A CLINICAL STUDY

ASSOCIATION BETWEEN URTICARIA ACTIVITY SCORE (UAS) AND DERMATOLOGY LIFE QUALITY INDEX (DLQI) AND CHANGE TRAJECTORIES ACROSS ALL TIME POINTS

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ARTICLE INFO	ABSTRACT
	Introduction: *Shara Muzmin* (Chronic Urticaria (CU) is a common skin disorder characterized by the recurrent appearance of wheals and/or angioedema for more than 6 weeks. The Urticaria Activity Score (UAS) score is commonly used to assess the CU disease activity. CU signs & symptoms affect a wide range of daily activities, from personal care to sleep/rest, work performance, and social relationships. The Dermatology Life Quality Index (DLQI) assesses QOL parameters across several types of dermatologic conditions. **Objective:** Aims of this study was to determine the association between UAS and DLQI in different follow-ups of patients and improvement UAS and DLQI. Compare change trajectories across all time points (follow-ups) simultaneously between UAS and DLQI using latent class growth models (LCGM). **Methods:** In this study 29 patients were registered for protocol and used to calculate UAS and DLQI over the time points. Unani pharmacopoeial formulation *Qurs Asfar* 775mg was given twice daily with water after meals for the period of two weeks. Simple regression model used to determine the association between UAS and DLQI in different follow-ups of patients and improvement, r^2 (Pearson) values used to assess the validity of symptom scores and how strong association of them. Latent Class Growth Model (LCGM) used to find individual trajectories of change, allowing correlation of patterns of changes between multiple outcome measures across multiple time points simultaneously. **Result:** The UAS values were found to positively associated and significantly with DLQI values (r^2 = 0.31, P< 0.01) at before stating of this study. UAS values were found to positively associated and significantly with DLQI values (r^2 = 0.33, P< 0.01) at 1st follow-up. UAS values were found to highly positively associated and significantly with DLQI values (r^2 = 0.72, P< 0.01) at 2nd follow-up. Percentage improvement in UAS values were found to highly positively associated and significantly with DLQI values (r^2 = 0.72, P< 0.01). LCGM for A single quadratic trajectory model was found for UAS over the time points using LCGM and two quadratic trajectory model DLQI. **Conclusion:** The study conclusion that impact of the disease state on a patient's life: improvements in signs and symptoms, as measured by the UAS, were reflected in improvements in DLQI. The latent class growth models shows that the daily average urticarial activity over seven days and the DLQI over time points are nearly identical.

INTRODUCTION

The *Shara* (Urticaria) is defined as a transient eruption of circumscribed edematous and usually itchy swellings of the dermis (Warin, 1974).

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Unani System of medicine *Shara* (Urticaria) is the maculopapular lesion of the skin with reddishness sometimes these lesion are small and sometimes they are big, most of the times colour of the lesion is red but it may be white sometimes itching is associated with these lesion. Itching is abrupt. Duration of *Shara* (Urticaria) varies few hours to few days (Ibn Sina; Abdul, 2010; Hakim Mohammad Rafeeq Hujazi, 1980;

Hakim Gulam Jeelani Khan, 1935; Allama Najeebuddin Samarqandi, 2007; Hakim Ajmal Khan, 1987). Urticaria is a vascular reaction of the skin characterized by the appearance of wheals, generally surrounded by a red hals or flare and associated with severe itching, stinging or pricking sensation. These wheals are caused by localized edema. Clearing of the central region may occur and lesion may unite, producing an annular or polycyclic pattern (William D.J, 2006). *Shara* (Urticaria) is generally divided into two forms as acute and chronic. The actual cause of *Shara* (Urticaria) *is* believed to be the *Fasad e Dam* (blood impairment) caused by the *vapors* of *Dam e Merari* (bilious blood) or *Balgham e Boraqi* (acidic phlegm) coming towards the skin or periphery of the body (Ibn Sina; Abdul, 2010; Abu Al M.H.A, 2008; Allama Najeebuddin Samarqandi, 2007). The chronic cause of *Shara* (Urticaria) is associated with diverse clinical presentations and causes. Conventionally it is defined as the repeated occurrence of daily or almost daily cutaneous wheals accompanied by redness and itching for more than 6 weeks (Yadav S, 2006). The wheals are often pale and surrounded by reddened skin, although occasionally the wheals themselves are red. The individual wheals typically last less than 24 hours, and symptoms are often worse at night. *Shara Muzmin* (Chronic Urticaria) affects in at least 0.1% and possibly up to 3% of the population (Yadav S, 2006). *Shara Muzmin* (Chronic Urticaria) is twice as common in women as in men (Singh M, 1990).

Chronic urticaria severity is assessed by evaluating signs [hives (changing daily)] and symptoms (itch). Patients count and record these using a daily diary such as the Urticaria Activity Score (UAS). CU signs & symptoms affect a wide range of daily activities, from personal care to sleep/rest, work performance, and social relationships. Physical and emotional functioning is subjectively impaired beyond the severity of the actual disease symptoms. As with other chronic skin disease that affects patients' quality of life (QOL). The Dermatology Life Quality Index (DLQI) assesses QOL parameters across several types of dermatologic conditions (Godse, 2006). The efficacy CU treatment, clinicians must assess changes in the patient's condition. The DLQI is an easy and efficient instrument for assessing quality of life in dermatology patients. Impact of skin diseases of the measurement on patient's quality of life is important. Skin diseases can have a major impact on patient's lives in terms of psychological well-being, social functioning and everyday activities. Measurement techniques include general health, disease specific and dermatology specific questionnaires: experience with the Dermatology Life Quality Index (DLQI). A comparable understanding of a patient's condition and response to treatment can be obtained from a single assessment referring to the past week (DLQI), physicians could administer the DLQI in lieu of UAS. The purpose of this study was to determine the association between UAS and DLQI in different follow-ups of patients and improvement UAS and DLQI. Compare change trajectories across all follow ups simultaneously between UAS and DLQI using latent class growth models (LCGM).

MATERIALS AND METHODS

An open level clinical study, approved by the institutional ethics committee, was carried- out on the patients of *Shara Muzmin* (Chronic Urticaria) in GOPD/IPD of Regional Research Institute of Unani Medicine, Patna during the year 2015-16.

Drugs Administrative

In this study unani pharmacopoeial formulation *Qurs Asfar* was used 775 mg twice daily with water after meals. The total duration of treatment was 14 days. All clinical follow-ups were done once every 07 days.

Patients Selection

The patients were selected on the basis of inclusion and exclusion criteria given below:

Inclusion Criteria

- Patients of either sex with age 18-55 years
- Clinically diagnosed case of chronic urticaria (urticaria more than six weeks) presenting with any one of the following signs and symptoms.
  - H/o recurrent evanescent skin eruptions
  - Feeling of heat and pricking sensation just before the appearance of lesions
  - Edematous wheals surrounded by a red flare
  - Intense itching which is usually very intense with burning sensation and increase in the evening time
  - Mild to severe pruritus
  - Physical urticaria (cold, heat, sun exposure, vibration, pressure, sweating and exercise)
  - Dermatographism

Exclusion Criteria

- Patients with difficulty in breathing in acute urticaria.
- Urticaria due to worm infestation
- Anaphylactic shock
- Known cases of Thyroid disease/ Lupus/Rheumatoid arthritis
- Known cases of severe Renal/ Hepatic/ Cardiac ailments
- Pregnant and lactating women

Data

Information of patients' history, physical examination, clinical and laboratory investigations data were collected from case record forms.

Measures of Urticaria Activity Score (UAS)

The improvement in *Shara Muzmin* (Chronic Urticaria) for which Urticaria Activity Score (UAS) was used. The UAS is the sum of the daily urticarial activity scores over 7 days and ranges from 0 to 42. The daily urticarial activity score is the average of the morning and evening urticarial activity scores and ranges from 0 to 6. The urticarial activity score is the sum of ratings on a scale of 0 to 3 (0=none to 3=intense/severe) for the number of wheals (hives) and itch intensity over the previous 12 hours, ranges from 0 to 6, and is measured twice daily (morning and evening). The Baseline score is the sum of the daily urticarial activity scores over the 7 days prior to the first treatment. A higher urticarial activity score indicates more urticaria activity (Mathias, 2010; Mathias, 2014; Zazzali, 2012). Percentage improvement of UAS done by after end of treatment as (base line – end line)/end line *100.

Tabl 1. Scale of Urticaria Activity Score (UAS)

S. No.	Score	Wheals	Pruritus
1.	0	None	None
2.	1	Mild (Less than 20 wheals /24hrs)	Mild (present but not annoying)
3.	2	Moderate (20-50 wheals/24hr)	Troublesome but does not interfere with sleep
4.	3	Intense >50 wheals/24hrs or large confluent areas of wheals	Severe Pruritus which is sufficiently troublesome to interfere with normal daily activity /sleep

Measures of Dermatology Life Quality Index (DLQI)

The DLQI was used at base line and end of the week to assess the levels of QoL impairment. The DLQI is a simple 10-question validated QoL questionnaire used for patients with skin diseases that was shown to be a valid, reliable, and clinically useful outcome measure for assessing health-related QoL in CU patients. The DLQI contains six main items: symptoms and feelings (questions 1 and 2), daily activities (questions 3 and 4), leisure (questions 5 and 6), work and school (question 7), personal relationships (questions 8 and 9), and treatment (question 10). All questions are related to the week prior to testing, and response categories include 'not at all', 'a little', 'a lot', and 'very much' with corresponding scores 0, 1, 2, and 3, respectively; the response 'not relevant' was scored as 0. The summing of all responses gave a total index score. The minimum index scoring was from 0 to 1 (no effect at all on patient's life) and the maximum from 21 to 30 (extremely large effect on patient's life) (Lennox, 2004; Finlay, 1994). Percentage improvement of DLQI done by after end of treatment as (base line – end line)/end line *100.

Statistical Analysis

All statistical analyses were carried out in R Software (version 3.3.2) and SAS 9.4 (Andruff, 2009). Simple regression model used to determine the association between UAS and DLQI in different follow-up of patients and improvement UAS and DLQI in 29 patients. To assess the validity of symptom scores and how strong association of them, r^2 (Pearson) values, which quantify the proportion of variance of the DLQI explained by these scores, were calculated. Latent class growth model (LCGM) is a semi parametric technique applied to data from of this study using information from every available time point or follow-ups. LCGM is a growth curve analysis based on structural equation modelling; it models individual trajectories of change, allowing correlation of patterns of changes between multiple outcome measures across multiple time points simultaneously (Stull, 2008). Analysis of that compare mean changes among groups of patients, e.g., analyses of variance, LCGM examine how the change in one variable across all time points for a given patient matches the change in another variable for that patient. LCGM fixes the slope and the intercept to equality across individuals within a trajectory. Analyses of mean change are limited to change between two time points and cannot correlate changes involving multiple variables. However, LCGM calculate a slope of change and its corresponding intercept for every patient for each variable and correlate those intercepts and slopes of change. The intercept is the value of the growth curve (slope of change) at the first assessment point, similar to the value of the initial observation for a patient. The best-fitting classification model was determined based on the Bayesian Information Criterion (BIC)

(Schwartz, 1978); a criterion calculated from the log-likelihood of the model and the number of parameters in the model. The lowest BIC suggests the best fit. The LCGM were conducted so that UAS7 scores were modelled across all time points or follow ups simultaneously with DLQI, allowing the intercepts and slopes.
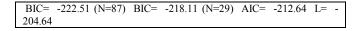
RESULTS

The mean ± SEM of average daily UAS and DLQI values at before starting of the study was 5.76 ± 0.13 and 16.07±0.39 respectively. UAS values were found to positively associated and significantly with DLQI values ($r^2 = 0.31$, P< 0.01, Fig. 1-A). The mean ± SEM of average daily UAS and DLQI values after 07 days i.e. 1st follow-up was 3.54 ± 0.24 and 11.31±0.60 respectively. UAS values were found to positively associated and significantly with DLQI values ($r^2 = 0.33$, P< 0.01, Fig. 1-B). The mean ± SEM of average daily UAS and DLQI values after 14 days i.e. 2nd follow-up was 2.26 ± 0.22 and 5.21±0.68 respectively. UAS values were found to highly positively associated and significantly with DLQI values ($r^2 = 0.72$, P< 0.01, Fig. 1-C). In addition, the mean ± SEM of average daily percentage improvement of UAS and DLQI values after the treatment was 60.93 ± 3.36 and 68.27±3.77 respectively. UAS values were found to highly positively associated and significantly with DLQI values ($r^2 = 0.72$, P< 0.01, Fig. 1-D).
In this study, data was analyses on base line, 1st follow-up and 2nd follow-up, LCGM applied to find out trajectory of UAS. A single quadratic trajectory model was tested, the linear and quadratic components of this model were significant and BIC value was minimum compare as two trajectory model (Table-2). The output of this model, displayed in Fig. 2-A, shows that the quadratic terms of trajectory one. To find trajectory of DLQI, the linear and quadratic components of single quadratic trajectory model were no significant. In addition, the quadratic model for two trajectories was performed, linear and quadratic components of two quadratic trajectory model were significant with BIC value was minimum compared as one trajectory model (Table-3). The output of this model, displayed in Fig. 2-B, shows that the quadratic terms of trajectory one & two.

Table 2. Output of Urticaria Activity Score (UAS) of quadratic model for Trajectories One

Group	Parameter	Estimate	Standard Error	T for H0: Parameter=0	
				t-value	p-value
1	Intercept	7.17772	0.40209	17.851	0.0000
	Linear	-4.73438	0.80322	-5.894	0.0000
	Quadratic	1.13802	0.35182	3.235	0.0017
Sigma		1.36890	0.13194	10.375	0.0000
BIC= -124.68 (N=87) BIC= -122.48 (N=29) AIC= -119.75 L= -115.75					

Table 3. Output of Dermatology Life Quality Index (DLQI) of quadratic model for Trajectories one and two

Group	Parameter	Estimate	Standard Error	T for H0: Parameter=0	
				t-value	p-value
1	Intercept	15.88201	0.46745	33.976	0.0000
	Linear	-4.21932	1.19187	-3.540	0.0006
	Quadratic	-0.81644	0.57409	-1.422	0.1586
2	Intercept	17.72993	1.42213	12.467	0.0000
	Linear	-2.90357	3.57766	-0.812	0.4192
	Quadratic	0.60718	1.72498	0.352	0.7257
Sigma		2.28780	0.18513	12.358	0.0000
	Group membership				
1	(%)	89.88283	5.94338	15.123	0.0000
2	(%)	10.11717	5.94338	1.702	0.0923

BIC= -222.51 (N=87) BIC= -218.11 (N=29) AIC= -212.64 L= -204.64

this disease, such as feelings, daily activities, leisure, work and school, personal relationships etc.
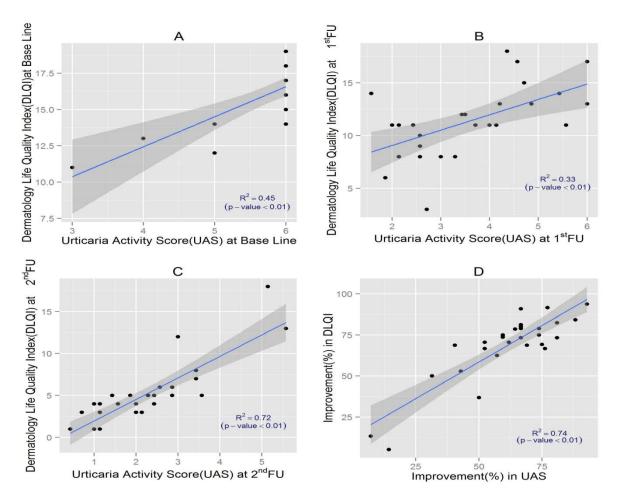

Figure 1. Association between UAS and DLQI in different follow-ups of patients and improvement UAS and DLQI
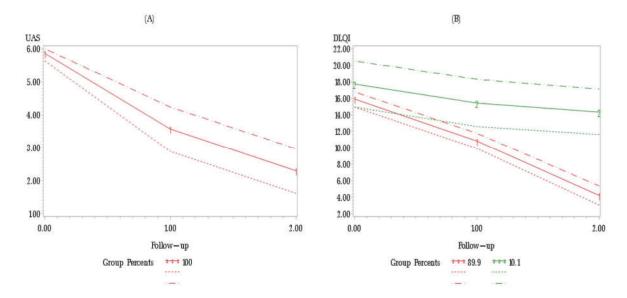

Figure 2. Trajectories across all follow ups simultaneously between UAS and DLQI using latent class growth models (LCGM)

DISCUSSION

A linear impact or association is present between *Shara Muzmin* (Chronic Urticaria) and DLQI of patients due to debilitating and uncomfortable symptoms. In addition to classical sign & symptoms of patients with Chronic Urticaria, like pruritus and papules, other factors are more relevant for

Thus, merely evaluating urticaria progress by counting lesions and measuring pruritus intensity is insufficient. A holistic evaluation of the patient is required for a better understanding of disease impact on QoL. The results of LCGM showed a near-perfect association between changes in signs and symptoms of Chronic Urticaria and dermatologic QoL over

time (follow-ups) for one quadratic trajectory and two quadratic trajectories respectively. Changes in sign and symptom with CU patients' severity are closely linked to changes in dermatologic QoL. If improvement over time is found using the UAS, it is highly likely that DLQI.

Conclusion

The results of the study concluded that the impact of the disease state based on signs and symptoms in base line, 1st follow up and 2nd follow up using UAS scores on a patient's life: improvements in signs and symptoms were reflected in improvements in DLQI. The result of these latent class growth models shows that the daily average urticarial activity over seven days, and the DLQI over time points is nearly identical.The chronic urticaria disease is associated DLQI. If sign & symptoms of disease increase then the QoL is more trouble.

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