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Urinary Orosomucoid as a Potential Marker of Inflammation in Psoriasis Vulgaris

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ABSTRACT

Background: Psoriasis vulgaris (PV) is a chronic proliferative inflammatory dermal disease. Orosomucoid (ORM) is an acute phase protein (APP) primarily formed in the liver. Novel research revealed urinary orosomucoid (uORM) as a more sensitive, noninvasive biomarker of inflammatory activation compared to serum ORM (se-ORM).

Objective: To investigate the role of uORM as a surrogate marker for psoriasis and to correlate its urinary values with the PV severity. **Patients and Methods:** This was a case-control study, comprised 50 cases with confirmed diagnosis of psoriasis and control group included 50 healthy controls. The included cases were classified based on PASI score into; mild PV (≤10), moderate PV (>10 -<20) and severe PV (≥20). Morning urine samples were acquired from all cases and controls to measure urinary ORM.

Results: The AUC for uORM A in differentiating cases from control was fair with the best detected cutoff point was 53.18 yielding sensitivity of 74% and specificity 58%, and for uORM A/creatinine in differentiating cases from control was fair with the best detected cutoff point was 0.293 yielding sensitivity of 70% and specificity 52%. There was a statistically significant higher median uORM A, uORM A/ creatinine among severe cases than mild and, moderate cases.

Conclusions: A highly sensitive, inexpensive, and easily available noninvasive biomarker, uORM demonstrates itself ability to become a new inflammatory marker in PV offering further data on disease severity and progression.

Keywords: Psoriasis, Urinary Orosomucoid, Erythematous Plaques, Psoriasis Area and Severity Index.

INTRODUCTION

Psoriasis vulgaris (PV) is a chronic proliferative and inflammatory dermal disease skin [(1,2)]. It has been demonstrated that two percent of populations suffer from different forms of PV [(3)]. Although PV is a benign dermal disease, it is a chronic disease with remission and exacerbation, it has been associated with poor quality of life (QoL) [(4)]. Of note, the median age of the initial presentation of PV ranges from 15 to 20 years of age, while the second presentation happening within the fifth decade [(5,6)].

The pathophysiology of PV includes dermal infiltration by stimulated T cells with subsequent activation of keratinocytes proliferation. Such dysregulation in keratinocyte turnover has been demonstrated to be associated with thick plaques formation. Other accompanying characteristics involve epidermal hyperplasia and parakeratosis. Additionally, the epidermal cells could not form lipids resulting in scaly skin (characteristic feature of PV) [(7,8)].

C-reactive protein (CRP) is a broadly utilized inflammatory marker. Earlier researches demonstrated an increase in CRP values in cases complaining from PV; some of which recommended that CRP may be utilized as a marker of PV severity [(9,10)].

Orosomucoid (ORM) has been considered as a major APP primarily formed by the liver, representing about 0.5-1.2 g/L of serum proteins [(11)].

Even though novel researches have demonstrated uORM as a sensitive, noninvasive marker of inflammatory stimulation, the clinical value of the urinary marker is poorly evaluated in the current literature [(12,13)]. Under normal physiological conditions, uORM excretion is low and its urinary concentrations represent a few mg/L (0.01-0.3 mg/mmol), on the other hand, increased uORM levels are described in particular disorders [(14,15)]. The increased uORM appears to be accompanied by systemic inflammatory processes and impaired endothelial functions, which are reported also to play essential roles in the PV pathomechanism [(12,16)].

Based on the previous concept and due to the lack of relevant studies regarding this perspective, this study was conducted aiming to assess uORM role as a surrogate marker for psoriasis, and to correlate its urinary levels with the disease severity.

PATIENTS AND METHODS

This was a prospective case-control study that was conducted at Dermatology, Andrology and STDs Department in Mansoura University.

Inclusion criteria: This study included a total of 100 subjects, who were divided into two equal groups; cases group included 50 cases aged between 18 and 60 years with confirmed diagnosis of psoriasis based on the typical clinical and dermoscopic examination and control group included 50 healthy controls. **Exclusion criteria**: we excluded patients who had systemic treatments, pregnant females, patients with impaired kidney functions (eGFR < 60 ml/min/1.73m^2), patients with acute inflammation and patients with autoimmune diseases (AIDs).

Methods:

All of the included cases were subjected to complete history taking that comprised personal history (name, age, sex, occupation and residence), history of the current illness (onset, course and duration of PV and predisposing factors), history of drugs (nature, route, dosage, duration, effects and adverse events), family history of PV or different dermatologic diseases and

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previous history of any accompanying systemic and dermatologic diseases or major surgeries.

Thorough physical examination included general examination to rule out any systemic disorders, dermatologic examination that included skin, hair, nails and mucous membranes to assess the PV type, distribution and severity and to rule out different cutaneous AIDs.

Lesions were scored based on psoriasis area and severity index (PASI) score which is the most frequently utilized approach to assess PV severity. It measures erythema, scaling and thickness of lesions and is weighted by the affected area. In addition, it is an essential approach in measurement of PV impact on QoL [17]. The included cases were classified based on PASI score into; mild PV (≤10), moderate PV (>10 - <20), severe PV (≥20) [18].

Laboratory Investigations:

Midstream 1st morning urine samples were acquired from all cases and controls to measure urinary ORM and urinary creatinine. Venous blood samples were obtained to measure CRP, creatinine and creatinine clearance (CrCl).

Test principle:

Double-antibody (AB) sandwich ELISA was utilized to assay the value of human α1-acid glycoprotein (α1-AGP) in samples, α1-AGP was added to monoclonal AB (MAB). Enzyme well was precoated with human α1-AGP MAB, incubation; after that, α1-AGP antibodies labelled with biotin were added, and combined with streptavidin-HRP forming immune complex; after that incubation was conducted and washing was done again to remove the uncombined enzyme. After that, chromogen solution A, B was added, the colour of the liquid became bluish, and by the effect of acid changed into yellow.

Materials:

The kit was balanced 30 minutes in the ambient temperature then used. For each step, sample was added with sample injector that has to be calibrated regularly, to evade needless experimental tolerance. The process was conducted according to the instructions.

Specimen Requirements:

Specimen was kept in -20℃ to preserve. Centrifugation was done for 20 minutes at the speed of 3000 rpm and the supernatant was discarded.

Assay Procedure:

Injected samples; in blank well**;** samples and (α1-AGP)-AB labelled with biotin, streptavidin-HRP shouldn't be added, only chromogen solution A and B, and stop solution were allowed. In standard wells; 50 µl, streptavidin and HRP 50 µl were added, in tested wells; sample 40 µl was added, and after that (α1-AGP) AB 10 µl and streptavidin-HRP 50 µl were added. After that, the sealing membrane was sealed followed by gentle shaking, and incubation for one hour at 37℃.

Confection started by dilute thirty times the 30×washing concentrate with deionized water. In washing; membrane was excised cautiously, and the liquid was drained, the residual water was removed. 50 µl of chromogen solution A were added, then 50 µl of chromogen solution B to all wells. Gentle mixing was done followed by incubation for 10 min at 37℃ in a dark room.

Termination was done by adding 50 µl of stop solution and the appearance of yellow discoloration.

In final measurement, we considered blank well as zero, the OD was measured under 450 nm wavelength, which was conducted within fifteen minutes following the addition of the stop solution.

Ethical consideration:

Study protocol was approved frm Institutional Research Board (IRB) of the Faculty of Medicine, Mansoura University with code number MS.21.11.1748. An informed written consent was obtained from all participants after complete explanation of the benefits and drawbacks of each intervention. Patients and controls were free to withdraw from the study upon their request. Privacy of the patients was respected. The collected data were used for scientific purposes only. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

Data analysis was conducted by SPSS software, (PASW statistics for windows version 25). Qualitative data were defined by utilizing number and percent and were compared by chi-square test or Fisher exact test. Quantitative data were defined by utilizing median and range for nonnormal distribution of data and mean±standard deviation (SD) for normal distribution of data following assessing normality by utilizing Kolmogorov-Smirnov test and these data were compared by Mann Whitney U test or Student t test respectively. ROC curve was utilized to assess validity. In terms of all the previous tests, p was considered significant when its vales less than 0.05.

RESULTS

The present study was case-control study that was conducted on 50 cases with psoriasis and 50 healthy controls to assess the role of orosomucoid as potential marker of psoriasis vulgaris.

Table (1) demonstrates non-statistically significant difference between studied groups in terms of age, sex, occupation, marital status, and smoking. There was statistically significant higher frequency of positive CRP among cases than control group. Median serum creatinine (Ser Cr), median urinary orosomucoid A, and urinary orosomucoid A/creatinine ratio were higher among case than control group with statistically significant difference. No statistically significant difference was found between patients and healthy controls as regard creatinine clearance.

Table (1): Sociodemographic characteristics and laboratory finding of the studied groups.

	Cases N=50(%)	Control N=50(%)	Test of significance
Sociodemographic Characteristics			
Age/years mean±SD	45.32±12.95	40.86±12.25	t=1.77 p=0.08
Sex			
Male	24(48.0)	17(34.0)	χ^2=2.03
Female	26(52.0)	33(66.0)	P=0.155
Occupation			
Not working	7(14.0)	3(6.0)	
Manual worker	11(22.0)	15(30.0)	
Employee	2(4.0)	5(10.0)	MC=8.88
Student	4(8.0)	2(4.0)	P=0.114
HCWS	16(32.0)	22(44.0)	
Housewife	10(20.0)	3(6.0)	
Marital status			
Single	5(10.0)	4(8.0)	P=1
Married	45(90.0)	46(92.0)	
Smoking	10.6(16.7)	9(15.0)	χ^2=0.063 P=0.803
Laboratory Finding			
CRP (mg/L) +ve	33(66.0)	14(28.0)	χ^2=14.492 P<0.001*
CRP (mg/L) Median (min-max)	24(6-116)	12(6-24)	Z=1.38 P=0.16
Creatinine (mg/dl)	1.17±0.25	1.0±0.25	t=3.40 p=0.001*
Urinary orosomucoid A	66.70(20.18-118.44)	51.49(26.7-91.99)	Z=2.15 P=0.03*
Creatinine clearance	94.26(74.35-130)	90(60-120)	Z=0.825 P=0.409
Urinary orosomucoid A/ Creatinine	0.413(0.1-2.59)	0.293(0.1-1.28)	Z=2.26 P=0.024*

Median and min-max: nonparametric test. *: Significant.

Table (2) demonstrates that 68% of the studied cases had gradual onset of disease, 62.9% progressive course. Median duration of disease was 6 years, mean age of onset was 36.59, 22% of the studied cases had systemic disease, 100% topical therapy, 18% positive family history, 100% skin affection, 100% history of trauma, 100% positive grattage test and 38% had hair affection. Median PASI score was 7.8.

Table (2): Disease characters, systemic disease, clinical presentation and treatment history among studied cases

	N=50	%
Onset		
Acute	16	32.0
Gradual	34	68.0
Course		
Progressive	22	62.9
Intermittent	13	37.1
Duration / years		
Median (min-max)	6.0(1.0-40.0)	
Age of onset		
Mean (min-max)	36.59(9.0-65.0)	
Systemic disease	11	22.0
Hypertension	5	10.0
Diabetes mellitus	4	8.0
Cardiac disease	2	4.0
Topical therapy	50	100.0
Previous systematic therapy	20	40.0
Previous phototherapy	13	26.0
Family history (+ve)	9	18.0
Skin	50	100.0
Trauma	50	100.0
Grattage test	50	100.0
Scalp psoriasis	19	38.0
PASI score		
Mean	12.06±10.51	
Median (min-max)	7.8(0.9-39.8)	

Table (3) Demonstrates that area under curve for urinary orosomucoid A in differentiating cases from control was fair with the best detected cutoff point was 53.18.

Table (3): Urinary Orosomucoid A validity in differentiating between cases and control groups.

	AUC (95%CI)	P value	Cutoff point	Sensitivity %	Specificity %
Urinary orosomucoid A	0.625 (0.513-0.736)	0.03*	53.18	74.0	58.0

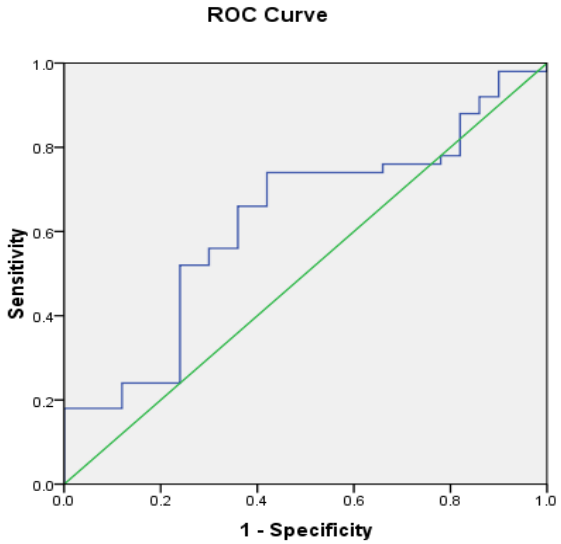

Figure (1): ROC curve of urinary orosomucoid A validity in differentiating between cases and control groups.

Table (4) Demonstrates that area under curve for urinary orosomucoid A/creatinine in differentiating cases from control was fair with the best detected cutoff point was 0.293.

Table (4): Urinary orosomucoid/creatinine validity in the differentiation between both groups

	AUC (95%CI)	P value	Cutoff point	Sensitivity %	Specificity %
Urinary orosomucoid / creatinine	0.631 (0.519-0.743)	0.024*	0.293	70.0	52.0

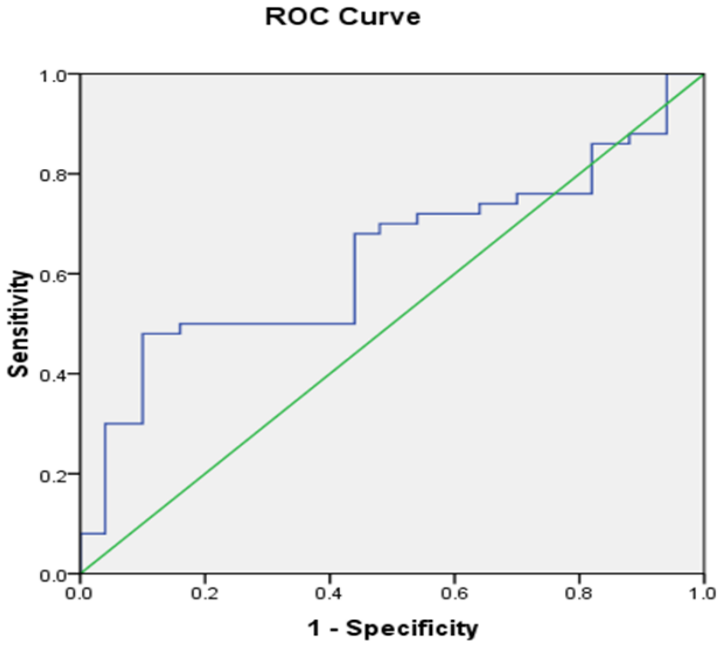

Figure (2): ROC curve of urinary orosomucoid/creatinine Validity in differentiating between cases and control groups.

Table (5) illustrates that AUC for serum creatinine in the differentiation between cases and controls was good with the best detected cutoff point was 0.950.

Table (5): Serum creatinine validity in the differentiation between cases and control groups.

	AUC (95%CI)	P value	Cutoff point	Sensitivity %	Specificity %
Creatinine (mg/dl)	0.700 (0.595-0.804)	0.001*	0.950	84.0	38.0

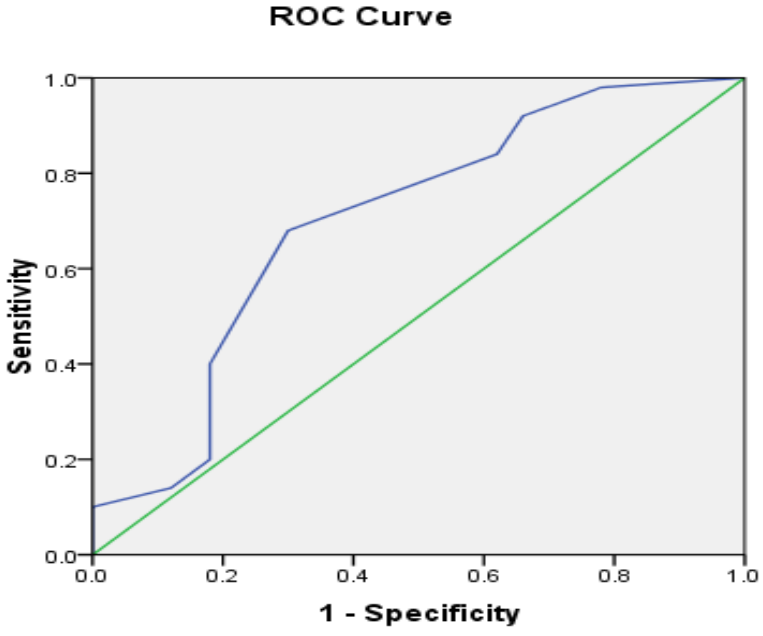

Figure (3): ROC curve of creatinine validity in differentiating between cases and control groups.

Table (6) shows non-statistically significant relation between that urinary orosomucoid A and disease characteristics, family history and clinical characteristics of the studied cases.

Table (6): Association between urinary orosomucoid A and disease characters and PASI score among studied cases

	Urinary Orosomucoid A Median (min-max)	Test of significance
Onset		
Acute	73.67(41.44-109.97)	Z=1.33
Gradual	63.11(20.18-118.44)	P=0.183
Course		
Progressive	61.24(29.22-118.44)	Z=0.383
Intermittent	67.82(20.18-111.31)	P=0.702
Systemic disease		
-ve	67.04(29.22-111.31)	Z=0.269
+ve	58.80(20.18-118.44)	P=0.788
Previous systematic therapy		
-ve	60.50(29.22-96.86)	Z=0.931
+ve	71.45(20.18-118.44)	P=0.352
Previous phototherapy		
-ve	58.96(29.22-96.86)	Z=1.69
+ve	76.36(20.18-118.44)	P=0.091
Family history		
-ve	70.42(20.18-118.44)	Z=0.846
+ve	56.30(46.86-111.31)	P=0.398
Hair		
-ve	61.24(20.18-118.44)	Z=0.630
+ve	67.04(29.22-111.31)	P=0.529
PASI score	r=0.204 p=0.155	
Duration / years	r=0.224 p=0.118	
Creatinine Clearance	r=0.009 p=0.9550	

Table (7) shows that there was a statistically significant higher median urinary orosomucoid A, urinary orosomucoid A/creatinine among severe cases than mild and moderate cases. Also statistically significant higher CRP was detected with severe disease than mild and moderate disease.

Table (7): Orosomucoid A and urinary orosomucoid A/creatinine among cases according to severity of psoriasis vulgaris

	Mild	Moderate	Severe	test of significance
Urinary Orosomucoid A	35.0 (29.22-111.31)	47.49 (20.18-96.86)	79.21 (45.03-118.44)	KW=0.681 P=0.03*
Urinary Orosomucoid A/ creatinine	0.327 (0.1-2.4)	0.313 (0.11-1.07)	0.756 (0.22-2.59)	KW=5.12 P=0.024*
CRP	8(6-112)	24(8-96)	62(12-116)	KW=7.73 P=0.02*

DISCUSSION

Psoriasis is a chronic inflammatory dermal lesion, featured by erythematous plaques covered with silvery scales. It often affects the scalp, knees, elbows, and trunk. In addition, it could affect the joints and eyes. It is a chronic disease with remission and exacerbation. There are a lot of types of PV, however the plaque type is the commonest [19].

Its prevalence ranges from 0.2% to 4.8%. The actual cause is not well understood; however, it is believed that it is a T-lymphocyte-mediated AID. There is a correlation between HLA antigens and familial occurrence reinforces its genetic background. Of note, mechanical and chemical injuries cause psoriatic lesions. In addition, some medications which include chloroquine, lithium, corticosteroids, and NSAIDs could deteriorate PV. In general, summer improves PV, whereas winter worsens it. In addition, infections, stressful conditions, alcohols, tobacco smoking, overweight, and hypocalcemia have been considered as other predisposing factors for PV [20].

Orosomucoid is a major APP mostly synthesized in the liver, representing about 0.5-1.2 g/L of serum proteins. In addition, se-ORM values could be increased also in a lot of diseases owing to systemic inflammation [13]. On the other hand, several researches revealed uORM as a more sensitive, noninvasive biomarker of inflammatory stimulation than se-ORM. Under normal physiological conditions, uORM execration is low as its concentrations represent a few mg/L (0.01-0.3 mg/mmol) [12].

Increased uORM appears to be accompanied by systemic inflammatory conditions and impaired endothelial function and both factors are thought to have essential roles in terms of PV pathomechanism [21].

Hence, the aim of the current prospective case control study was to assess the role of uORM as a surrogate marker for psoriasis and to correlate its urinary values with the disease severity.

The present study was conducted on 50 cases with psoriasis recruited from the Dermatology and Venereology Department of Mansoura University Hospitals in addition to 50 healthy controls.

Regarding the demographic data of the present cases, our study revealed that; the mean age of PV was at 45 years with female predominance (52%) with no significant difference between both groups with regard to both age and sex. **Parisi *et al.*** [22] found that the mean age of onset of PV was at 33 years with female's predominance (65%).

The present study revealed that that 68% of the studied cases had gradual onset of disease, 62.9% with progressive course and median duration of disease was 6 years ranging from 1 to 40 years. Other studies [23-25] found that most of psoriatic cases had gradual onset (96%) and 32% were progressive. The median duration of psoriasis was 18 years [26].

In our study 38% of cases had scalp affection. In another study by **Chan *et al*.** [27], about eighty percent of PV cases were associated with scalp PV.

Our study revealed that 22% of their studied cases had systemic disease. Hypertension (HTN) (n=5) and diabetes mellitus (DM) (n=4) were the most common. 16.7% of the cases were current smokers. In contrast, **Karabay *et al.*** [28] have demonstrated that the prevalence of an associated disease in their psoriatic cases was 14%, in which HTN, DM and dyslipidemia were the most frequent disorders. In addition, sixty percent of their study cases were smokers.

The present study revealed that 18% of the studied cases had positive family history (PFH) of PV. **Solmaz *et al.*** [29] found that 31.9% of studied psoriatic cases had a PFH of similar condition. In addition, they revealed that such history was correlated positively with younger age at onset of PV and existence of enthesitis.

In our study, the median PASI score of the cases was 12.06, while **Karabay *et al.*** [28] found that the mean PASI score of the cases was 15.08±8.8.

The current study revealed a statistically significant higher frequency of positive CRP among cases than control group. CRP significantly increased in cases with severe PV than moderate and mild ones (p=0.02). Our results of CRP was in accordance with **Vadakayil *et al.*** [10] who revealed that CRP was significantly increased among cases with PV in comparison to the controls (p=0.001). It has been demonstrated that; CRP was significantly increased among cases with severe PV compared to mild ones.

Other studies evaluated the association between PV severity and CRP values. Based on the meta-analysis reported by **Dowlatshahi *et al.*** [30] CRP values are significantly greater in cases complaining from PV in comparison with normal subjects (p=0.001).

The current study revealed that mean serum creatinine was higher among cases than control group (p=0.001), while serum creatinine wasn't significantly different between both groups. Also, other report conducted by **Tehranchinia *et al.*** [31] have revealed that median serum levels of creatinine and CrCl weren't significantly different between both groups

The current study revealed that median uORM A statistically increased among PV cases compared to the controls and also among severe PV cases compared to mild and moderate ones (P=0.03). Likewise, **Khalid *et al.*** [32] noted a significant increase in uORM values among PV cases compared to the controls which is in agreement with the current study. Also, **Kustán *et al.*** [13] **and Nowowiejski *et al.*** [33] came to the same conclusion.

Of note, uORM has been considered to be of great sensitivity as an inflammatory marker in comparison with se-ORM, since it increases in PV cases even with a minimal degree of inflammations.

In the same line, **Németh *et al.*** [21] have illustrated that there was a significant increase in uORM

value in moderate cases then the uORM values of the mild psoriatic cases to the uORM values of moderate ones.

Urinary orosomucoid (uORM) A/creatinine ratio was also higher among PC cases than the control group with a significant difference that was also detected among severe, moderate and mild cases (p=0.024). Likewise, **Khalid *et al.*** [32] revealed that there was a significant correlation between PV severity and uORM/u-CREAT level ($p<0.001$) it was greater in severe PV compared to mild and moderate ones.

In accordance **Kustán *et al.*** [13] recorded that based on PV severity, uORM/u-CREAT was associated with a significant increase among cases with severe PV in comparison with mild and moderate ones. Also **Németh *et al.*** [21] noticed that uORM/uCREAT was associated with a significant increase in moderate PV cases in comparison with mild PV cases (p=0.005).

On contrary, **Nowowiejska *et al.*** [33] observed that no significant difference was found between cases with PV and controls as regard uORM/uCREAT. The difference between this study and our study may be related to differences in the study design.

Other studies displayed extensive uORM excretion in a lot of inflammatory situations [34]. Moderate uORM values were demonstrated in DM and in cardiac disorders, presumably accompanied minimal degree of inflammation, impaired endothelial functions and generation of free radicals, which are also pathophysiological factors in PV [35].

The small sample size as well as the few studies that investigate the relationship between uORM protein and the severity of psoriasis has been considered the main limitations. So many multicenter case control researches should be conducted to confirm the presenting results.

CONCLUSION

In conclusion, a highly sensitive, inexpensive and easily available noninvasive biomarker, uORM reveals its ability to become a new inflammatory marker in PV offering further data on PV severity and progression.

On the other hand, additional studies are required to explain its predictive values and actual role in the context of PV pathophysiology. The present study revealed a significant association between uORM protein, uORM/ uCREAT ratio and PV. As a result, they may be highly sensitive, available, and novel inflammatory biomarkers of PV that correlate to the PV severity.

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REFERENCES

1. **Korman N (2020):** Management of psoriasis as a systemic disease: what is the evidence? British Journal of Dermatology, 182(4):840-8.
2. **Novartis P, Weinblatt M, Merola J (2018):** Targeted therapies for psoriatic arthritis: an update for the dermatologist. Semin Cutan Med Surg., 37(3):173-181.
3. **Raharja A, Mahil S, Barker J (2021):** Psoriasis: a brief overview. Clinical Medicine, 21(3):170-75.
4. **Yang E, Beck K, Sanchez I *et al.* (2018):** The impact of genital psoriasis on quality of life: a systematic review. Psoriasis: Targets and Therapy, 8: 41-47.
5. **Eder L, Widdifield J, Rosen C *et al.* (2019):** Trends in the prevalence and incidence of psoriasis and psoriatic arthritis in Ontario, Canada: a population-based study. Arthritis Care and Research, 71(8):1084-91.
6. **Larsabal M, Ly S, Sbidian E *et al.* (2019):** GENIPSO: a French prospective study assessing instantaneous prevalence, clinical features and impact on quality of life of genital psoriasis among patients consulting for psoriasis. British Journal of Dermatology, 180(3):647-56.
7. **Hugh J, Weinberg J (2018):** Update on the pathophysiology of psoriasis. Cutis, 102(5):6-12.
8. **Kahn J, Deverapalli S, Rosmarin D (2018):** JAK-STAT signaling pathway inhibition: a role for treatment of discoid lupus erythematosus and dermatomyositis. International Journal of Dermatology, 57(8):1007-14.
9. **Isha, Jain V, Lal H (2011):** C-reactive protein and uric acid levels in patients with psoriasis. Indian Journal of Clinical Biochemistry, 26:309-11.
10. **Vadakayil A, Dandekeri S, Kambil S *et al.* (2015):** Role of C-reactive protein as a marker of disease severity and cardiovascular risk in patients with psoriasis. Indian Dermatology Online Journal, 6(5):322-27.
11. **Fournier T, Medjoubi N, Porquet D (2000):** Alpha-1-acid glycoprotein. Biochim Biophys Acta., 1482(1-2):157-71.
12. **Kustán P, Szirmay B, Kőszegi T *et al.* (2017):** Monitoring urinary orosomucoid in patients undergoing cardiac surgery: A promising novel inflammatory marker. Clinical Biochemistry, 50(18): 1002-6.
13. **Kustán P, Kőszegi T, Miseta A *et al.* (2018):** Urinary orosomucoid a potential marker of inflammation in psoriasis. International Journal of Medical Sciences, 15(11):1113-17.
14. **Svendstrup M, Christiansen M, Magid E *et al.* (2013):** Increased orosomucoid in urine is an independent predictor of cardiovascular and all-cause mortality in patients with type 2 diabetes at 10 years of follow-up. Journal of Diabetes and its Complications, 27(6):570-5.
15. **Kustán P, Szirmay B, Horváth-Szalai Z *et al.* (2016):** Urinary orosomucoid: validation of an automated immune turbidimetric test and its possible clinical use. Biochemia Medica, 26(3):421-30.
16. **Christiansen M, Iversen K, Larsen C *et al.* (2009):** Increased urinary orosomucoid excretion: a proposed marker for inflammation and endothelial dysfunction in patients with type 2 diabetes. Scandinavian Journal of Clinical and Laboratory Investigation, 69(2):272-81.
17. **Feldman S, Krueger G (2005):** Psoriasis assessment tools in clinical trials. Annals of the Rheumatic Diseases, 64(2): 65-68.
18. **Mrowietz U, Kragballe K, Reich K *et al.* (2011):** Definition of treatment goals for moderate to severe psoriasis: a European consensus. Archives of Dermatological Research, 303: 1-10.

19. **Nair P, Badri T (2023):** Psoriasis. In: StatPearls. Treasure Island (FL): StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK448194/
20. **Nguyen C, Bloch Y, Składanowska K *et al.* (2019):** Pathophysiology and inhibition of IL-23 signaling in psoriatic arthritis: A molecular insight. Clinical Immunology, 206: 15-22.
21. **Németh B, Péter I, Boncz I *et al.* (2019):** Urinary orosomucoid: a new marker of cardiovascular risk in psoriatic patients? Therapeutics and Clinical Risk Management, 15: 831-37.
22. **Parisi R, Iskandar I, Kontopantelis E *et al.* (2020):** National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ., 20: 369. doi: https://doi.org/10.1136/bmj.m1590
23. **Bayomy H, Albedaiwi Y, Alabdulatif S *et al.* (2022):** Psoriasis in Northern Saudi Arabia: Clinical features and implications for quality of life. Journal of Public Health Research, 11(4):22799036221123961. doi: 10.1177/22799036221123961
24. **Jankowiak B, Kowalewska B, Krajewska-Kułak E *et al.* (2020):** Stigmatization and quality of life in patients with psoriasis. Dermatology and Therapy, 10(2):285-96.
25. **Sanad E, Nazmy N, Abd-El Hamid El Sayed R *et al.* (2022):** Interleukin-17A gene single nucleotide polymorphism and its relation to fungal growth in psoriatic patients: A preliminary study. Journal of Cosmetic Dermatology, 21(7): 3059-67.
26. **Yalici-Armagan B, Tabak G, Dogan-Gunaydin S *et al.*(2021):** Treatment of psoriasis with biologics in the early COVID-19 pandemic: A study examining patient attitudes toward the treatment and disease course. Journal of Cosmetic Dermatology, 20(10):3098-102.
27. **Chan C, Van Voorhees A, Lebwohl M *et al.* (2009):** Treatment of severe scalp psoriasis: from the Medical Board of the National Psoriasis Foundation. Journal of the American Academy of Dermatology, 60(6):962-71.
28. **Karabay E, Çerman A, Demir D *et al.* (2019):** The effects of systemic psoriasis therapies on the C-reactive protein and the neutrophil-lymphocyte ratio. Annals of Dermatology, 31(6):601-10.
29. **Solmaz D, Bakirci S, Kimyon G *et al.* (2020):** Impact of having family history of psoriasis or psoriatic arthritis on psoriatic disease. Arthritis Care and Research, 72(1):63-68.
30. **Dowlatshahi E, Van Der Voort E, Arends L *et al.* (2013):** Markers of systemic inflammation in psoriasis: a systematic review and meta-analysis. British Journal of Dermatology, 169(2):266-82.
31. **Tehranchinia Z, Ghanei E, Mohammadi N *et al.* (2018):** No relation between psoriasis and renal abnormalities: a case-control study. Scientific World Journal, 18:5301631. doi: 10.1155/2018/5301631.
32. **Khalid H, Abd El Gayed E, Elrsool A *et al.* (2022):** Evaluation of serum and urinary orsomucoid protein A in psoriatic patients and their relation to severity of disease. Journal of Cosmetic Dermatology, 21(3):1185-92.
33. **Nowowiejska J, Baran A, Hermanowicz J *et al.* (2023):** Tumor necrosis factor (TNF) α, endothelin (ET) 1 and α1-acid glycoprotein (AGP) as potential urine and serum markers of metabolic complications in psoriasis? Dermatol Ther (Heidelb), 13(10):2217-2227.
34. **Park Y, Yoo S, Hwang D *et al.* (2016):** Identification of novel urinary biomarkers for assessing disease activity and prognosis of rheumatoid arthritis. Experimental and Molecular Medicine, 48(2): 211. doi: 10.1038/emm.2015.120.
35. **El-Beblawy N, Andrawes N, Ismail E *et al.* (2016):** Serum and urinary orosomucoid in young patients with type 1 diabetes: a link between inflammation, microvascular complications, and subclinical atherosclerosis. Clinical and Applied Thrombosis/Hemostasis, 22(8):718-26.