Severity of Psoriasis Associated with Metabolic Syndrome

ANA MARIA ALEXANDRA STANESCU[1]*, CONSTANTIN STEFANI[1], IOANA VERONICA GRAJDEANU[1], BOGDAN SERBAN[12], GHEORGHE CIOBANU[3], CAMELIA CRISTINA DIACONU[1,4]

[1]University of Medicine and Pharmacy Carol Davila, 8 Eroii Sanitari Str, 050474, Bucharest, Romania
[2]Emergency University Hospital Bucharest, 169 Splaiul Independenei, 050098, Bucharest, Romania
[3]State University of Medicine and Pharmacy Nicolae Testemitanu Chisinau, Republic of Moldova
[4]Clinical Emergency Hospital of Bucharest, 8 Calea Floreasca, 014461, Bucharest, Romania

Although extensively studied, psoriasis still has negative consequences and is associated with multiple comorbidities, including metabolic syndrome. The severity of psoriasis seems to influence the occurrence of diagnostic criteria for metabolic syndrome. 208 patients diagnosed with psoriasis were identified, who were divided into lots depending on the severity of psoriasis, but also to the presence or absence of metabolic syndrome. Interpretation of statistical data was done with SPSS V21 (Statistical Package for Social Science) and MEDCALC (Statistical Software). The coexistence of severe psoriasis with metabolic syndrome increases the risk of developing cardiovascular diseases by 2.97 or greater, with a confidence interval of [1.60, 5.51], than that of patients with severe psoriasis who have no metabolic syndrome. The hypothesis was statistically confirmed by p = 0.003. Analyzing the total group with psoriasis by severity, we found the following distribution: from the total number of 208 patients, 39 (18.8%) had severe psoriasis, 83 (39.9%) moderate psoriasis and 86 (41.3%) mild psoriasis. The higher incidence of metabolic syndrome in patients with psoriasis is evidenced by the Pearson Chi-Square test, where p <0.001. The association of metabolic syndrome in patients with psoriasis is evident. The more severe the psoriasis, the more likely it is to develop metabolic syndrome.

Keywords: psoriasis, cardiovascular diseases, metabolic syndrome.

Psoriasis is a global health problem. Methods of preventing psoriasis have not yet been discovered, genetic predisposition cannot be altered, and eliminating triggering and aggravating factors cannot predict the activation, duration or remission of the disease. As there is an increased incidence of cardiovascular disease, diabetes mellitus and obesity (components of metabolic syndrome) in patients with psoriasis, the problem of the increased incidence of metabolic syndrome in these patients has been raised [1-3].

A recent study has shown that the prevalence of metabolic syndrome was significantly higher in psoriatic patients than in controls (39.3% vs. 17.1%, odds ratio = 3.13), with a significantly higher prevalence of hypertension, abdominal obesity and diabetes; there was a significant trend of increasing prevalence of metabolic syndrome, hypertension and type 2 diabetes with increased severity and longer duration of the psoriasis [4].

Cytokines involved in pathogenesis of psoriasis, like IL-1, IL-4, IL-6, IL-8, IL-12 and TNF, are also involved in metabolic syndrome [5,6]. Regarding the association of psoriasis with metabolic syndrome, besides inflammation and genetic factors, life style contributes as well [7-9]. More recently, vitamin D appears to play a very important role, both in the treatment of psoriasis and in the components of metabolic syndrome [10,11].

The objective of this study was to determine the prevalence of metabolic syndrome in patients with psoriasis depending on its severity.

Experimental part

The study was conducted in Bucharest and Ilfov county, between 2010-2017, with the participation of family doctors, dermatologists and Elias Emergency Hospital - Department of Dermatology, Bucharest, Romania. Selection of patients with psoriasis was made following a definite diagnosis by a dermatologist. The control group consisted of the general population who had no conditions that could influence the study. The inclusion age for all participants was ≥ 18 years. To monitor the correlation of the severity of psoriasis with metabolic syndrome, 5 lots were formed:

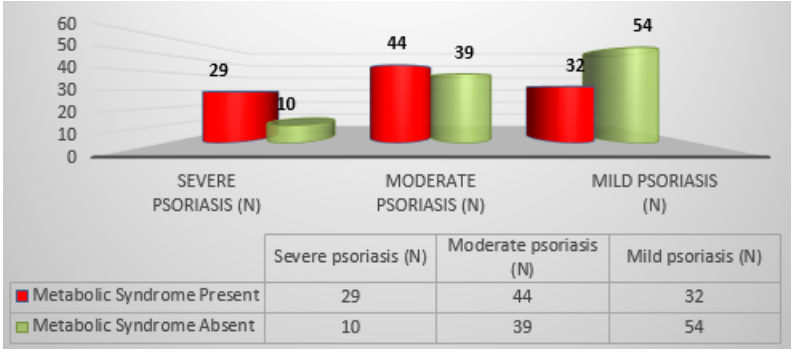
- Lot 1 - patients with severe psoriasis who have metabolic syndrome.
- Lot 2 - patients with moderate psoriasis who have metabolic syndrome.
- Lot 3 - patients with mild psoriasis who have metabolic syndrome.
- Lot 4 - patients with psoriasis without metabolic syndrome.
- Lot 5 - patients who do not have psoriasis but have metabolic syndrome.

The privacy of personal data during the study was completely respected. Follow-up: heredo-collateral history, pathological personal history, personal physiological history, living and working conditions, history of psoriasis, clinical assessments and laboratory examinations.

To determine the severity of psoriasis, we used the BSA score [12] and the criteria of the International Diabetes Federation (IDF) for the diagnosis of metabolic syndrome [13].

Interpretation of statistical data was done with SPSS V21 (Statistical Package for Social Science) and MEDCALC (Statistical Softwer). For the parametric and nonparametric data, we used the ANOVA test (compares three or more groups simultaneously), Pearson Chi-Square, Likelihood Ratio, Kruskal Wallis, Fisher's Exact Test, Mann-Whitney, Student T, McNemar-Bowker Test, Cramer's and the Bonferroni Corrected Test. We took into account the statistical significance p <0.05 for validation. The confidence interval of 95% for the variance intervals of the studied parameters was respected.

* email: alexandrazotta@yahoo.com; Phone: +40730486709 All authors had equal contribution and share the first authorship



	Severe psoriasis (N)	Moderate psoriasis (N)	Mild psoriasis (N)
Metabolic Syndrome Present	29	44	32
Metabolic Syndrome Absent	10	39	54

Fig. 1. The presence of metabolic syndrome in patients with psoriasis depending on the severity of psoriasis

Table 1

DISTRIBUTION OF THE FIVE LOTS BY AGE AND SEX

Age	Lot 1 (N = 29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
V1*	2/29 (6.9%)	2/44 (4.5%)	0/32 (0.0%)	19/103(18.4%)	8/122 (6.6%)	0.013 (Pearson Chi-Square)
V2*	7/29 (24.1%)	9/44 (20.5%)	6/32 (18.8%)	29/103 (28.2%) 28/103 (27.2%)	31/122 (25.4%)	
V3*	12/29 (41.4%)	11/44 (25.0%)	9/32 (28.1%)	14/103 (13.6%) 13/103 (12.6%)	36/122 (29.5%) 29/122 (23.8%)	
V4*	7/29 (24.1%)	16/44 (36.4%)	13/32 (40.6%)		18/122 (14.8%)	
V5*	1/29 (3.4%)	6/44 (13.6%)	4/32 (12.5%)			
Sex=F	19/29 (65.5%)	24/44 (54.5%)	15/32 (46.9%)	64/103 (62.1%)	77/122 (63.1%)	0.420 (Pearson Chi-Square)

*V1 =18-40 years, V2 = 41-50 years, V3 = 51-60 years, V4 = 61-70 years, V5 = >70 years.

Results and discussions

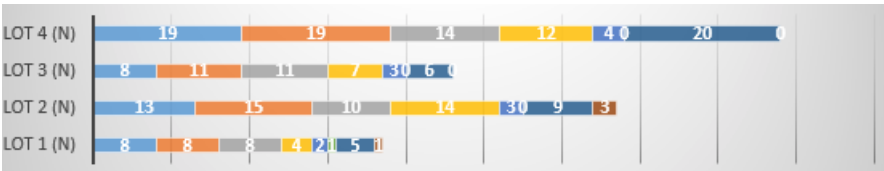
The presence of metabolic syndrome among patients with psoriasis, depending on the severity of psoriasis, is shown in figure 1.

We analyzed each lot, the correlations between them and the statistical significance of the interest between the lots and the studied components. We found statistically significant differences only in the age group 61-70 years (p = 0.013). Among the remaining age groups, there were no statistically significant differences. We did not find statistically significant differences regarding sex in the studied groups.

Regarding the heredo-collateral history, we most commonly encountered the cardiovascular disease in patients with psoriasis (25.5% of cases), 34 of these cases were in patients with psoriasis and metabolic syndrome and 19 in patients with psoriasis without metabolic syndrome. Of the patients with psoriasis and metabolic syndrome, 29 have or have had psoriasis in their family medical history. In Lot 5, no patient with psoriasis was found in the heredo-collateral history and we can say that we have a very strong statistical significance with p = 0.000.

In Lot 1, the most common comorbidities are: psoriasis 27.6%, cardiovascular disease 27.6%, obesity 27.6%, arthritis 17.2%, diabetes mellitus 13.8%, neoplasms 6.9%. In Lot 2 we encountered: cardiovascular diseases 34.1%, diabetes 31.8%, psoriasis 29.5%, obesity 22.7%, arthritis 20.5%, neoplasms and metabolic syndrome 6.8%. In Lot 3 we encountered: 34.4% cardiovascular disease, 34.4% obesity, 25.0% psoriasis, 21.9% diabetes, 18.8% of arthritis and 9.4% of neoplasms. In Lot 4 we found: 19.4% arthritis, 18.4% psoriasis, 18.4% cardiovascular disease, 13.6% obesity, 11.7% diabetes and 1.9% neoplasms. The low incidence of metabolic syndrome may be due to non-diagnosis, being poorly known in the past and nearly impossible to diagnose.

We found significant differences in the presence of cardiovascular disease between lots (p_value = 0.001), namely: between Lot 1 and Lot 4, Lot 1 and Lot 5, Lot 2 and Lot 4, Lot 2 and Lot 5, Lot 3 and Lot 4. Cardiovascular disease was present in all five groups, being associated



	Lot 1 (N)	Lot 2 (N)	Lot 3 (N)	Lot 4 (N)
Psoriasis	8	13	8	19
Cardiovascular diseases	8	15	11	19
Obesity	8	10	11	14
Diabetes	4	14	7	12
Neoplasms	2	3	3	4
Psychic diseases	1	0	0	0
Arthritis	5	9	6	20
Metabolic syndrome	1	3	0	0

Fig. 2. Identification of heredo-collateral history

Table 2
PATHOLOGICAL PERSONAL HISTORY OF THE FIVE STUDIED GROUPS

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Psoriasis=Yes	29/29 (100%)	44/44 (100%)	32/32 (100%)	103/103 (100%)	0/122 (0.0%)	0.001 (Pearson Chi-Square)
Cardiovascular diseases = Yes	12/29 (41.4%)	16/44 (36.4%)	11/32 (34.4%)	9/103 (8.7%)	17/122 (13.9%)	0.001 (Pearson Chi-Square)
Diabetes=Yes	6/29 (20.7%)	10/44 (22.7%)	7/32 (21.9%)	6/103 (5.8%)	16/122 (13.1%)	0.021 (Pearson Chi-Square)
Neoplasms=Yes	3/29 (10.3%)	3/44 (6.8%)	1/32 (3.1%)	0/103 (0.0%)	4/122 (3.3%)	0.024909 (LikelihoodRatio)
Psychic diseases=Yes	4/29 (13.8%)	0/44 (0.0%)	0/32 (0.0%)	0/103 (0.0%)	0/122 (0.0%)	0.001 (LikelihoodRatio)
Arthritis=Yes	10/29 (34.5%)	11/44 (25.0%)	7/32 (21.9%)	18/103 (17.5%)	6/122 (4.9%)	0.001 (Pearson Chi-Square)
Metabolic syndrome=Yes	29/29 (100%)	44/44 (100%)	32/32 (100%)	0/103 (0.0%)	122/122 (100%)	0.001 (Pearson Chi-Square)
Other dermatological diseases=Yes	1/29 (3.4%)	2/44 (4.5%)	0/32 (0.0%)	0/103 (0.0%)	0/122 (0.0%)	0.05 (Likelihood Ratio)
Allergies=Yes	8/29 (27.6%)	12/44 (27.3%)	10/32 (31.3%)	15/103 (14.6%)	8/122 (6.6%)	0.001 (Pearson Chi-Square)
HIV/AIDS=Yes	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	2/103 (1.9%)	0/122 (0.0%)	0.32 (Likelihood Ratio)

with both psoriasis and metabolic syndrome. We determined the relative risk of cardiovascular disease in patients with severe psoriasis and metabolic syndrome compared to patients with severe psoriasis without metabolic syndrome. Using descriptive statistics, we estimated the risk of developing CVD depending on the presence or absence of metabolic syndrome in patients with severe psoriasis. The coexistence of severe psoriasis with metabolic syndrome increases the risk of developing CVD of 2.97 or greater with a confidence interval of [1.60, 5.51] than that of patients with severe psoriasis who have no metabolic syndrome. The hypothesis was statistically confirmed by p = 0.003.

With regard to diabetes mellitus, we have statistical significance between Lot 2 with the highest distribution of DM and Lot 4 with the lowest DM distribution (p = 0.021.) The presence of diabetes mellitus is increased in Lot 1, Lot 2 and Lot 3 versus the other, which indicates the more frequent association of diabetes in patients with psoriasis and metabolic syndrome.

In Lot 1 we found in 10.3% of the cases the presence of neoplasms, compared to Lot 4 where they are non-existent, and having statistical significance (p = 0.024). The presence of arthritis is most common in Lot 1 and much more common in association with psoriasis than metabolic syndrome (p_value = 0.0001). Allergies are also more prevalent in people with psoriasis and metabolic syndrome (p_value = 0.0003). In the personal physiological history of the psoriasis group, there were no relevant changes for the current study. Undetectable differences between lots.

During pregnancy, gestational diabetes was reported in five cases of psoriasis patients.

Table 3
DISTRIBUTION OF VARIABLES: SMOKING, ALCOHOL, DRUGS AND COLA / COFFEE

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Smoking F1*	10/29 (34.5%)	13/44 (29.5%)	10/32 (31.3%)	39/103 (37.9%)	20/122 (16.4%)	0.0004 (Pearson Chi-Square)
F2*	17/29 (58.6%)	16/44 (36.4%)	9/32 (28.1%)	33/103 (32.0%)	43/122 (35.2%)	
F3*	2/29 (6.9%)	15/44 (34.1%)	13/32 (40.6%)	31/103 (30.1%)	59/122 (48.4%)	
Alcohol						
A1*	8/29 (27.6%)	14/44 (31.8%)	12/32 (37.5%)	32/103 (31.1%)	22/122 (18.0%)	0.0004 (Pearson Chi-Square)
A2*	9/29 (31.0%)	13/44 (29.5%)	10/32 (31.3%)	41/103 (39.8%)	25/122 (20.5%)	
A3*	12/29 (41.4%)	17/44 (38.6%)	10/32 (31.3%)	30/103 (29.1%)	75/122 (61.5%)	
Drugs=Yes	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	0/103 (0.0%)	0/122 (0.0%)	-
Cola / Coffee=Yes	21/29 (72.4%)	25/44 (56.8%)	22/32 (68.8%)	60/103 (58.3%)	58/122 (47.5%)	0.059 (Pearson Chi-Square)

*F1 = smokers, F2 = former smokers, F3 = non-smoking; A1 = consumers, A2 = occasional consumers, A3 = non-consumers.

In the groups with psoriasis, smokers were shown in comparison with the group with metabolic syndrome. Former smokers are in a higher percentage (58.6%) in group 1, where there is association of psoriasis - metabolic syndrome.

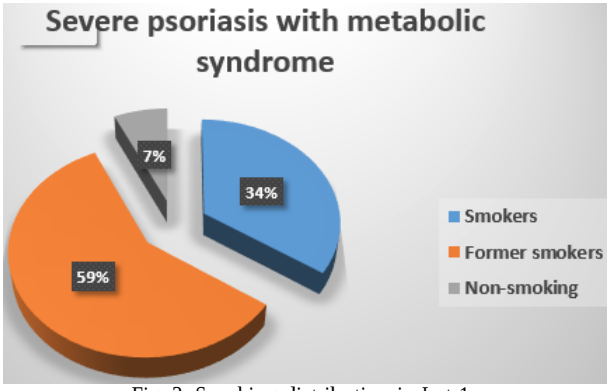


Fig. 3. Smoking distribution in Lot 1

Most non-smokers were found in group 5, those with metabolic syndrome without psoriasis. We found a significantly higher alcohol consumption in patients with psoriasis, without being influenced by the presence of metabolic syndrome. The highest percentage of coffee/ cola consumption was found in patients with severe psoriasis and metabolic syndrome (lot 1 - 72.4%), but the rest of the lots had high percentages in this variable, the smallest percentage being in group 5 (47.5%).

We found significant differences in the various stages of stress between lots ($p = 0.001$). Intensive stress prevailed in lots 1 (51.7%), 2 (47.7%), 3 (59.4%), 4 (52.4%), compared to lot 5 (6.6%). Patients with psoriasis are more frequently exposed to intense stress compared to patients with metabolic syndrome without psoriasis. Low stress is the most common in group 5 (55.7%) lacking psoriasis, and the least common is in group 3 (9.4%) with mild psoriasis and metabolic syndrome.

Reduced physical activity is predominant in all 5 lots. Intense physical activity is missing in groups 1, 2 and 3, where there are patients with psoriasis and metabolic syndrome. In a small percentage, we found intense physical activity in group 2 (5.8%) of patients with psoriasis without metabolic syndrome, and in group 5 (1.6%) patients with metabolic syndrome without psoriasis. From the point of view of the severity of psoriasis, there was a lack of physical activity in patients with severe psoriasis and metabolic syndrome (93.1%), compared to those with mild psoriasis and metabolic syndrome (71.9%).

Table 4

COMPARISON OF STRESS LEVELS AND PHYSICAL ACTIVITY

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Stress						
T1*	15/29 (51.7%)	21/44 (47.7%)	19/32 (59.4%)	54/103 (52.4%)	8/122 (6.6%)	0.001 (Pearson Chi-Square)
T2*	7/29 (24.1%)	11/44 (25.0%)	10/32 (31.1%)	31/103 (30.1%)	46/122 (37.7%)	
T3*	7/29 (24.1%)	12/44 (27.3%)	3/32 (9.4%)	18/103 (17.5%)	68/122 (55.7%)	
Physical activity						
AC1*	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	6/103 (5.8%)	2/122 (1.6%)	0.003 (Pearson Chi-Square)
AC2*	2/29 (6.9%)	11/44 (25.0%)	9/32 (28.1%)	28/103 (27.2%)	49/122 (40.2%)	
AC3*	27/29 (93.1%)	33/44 (75.0%)	23/32 (71.9%)	69/103 (67.0%)	71/122 (58.2%)	

*T1 = intense stress, T2 = moderate stress, T3 = minimal stress; AC1 = intense physical activity, AC2 = moderate physical activity, AC3 = minimal physical activity.

Table 5

DISEASE HISTORY IN PATIENTS WITH PSORIASIS, LOTS 1, 2, 3 AND 4

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N =122)	Test - Comparison of the 5 lots
Diagnosis History = New	0/29 (0.0%)	2/44 (4.5%)	0/32 (0.0%)	0/103 (0.0%)	-	0.09 (Likelihood Ratio)
History Old lesions Undiagnosed = Yes	0/29 (0.0%)	2/44 (4.5%)	0/32 (0.0%)	0/103 (0.0%)	-	0.09 (Likelihood Ratio)
Intensity Psoriasis severity = Yes					-	0.001 (Pearson Chi-Square)
P1*	29/29 (100%)	0/44 (0.0%)	0/32 (0.0%)	10/103 (9.7%)	-	
P2*	0/29 (0.0%)	44/44 (100%)		39/103 (37.9%)	-	
P3*	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	54/103 (52.4%)	-	
			32/32 (100%)			
History Duration of the disease in years	8.86±2.386 9.00 [7.00, 11.00]	8.34±4.387 8.00 [5.00, 11.00]	8.87±3.824 9.00 [7.00, 11.00]	5.36±2.619 5.00 [3.00, 7.00]	-	0.001 (Kruskal Wallis)
RecurrentHistory = Yes	29/29 (100%)	42/44 (95.5%)	30/32 (93.8%)	77/103 (74.8%)		0.001 (Likelihood Ratio)
History of Biopsy	3/29 (10.3%)	0/44 (0.0%)	1/32 (3.1%)	0/103 (11.7%)	-	0.01 (Likelihood Ratio)

*P1 = severe psoriasis, P2 = moderate psoriasis, P3 = mild psoriasis.

Regarding the history of psoriasis, we found two new cases of moderate psoriasis with undiagnosed old lesions and metabolic syndrome. Those with a new diagnosis of psoriasis represent 0.96% of the total group of patients with psoriasis and 4.5% of group 2 (patients with moderate psoriasis and metabolic syndrome). Analyzing the total group with psoriasis by severity we found the following distribution: of the total number of 208, 39 (18.8%) with severe psoriasis, 83 (39.9%) moderate psoriasis and 86 (41.3%) mild psoriasis. A percentage of 85.6% of the total group of 208 patients with psoriasis had relapses over time. Of the 105 patients with psoriasis and metabolic syndrome, 96.2% claimed that they had relapses compared to 103 patients with non-metabolic psoriasis, of whom 74.8% had relapses. All patients with severe psoriasis and metabolic syndrome (group 1) had relapses.

Statistically significant differences between waist circumference values were found between lot 4 and lot 5 ($p = 0.029$), lot 1 and lot 4 ($p = 0.019$), lot 2 and lot 4 ($p\_value = 0.001$), lot 3 and lot 4 ($p = 0.001$), lot 5 and lot 2 ($p = 0.030$). Increased waist circumference is highlighted in patients with both psoriasis and metabolic syndrome, as well as in those with metabolic syndrome, compared to patients with psoriasis without metabolic syndrome. According to the definition of the International Diabetes Federation, the first condition is the circumference of the enlarged waist without which the diagnosis of metabolic syndrome cannot be confirmed.

We found statistically significant differences in the body mass index between lot 4 and lot 5 ($p = 0.022$), lot 3 and lot 4 ($p = 0.049$), lot 2 and lot 4 ($p = 0.000$) Lot 1 and Lot 4 ($p = 0.001$). Of the studied groups, a smaller BMI was observed in the absence of metabolic syndrome. Increased BMI can be observed in proportion to the occurrence of metabolic syndrome and increased psoriasis severity.

From the point of view of the differences between the groups of systolic blood pressure ($p = 0.470$) and the diastolic blood pressure lots ($p = 0.332$), we did not find statistically significant differences. The presence of high blood pressure in the association of psoriasis - metabolic syndrome is higher than in the other groups, being present in all patients with severe psoriasis and metabolic syndrome (fig. 4).

We found statistically significant differences with respect to the blood glucose value between lot 3 and lot 5 ($p\_value = 0.038$), lot 1 and lot 3 ($p\_value = 0.003$), lot 2 and lot 1 ($p\_value = 0.046$) (table 8). The highest mean value of glycemia was in patients with severe psoriasis and metabolic syndrome of 120.65 ± 34.58. The highest blood glucose, found in a patient without a diabetes

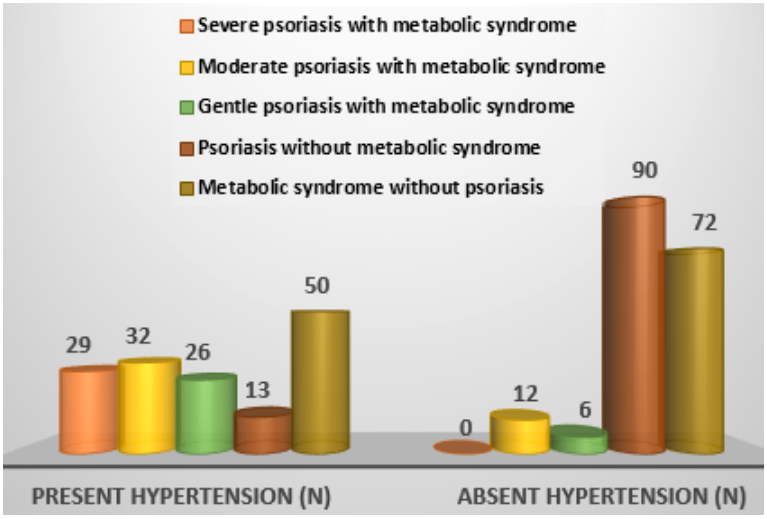


Fig. 4. Presence or absence of hypertension in the studied groups

Table 6

WAIST CIRCUMFERENCE AND BODY MASS INDEX FOR THE 5 LOTS

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Waist circumference evaluation (cm)	107.53±16.9 10 102.0 [93.2, 122.5]	111.67±15.379 106.2 [98.2, 126.0]	111.71±15.544 109.5 [99.0, 126.0]	95.08±19.039 93.5 [80.5, 108.7]	102.90±12.371 101.0 [93.7, 112.5]	0.001 (Kruskal Wallis)
Body Mass Index Assessment	30.89±4.349 30.0 [28.0, 32.7]	30.00±4.859 28.0 [26.0, 33.0]	29.43±5.339 27.5 [25.0, 32.0]	26.47±4.677 26.0 [23.0, 29.0]	28.10±3.172 28.0 [25.7, 30.0]	0.001 (Kruskal Wallis)

Table 7

REPRESENTATION OF ELEVATED SYSTOLIC AND DIASTOLIC BLOOD PRESSURE

	Lot 1 (N = 29)	Lot 2 (N = 32)	Lot 3 (N = 26)	Lot 4 (N = 13)	Lot 5 (N = 50)	Test - Comparison of the 5 lots
Rating Systolic blood pressure (mmHg)	151.06±11.910 148.0 [140.0, 157.0]	150.96±11.292 148.0 [143.0, 155.7]	148.73±9.958 148.0 [139.7, 155.0]	152.46±11.442 150.0 [144.0, 160.0]	147.96±8.436 148.0 [140.0, 155.0]	0.470 (ANOVA)
Rating diastolic blood pressure (mmHg)	88.62±4.345 87.0 [86.0, 89.5]	88.65±4.178 87.0 [86.0, 89.0]	87.61±3.441 87.0 [85.7, 89.0]	89.00±3.958 88.0 [86.5, 91.0]	87.38±2.609 87.0 [86.0, 89.0]	0.332 (ANOVA)

diagnosis, was 201 mg/dL, this patient having both severe psoriasis and metabolic syndrome. The lowest glycemic value in the patient without diabetes was 60 mg/dL, the patient with moderate psoriasis and the metabolic syndrome. Concerning glycosylated hemoglobin, there were significant differences between lot 3 and lot 5 (p value = 0.017). Mean glycosylated hemoglobin is slightly lower in lot 5 compared to other batches, with a standard deviation of 5.97 ± 0.75. There were no statistically significant differences in HOMA-IR mean values between the five lots.

The HDL cholesterol value has significant differences between lot 1 and group 5 (p value = 0.01), lot 1 and lot 4 (p value = 0.001), lot 2 and lot 5 (p value = 0.009), lot 2 and lot 4 (p value = 0.001) , lot 3 and lot 4 (p value = 0.013). The lowest mean HDL cholesterol values were found in patients with severe psoriasis and metabolic syndrome, with an average of 36.58±8.244, compared to the highest average in patients with psoriasis without metabolic syndrome, with an average of 49.50±11.077. The presence of metabolic syndrome influences the HDL cholesterol average, which is lower in those with metabolic syndrome, and also the average decreases in close relation to with the increase in psoriasis severity. We found significant differences between batches and triglyceride value, batch 2 and batch 5 (p value = 0.001), batch 4 and batch 5 (p value = 0.001). The highest triglycerides were found in the association of severe psoriasis with metabolic syndrome (163.44±46.173), followed by metabolic syndrome without psoriasis (160.79±23.594), and the lowest was found in patients with moderate psoriasis and metabolic syndrome (141.63±21.360).

There was no case of increased serum calcium in patients with severe psoriasis and metabolic syndrome, 44.8% of which had serum calcium in normal range and 55.2% had low serum calcium. In group 5 of the 122 study participants, 1 patient had elevated serum calcium (0.8%), most (70.5%) had normal values and 35 (28.7%) had low values. Lots 2, 3 and 4 predominate in normal and low serum calcium levels.

The distribution of biomarkers of systemic inflammation

Significant differences across different fibrinogen groups were found between batches (p = 0.001), namely:

-Lot 5 has the highest percentage of normal fibrinogen. Lots 1, 2 and 3 have no normal value for fibrinogen.

Table 8

DISTRIBUTION OF LABORATORY TESTS PERFORMED ON THE 5 LOTS

Laboratory Exam	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Glucose (mg/dL)	120.65±34.586 115.0 [92.0, 140.0]	100.77±28.835 92.0 [79.5, 121.5]	94.31±24.819 90.0 [76.2, 99.0]	106.10±27.476 98.0 [87.0, 128.0]	105.96±21.408 104.0 [88.0, 122.0]	0.003094 (Kruskal Wallis)
Hemoglobin glycosylated	6.42±0.909 6.0 [5.7, 7.0]	6.44±0.629 6.4 [5.8, 6.8]	6.67±0.659 6.7 [6.3, 7.0]	6.16±0.601 6.2 [5.7, 6.6]	5.97±0.758 5.9 [5.4, 6.4]	0.002 (ANOVA)
HOMA-IR	3.05±1.350 2.5 [2.0, 4.8]	3.04±1.342 2.5 [2.0, 4.2]	3.02±1.348 2.3 [2.0, 4.0]	2.64±1.096 2.2 [1.9, 3.1]	2.64±1.500 2.0 [1.6, 3.4]	0.23 (Kruskal Wallis)
HDL cholesterol (mg/dL)	36.58±8.244 37.0 [29.5, 43.5]	38.34±12.001 36.0 [31.2, 43.5]	41.50±12.791 39.5 [31.2, 49.0]	49.50±11.077 49.0 [41.0, 59.0]	46.02±13.671 44.0 [36.0, 58.0]	0.001 (Kruskal Wallis)
Triglycerides (mg/dL)	163.44±46.173 155.0 [134.5, 190.0]	141.63±21.360 140.0 [126.2, 161.2]	151.78±21.982 151.0 [136.2, 169.2]	143.91±20.770 139.0 [132.0, 149.0]	160.79±23.594 157.5 [140.0, 179.2]	0.04 (Kruskal Wallis)
Serum calcium (mg/dL)						0.00005 (Likelihood Ratio)
CA1*	16/29 (55.2%)	19/44 (43.2%)	17/32 (53.1%)	50/103 (48.5%)	35/122 (28.7%)	
CA2*	13/29 (44.8%)	20/44 (45.5%)	14/32 (43.8%) 1/32 (3.1%)	44/103 (42.7%)	86/122 (70.5%)	
CA3*	0/29 (0.0%)	5/44 (11.4%)		9/103 (8.7%)	1/122 (0.8%)	
Fibrinogen (mg/dL)						0.001 (Pearson Chi-Square)
FB1*	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	13/103 (12.6%)	70/121 (57.9%)	
FB2*	9/29 (31.0%)	18/44 (40.9%)	19/32 (59.4%)	50/103 (48.5%)	22/121 (18.2%)	
FB3*	20/29 (69.0%)	26/44 (59.1%)	13/32 (40.6%)	40/103 (38.8%)	29/121 (24.0%)	
ESR increased (mm/h)	19/29 (65.5%)	23/44 (52.3%)	13/32 (40.6%)	27/103 (26.2%)	39/122 (32.0%)	0.0002 (Pearson Chi-Square)
Protein C reactive (mg/L)						0.001 (Pearson Chi-Square)
C1*	0/29 (0.0%)	0/44 (0.0%)	0/32 (0.0%)	0/103 (11.7%)	64/121 (52.9%	
C2*	0/29 (0.0%)	6/44 (13.6%)	9/32 (28.1%) 9/32 (28.1%)	22/103 (21.4%)	30/121 (24.8%)	
C3*	8/29 (27.6%)	12/44 (27.3%)	14/32 (43.8%)	40/103 (38.8%)	27/121 (22.3%)	
C4*	21/29 (72.4%)	26/44 (59.1%)		41/103 (39.8%)	0/121 (0.0%)	

**CA1 = low, CA2 = normal, CA3 = high; FB1 = normal, FB2 = moderately high, FB3 = increased risk of coronary and cerebrovascular disease; C1 = low cardiovascular risk, C2 = moderate cardiovascular risk, C3 = increased cardiovascular risk, C4 = non cardiovascular diseases - inflammatory processes.*

Table 9
VITAMIN D VALUES AND SUN EXPOSURE ACCORDING TO SEASON

	Lot 1 (N=29)	Lot 2 (N = 44)	Lot 3 (N = 32)	Lot 4 (N = 103)	Lot 5 (N = 122)	Test - Comparison of the 5 lots
Vitamin D (ng/mL)	16.34±7.227 15.0 [11.0, 22.0]	26.75±19.539 23.0 [11.5, 34.7]	31.15±20.307 26.0 [14.2, 46.2]	31.35±19.707 26.0 [16.0, 47.0]	43.72±23.561 43.5 [22.0, 61.0]	0.0008 (Kruskal Wallis)
Exposure to the sun **E1*** **E2*** **E3***	5/29 (17.2%) 4/29 (13.8%) 20/29 (69.0%)	1/44 (2.3%) 17/44 (38.6%) 26/44 (59.1%)	6/32 (18.8%) 14/32 (43.8%) 12/32 (37.5%)	16/103 (15.5%) 27/103 (26.2%) 60/103 (58.3%)	35/122 (28.7%) 43/122 (35.2%) 44/122 (36.1%)	0.0002 (Pearson Chi-Square)

*E1 = intensive, E2 = occasional, E3 = minimal.

-Lot 3 has the highest percentage with moderately high values.

-Lot 1 has the highest percentage with increased risk of coronary and cerebrovascular disease.

The higher ESR value occurs more predominantly in lot 1 (65.5%), lot 2 (52.3%) and group 3 (40.6%) than lot 4 (26.2%) and lot 5 (32.0%). Increases in ESR are seen in patients with psoriasis and metabolic syndrome, with an increasing trend as the psoriasis increases. There are statistically significant differences in the presence of ESR increased among lots (= 0.001), namely: Lot 1 and Lot 4, Lot 1 and Lot 5, Lot 2 and Lot 4.

Reactive C protein values are consistent with the presence of the inflammatory process in psoriasis. In patients with severe psoriasis and metabolic syndrome, the C-reactive protein with a value greater than 10 mg/dL occurs in 72.4% and decreases proportionally with the decrease in the severity of psoriasis and the presence/ absence of metabolic syndrome. In patients with metabolic syndrome without psoriasis, we found no higher than 10 mg/dL .

Sun exposure is generally low, predominantly in patients with psoriasis. Sun exposure is even lower as the severity of psoriasis increases.

With regard to serum vitamin D, significant differences were found between lot 1 and group 3 ($p = 0.036$), lot 1 and lot 4 ($p = 0.002$), lot 1 and lot 5 ($p = 0.001$), lot 2 and lot 5 ($p = 0.001$), batch 4 and batch 5 ($p = 0.001$) (table 9). Low vitamin D values were found in the severe psoriasis and metabolic syndrome groups, with an average of 16.34±7.227 ng/mL. The highest values were in lot 5 (metabolic syndrome without psoriasis), with a mean of 43.72±23.56 ng/mL. We correlated the initial values of vitamin D in patients with psoriasis, compared with those with metabolic syndrome. We can assert that psoriasis has a negative correlation with the vitamin D value ($p <0.001$), the higher the intensity of psoriasis, the lower the vitamin D value, while between the MS and the vitamin D value we have not found a correlation ($p = 0.01$).

Description of initial values of vitamin D:

- Severe psoriasis (regardless of the presence or absence of metabolic syndrome) - mean value 16.34±7.22 ng/mL, 95% [13.60, 19.09] with a minimum of 7 ng/mL and a maximum of 33 ng/mL.

- Moderate psoriasis (regardless of the presence or absence of metabolic syndrome) - mean value of 26.75±19.53 ng/mL, 95% [20.81, 32.69] with a minimum of 6 ng/mL and a maximum of 80 ng/mL.

- Mild psoriasis (regardless of the presence or absence of metabolic syndrome) - mean value of 31.16±20.30 ng/mL, 95% [23,83, 38,48] with a minimum of 8 ng/mL and a maximum of 83 ng/mL.

- Total psoriasis without metabolic syndrome - mean value 31.36±19.07 ng/mL, 95% [27.51, 47.95] with a minimum of 6 ng/mL and a maximum of 90 ng/mL.

- Metabolic syndrome without psoriasis - mean value 43.73±23.56 ng/mL, 95% [39.51, 38.48] with a minimum of 7 ng/mL and a maximum of 92 ng/mL.

- Psoriasis with metabolic syndrome - mean value 25.22±18.12 ng/mL, 95% [21.71, 28.73] with a minimum of 6 ng/mL and a maximum of 83 ng/mL.

Percentage distribution on vitamin D levels (deficiency, insufficiency and normal) is highlighted in figure 5. The frequency of cases of vitamin D deficiency is significantly higher in the case of psoriasis association with metabolic syndrome, metabolic syndrome $p <0.001$ and psoriasis $p = 0.003$. Between psoriasis and metabolic syndrome we also have a statistically significant significance $p <0.001$.

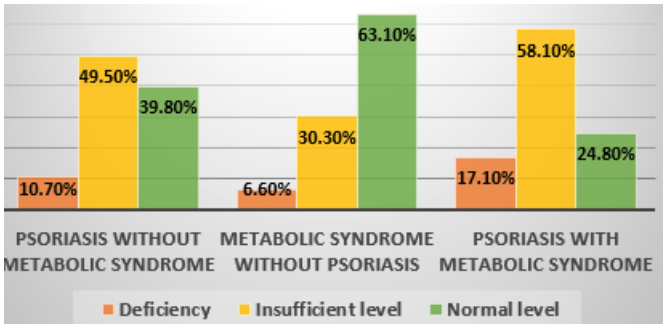


Fig. 5. Distribution of vitamin D levels on lots.

Distribution of metabolic syndrome components in patients with psoriasis in the absence of metabolic syndrome diagnosis

The predictive factors of the metabolic syndrome are even its components. We tracked the presence of metabolic syndrome components in patients with psoriasis that did not meet the criteria for the diagnosis of metabolic syndrome. We studied 103 patients with psoriasis who did not meet the requirements for the diagnosis of metabolic syndrome. However, we have noticed the presence of metabolic syndrome components in these patients, either independently or as a component.

The female gender was dominant, of the 103 patients we had 64 women and 39 men. In the first phase, we followed the presence of each diagnosis criterion of the metabolic syndrome, by gender.

The distribution of the components of metabolic syndrome is: in women, the increased waist circumference, followed by HDL cholesterol and hyperglycemia, while men show increased waist circumference and hyperglycemia.

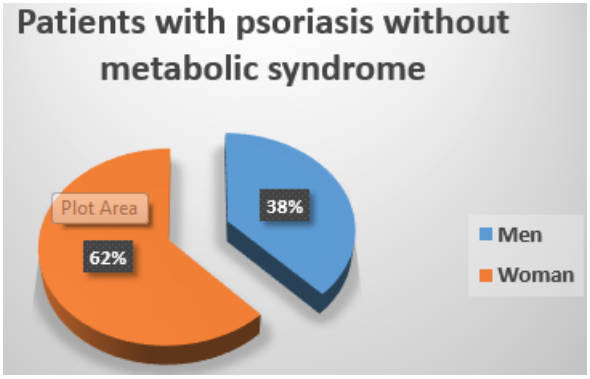


Fig. 6. Gender distribution of patients with psoriasis without metabolic syndrome

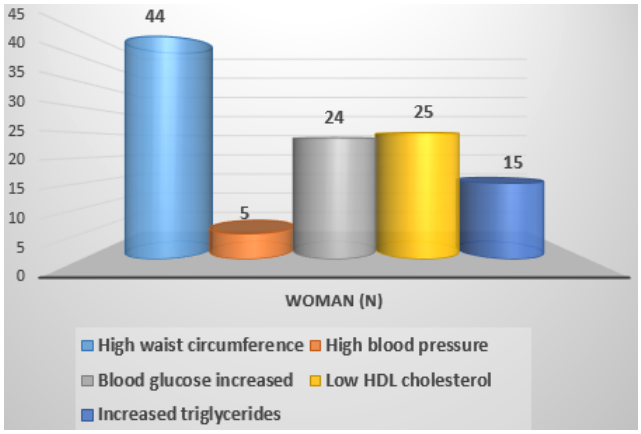


Fig. 7. Presence of metabolic syndrome components in woman

Psoriasis correlation - metabolic syndroma

In order to analyze and verify the data obtained from the study, we used statistical tests to determine the correlation between psoriasis and the metabolic syndrome that best correspond to the criteria imposed by the data obtained: Pearson Chi-square test, cross-tabulation for category data, Phi, Cramer, Fisher Exact Test. The value of the Pearson Chi-Square test of $p < 0.001$ is well below the value of 0.05 representing the acceptance threshold (alpha = 0.05 critical value). Also, the values obtained from the Phi and Cramer tests show that the degree of correlation is high and the acceptance level is very good, under the threshold of 0.05 (practically very small, approx. 0.001).

By comparing the prevalence of metabolic syndrome among the patients studied with the metabolic syndrome prevalence of 30% among the general population, we found a strong statistical correlation. The higher incidence of metabolic syndrome in patients with psoriasis is evidenced by the Pearson Chi-Square test, where $p < 0.001$. With the increase in psoriasis severity, the risk of developing metabolic syndrome increases. The presence of metabolic syndrome is greater in those with severe psoriasis and moderate psoriasis versus those with mild psoriasis.

Regarding the duration of the disease (years after the diagnosis of psoriasis), we compared the values between the four groups. We used the Kruskal-Wallis test, the values in each group being not normally distributed. Significant differences between Lot 1 and Lot 4 (p value = 0.001), Lot 2 and Lot 4 (p value = 0.001), Lot 3 and Lot 4 (p value = 0.001) were obtained.

One can observe the association of metabolic syndrome with the duration of psoriasis. In the first 3 lots in which the metabolic syndrome is present, the duration of psoriasis is

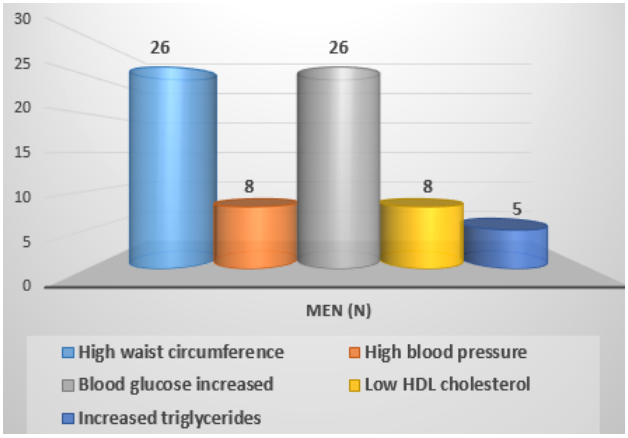


Fig. 8. Presence of metabolic syndrome components in men

higher (mean ± DS is in lot 1 = 8.86±2.38, lot 2 = 8.34±4.38, group 3 = 8.87±3.82) versus group 4 where metabolic syndrome is not present (standard deviation group 4 = 5.36±2.61).

Conclusions

The association of metabolic syndrome in patients with psoriasis is evident. The more severe psoriasis, the more likely it is to develop metabolic syndrome. Also, metabolic syndrome is associated with longer duration of psoriatic disease. Differential approach of patients with psoriasis is required due to the increased risk of developing metabolic syndrome.

References

1. ARMSTRONG, A.W., HARSKAMP, C.T., ARMSTRONG, E.J. J Am Acad Dermatol., **68**, no. 4, 2013, p. 654–62.
2. LANGAN, S.M., SEMINARA, N.M., SHIN, D.B., TROXEL, A.B., KIMMEL, S.E., MEHTA, N.N., MARGOLIS, D.J., GELFAND, J.M. J Invest Dermatol., **132**, no. 3 Pt 1, 2012, p. 556–62.
3. ROMAN, G., GRAMMA, R., ENACHE, A., PARVU, A., MOISA, S.M., DUMITRAS, S., IOAN, B. Med Health Care and Philos, **16**, no. 4, 2013, p. 843-856.
4. KOTHIWALA, S.K., KHANNA, N., TANDON, N., NAIK, N., SHARMA, V.K., SHARMA, S., SREENIVAS, V. Indian J Dermatol Venereol Leprol, **82**, no. 5, 2016, p. 510-518.
5. KAPLAN, J.M. Vasc Health Risc Manag., **4**, no. 6, 2008, p. 1229–1235.
6. RADULESCU, C., MIRICESCU, D., CALENIC, B., RADULESCU, R., STANESCU, I., CALENIC, A., TOTAN, A., VIRGOLICI, B., BALAN, D., GREABU, M., Mat. Plast, **55**, no. 3, 2018, p. 291-294.
7. NISA, N., QAZI, M.A. Indian J Dermatol Venereol Leprol., **76**, no. 6, 2010, p. 662–665.
8. IORGA, M., DASCALU, N, SOPONARU, C., IOAN, B. The Medical-Surgical Journal, **119**, no. 4, 2015, p. 1128-1133.
9. TOTAN, A., BALAN, D.G., MIRICESCU, D., RADULESCU, R., STANESCU, I.I., VIRGOLICI, B., MOHORA, M., GREABU, M., Rev. Chim. (Bucharest), **70**, no.1, 2019, p. 78-83.
10. HAMBLY, R., KIRBY, B. Arch Dermatol Res., **209**, no. 7, 2017, p. 499-517.
11. MIRICESCU, D., STANESCU, I., PERLEA, P., CALENIC, B., RADULESCU, R., TOTAN, A., VIRGOLICI, B., SABLIOV, C., GREABU, M., Mat. Plast., **54**, no. 2, 2017, p. 249-252.
12. DUFFIN, K.C., PAPP, K.A., BAGEL, J., LEVI, E., CHEN, R., GOTTLIEB, A.B. J Drugs Dermatol., **16**, no. 2, 2017, p. 147–153.
13. RODRIGUEZ-ORTIZ, D., REYES-PEREZ, A., LEON, P., SANCHEZ, H., MOSTI, M., AGUILAR-SALINAS, C.A., VELAZQUEZ-FERNANDEZ, D., HERRERA, M.F. Surgery, **159**, no. 4, 2016, p. 1121-1128.

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