CHRONIC VENOUS DISEASE AND PSORIASIS - A RANDOM ASSOCIATION?

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CHRONIC VENOUS DISEASE AND PSORIASIS- JUST A RANDOM ASSOCIATION? (Abstract): **Aims:** Chronic venous disease and psoriasis are two common pathologies in dermatological practice. The aim of this study is to determine the prevalence of venous disease among the psoriatic population and to identify risk factors that lead to their association**.** **Materials and methods**: This study included 375 patients diagnosed with psoriasis vulgaris, hospitalized in "Sf. Spiridon" County Clinical Emergency Hospital's Dermatology-Venereology Clinic, between 01.01.2019 and 31.05.2021. **Results**: The prevalence of chronic venous disease in the study group was 37.3%, reaching the highest values in the age group of 36-60 years (women: 40.7%, men: 48.6%, $P = 0.040$). Among the common risk factors, obesity had a prevalence of 19.2% and smoking 24.3% ($P = <0.001$). Among common comorbidities, hypertension had a prevalence of 47.1% and diabetes mellitus 13.6% ($P = <0.001$). **Conclusions**: In the future, more studies are required, in order to fully elucidate the mechanisms by which venous disease can be associated with psoriasis. **Keywords**: PSORIASIS, CHRONIC VENOUS DISEASE, OBESITY, SMOKING.

INTRODUCTION

Psoriasis is a chronic inflammatory disease, with a global prevalence of 2-4% and a mild evolution in 2/3 of cases (1). The etiopathogenesis of psoriasis is not fully elucidated. Clinical manifestations of psoriasis vulgaris include the appearance of erythematous-scaly plaques, well delimited, with the surface covered by white, fine, easily removable scales (2, 3). Other clinical types are guttate, pustular, erythrodermic and inverse psoriasis. It usually affects young people, between the ages of 20 and 40 years (1). Internal or external risk factors cause immunologic and metabolic dysregulations, that can trigger the disease in genetically predisposed individuals (4, 5). The immune system responds with T cells hyperactivation and T-helper 1 cells upregulation

(6, 7).

Chronic venous disease (CVD) is a common vascular pathology, produced by disturbances in the return of blood in the deep, superficial and perforating venous systems. Increased venous pressure occurs most often by weakening of the vascular wall and secondary to valvular insufficiency. Venous hypertension causes extravasation of water and erythrocytes in the tissues, leading to skin lesions (8). Clinical manifestations of CVD include discomfort and pruritus of lower limbs and suggestive signs include the appearance of varicose veins, leg edema, purple lesions or lipodermatosclerosis, as well as ulcers (9).

Common risk factors involved in the etiopathogenesis of psoriasis and chronic venous disease are obesity and smoking. Obesity is a risk factor in the development of venous valvular insufficiency in CVD due to the mechanical component and the systemic proinflammatory status produced by adipose tissue, accentuated by sedentary lifestyle and impaired pumping function of the leg muscles (10). Obesity can also lead to psoriasis (11). Hypertension is considered a comorbidity of psoriasis but there are studies in which hypertensive patients have associated an increased incidence of psoriasis (12). Also, high blood pressure can be a factor in the onset or worsening of venous disease (13).

We performed a cross-sectional study, including 375 patients, aiming to determine the prevalence of CVD among the psoriasis population and to identify risk factors that lead to their association.

MATERIALS AND METHODS

We included in this study all patients diagnosed with psoriasis vulgaris (L40.0) between 01.01.2019 and 31.05.2021, resulting 375 patients, hospitalized in "Sf. Spiridon" County Clinical Emergency Hospital's Dermatology-Venereology Clinic. The characteristics of the patients admitted in the study were: age, sex, environment, primary diagnosis and secondary diagnoses, PASI and DLQI severity scores. All patients included in the study signed their consent to the processing of personal data.

The assessment of the severity of psoriasis was performed by the doctors, using the PASI score (Psoriasis Area and Severity Index) and the impact on the quality of life was quantified using the DLQI score (Dermatology Life Quality Index). The assessment of the severity of chronic venous disease was performed using the CEAP (Clinical Etiology Anatomy Pathophysiology) classification, as follows: C0-without signs of venous disease; C1-intradermal telangiectasias or subdermal reticular veins (diameter between 1-3mm); C2- varicose veins (diameter over 3 mm); C3-edema in the ankle or calf; C4-venous eczema, lipodermatosclerosis or white atrophy; C5-healed venous ulcer; C6- active venous stasis ulcer (14).

In determining the obesity class, we used the Body Mass Index (BMI), as follows: grade I-BMI obesity with values between 30 and 34.99; grade II-BMI obesity with values between 35 and 39.99 and grade III-BMI or morbid obesity with values of 40 or more (15).

The statistical analysis of the patients' data was performed using the SPSS program version 20.0 and the calculation of the chi-square test, as follows: p <0.05, the statistical value is moderately significant (S, 95% c); p <0.01, the statistical value is very significant (S, 99% confidence); p <0.001, the statistical value is highly significant (HS, 99.9% confidence); p> 0.05, the statistical value is not significant (NS).

RESULTS

The prevalence of chronic venous disease among the psoriatic patients was 37.3%, representing 140 patients out of a total of 375 patients included in the study.

From first table, we can observe that the prevalence of CVD in the psoriatic population has the highest values in the age category 36-60 years, both in females and males, with values of 40.7% and 48.6%, followed by the age category with patients over 60 years, with a percentage of 35.9% for females and 38.0% for males. The lowest prevalence was in the age category 18-35 years, with a value of 23.4% in women and 13.5% in men (P = 0.040).

In the group of psoriatic patients who also associated the diagnosis of CVD, there was a slight predominance of males (55%) (P = 0.055) and the mean age was 60.06 ± 12.35 years (P = 0.027). Regarding the local environment, 55.7% of patients belong to urban areas (P = 0.033) and 44.3% come from rural areas (P = 0.041).

From second table, we can observe that after the classification according to the clinical stage of the chronic venous disease, most of the patients were classified in CEAP C3 (32.1%), followed by C4 (28.6%) and C2 (26.4 %) (P = <0.001). Stages C5 and C6 had a lower representation, of 6.4% (P = 0.047).

After classifying the patients according to the PASI score, most of the patients included in our study fall into the moderate-severe type of the disease (61.4%), followed by the moderate type (20.7%). The severe (11.4%) and mild (6.4%) types had lower percentages. Regarding other forms of psoriasis associated with CVD, we noticed that the pustular type had the highest prevalence, being diagnosed in 3.6% of patients, followed by guttate and inverted types, with a prevalence of 2.9% and 2.1%, (P = <0.001).

TABLE I.

Chronic venous disease prevalence by age and gender

		Gender				
		Female		Male		
		N	N %	N	N %	p- value
Age	18-35	39	23.4%	28	13.5%	0.040
	36-60	68	40.7%	101	48.6%	
	over 60	60	35.9%	79	38.0%	

TABLE II
Characteristics and risk factors of patients diagnosed with chronic venous disease and psoriasis vulgaris

Parameter	N (%)	P-value	Parameter	N (%)	P-value
Gender			Environment		
• female	63 (45%)	0.041	• Rural	62 (44.3%)	0.041
• male	77 (55%)	0.055	• Urban	78 (55.7%)	0.033
Age	60,06±12,35	0.027	Severity of psoriasis		
CEAP C categories			Moderate-to-severe	86 (61.4%)	
• C2	37 (26.4%)	<0.001	Moderate	29 (20.7%)	
• C3	45 (32.1%)	<0.001	Severe	16 (11.4%)	
• C4	40 (28.6%)	<0.001	Mild	9 (6.4%)	
• C5	9 (6.4%)	0.047	PASI <10	123 (87.9%)	0.043
• C6	9 (6.4%)	0.047	PASI 10-20	12 (8.6%)	0.068
Obesity	27(19.2%)	<0.001	PASI >20	5 (3.6%)	0.055
• grade I	7 (5%)	0.012	DLQI <10	117 (83.6%)	0.001
• grade II	16 (11.4%)	0.009	DLQI 10-20	19 (13.6%)	0.033
• grade III	4 (2.9%)	0.029	DLQI >20	5 (3.6%)	0.074
Other types of psoriasis			Hypertension	66 (47.1%)	<0.001
• Guttate	4 (2.9%)	<0.001	Diabetes mellitus	19 (13.6%)	<0.001
• Inverse	3 (2.1%)	<0.001	Smoking	34 (24.3%)	<0.001
• Pustular	5 (3.6%)	<0.001			

From first figure we can observe that the moderate-severe forms of Psoriasis are mainly associated with CEAP C3 (19.3%) and C4 (17.1%), the moderate type is associated with class C3 (8.6%) and C2 (7.1%) predominantly. The severe type is associated especially with the C4 class (5.0%) and the mild type is especially associated with the C2 class (2.9%), (P = 0.099).

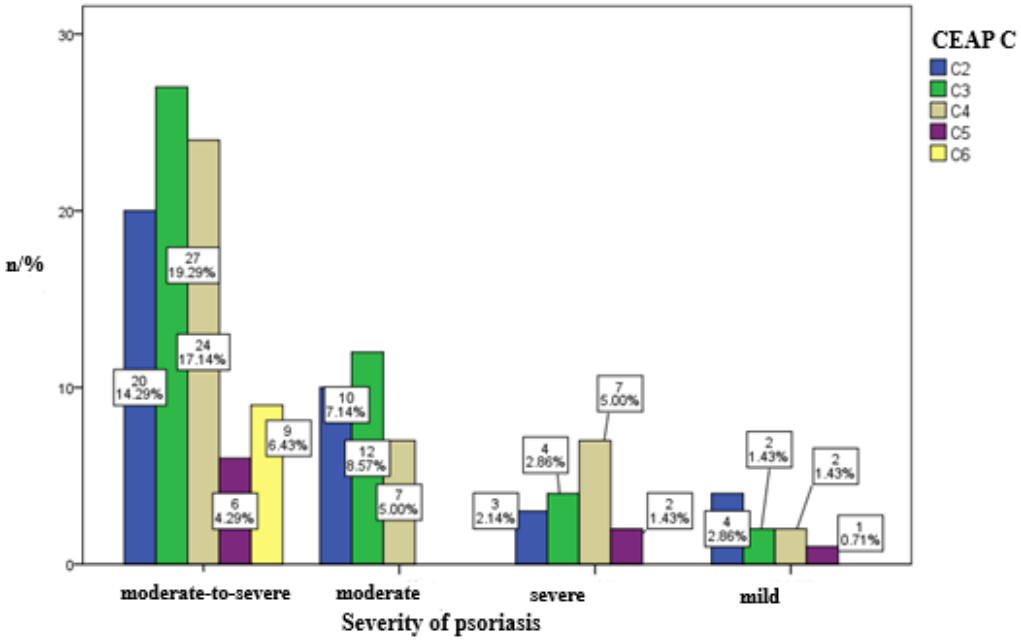

Fig. 1. Distribution of the severity forms of CVD on the severity of Psoriasis.

DISCUSSION

Compared to the experience of other medical centers, we can consider that in our study, the prevalence of chronic venous disease among the psoriatic population is high. A study conducted at the Sibiu Dermatology Clinic, during 2010-2013, on a cohort of 270 patients diagnosed with psoriasis, CVD prevalence was 22.22% (16). In another study conducted in Tunis, published in 2019, evaluating a cohort of 163 patients diagnosed with Psoriasis, the prevalence of CVD was 1% (17) There are, however, few studies published in the literature on this association. The highest prevalence of venous disease was in the age group 36-60 years, followed by the age group over 60 years. Women have a higher prevalence compared to men in the age group 18-35 years, and males have a higher prevalence in the age groups 36-60 years and over 60 years. Most patients included in the study have mild to moderate forms of venous disease. Psoriatic lesions cause the patient to consult a dermatologist, thus facilitating the early diagnosis and treatment of venous disease.

There are common risk factors involved in the etiopathogenesis of psoriasis and chronic venous disease (CVD) (1, 18). Excess body weight can trigger or maintain psoriasis or venous disease. Adipose tissue acts as an accessory endocrine organ, synthesizing over 700 peptides with a proinflammatory or metabolic role, called adipokines. Leptin, an adipokine involved in regulating appetite but also in perpetuating systemic inflammatory syndrome, has elevated serum values in psoriatic

patients (19). Other molecules involved in the onset of psoriasis are Tumor Necrosis Factor α (TNFα), Interleukin-6 and Interleukin-1 (1, 10). Obesity is also a risk factor for CVD. Recent studies show that elevated body mass index values are associated with more severe forms of venous disease (10, 13). In vivo, obesity is associated with decreased venous tonus in animal studies (11). In our study, we found a high prevalence of obesity, 19.2% of patients associated a BMI> 30 kg/m^2 (statistical value is highly significant, P = <0.001). Vlajinac *et al.* conducted a study on a group of 1116 patients diagnosed with CVD, and 15.8% had associated obesity (20). In a study of a group of psoriatic patients, Jacobi *et al.* found a prevalence of 27.6% in obesity (21). We can consider that in this study this association is also verified.

Smoking has been demonstrated as a risk factor for both psoriasis and chronic venous disease (18, 22). A meta-analysis study showed that among smokers or ex-smokers there is an increased prevalence of psoriasis. Smoking is responsible for the development of a chronic proinflammatory status and is especially associated with pustular forms of psoriasis (18). The number of packs/years is directly proportional to the severity of psoriasis. For CVD, smoking is a risk factor in young patients (<35 years) and especially in males (23). Gourgou *et al.* demonstrated that the appearance of varicose veins is closely related to the number of cigarettes consumed per day (24). In this study, 24.3% of patients are smokers or ex-smokers. Adışen *et al.* conducted a study on 563 patients diagnosed with plaque psoriasis between 2007 and 2013, and the prevalence of smoking in this population was 50.1% (25). Regarding the association of smoking with CVD, Gourgou *et al.* conducted a study on 1806 patients with venous disease and the prevalence of smoking in this group was 37% (24).

Cardiovascular comorbidities are associated with both psoriasis and venous disease. Psoriatic patients, especially those with severe forms, have an increased prevalence of hypertension (26). On the other hand, hypertension is a risk factor involved in the onset of psoriatic disease, as demonstrated in the study performed by Kim *et al*. in 2018, in which hypertensive patients had an increased incidence of psoriatic disease (12). Criqui *et al*. found that elevated blood pressure, both systolic and diastolic, is associated with chronic venous disease (22). A study conducted in Catalonia on a population of psoriatic patients, concluded that the most common comorbidities of psoriasis are hypertension and type II Diabetes, with prevalences of 34.4% and 14.7% (27). In our study, the prevalence of hypertension was high, with a value of 47.1%, and diabetes mellitus had a prevalence of 13.6%. Psoriasis is a risk factor for the onset of type II diabetes, regardless of age or disease severity (18). Diabetes mellitus may be considered a comorbidity in the patient with CVD. The vascular pathological changes induced by chronic hyperglycemia are represented by endothelial dysfunction, reduced peripheral perfusion and local angiogenesis (13).

CONCLUSIONS

Both psoriasis and chronic venous disease are common pathologies in dermatological medical practice, both of which have a negative impact on the patient's quality of life. In this study, the prevalence of CVD among psoriatic patients was significantly higher than the worldwide published results. There are, however, very few studies that have included this association.

In this population, there is a statistically significant high connection with hypertension, diabetes, obesity and smoking. Considering the results of our study, we consider that it is necessary to deepen this topic in future studies.

CONFLICT OF INTEREST AND FUNDING

The authors declare that there is no conflict of interest and they received no funding.

REFERENCES

1. Barrea L, Nappi F, Di Somma C, *et al*. Environmental Risk Factors in Psoriasis: The Point of View of the Nutritionist. *Int J Environ Res Public Health* 2016; 13(5): 743.
2. Petrescu Z, Ţăranu T, Brănişteanu D, *et al*. *Dermatologie şi infecţii transmise sexuală*. Iasi: Ed Junimea, 2008.
3. Grajdeanu IA, Statescu L, Vata D, Popescu IA, Porumb-Andrese E, Solovastru Gheuca L. Imaging techniques in the diagnosis and monitoring of psoriasis. *Exp Ther Med*. 2019; 18(6): 4974-4980.
4. Ţolea I. *Dermatovenerologie clinică.* Craiova: Editura Medicală Universitară, 2002.
5. Solovăstru Gheuca L, Vâţă D, Batog AH, *et al*. Comorbidities in psoriatic patients of Iasi Dermatological Clinic from 2004-2008. *Med Surg J -Rev Med Chir Soc Med Nat, Iasi* 2009; 113(3), 751-756.
6. Sundarrajan S, Arumugam M. Comorbidities of Psoriasis - Exploring the Links by Network Approach. *PLoS One* 2016; 11(3): e0149175.
7. Grechin C, Solovăstru Gheuca L, Vâţă D, *et al*. Inflammatory marker alteration in response to systemic therapies in psoriasis. *Experimental and Therapeutic Medicine* 2020; 20: 42-46.
8. Spiridon M, Corduneanu D. Chronic Venous Insufficiency: Frequently Underdiagnosed and Undertreated Pathology. *MAEDICA Journal of Clinical Medicine* 2017; 12(1): 59-61.
9. Matthew Leach. Chronic venous insufficiency; In *Basic medical Key* 2015, chapter 11.
10. Davies HO, Popplewell M, Singhal R, Smith N, Bradbury AW. Obesity and lower limb venous disease - The epidemic of phlebesity. *Phlebology: The Journal of Venous Disease* 2016; 32(4): 227-233.
11. Cotter C, Walsh S. Cutaneous sequelae of a national health crisis: Obesity and the skin. *Skin health and disease* 2021, 1(1): e7.
12. Kim HN, Han K, Song SW, Lee JH. Hypertension and risk of psoriasis incidence: An 11-year nationwide population-based cohort study. *PLoS ONE* 2018, 13.
13. Mahapatra S, Ramakrishna P, Gupta B, Anusha A, Para MA. Correlation of obesity & comorbid conditions with chronic venous insufficiency: Results of a single-center study. *Indian J Med Res* 2018; 147(5): 471-476.

14. Carman TL, Al-Omari A. Evaluation and Management of Chronic Venous Disease Using the Foundation of CEAP. *Curr Cardiol Rep* 2019: 21(10): 114.
15. Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. *Nutr Today* 2015; 50(3): 117-128.
16. Rotaru M. Psoriasis and associated cardiometabolic comorbidities. *Acta Medica Transilvanica* 2015; 20(1): 76-79.
17. Jendoubi F, Ben L, Rabhi F, *et al*. Nail Involvement in Psoriatic Patients and Association with Onychomycosis: Results from a Cross-Sectional Study Performed in a Military Hospital in Tunisia. *Skin Appendage Disorders* 2019; 5(5): 299-303.
18. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk Factors for the Development of Psoriasis. *Int J Mol Sci* 2019; 20(18): 4347.
19. Stîncanu A, Andrese E, Stătescu L, Vâță D, Solovastru Gheuca L. Leptin - a systemic inflammation marker in vulgar psoriasis associated with metabolic syndrome. *Revista Societății Romane de Dermatologie* 2014; 59; 209-216.
20. Vlajinac HD, Marinkovic, Maksimovic MZ, Matic PA, Radak DJ, Body Mass Index and Primary Chronic Venous Disease - A Cross-sectional Study. *European Journal of Vascular and Endovascular Surgery* 2013; 45(3): 293-298.
21. Jacobi A, Langenbruch A, Purwins S, Augustin M, Radtke MA. Prevalence of Obesity in Patients with Psoriasis: Results of the National Study PsoHealth3. *Dermatology* 2015; 231(3): 231-238.
22. Criqui MH, Denenberg JO, Langer RD, Fronek A. Risk factors for chronic venous disease: The San Diego Population Study. *J Vasc Surg* 2007; 46(2): 331-337.
23. Vuylsteke ME, Colman R, Bergan J, Langer RD, Fronek A. An Epidemiological Survey of Venous Disease Among General Practitioner Attendees in Different Geographical Regions on the Globe: The Final Results of the Vein Consult Program. *Angiology* 2018; 69(9): 779-785.
24. Gourgou S, Dedieu F, Sancho-Garnier H. Lower Limb Venous Insufficiency and Tobacco Smoking: A Case-Control Study, *American Journal of Epidemiology* 2002; 155(11): 1007-1015;
25. Adışen E, Uzun S, Erduran F, Gürer MA. Prevalence of smoking, alcohol consumption and metabolic syndrome in patients with psoriasis. *An Bras Dermatol* 2018; 93(2): 205-211.
26. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and hypertension: A systematic review and meta-analysis of observational studies. *J Hypertens* 2013; 31: 433-442.
27. Puig L, Ferrándiz C, Pujol RM, *et al*. Burden of Psoriasis in Catalonia: Epidemiology, Associated Comorbidities, Health Care Utilization, and Sick Leave. *Actas Dermosifiliogr (Engl Ed)* 2021; 112(5): 425-433.