

**Association of Blood Eosinophils in Patients with Acute & Chronic Urticaria****Karthik Ramappa<sup>1</sup>, Annie Rose L<sup>2</sup>**<sup>1</sup>Assistant Professor, Department of Dermatology, St Peter's Medical College, Hospital and Research Institute, Tamil Nadu, India<sup>2</sup>Assistant Professor, Department of Pathology, St Peter's Medical College, Hospital and Research Institute, Tamil Nadu, India

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Corresponding author: Dr. Karthik Ramappa

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**Abstract:**

**Introduction:** Eosinophilia, characterized by an elevated blood eosinophil count exceeding 500 cells/mm<sup>3</sup>, is frequently encountered in routine medical tests. However, the interpretation of eosinophilia can be complex in clinical practice due to its association with various underlying conditions. In the context of urticaria, eosinophils are thought to play a significant role in contributing to tissue damage. This potential impact of eosinophils on the inflammatory process of urticaria is supported by the link between urticarial skin lesions and eosinophil-related conditions, such as hyper-eosinophilic syndrome.

**Aim and Objectives:** To assess the relationship of absolute eosinophil count in patients with acute and chronic urticaria.

**Material and Methods:** A prospective observational study was conducted in a rural tertiary care hospital in southern India, in the dermatology department. The study aimed to involve 30 patients with acute urticaria, 30 patients of chronic urticaria, and 60 study subjects with age sex matched control were selected. In chronic urticaria 15 study subjects were symptomatic and 15 patients were asymptomatic at the time of sampling. Before participating in the study, all patients provided their informed written consent.

**Result:** In acute urticaria, the mean AEC of the study subjects 756.67±437.64, in chronic asymptomatic urticaria the mean 246.0±115.0, in chronic symptomatic urticaria group the mean AEC was 422.67±246.07, in control group the mean AEC group 194.10±120.05, on comparing there is significant difference with p value 0.0. On applying regression analysis there is almost no association between age of study subjects with AEC with R square 0.002.

**Conclusions:** The mean absolute eosinophil counts were significantly higher both in patients with acute urticaria and in patients with chronic symptomatic urticaria compared to that of the healthy subjects. Patients affected by acute urticaria showed eosinophil count values significantly higher than patients affected by chronic urticaria.

**Keywords:** Urticaria, AEC, Eosinophil Count, Wheals.

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**Introduction**

Urticaria is a common condition marked by recurring itchy wheals and swelling, thought to stem from occasional activation of skin mast cells by unknown means. The wheals appear on the upper and mid-dermis, forming a raised, red, and itchy rash caused by increased blood flow, vasodilation, and heightened vascular permeability. Although a subset of urticaria patients shows autoantibodies against the high-affinity IgE receptor (FceR1), indicating a potential autoimmune origin, the exact significance of this discovery remains uncertain.[1]

Wheals are raised areas of varying sizes and shapes accompanied by noticeable redness, often causing

itching. These lesions typically vanish within a day. The prognosis for both life and well-being in chronic urticaria (CU) is generally positive. However, the condition can be accompanied by other health issues. Overall, CU is a condition with an uncertain underlying cause, leading to frequent consultations with specialists and unnecessary diagnostic investigations. These efforts often aim to identify a triggering factor that might not be evident based solely on medical history[2].

Previous research has suggested that when it comes to urticaria, there is an increased presence of mast cells, monocytes, T-lymphocytes, and eosinophils in biopsy samples. However, the specific role of

eosinophils in causing skin lesions remains somewhat unclear. When eosinophils are activated, they release various inflammatory substances, including leukotrienes, the major basic protein, eosinophil cationic protein (ECP), eosinophil protein X/eosinophil-derived neurotoxin, and eosinophil peroxidase. This array of released substances suggests that eosinophils may be involved in both allergic and non-allergic mechanisms.[3]

Eosinophilia, which refers to an elevated blood eosinophil count exceeding 500 cells/mm<sup>3</sup>, is a common discovery in routine tests. This finding can be associated with various underlying conditions, making the evaluation of eosinophilia challenging in clinical practice. Eosinophils are believed to have a significant role in contributing to tissue damage in urticaria. The potential impact of eosinophils on the inflammatory process of urticaria is substantiated by the connection between urticarial skin lesions and eosinophilic disorders like hyper-eosinophilic syndrome [4].

Interestingly, while we can't rule out the involvement of other cells entirely, our investigation into the activation of the coagulation cascade revealed that in chronic urticaria, the cells expressing tissue factor, which triggers the activation of the extrinsic pathway, are eosinophils. In fact, immunohistochemical experiments demonstrated that tissue factor was co-located with eosinophil cationic protein, a well-established marker of eosinophils. These findings underscore the significance of eosinophils in chronic urticaria as a source of tissue factor. This aligns with recent studies indicating that eosinophils store tissue factor and promptly transfer it to the cell membrane upon activation.[5]

### Aim and Objective

To assess the relationship of absolute eosinophil count in patients with acute and chronic urticaria.

### Material and Methods

A prospective observational study was conducted in a rural tertiary care hospital in southern India, in the dermatology department. The study aimed to involve 30 patients with acute urticaria, 30 patients of chronic urticaria, and 60 study subjects with age-sex-matched control were selected. In chronic urticaria 15 study subjects were symptomatic and 15 patients were asymptomatic at the time of sampling. Before participating in the study, all patients provided their informed written consent. The research process involved a thorough examination of the patients' condition. 15 patients with chronic urticaria were symptomatic with daily eruptions, whereas 15 patients were asymptomatic for at least 3 weeks. Patients with urticaria, resulting predominantly from physical causes were excluded. Anti-histamine treatment was stopped at least 48h before the blood samples were collected. None of the patients was taking steroids or immuno-suppressive drugs at the time of the study.

The following information was collected from each participant:

For the purpose of analysis, blood samples were drawn from the patients' veins using K2 EDTA tubes. Complete blood counts, including absolute eosinophil counts (AEC), were measured using a Abbot celldyn 5 part analyzer. A normal AEC range of 40 - 440 was considered standard. The statistical analysis of the data involved the use of SPSS software version 16. A comparative analysis was performed between the patient group and a control group (presumably individuals without chronic urticaria). In addition, Spearman's rank correlation coefficient (Spearman's rho) was employed when necessary to explore potential associations between variables. Statistical significance was set at a two-tailed p-value of less than 0.05.

### Result

**Table 1: Distribution of study subjects as per age group**

Diagnosis	Mean	N	Std. Deviation
Acute Urticaria	39.83	30	11.277
Chronic asymptomatic Urticaria	39.60	15	11.432
Chronic symptomatic Urticaria	34.40	15	10.162
Control	35.77	60	12.141
Total	37.09	120	11.666

ANOVA test applied, F value – 1.22, p value – 0.299

Tab 1 shows distribution of study subjects as per age group, The mean age of the study subjects in acute urticaria was 39.83±11.28 yr, in chronic asymptomatic urticaria was 39.60±11.43 yr, in chronic symptomatic urticaria the mean age was 34.40±10.16yr, whereas in control the mean age was 35.77±12.14 yr, on comparing there is non-significant difference among them.

**Table 2: Distribution of study subjects as per sex**

		Diagnosis				Total
		acute	chronic asymptomatic	chronic symptomatic	Control	
Sex	F	20	11	11	38	80
	M	10	4	4	22	40
Total		30	15	15	60	120

Chi-square value- 0.9, p value- 0.82, non-significant

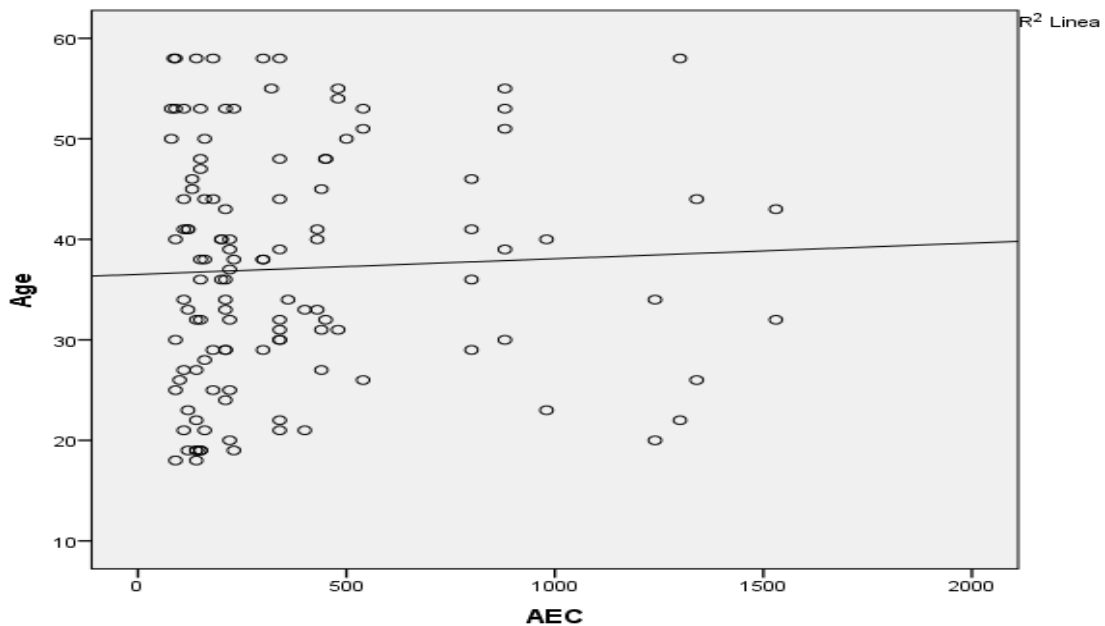
Tab 2 shows Distribution of study subjects as per sex, In acute urticaria out of 30 study subjects, 20 study subjects were female, in chronic asymptomatic urticaria as well as chronic symptomatic group out of 15 study subjects 11 were female respectively, In control group out of 60 study subjects 38 subjects were female. On comparing there is non-significant difference with p value 0.82.

**Table 3: Mean AEC of the study subjects**

Diagnosis	Mean	N	Std. Deviation
Acute	756.67	30	437.645
Chronic asymptomatic	246.00	15	115.003
Chronic symptomatic	422.67	15	246.068
Control	194.10	60	120.050
Total	369.80	120	343.629

Anova test applied, F value- 48.65, p value- 0.0

Table 3 shows Mean AEC of the study subjects, In acute urticaria, the mean AEC of the study subjects 756.67±437.64, in chronic asymptomatic urticaria the mean 246.0±115.0, in chronic symptomatic urticaria group the mean AEC was 422.67±246.07, in control group the mean AEC group 194.10±120.05, on comparing there is significant difference with p value 0.0



**Figure 1: Association of Age of study subjects with AEC**

Fig 1 shows Association of Age of study subjects with AEC, On applying regression analysis there is almost no association between age of study subjects with AEC with R square 0.002

**Discussion**

Urticaria is a common allergic skin disease affecting 15% to 25% of the population at least once in lifetime, which occurs either acutely or evolve in chronic course. Acute urticaria can present as acute onset of transient wheals with or without associated angioedema for less than 6 weeks, whereas chronic urticaria presents with

wheals occurring continuously or intermittently for at least 6 or more weeks. Urticaria has a major psychological impact on the quality of life of patients.

Chronic urticaria (CU) affects 0.5–1% of the general population worldwide with CSU accounting for more than two-thirds of CU cases. Urticaria is a mast cell- driven disease. Histamine

and other mediators, such as platelet-activating factor (PAF) and cytokines released from activated skin mast cells, result in sensory nerve activation, vasodilatation and plasma extravasation as well as cell recruitment to urticarial lesions. The mast cell-activating signals in urticaria are ill-defined and likely to be heterogeneous and diverse. Highly selective ligand interactions ELAM 1 and ICAM 1 provide a powerful mechanism to control the sequential evolution of inflammatory cell infiltration in urticarial wheals during their development in time. Mast cells (MC) are the primary effector cells in urticaria and in many cases of angioedema. These cells are widely distributed in the skin, mucosa, and other areas of the body, and have high-affinity immunoglobulin E (IgE) receptors. Immunoglobulin E is believed to be one of the major mediators of immediate hypersensitivity reactions that underlie atopic conditions such as urticarial, IgE-mediated allergic mechanisms are incriminated in certain cases of chronic urticaria, because elevated serum IgE levels are found in these patients.

In the present study the mean age of the study subjects in acute urticaria was  $39.83 \pm 11.28$  yr, in chronic asymptomatic urticaria was  $39.60 \pm 11.43$  yr, in chronic symptomatic urticaria the mean age was  $34.40 \pm 10.16$ yr, whereas in control the mean age was  $35.77 \pm 12.14$  yr, on comparing there is non-significant difference among them. Study by Naveen N et al [6] shows The mean age of cases was  $29.23 \pm 1.27$  years (3 months to 62 years). Amongst which 23 patients (22.33%) were of paediatric age group (<18 years) and 82 patients (79.61%) were between 19 and 60 years and one patient was more than 60 years.

These findings suggest that urticaria, whether acute or chronic, does not appear to be strongly influenced by age in this study. This could have clinical implications, indicating that the likelihood of developing urticaria or the type of urticaria a patient might have is not strongly associated with their age within this age range.

Other factors, such as allergens, immune system responses, genetics, or environmental factors, may play more significant roles in determining the presence and nature of urticaria in these individuals. Study by AB KAY et al [7] in their study found that mean age of the study subjects was 51 years, and age range 32–71 years. Immune responses can vary with age. For instance, children and elderly individuals might have different immune reactions compared to adults. Younger individuals might have more robust responses due to a more active immune system, while elderly individuals might experience changes in immune function.

In the present study In acute urticaria out of 30 study subjects, 20 study subjects were female, in chronic asymptomatic urticaria as well as chronic symptomatic group out of 15 study subjects 11 were female respectively, In control group out of 60 study subjects 38 subjects were female. On comparing there is non-significant difference with p value 0.82. Gender-based differences in immune responses are well documented. Hormonal differences between males and females can influence immune system activity and responses to allergic conditions. For instance, estrogen has been associated with enhancing allergic reactions, potentially leading to differences in how eosinophils are activated and their role in allergic conditions like urticaria. Eosinophils have been studied in the context of gender differences and allergic diseases. Some research suggests that females may have a higher baseline eosinophil count compared to males, which might contribute to variations in allergic reactions. This could be due to hormonal factors, genetic predisposition, or a combination of both. Study by AB KAY et al [7] shows 62.5% study subjects were female which corresponds to our present study.

In the present study In acute urticaria, the mean AEC of the study subjects  $756.67 \pm 437.64$ , in chronic asymptomatic urticaria the mean  $246.0 \pm 115.0$ , in chronic symptomatic urticaria group the mean AEC was  $422.67 \pm 246.07$ , in control group the mean AEC group  $194.10 \pm 120.05$ , on comparing there is significant difference with p value 0.0. Study by Agrawal A. et al [8] shows in their study Absolute eosinophil count ranged from 300-2000 cells/cu mm with mean Absolute eosinophil count of 553 cells/cu mm. Study by Kai-Lin Chang et al [9] shows the significance of eosinophil percentage between the acute and chronic groups, 84 and 54 patients were included, respectively, and the results showed no statistical difference (median of 2.1% in the acute group vs. 2.0% in the chronic group,  $p = 0.836$ ). The proportion of patients with elevated eosinophil percentages was also analyzed and compared between the two groups.

Absolute Eosinophil Count (AEC), which implies that as eosinophil levels increase or decrease, there are corresponding changes in the severity of urticarial symptoms. Eosinophils are known to play a role in various allergic reactions, including urticaria.

They release pro-inflammatory molecules that can contribute to tissue damage and itching. Eosinophil infiltration in urticarial lesions has been observed, which might correlate with disease activity.

### Conclusions

The absolute eosinophil counts were significantly higher both inpatients with acute urticaria and in

patients with chronic symptomatic urticaria compared to that of the healthy subjects. Patients affected by acute urticaria showed eosinophil count values significantly higher than patients affected by chronic urticaria. No significant difference was found between the healthy subjects and the patients with asymptomatic chronic urticaria. So absolute eosinophil counts adds value as routine test in case of acute urticaria & chronic symptomatic urticaria in case of rural set up where patient can't afford expensive tests.

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