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Original article

Urotensin II in Psoriasis in relation to disease severity

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Abstract:

Background: Up to 3% of people worldwide suffer from chronic inflammatory skin condition psoriasis. When combined with risk factors for atherosclerosis, psoriasis may increase the incidence of metabolic syndrome and other cardiovascular diseases. Urotensin II (UII) is a vasoactive peptide that has been suggested to be increased in metabolic syndrome. **Aim:** It was to analyze the connection between the severity of the illness and the serum level of Urotensin II (UII) in psoriasis patients. **Methods:** 40 patients with psoriasis and 40 control participants participated in this study; they were age- and sex-matched. The cases underwent a thorough history taking and clinical examination, along with an evaluation of the extent and severity of the psoriasis. All subjects' serum UII and lipid profile were measured using ELISA. **Results:** The case and control groups' fundamental demographic and clinical data did not statistically differ from one another. When comparing the median level of UII (1.28-17.35 ng/ml) in control group versus that in patients' group; the latter showed a statistically higher significant level (p= 0.001) than the control group (26.26 ng/ml). The best urotensin II cutoff point for identifying psoriasis cases from controls was > 12.825 ng/ml, with 97.5 % sensitivity, 90 % specificity, 95% NPV, 97.5 % PPV, and a total accuracy of 92.5 %. With a statistically significant value of p< 0.001, the AUC was 0.987. Conclusion**:** Based on our findings, Urotensin II could be used to diagnose psoriasis in susceptible people.

Keywords: Psoriasis, Metabolic syndrome, Cardiovascular, Urotensin, hyperlipidemia.

Introduction

Skin, nails, and joints are all affected by the T-cell mediated autoimmune disease known as psoriasis. About 2 to 3 % of the population is affected (1). The red plaques with distinct borders and adherent silvery white scales are distributed symmetrically over the body as its main distinguishing feature (2).

The severity of psoriasis is typically evaluated using the PASI and other clinical tools, of limited subjectivity. Clinicians choose the therapy based on psoriasis severity, hoping to help patients experience longer remission times and improve their quality of life (3).

Psoriasis is linked to cardiovascular diseases like stroke, coronary heart disease, and peripheral vascular disease, according to clinical and epidemiological evidence(4). This association's exact mechanisms are unknown. Some have hypothesized that chronic inflammation via Th1 and Th17, a critical component of the pathogenesis of psoriasis, also contributes to the emergence of atherosclerosis(5 ,6). Urotensin II (U-II) is an effective vasoconstrictor (7). It's produced by blood vessel, heart, kidney, and liver cells, but also in the GI tract and CNS (8, 9).

Numerous studies link the pathophysiological chain that leads to atherosclerosis and low-grade inflammation and U-II (7,9), which is one of the psoriasis' included mechanisms.

This study examined the relationship between serum UII levels and disease severity in psoriasis patients at risk for metabolic syndrome.

Patients and methods

This case-control investigation was done between August 2021 and February 2022 at the outpatient clinic of Dermatology and Andrology Departments at Benha University Hospital. This study was carried out on 40 patients with psoriasis and 40 age and sex matched control individuals.

We included subjects with a psoriasis diagnosis who were over 18 years and of either gender. Cases with the following criteria were excluded; patients who are suffering from another dermatological disease, patients' receiving systemic or topical treatment or phototherapy for psoriasis for less than one month before enrolling to the study and patients with a history or clinical evidence of any of the following: acute or chronic infection, chronic renal or liver disease, pregnancy and breastfeeding and heavy smokers.

The research is done in accordance with the 2013-revised Helsinki Standards (10). Written or verbal informed consent was obtained from the included cases before the study was conducted and after the

ethical approval of faculty of medicine, Benha University (MS 32-11-2020)

The cases underwent a clinical examination to rule out any systemic diseases as well as a history taking procedure that included demographic information and a history of the current illness. The general examination also included measurements of blood pressure, body mass index, height, and weight. BMI > 25 kg/m2 was used to diagnose obesity(11).

The psoriasis assessment included assessment of disease distribution, joint affection, nail affection and/or presence of pruritus. The severity of the disease was assessed using the Psoriasis Area and Severity Index (PASI) score(12).

Laboratory tests measured fasting plasma glucose, HDL, cholesterol, triglycerides and serum Urotensin II level by Human Urotensin II ELISSA Kit (by Bioassay Technology Laboratory, Korian Biotech Co., Ltd) (Cat. No. E3108Hu)

Statistical analysis of data

SPSS version 27 for Windows® was used to code, process, and analyse the data (IBM, SPSS Inc, Chicago, IL, USA). Percentages and numbers were used to present quantitative data (frequency). Chi-Square, also called Fischer's exact test, was used to compare the groups.

The Kolmogorov-Smirnov test assessed whether quantitative data were normally distributed. While parametric data was expressed as median with standard deviation, non-parametric data was expressed as median (Range). Independent samples t-test and Mann-Whitney test were used to compare two groups with normally distributed quantitative variables if the data were non-parametric. ROC curve: Plotting sensitivity (TP) versus 1-specificity (FP) at different cut-off values. The ROC curve's area indicates the test's diagnostic performance. The Spearman correlation was used to correlate numerical data. *P* values less than 0.05 are regarded as significant for all tests.

Results

The current study demonstrates the fundamental clinical and demographic information about the study's participants. The mean age of control group was 46.13 ± 11.44 years, while the mean age of psoriasis group was 44.43± 9.71 years; neither group differed statistically (p=0.476).

In the psoriasis group, there were 42.5 percent of men and 57.5 percent of women, whereas in the control group, 55% men, 45% women; with no significant difference between both groups (p=0.263).

Control group's mean BMI was 29.42± 4.42 kg/m2, while psoriasis group had a mean BMI of 31.52± 5.70 kg/m2, with

statistically insignificant difference (*p*=0.069).

Diabetes was present in 20% of psoriasis cases compared to 27.5% of control cases, but neither group differed significantly (*p*=0.431).

Hypertension was present in 30% of cases of psoriasis compared to 42.5 percent of cases in the control group, but neither group differed significantly (*p*=0.245).

Metabolic syndrome was present in 32.5% of the psoriasis group and 40% of the control group, with no statistical difference (*p*=0.485).

Table (1) shows psoriasis's mean duration was 2.93 ± 4.27 years which ranged between 2 months and 20 years. The mean PASI was 6.47 ± 8.02 with range between 1.2 and 47.4.

Ten psoriasis cases (25%) had a positive family history. Joint affection was reported in 4 cases (10%), nail affection in 3 cases (7.5%) and pruritus was reported in 26 cases (65%).

Blood pressure (mmHg), fasting blood glucose level (mg/dl), and lipid profile including HDL (mg/dl), cholesterol (mg/dl) and triglycerides (mmol/L) prevalence were not statistically different between psoriasis cases and controls (*p* was 0.077, 0.576 , 1, 0.592, 0.745 respectively)

Figure 1, demonstrates, the median level of urotensin II (26.26 ng/ml with a range of 5.99–48.12 ng/ml), which was statistically higher than the control group (3.78 ng/ml with a range of 1.28–17.35 ng/ml) (*p* less than 0.001).

Figure (2**)** shows that best urotensin II cutoff point for psoriasis cases and controls was > 12.825 ng/ml with 97.5 percent sensitivity, 90 percent specificity, 95 percent NPV, 97.5 percent PPV, and 92.5 percent accuracy. The AUC was 0.987 (p less than 0.001).

Table (1): Psoriasis disease criteria analysis.

Variables		Psoriasis group n= 40
Disease duration (Years)	Mean ± SD	2.93 ± 4.27
	Median (min-max)	1 (0.17 -20)
PASI	Mean ± SD	6.47 ± 8.02
	Median (min-max)	4.20 (1.20 – 47.40)
Family history of psoriasis		
	Negative	30 (75%)
	Positive	10 (25%)
Associated features		
	Joint affection	4 (10%)
	Nail affection	3 (7.5%)
	Pruritus	26 (65%)

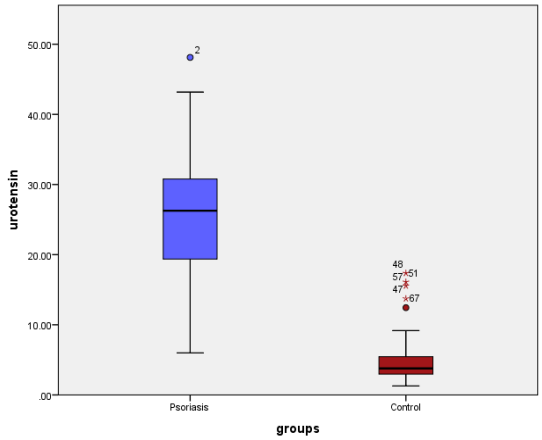

Figure (1): Urotensin II level in the study groups.

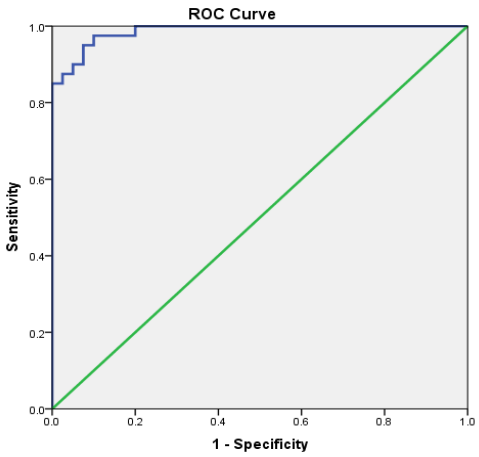

Figure (2): ROC curve for urotensin II in differentiating psoriasis cases from controls.

As shown in table 2, Urotensin II level showed a statistically positive correlation to weight (r= 0.366, p= 0.020) and BMI (r= 0.385, p= 0.014). There was no statistically significant correlation between other variables and urotensin II. Additionally, there was no statistically significant relationship between urotensin II and the other variables in the control group.

Table (3) demonstrates that the median level of urotensin II was 26.26 ng/ml (5.99–48.12 ng/ml), which was statistically higher than the control group 3.78 ng/ml (1.28–17.35 ng/ml) (p less than 0.001).

Table (2): Correlation between urotensin II level with other variables in the psoriasis and control groups.

Variable	Urotensin (ng/ml)		
	Psoriasis group		Control group
	r	p	
Age (years)	0.127	0.434	0.223
Weight (kg)	0.366	0.020*	0.003
Height (m)	-0.222	0.169	0.109
BMI (kg/m^2)	0.385	0.014*	0.121
PASI	0.053	0.746	
Disease duration (years)	0.167	0.302	

p < 0.05= statistically significant; r= spearman correlation, BMI = Body mass index, PASI = psoriasis area and severity index

Table (3) lipid profile, blood glucose level, and high blood pressure prevalence were not statistically different between psoriasis cases and controls.

	Groups				*P* value
	Psoriasis group (N=40)		Control group (N=40)		
Blood pressure					
Normal	36	90%	30	75%	0.077
High	4	10%	10	25%	
FBG					
Normal	31	77.5%	33	82.5%	0.576
High	9	22.5%	7	17.5%	
HDL					
Normal	36	90%	36	90%	1
High	4	10%	4	10%	
Cholesterol					
Normal	30	75%	32	80%	0.592
High	10	25%	8	20%	
TGs					
Normal	35	87.5%	34	85%	0.745
High	5	12.5%	6	15%	
Urotensin (ng/ml)	26.26 (5.99-48.12)		3.78 (1.28- 17.35)		**< 0.001***

P= probability; FBG=fasting blood glucose; HDL = high density lipoprotein ; TGs = triglycerides.

Discussion

In psoriasis patients, the current study sought to determine the relationship between serum UII levels and disease severity.

The current study enrolled psoriasis patients with mean age of 44.43 ± 9.71 years. In the psoriasis group, the proportion of men and women was 42.5 percent and 57.5 percent, respectively.

Similar findings were made by another study (13) who looked at 60 psoriasis patients. The patients included 35 males, with a mean age of 38.43. Men made up 56.3 percent in another Egyptian study (14), with a mean age of 39.3 ±17.9 years (range, 1-94 years). On the other hand, a Denmark study reported a female majority (53.2%) (15).

In contrast, some authors explained this variation due to racial differences between the different studied communities. From the researcher point of view, the differences between the studies in the same country could be explained due to variations in access to different health care facilities.

Current research, the mean BMI of psoriasis cases was 31.52 ±5.70 kg/m2 and 29.42 ±4.42 kg/m2, no significant difference in the control group.

In the current study, psoriasis lasted 2.93±4.27 years, ranging from 2 months to 20 years. This agreed with another study which demonstrated that Psoriasis lasts between 1 and 35 years on average(16).

Another study reported that Psoriasis patients' disease duration ranged from 1 to 40 years (mean: 13.8 ±12.0 years)(17).

Positive family history of psoriasis is considered a risk factor for psoriasis(18). Ten cases (or 25%) of the psoriasis cases had a confirmed family history of the condition. This is comparable to studies done in the Maghreb, China, and Malaysia, where family history was reported for 28.6%, 23.1%, and 23.1% of patients, respectively (19-23).

This percentage was higher than the findings from another study (24), A family history was present in 10.5% of their patients(24). Patients may conceal family illnesses as a result of cultural and social factors. Such a denial could ease patients' fears of social exclusion and stigma, which are made worse by the regional culture "ideal mate " Patients with psoriasis have established social networking groups to network for marriage(25, 26).

In the present study, there was a statistically significant positive correlation between the Urotensin level in patients' group and BMI.

Receptors of U-II were discovered in the hypothalamus of the experimental model, and U-II may have an impact on the network that regulates appetite (8,30). U-II affects glucose-6-phosphate dehydrogenase and NADPH activity, which affects liver lipogenesis (8, 30, 9).

Numerous studies have linked U-II to low-grade inflammation and atherosclerosis, two of MS's main pathologies (7-9, 31). Recently, a positive correlation between U-II and high sensitivity C-reactive protein, a biomarker of low-grade inflammation, was discovered [33].

Numerous studies linked U-II to impaired glucose tolerance, insulin resistance, and hyperinsulinemia in hypertensive patients (8, 31, 32).

The median level of urotensin II in the current study was 26.26 ng/ml, statistically higher than the control group 3.78 ng/ml level. No studies have measured UII in psoriasis patients, to the best of our knowledge.

Without other conventional risk factors, people with psoriasis may have a higher risk of myocardial infarction, stroke, vascular inflammation, and atherosclerotic conditions (37-39). The metabolic syndrome, which includes obesity, hypertension, dyslipidemia, and insulin resistance, is associated with chronic inflammation (40, 41).

Metabolic syndrome and psoriasis may have overlapping inflammatory pathways and genetic predisposition (42). In addition to promoting epidermal hyperplasia in psoriasis TNF- and IL-6 dysregulation in chronic Th-1 and Th-17-mediated inflammation may inhibit insulin signaling, alter adipokine expression, and

result in insulin resistance and obesity (43, 44).

By encouraging chronic inflammation and angiogenesis, hyperinsulinemia associated with the metabolic syndrome may aggravate psoriasis(43, 44).

Furthermore, the severity of the psoriasis disease and the treatment response are all linked to obesity, dyslipidemia, and diabetes (45 ,46).

The primary strength of the current study is that we reported the direct link between psoriasis and UII for the first time to the best of our knowledge. Additionally, the current study demonstrated that, with high sensitivity and specificity, the best UII cutoff point for differentiating psoriasis cases from controls was > 12.825 ng/ml.

The sample size was one of the limitation in the current study.

Conclusion

Based on our findings, it could be included that Urotensin II could be utilized as a biomarker for diagnosis of psoriasis in susceptible individuals. The marker revealed high degree of sensitivity and specificity in differentiating case with psoriasis from controls. Moreover, urotensin II showed positive but insignificant correlation with the disease severity and duration which reflects its ability in assessment of the disease severity in psoriasis. The latter issue still requires further validation studies with larger sample size.

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