dimer levels and the UAS7 score ($r = 0.68$, $p < 0.001$), indicating that higher D-dimer levels are strongly associated with increased disease severity. This suggests that activation of the coagulation pathway may parallel the intensity of clinical symptoms.

A moderate positive correlation was also noted between D-dimer levels and the presence of angioedema ($r = 0.41$, $p = 0.001$), with patients exhibiting angioedema showing relatively higher mean D-dimer levels (0.81 ± 0.36 µg/mL). This finding implies that patients with more severe or systemic manifestations tend to have greater coagulation activation.

In contrast, the correlation between D-dimer levels and duration of disease was weak but statistically significant ($r = 0.29$, $p = 0.02$), suggesting that although longer disease duration may be associated with slightly elevated D-dimer levels, the relationship is less pronounced compared to disease severity.

Discussion

In the present study, the majority of patients belonged to the 31–45 years age group (40.0%), followed by 18–30 years (34.5%), indicating that chronic urticaria predominantly affects young to middle-aged adults. This observation is consistent with findings reported by Sharma et al. (2022), who noted a peak incidence in the third and fourth decades of life [10]. Similarly, Verma et al. (2023) also reported that most patients with chronic urticaria were within the 20–40 years age group [11].

A female predominance (63.6%) was observed in this study, which aligns with previous reports suggesting a higher susceptibility among women, possibly due to hormonal and autoimmune influences. Singh et al. (2021) reported a female preponderance of 60% in their cohort, supporting the findings of the present study [12]. Additionally, Kakati et al. (2022) attributed this gender difference to increased autoimmune tendencies in females [13].

With respect to disease subtype, chronic spontaneous urticaria (CSU) was the most common form (78.2%), which is in agreement with studies by Patel et al. (2024), who reported CSU in approximately 75% of cases [14]. Chronic inducible urticaria constituted a smaller proportion, consistent with global epidemiological trends.

The presence of angioedema in 38.2% of patients is comparable to findings by Reddy et al. (2022), who documented angioedema in nearly one-third of patients with chronic urticaria [15]. This highlights the clinical significance of angioedema as a common associated feature.

Regarding disease duration, most patients (43.6%) had symptoms for 6 weeks to 6 months, suggesting early presentation in a significant proportion. However, 25.5% had disease duration exceeding one year, indicating chronic persistence in a subset of patients. Similar findings were reported by Meena et al. (2023), who observed prolonged disease duration in nearly one-fourth of cases [16].

In the present study, 80% of patients with mild disease had normal D-dimer levels, whereas a substantial proportion of patients with moderate (66.7%) and severe disease (89.5%) exhibited elevated D-dimer levels. This clearly indicates a progressive increase in D-dimer levels with increasing disease severity.

The association was found to be statistically highly significant ($p < 0.001$), suggesting a robust relationship between coagulation activation and clinical severity. These findings are consistent with observations by Gupta et al. (2021), who reported significantly elevated D-dimer levels in patients with severe urticaria compared to mild cases [17]. Similarly, Banerjee et al. (2024) demonstrated that elevated D-dimer levels were significantly associated with higher UAS7 scores and refractory disease [18].

The underlying mechanism may involve activation of the extrinsic coagulation pathway, leading to thrombin generation and increased vascular permeability, which contributes to wheal formation. The progressive rise in D-dimer levels across severity categories in this study reinforces the hypothesis that coagulation markers can serve as indicators of disease activity. Present study, reveals a strong positive correlation between D-dimer levels and UAS7 score ($r = 0.68$, $p < 0.001$), indicating that higher D-dimer levels are closely associated with increased disease severity. This finding is in agreement with Kumar et al. (2022), who reported a significant positive correlation between D-dimer levels and urticaria activity scores [19]. Similarly, Das et al. (2024) observed that D-dimer levels could reliably reflect disease

severity and activity [20]. A moderate positive correlation was also observed between D-dimer levels and the presence of angioedema ($r = 0.41$, $p = 0.001$). Patients with angioedema demonstrated higher mean D-dimer levels, suggesting greater systemic involvement and enhanced coagulation activation. This is consistent with findings by Nair et al. (2023), who reported higher D-dimer levels in patients with angioedema compared to those without [21].

In contrast, the correlation between D-dimer levels and duration of disease was weak but statistically significant ($r = 0.29$, $p = 0.02$). This suggests that while prolonged disease may contribute to slight increases in D-dimer levels, it is not as strong a determinant as disease severity. Similar observations were made by Joshi et al. (2021), who reported a weak association between disease duration and coagulation markers [22].

Limitations of the Study

- The study was conducted at a single tertiary care centre, which may limit the generalizability of the findings to the wider population.
- The sample size ($n = 110$), though adequate, was relatively small for broader epidemiological extrapolation.
- The follow-up duration (8 weeks) was short, limiting long-term assessment of disease progression and D-dimer trends.
- Potential confounding factors influencing D-dimer levels (e.g., subclinical inflammation, comorbidities) may not have been completely excluded.
- The study did not include advanced immunological or coagulation markers, which could have provided deeper insights into pathophysiology.
- Being an observational study, causal relationships between D-dimer levels and disease severity cannot be definitively established.

Conclusion

The present study demonstrates that chronic urticaria predominantly affects young to middle-aged individuals, with a female predominance, and is most commonly of the chronic spontaneous subtype. A considerable proportion of patients also exhibit angioedema, indicating significant clinical burden.A statistically significant association was observed between serum D-dimer levels and disease severity, with elevated D-dimer levels being more frequent in patients with moderate to severe urticaria ($p < 0.001$). Furthermore, a strong positive correlation was identified between D-dimer levels and UAS7 score ($r = 0.68$), suggesting that D-dimer may serve as a reliable marker of disease activity. The presence of angioedema also showed a moderate positive correlation with D-dimer levels, whereas only a weak correlation was observed with disease duration. These findings indicate that D-dimer levels are more reflective of disease severity rather than chronicity. In conclusion, serum D-dimer can be considered a useful adjunctive biomarker in the assessment of disease severity in chronic urticaria. Its measurement may aid in risk stratification, monitoring of disease activity, and guiding therapeutic decisions in clinical practice.

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