

# Chronic Spontaneous Urticaria: Clinical Profile, Autologous Serum Skin Test Positivity and Associated Impairment in Quality of Life in Nepalese Patients

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## ABSTRACT

### Background

Chronic Spontaneous Urticaria is considered to be an autoimmune phenomenon in half of the total cases. Autologous serum skin test is a simple screening test for the presence of auto-antibodies in chronic urticaria. Significant impairment in quality of life have been observed in autologous serum skin test positive cases. There are limited literatures on chronic spontaneous urticaria, autologous serum skin test and associated Dermatology Life Quality Index in Nepal till date.

### Objective

To find the proportion of autologous serum skin test positive cases in chronic urticaria and impairment in quality of life in such patients.

### Method

This was a retrospective review of outpatient records of patients diagnosed with chronic spontaneous urticaria, from January 2018 to December 2019, from a tertiary care hospital in Kathmandu, Nepal. Details of the patients, autologous serum skin test and dermatology life quality index scores were analyzed and presented.

### Result

Among the total 114 cases positive autologous serum skin test was seen in 48.2% of cases. The mean total Dermatology Life Quality Index score was  $8.06 \pm 6.64$ . A significantly higher quality of life impairment was observed in patients with positive autologous serum skin test as compared to the negative ones. The odds of finding a positive autologous serum skin test in patients with angioedema was 2.1, however the difference was not statistically significant.

### Conclusion

Chronic spontaneous urticaria was more common in females as compared to males. A positive autologous serum skin test was present in half of the patients which was in turn associated with a greater impairment of quality of life.

## KEY WORDS

*Autologous serum skin test, Chronic urticaria, Dermatology life quality index, Quality of life*

## INTRODUCTION

Chronic Urticaria (CU), is characterized by the sudden appearance of wheals, angioedema, or both and associated itching for more than six weeks. It is classified in two different types: Chronic Spontaneous Urticaria (CSU) and Chronic Induced Urticaria (CIU).<sup>1</sup> In the patients with CSU, the etiology is either uncertain or believed to be of autoimmune in origin which is in contrast with CIU where the physical factors like heat or cold are responsible. The worldwide prevalence of the CSU is estimated to be 0.5% -1%.<sup>2</sup> In a study conducted in rural Nepal, the prevalence of Urticaria was 2.4%.<sup>3</sup>

In all cases of CSU, complete blood count (CBC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are routinely recommended based on European guidelines, and other tests based on history and examination to establish the cause.<sup>1</sup> The patient reported measures of disease severity are equally important in patient management and Dermatology Life Quality Index (DLQI) is one of the tools to measure them.<sup>4</sup> It is a well validated tool for measuring the impact in quality of life (QoL) due to CU.<sup>5</sup>

CSU is considered to be an auto-immune phenomenon in almost half of the total cases.<sup>6</sup> Autologous serum skin test (ASST) is a simple screening test for the presence of autoantibodies in patient with CSU with the negative predictive value of 92.8% (range 81.4-100%).<sup>7</sup> It is one of the most feasible tests in our setting for that purpose. Positive ASST is associated with prolonged disease and poor response to routine therapy.<sup>8</sup> There are limited literatures on ASST in CU and DLQI published from Nepal till now. This study assesses the frequency of ASST in patients with CSU and also analyzes the impairment of quality of life in ASST positive CSU patients. This will help clinician to understand the etiology of CSU and its impact on quality of life and hence helps in making better decision for long term management of these patients.

## METHODS

This was a retrospective study carried out by reviewing records of Out Patient Department (OPD) of Dermatology and Venereology, Civil Service Hospital, Kathmandu, Nepal from January 2018 to December 2019. The patients diagnosed with CSU and CSU associated with CIU of 16 years of age and above were included in the study. Patients with diagnosis of CIU, Urticaria associated with syndromes, systemic inflammatory conditions, and Urticarial vasculitis were excluded from the study. The DLQI questionnaire's Nepali version was also completed by the patients. The questionnaire has been a standard patient reported tool to measure the quality of life impairment in skin conditions including chronic urticaria in our OPD. The study variables included demographic and clinical data, positivity of ASST, association of CSU with CIU, association with angioedema, other associated factors (systemic symptoms, food

allergens, aggravation during menstrual periods) and DLQI.

The patients of chronic urticaria were subjected to a baseline investigation (CBC, ESR, CRP) to rule out underlying infections or systemic inflammatory conditions as per European guidelines.<sup>1</sup> All patients with CSU underwent an ASST which was also done routinely in our hospital in cases of CSU.

Procedure of ASST was carried out as recommended by the European Academy of Allergy and Clinical Immunology/Global Allergy and Asthma European Network (EAACI/GA2 LEN) task force consensus report.<sup>7</sup> In a plain sterile container, 3ml of the patient's venous blood was collected and left to clot for 30 minutes. Then it was centrifuged for 10 minutes at 500 rpm which separated blood from serum. A 0.05 ml of the freshly prepared serum was then injected over the volar aspect of patient's forearm with the help of 27G needle. Sterile saline (0.05 ml) was injected 5 cm below the serum as the negative control. Induction of wheal greater than 1.5 mm diameter with the serum as compared to the wheal induced by normal saline was considered to be positive. Due to the unavailability of histamine, the positive control was not used in any of the cases.

Along with all the demographics, ASST and lab reports were also reviewed, tabulated and analyzed. Similarly, the total scores from DLQI questionnaires were also included.

Ethical approval for this study was taken from Institution Review Committee (IRC) of Civil Service Hospital (IRC protocol no. 21/2020).

Based on the distribution of continuous variables independent T-test or Mann Whitney U test were used to compare means of ASST positive and ASST negative patients. Odds of ASST positive in different categorical variables were calculated and association was tested by using Chi square test. All statistical analyses were performed using Statistical Package for Social Science (SPSS), v.25. In all analyses  $\alpha$  was set at 5%.

## RESULTS

In total, 114 cases were included in the final analysis. The mean age ( $\pm$  SD) of the population included was  $32.99 \pm 12.84$  years. Females outnumbered males with a male:female ratio of 1:1.65. Out of 114 patients with CSU, 48.2% tested positive for ASST. The mean ( $\pm$  SD) of total DLQI score was  $8.06 \pm 6.64$ . Other demographic findings are summarized in table 1.

Mann Whitney U test revealed a significantly higher QoL impairment in ASST positive patients compared to ASST negative ones (table 2).

The odds of finding positive ASST in patients with angioedema was found to be 2.1. Similarly those who had systemic symptoms and male sex had odds greater than 1 for positive ASST (table 3).

**Table 1. Demographic characteristics of the study population**

| Characteristics                                     | Number (%)          |
|---|---------------------|
| ASST  | Positive 55 (48.2)  |
|   | Negative 59 (51.8)  |
| Sex   | Male 43 (37.7)      |
|   | Female 71 (62.3)    |
| Occupation  | Housewife 50 (43.9) |
|   | Student 31 (27.2)   |
|   | Employed 33 (28.9)  |
| Angioedema  | Yes 38 (33.3)       |
|   | No 76 (66.7)        |
| Family History                                      | Yes 8 (7.0)         |
|   | No 106 (93.0)       |
| Systemic symptoms                                   | Yes 28 (21.9)       |
|   | No 89 (78.1)        |
| Chronic Inducible Urticaria                         | Yes 26 (22.8)       |
|   | No 88 (77.2)        |
| Food or Drug Intolerance                            | Yes 5 (4.4)         |
|   | No 109 (95.6)       |
| Aggravation with menstrual cycle (Total number =71) | Yes 5 (7.0)         |
|   | No 66 (93.0)        |

**Table 2. Mean  $\pm$  SEM of the continuous variables grouped as ASST positive and negative groups and compared with Mann Whitney U test (p value)**

|                    | ASST positive    | ASST negative    | p value |
|--------------------|------------------|------------------|---------|
| Total DLQI score   | 9.67 $\pm$ 0.98  | 6.56 $\pm$ 0.74  | 0.015   |
| Age in years       | 30.85 $\pm$ 1.49 | 34.98 $\pm$ 1.84 | 0.175   |
| Duration in months | 19.42 $\pm$ 3.69 | 11.44 $\pm$ 1.85 | 0.345   |
| ESR in mmHg/1hr    | 11.82 $\pm$ 1.03 | 12.97 $\pm$ 0.97 | 0.234   |

SEM: Standard Error of Mean, ASST: Autologous Serum Skin Test

**Table 3. Odds of ASST positive with other categorical variables**

|                    | Odds ratio | 95% CI        | p value |
|--------------------|------------|---------------|---------|
| Angioedema         | 2.10       | (0.95 - 4.67) | 0.064   |
| Systemic symptoms  | 1.49       | (0.61 - 3.64) | 0.380   |
| Physical urticaria | 0.89       | (0.37 - 2.15) | 0.808   |
| Male sex           | 1.20       | (0.56 - 2.57) | 0.628   |

CI: Confidence Interval

## DISCUSSION

The number of females presenting with CSU outnumbered males in our study, similar to most of the other studies as reviewed by Cassano et al.<sup>9</sup> The mean age of presentation of CSU in our study was 32.99  $\pm$  12.84 years. This was similar to other similar studies conducted at hospital settings as seen in a review by Niu et al.<sup>10</sup> This suggests that CSU is mainly an adult onset disease, but our inclusion criteria could have caused higher mean age.

CU is subdivided in CSU and CIU, but there is a considerable overlap in their presentation. In our study 22.8% of patients with CSU had one or the other form of CIU. Physical triggers

were found in 75.9% of CSU patients in a study by Sánchez et al., however, only 36.3% had positive challenge tests in that study.<sup>11</sup>

Angioedema was found in 33.3% of the patients of CSU in this study which was similar to the findings from a multi-centric European study (40.3%).<sup>12</sup>

Systemic symptoms were found in 21.9% of the patients in our study. However, the systemic symptoms were not recorded according to the different systems due to time constraints. The systemic symptoms in a similar epidemiological study by Doong et al., were joint pain or swelling (55.3%), headache/fatigue (47.6%), flushing (42.7%), wheezing (30.1%), gastrointestinal complaints (26.2%), and palpitations (9.7%).<sup>13</sup>

Food or drug intolerance was seen in 4.4% only, aggravation during menstrual cycle in 7% and a positive family history of CU in 7% of the cases.

ASST was found to be positive in 48.2% of the study population in our study. This was similar to findings by Kumar et al. (42%), higher than Karn et al., (36.2%), and Godse. (27.67%), but lower than Giri et al., (65.4%), Kocaturk et al., (63%), and Boonpiyathad et al. (63.7%).<sup>14-19</sup> A review of large pool of data conducted by Konstantinou et al. found ASST positivity of 45.5% (95% CI, 24.7–74.4%).<sup>7</sup> This study showed that we have almost half of the CSU patients with autoimmunity and will thus require long term treatment.

This study showed that ASST positive patients had a significantly higher impairment in QoL than those with a negative ASST. But similar finding was not found in other studies conducted in CSU.<sup>18,19</sup> However, in a study by Boonpiyathad et al, a mean wheal diameter of the ASST had a positive correlation with DLQI scoring.<sup>19</sup> The odds of getting a positive ASST was higher with the presence of angioedema, systemic symptoms and the male sex. But none of the associations reached statistical significance. This non-association of angioedema and ASST status was seen in other studies as well.<sup>18,19</sup>

Unavailability of Histamine as a positive control and inability of confirmation of autoantibodies with the Basophil Histamine Release Assay or Western-blot.

## CONCLUSION

CSU was more common in females as compared to males. A positive ASST was present in half of the patients which was in turn associated with a greater impairment of quality of life. However, no relation was noted, of ASST positivity, either with the duration of disease or with the presence of angioedema.

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