

# Acute Urticaria: Etiologies, Clinical Course and Quality of Life

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**SUMMARY** One hundred patients with acute urticaria were prospectively studied over a 2-year period with respect to etiology, clinical features and outcome, including the patient's quality of life using a Thai version of the Dermatologic Life Quality Index (DLQI). Twenty-one patients (21%) turned out to have chronic and 79 acute urticaria. Itchy sensations had the highest mean DLQI score translating to the highest negative impact on the quality of life. In more than half of the patients, the cause of the acute urticaria could not be identified. The most common identified causes of acute urticaria were infections (36.7%), followed by drugs, foods and insect bite reactions. Among those with acute urticaria, sixteen percent had co-existing angioedema, and one fourth had systemic symptoms, the most common being dyspnea. Patients with extensive wheals tended to have co-existing angioedema and also a statistically significant higher percentage of systemic symptoms, higher mean pruritus and mean DLQI scores than those with less body surface area involvement. Fifty-six percent of the patients with acute urticaria had complete remissions within 1 week; 78.5%, within 2 weeks and 91.1%, within 3 weeks.

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Acute urticaria is defined by a spontaneous appearance of wheals, sometimes accompanied by angioedema, for a duration of no more than 6 weeks.<sup>1</sup> Although acute urticaria is common, only few studies were published concerning its etiologies and clinical course.<sup>2,3</sup> Food allergy, infections and drug reactions are frequently regarded as possible causes.<sup>2-5</sup> Aoki *et al.*<sup>2</sup> studied patients with acute urticaria and suggested that urticaria is an immunologically erroneous reaction to foreign body inoculation, of which the large majority was supposed to be acute infections.

Some authors reported immunogenetic differences between Asian and Caucasian populations, resulting in differences in the clinical presentation and the frequency of autoantibodies in some autoimmune diseases.<sup>6,7</sup> Moreover, different dietary habits and environments, as well as the socioeconomic status, may cause different allergen sensitizations.

Several validated dermatology questionnaires have been created to measure the impact of skin diseases on the quality of life. The Dermatologic Life Quality Index (DLQI) is a 10-item self-administered English language questionnaire developed in Wales by Finlay and Khan<sup>8</sup> to measure the effects of different skin disorders on the quality of patients' lives. It is a simple, compact, uniform questionnaire, applicable to patients with any skin disease. Tiedra *et al.*<sup>9</sup> suggested that the DLQI was suitable as a transcultural equivalent instrument for international research. The DLQI has been translated into many languages including Thai. The Thai version of the DLQI was evaluated by Kulthanan *et al.*<sup>10</sup> to be highly valid and reliable.

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This study aimed to investigate etiologies, clinical features and outcome of acute urticaria at the Siriraj Hospital, Mahidol University. We also assessed the effects of acute urticaria on the patient's quality of life using the Thai version of the DLQI.

## MATERIALS AND METHODS

This study was approved by the Ethical Committee on Research Involving Human Subjects of Siriraj Hospital, Mahidol University, Thailand.

We prospectively studied patients with acute urticaria attending the outpatient clinic of the Department of Dermatology, Siriraj Hospital between August 2006 and July 2007. Patients aged over 18 years with newly developed (not more than 7 days from the initial onset) and untreated acute urticaria were enrolled. The diagnosis of urticaria was made clinically through the presence of itchy wheals of short duration. All patients were followed up by the same physician until remission.

Demographic data, etiologies, clinical features, course of the disease, treatment and outcome were studied. Associated acute infectious diseases were searched for. Drug reaction was regarded as a likely cause if a drug had been taken within 24 hours of the onset of the urticarial rash. Food intolerance was regarded as a likely cause if urticaria occurred within 2 hours after ingestion of suspected foods. Foods and drugs that were subsequently tolerated after a challenge in a remission period were excluded from the causes of urticaria. Other data obtained were personal histories of allergic rhinitis, asthma, atopic dermatitis and allergic conjunctivitis.

On the examining day, patients were also asked for a pruritus severity evaluation using the Visual Analog Scale (VAS), with a minimum score of 0 and a maximum score of 10, "0" meaning "no itch at all" and "10" "worst itch ever".

All patients were asked to complete the Thai version of the DLQI questionnaire by themselves. Dr. A.Y. Finlay had kindly given formal permission for its use in our study. This questionnaire consists of 10 questions, each referring to the previous 7 days. The questions cover disabilities at work, leisure, daily activities, personal relationships and treatment.

Each question has 5 possible answers: 'not relevant (not applicable)', 'not at all', 'a little', 'a lot', or 'very much' with the corresponding scores of 0, 0, 1, 2, and 3, respectively. The questions are simple and short and the questionnaire takes only a few minutes to complete. The DLQI total score is calculated by adding the scores of all 10 questions, with a maximum score of 30 and minimum score of 0. The higher the score, the greater the impairment of the quality of life.

All patients were prescribed antihistamines, mostly hydroxyzine 10 mg or loratadine 10 mg a day, but they were asked to take the medication as little as possible, and only to relieve intolerable symptoms. All patients were followed up until their urticaria cleared. Those who had a chronic course were followed up every 4 weeks.

The patients were instructed to record their symptoms in diary cards daily. The interview was repeated at a second visit a week later or by telephone if the patient did not appear at the follow up date.

## Statistical analyses

All statistical analyses were performed using SPSS 10.0 for windows software (SPSS Incorporated, Chicago, IL 60606). The categorical and continuous data were reported as the percentage and mean  $\pm$  SD, respectively. The Chi-Square test was used to analyze the association of categorical data. ANOVA and Bonferroni multiple comparisons were used to compare more than two groups for normal distribution. The T-test was used to compare two groups for normal distribution data (DLQI). The Mann-Whitney U test was used to compare two groups for non-normal distribution data. A  $p$ -value  $< 0.05$  was considered statistically significant.

## RESULTS

One hundred patients were enrolled in the study out of which 78 cases (78%) were female. The mean age of the patients was 37.6 (13.9) years with an age range of 18 to 84 years. Twenty-one patients (21%) turned out to have chronic urticaria. Of the 79 patients who had acute urticaria, 61 cases (77.2%) were female. The mean age of the patients with

**Table 1** Demographic data of the patients

Data	All patients (100 cases)		Acute urticaria (79 cases)	
	Number of patients	Percent	Number of patients	Percent
<b>Sex</b>				
• Male	22	22	18	22.8
• Female	78	78	61	77.2
<b>Dermographism</b>	27	27	22	27.8
<b>BSA*</b>				
• < 10%	44	44	30	38.0
• 10-50%	37	37	31	39.2
• > 50%	19	19	18	22.8
Angioedema	16	16	13	16.5
<b>Systemic symptoms</b>	28	28	22	27.8
• Dyspnea	20	20	16	20.3
• Abdominal pain	5	5	5	6.3
• Arthralgia	5	5	5	6.3
• Myalgia	2	2	0	0
• Fainting	1	1	1	1.3
<b>Episode</b>				
• First	49	49	38	48.1
• Recurrence	51	51	41	51.9
<b>Underlying disease</b>	29	29	24	30.4
• SLE	1	1	1	1.3
• Thyroid disease	5	5	3	3.8
• Other	24	24	21	26.6
<b>History of atopy</b>	33	33	25	31.9
<b>Patient</b>	22	22	18	22.8
• Asthma	2	2	2	2.5
• Allergic rhinitis	20	20	16	20.6
• Allergic conjunctivitis	4	4	3	3.8
• Atopic dermatitis	0	0	0	0
<b>Family</b>	22	22	17	21.5
• Asthma	7	7	5	6.3
• Allergic rhinitis	15	15	12	15.2
• Allergic conjunctivitis	1	1	0	0
• Atopic dermatitis	2	2	2	2.5

\*Body surface area

acute urticaria was 38.7 ( $\pm$  14.5) years (range 18-84 years). Demographic data of all patients and the group with a final diagnosis of acute urticaria are shown in Table 1.

Out of the 79 patients with acute urticaria, nearly half were experiencing the first attack of acute urticaria. The others had recurrent attacks (Table 1).

The mean amount of recurrences was 6.1 times (range 2-20). The average time interval between recurrences was 12.1 years. The patients with recurrent attacks had a higher percentage of personal histories of atopy as compared to those with the first episode of acute urticaria; however, the difference was not statistically significant. The patients with a higher rate of recurrences did not have a statistically

significant higher percentage of personal histories of atopy than those with fewer recurrences.

Sixteen percent of the patients had co-existing angioedema, and one fourth had systemic symptoms, the most common being dyspnea. The mean pruritus score was 7.4 (range 0.25-10). Eighteen of 79 patients (22.8%) had a personal history of atopy, the most common co-existing affliction was allergic rhinitis (16 cases, 20.6%).

Table 2 shows the possible causes of acute urticaria. For more than half of the patients, the cause could not be identified. The most common identified cause was infection, of which upper respiratory tract infection was the most frequent. Other causes were drugs, foods (yeast) and insect bite reactions (unknown names). The culprit drugs were coamoxiclav (2 cases), candesartan (1 case), omega-3, 6, 9 (1 case) and levofloxacin (1 case).

The interval between the start of the infectious symptoms and the onset of urticaria was approximately 6 days for most of the patients (26 of 29 cases, 89.7%). Three of 29 patients (10.3%) had the onset of the infectious symptoms at a mean of 3 days after the onset of urticarial symptoms. The mean duration of infectious symptoms was 3.9 days. Overall, the infections had a tendency to subside about 2 to 3 days before the remission of the urticarial symptoms. In fourteen of 26 cases (53.9%), the infectious symp-

toms had remissions before the urticarial symptoms at a mean (SD) of 5.14 (2.96) days (range 1-11 days). In 4 of 26 cases (15.4%), the remission of the infectious symptoms occurred simultaneously with the remission of the urticarial symptoms. In 8 of 26 cases (30.8 %), the infectious symptoms had remissions after the urticarial symptoms at a mean (SD) of 2.44 (1.76) days (range 0.5-5 days).

Fig. 1 shows the pruritus scores of the patients with acute urticaria. Most patients had moderate to severe itchy sensations with a mean (SD) pruritus score of 7.4 (2.0).

**Table 2** Possible causes of acute urticaria

Cause	Number of patients	Percent
<b>Unknown</b>	42	53.2
<b>Infections</b>	29	36.7
Upper respiratory tract infection	21	26.6
Diarrhea	5	6.3
Dental caries	2	2.5
Cystitis	1	1.3
<b>Drugs</b>	5	6.3
<b>Foods</b>	1	1.3
<b>Insect bite reactions</b>	2	2.5
<b>Total</b>	79	100

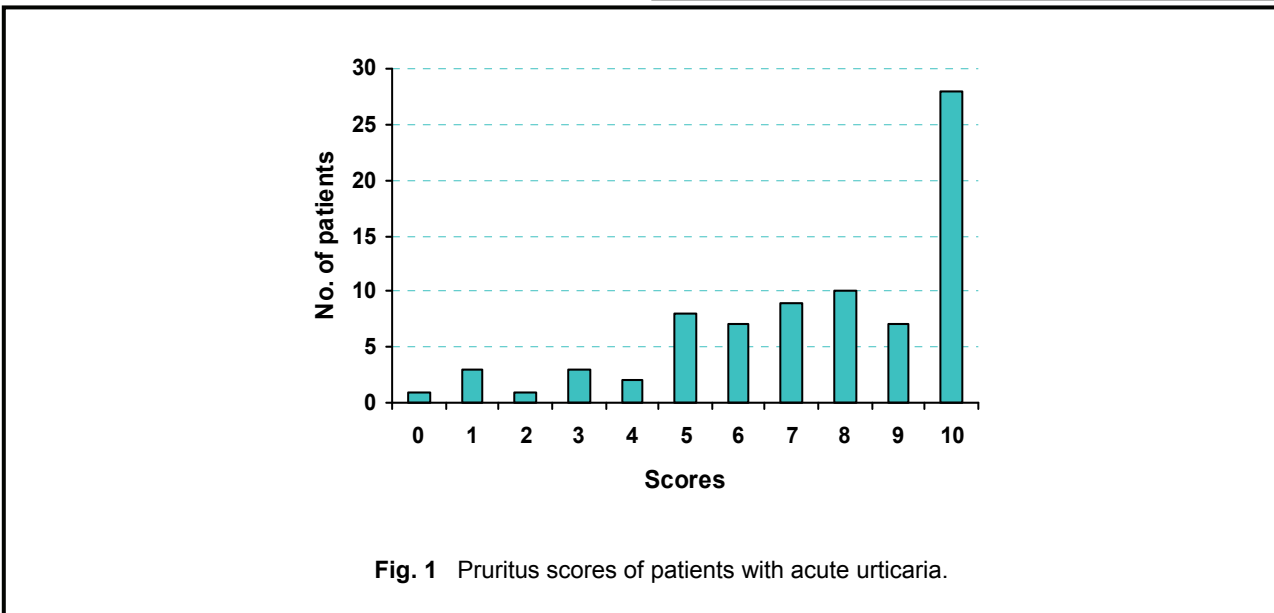


Fig. 1 Pruritus scores of patients with acute urticaria.

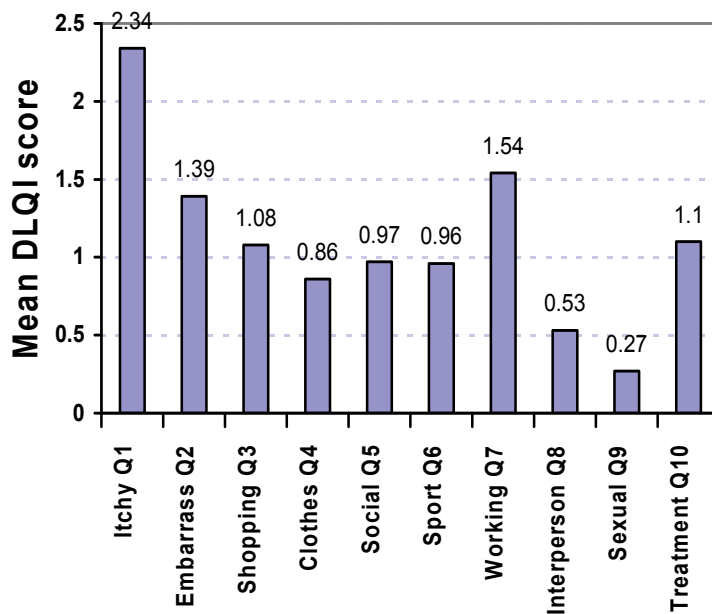
Fig. 2 shows the mean scores of each DLQI question in patients with acute urticaria. All patients completed all 10 questions in the questionnaire. The mean (SD) of the total DLQI score was 11.05 (7.3) with a range of 0 to 27. There was no statistically significant difference between the mean total DLQI score of males and females. Question 1 on itchy sensations had the highest mean DLQI score (2.34), while question 9, about sexual difficulties had the lowest mean DLQI score (0.27). Other questions that also had a high mean DLQI score were questions 7, 2, 10 and 3 which represented work/study, embar-

rassment, treatment and shopping. Tables 3 and 4 show the association of the body surface area (BSA) involvement of urticarial wheals with other clinical features. The patients with extensive wheals (> 50% BSA involvement) tended to have co-existing angioedema. They also had a statistically significant higher percentage of systemic symptoms, a higher mean pruritus score and mean total DLQI score compared to the patients with less BSA involvement. The most important factor that affected the mean total DLQI score was pruritus.

**Table 3** Body surface area (BSA) involvement in acute urticaria and clinical features (n = 79)

Clinical features	Number of patients	BSA			P value
		< 10% (n = 30) Number (%)	10-50% (n = 31) Number (%)	> 50% (n = 18) Number (%)	
Angioedema	13	4 (13.3)	3 (9.7)	6 (33.3)	0.08
Systemic symptoms	22	4 (13.3)	7 (22.6)	11 (61.1)*	0.001

\*p = 0.001 (Chi-square test), compare with BSA < 10% and 10-50% in the same data



**Note:** Q, question; Q1, itchy/sore/painful/stinging skin; Q2, embarrassment/self consciousness; Q3, Interfering with shopping/home working or gardening; Q4, clothes; Q5, social or leisure activities, Q6, sport difficulties; Q7, working or studying problems; Q8, interpersonal problems, Q9, sexual difficulties; Q10, treatment difficulties.

**Fig. 2** The mean scores of each DLQI question in patients with acute urticaria.

Fifty-six percent of the patients had complete remissions within 1 week; 78.5%, within 2 weeks and 91.1%, within 3 weeks. Acute urticaria with idiopathic cause had the longest mean remission (median = 8.5 days) (range 1-37 days) (Table 5). The others, in decreasing order of mean remission, were drugs, infectious causes, insect bite reactions and foods. It should be noted that there was only a small number of patients who had acute urticaria from drugs, insect bite reactions and foods. However, there was no statistically significant difference of the mean remission day between the idiopathic group and the others.

Most of the patients who had acute urticaria from infections had complete remission within 3 weeks. Among the patients who presented with acute urticaria of infectious etiology as verified by patient histories, physical examination and investigation, the

urticaria actually turned out to be acute in 82.9% and chronic in 17.1% of the cases. If the urticaria was of idiopathic causes, the probability that the patients turned out to have acute urticaria was 73.7% and chronic urticaria 26.3%. However, all (100%) of the patients who had urticaria from drugs, foods and insect bite reactions turned out to have acute urticaria.

## DISCUSSION

Previous studies reported a high prevalence of females and young to middle-aged patients with acute urticaria<sup>5</sup>, similar to our study. It should be noted here that we included only adult patients with acute urticaria.

Aoki *et al.*<sup>2</sup> published a study of 50 Japanese patients with acute urticaria, 31 of which (62%) experienced symptoms suggestive of infections, mostly

**Table 4** Urticaria severity according to BSA involvement (n = 79)

Score	BSA			p value
	< 10% (n = 30)	10-50% (n = 31)	> 50% (n = 18)	
<b>Pruritus score</b> Mean ± SD	6.3 ± 2.8	7.5 ± 2.6	9.06 ± 1.1 <sup>a</sup>	0.002
<b>Total DLQI score</b> Mean ± SD	8.5 ± 6.7	11.8 ± 7.3	13.9 ± 7 <sup>b</sup>	0.03

a, significantly compare with BSA < 10% in the same data, p value = 0.002 (ANOVA, Bonferroni multiple comparisons)

b, significantly compare with BSA < 10% in the same data, p value = 0.03 (ANOVA, Bonferroni multiple comparisons)

**Table 5** Course of acute urticaria (n = 79)

Causes	Number of patients	Remission in day(s)			
		Median	Minimum	Maximum	SD
<b>Unknown</b>	42	8.5	1	37	8.44
<b>Infections</b>	29	5	1	23	6.44
• URI*	21	6	1	23	7.12
• Diarrhea	5	5	2	12	3.91
• Dental caries	2	8	5	11	4.24
• Cystitis	1	2	2	2	-
<b>Drugs</b>	5	7	2	12	4.16
<b>Foods</b>	1	1	1	1	-
<b>Insect bite reactions</b>	2	3	3	3	0

\*upper respiratory tract infection.

respiratory tract infection. In most cases, infectious symptoms started 6 days before and 2 days after the onset of urticaria. Fifteen patients (30%) had no obvious causes. Similarly, most of our patients (89.7%) noted the infectious symptoms on average 6 days prior to the onset of urticarial symptoms. Ten percent had the onset of infectious symptoms at a mean of 3 days after the onset of urticarial symptoms.

Zuberbier *et al.*<sup>3</sup> reported in a study of 109 German patients with acute urticaria, that possible eliciting factors could only be identified in less than 50% of the cases. Associations with upper respiratory tract infections were found in 39.5%, drugs, mostly analgesics, in 9.2%, and suspected food intolerance 0.9% of the patients. They concluded that acute urticaria is frequently idiopathic and only rarely associated with IgE-mediated reactions.

In pediatric patients with acute urticaria, Schuller *et al.*<sup>11</sup> found 13 of 32 cases infected with streptococci. Kauppinen *et al.*<sup>12</sup> reported the prevalence of infections (mostly respiratory tract infections) at 28% in 40 children with acute urticaria. Legrain *et al.*<sup>13</sup> suspected mainly viral infections and/or drugs as etiologic factors in 28 infants older than 6 months with acute urticaria. Other infectious agents previously associated with acute urticaria were cytomegalovirus,<sup>14</sup> hepatitis A,<sup>15</sup> hepatitis B virus,<sup>16</sup> Coxsackie A9 virus,<sup>17</sup> Parvovirus B19,<sup>18,19</sup> *Strongyloides stercoralis*,<sup>20</sup> *Plasmodium falciparum*,<sup>21</sup> *Anisakis simplex*,<sup>22,23</sup> and *Mycoplasma pneumoniae*.<sup>24</sup>

Legrain *et al.*<sup>13</sup> reported food intolerance, mostly to cow's milk in 10 of 12 infants younger than 6 months old with acute urticaria. Kauppinen *et al.*<sup>12</sup> reported a 15% prevalence of food intolerance in children 6 months to 16 years of age with urticaria. In Thailand, Tuchinda *et al.*<sup>25</sup> reported that food was the possible cause in urticaria in 9.9% of pediatric patients under 12 years of age with urticaria. Sea food, fish, raw or preserved foods, eggs and food additives were cited as possible causes. Wanankul *et al.*<sup>26</sup> confirmed the contribution of food allergy to urticaria in 7% of 100 Thai pediatric patients and suspected food allergy in another 4 % of the patients. All patients were diagnosed as acute urticaria. The culprit foods were cow milk, egg, wheat and shrimp. In contrast, Aoki *et al.*<sup>2</sup> could not define any cases of food intolerance in their 50 patients with acute urti-

caria, while Zuberbier<sup>3</sup> reported a prevalence of 0.9%.

Similar to the study of Zuberbier *et al.*<sup>3</sup> in more than half of our adult patients no definite causes could be confirmed. Infectious causes were detected in 36.7% of the patients, mostly upper respiratory tract infections. The infectious signs and symptoms were mostly mild. Adverse reaction to drugs was the second most common identified cause. Food-induced urticaria was detected in only 1.3% of patients.

Tuchinda *et al.*<sup>27</sup> reported in 1978 that the prevalence of allergic rhinitis and asthma in Thai university students was 23.6% and 2.3% respectively. In 2001, Vichyanond *et al.*<sup>28</sup> found that the prevalence of allergic rhinitis and asthma in Thai university students was 26.3% and 8.8%. In the present study, the personal history of allergic rhinitis and asthma in patients with acute urticaria was 20.6% and 2.5%, respectively. These data implied that the prevalence of atopy was not increased in our patients with acute urticaria as compared to the general population. The patients with recurrent attacks had a higher percentage of personal histories of atopy as compared to those with the first episode of acute urticaria. There was, however, no statistically significant difference.

This study demonstrated that acute urticaria could cause impairment to the quality of life. The mean total DLQI score of our 79 patients with acute urticaria was 11.05. A study by Finlay and Khan<sup>8</sup> showed that the mean total DLQI scores for various dermatologic conditions were higher than that of the controls (7.3 vs. 0.5). However, in their study, they did not make specific mention about patients with urticaria. In a validated study using the Thai version DLQI, Kulthanan *et al.*<sup>10</sup> showed that active urticarial patients experienced a higher disability than active psoriatic patients (14.1 vs. 12.9).

In the present study, question 1 concerning itchy sensations had the highest mean DLQI score. This was supported by the high mean pruritus score by VAS of 7.4. These data implied that pruritus disturbed the quality of life of patients with acute urticaria. Question 9 asking about sexual difficulties had the lowest mean DLQI score. It should be noted

that a high percentage of patients marked “not relevant” for this item. It is probably a feature of Asian cultures that people are embarrassed when they are asked about sexual problems. The other questions that also had a high mean DLQI score were work/study, embarrassment, treatment and shopping.

Zuberbier *et al.*<sup>3</sup> reported that all 109 cases of their patients with acute urticaria had remission within 3 weeks. Aoki *et al.*<sup>2</sup> reported that 86% of their acute urticaria patients were cured within 2 weeks, 92% cured within a month and 96% cured within 3 months. Only 4% persisted over a year. In our study, 21% of cases presenting with acute urticaria turned out to have chronic urticaria.

The limitation of this study was that we did not study pediatric patients with acute urticaria. Moreover, the number of patients in some subgroups of acute urticaria such as insect bite reaction was too small. Further large scale studies should be performed in the future.

In summary, our study provided an overview of acute urticaria based on etiological aspects, clinical features and quality of life. Patients with extensive wheals tended to have co-existing angioedema, and also had a statistically significant higher percentage of systemic symptoms, a higher mean pruritus score and mean total DLQI score as compared to the group of patients with less BSA involvement.

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