Psoriasis is a chronic inflammatory cutaneous disorder, affecting both sexes, with possible onset at any age; psoriasis is only recently being recognized as a systemic disease, associated with a series of important comorbidities (cardiovascular, metabolic, psychiatric etc). Metabolic syndrome represents the association of abdominal obesity, dyslipidemia, hypertension and insulin resistance. There is a strong risk of developing metabolic syndrome with all its individual components among psoriatic patients. These two separated entities appear to be linked through a common pathway of inflammation; however, there are controversial data concerning the severity and duration of the psoriatic disease and the onset of metabolic syndrome. Correct psoriasis management should include extensive screening for the diagnosis of the MS even in younger patients, and they also should be encouraged towards a healthier life-style, and by this, reducing the associated cardiovascular risks. Our study sought to describe the epidemiology and clinical features of a population of psoriatic patients from an age-related point of view in relation to metabolic syndrome and to review the available literature.
Psoriazisul este o afecțiune cutanată inflamatorie cronică, ce afectează ambele sexe și cu posibil debut la orice vârstă; psoriazisul a fost clasificat recent ca făcând parte din grupul bolilor cu afectare sistemică, acestuia atribuindu-se o serie de comorbidități (cardiovasculare, metabolic, psihiatric, etc). Sindromul metabolic reprezintă asocierea dintre obezitate abdominală, dislipidemie, hipertensiune și rezistența insulinică. Există un risc foarte mare de a dezvolta sindrom metabolic, împreuna cu toate componentele sale individuale, printre pacienții diagnosticați cu psoriazis. Aceste două afecțiuni par a fi interconectate printr-o cale comună și anume cea a inflamației; cu toate acestea, datele privind asocierea dintre severitatea respectiv durata psoriazisului și instalarea sindromului metabolic, sunt controversate în prezent. Managementul corect al psoriazisului ar trebui să includă un screening extensiv pentru diagnosticarea sindromului metabolic, inclusiv la pacienții tineri și de asemenea aceștia ar trebui îndrumați să adopte un stil de viață cât mai sănătos, reducând astfel și riscurile cardiovasculare asociate. Studiul nostru a căutat să evidențieze și să descrie epidemiologia și aspectele clinice într-o populație de pacienți diagnosticați cu psoriazis, luând în considerare persectiva corelației dintre vârsta și instalarea sindromului metabolic și de asemenea să revizuască datele disponibile în literatura de specialitate legate de acest subiect.

Background
Psoriasis is a chronic, genetic, multifactorial disease, with an incomplete understanding of its complex pathogenesis, which nowadays affects 1-3% of worldwide population.

In the last few years, numerous studies and researches were conducted in order to demonstrate the association between psoriasis, an inflammatory chronic skin disease and metabolic syndrome (MS).

It has been highlighted that there is actually a high prevalence of MS, along with all of its composing elements, including arterial hypertension, central type obesity, impaired glucose tolerance, lipid disorder, among patients diagnosed with psoriasis; in the end this will lead to an increase regarding cardiovascular risk (atherosclerosis, stroke and myocardial infarction) and nonetheless the risk of mortality of these patients (life expectancy is decreased by 5 years among these patients)(4).

Regardless of the poor understanding of the true correlation between the two etiopathogenic mechanisms of MS and psoriasis, the latter is considered to be an important independent risk factor for the onset of former, the common bridge between the two being represented by inflammation, that leads to the production/secretion of pro-inflammatory cytokines (e.g. TNFα, IL-6, etc.)

Also a various number of factors were found that tend to play a significant part in completing the high risk cardiovascular profile; most frequently: nicotine dependence, alcohol consumption, lack of physical exercises, obesity, that is correlated with unhealthy food habits, psycho-emotional stress(2).

It has been shown that although there is no direct interdependence between patient sex, age, clinical type of psoriasis and the prevalence of MS, the majority of psoriatic patients with MS are generally older and have a longer disease duration compared with psoriatic patients without MS(3).

Taking into consideration the impact of cardiovascular diseases on life expectancy, a multidisciplinary long term management of the psoriatic patients should be necessary; the physician must not limit treatment goals to only alleviate skin and articular manifestations, but also has to look deeper into the health status of his patient screening for potential metabolic and cardiovascular abnormal changes. Psoriatic patients who are suspects of developing diabetes mellitus type II, should be guided to a nutritional advisor for regular check-ups, and efficient management of the underlying disease; also other specific tests for detecting heart activity, arterial hypertension and alterations of the lipid metabolism are necessary(4). Equally
important to the above is the psychological counseling of these patients, being aware of the fact that chronic psoriasis is associated with a multitude of psychiatric disturbances (lowered self-esteem, sexual dysfunction, anxiety, depression and even suicidal ideation) that could hasten the appearance of MS (3).

The aims of our study were to describe the epidemiology and clinical features of a population of psoriatic patients from an age-related point of view in relation to metabolic syndrome and to review the available literature.

**Material and methods**

We conducted a retrospective study with pooled data from a population of 186 psoriatic patients who attended “Elias” University Emergency Hospital. Metabolic syndrome was defined in accordance with the 2006 International Diabetes Federation (IDF) criteria and in agreement with European epidemiology as follows: waist circumference ≥ 94 cm for men and ≥ 80 cm for women plus any other two of the following: fasting plasma glucose >100 mg/dl or previously diagnosed type 2 diabetes mellitus, HDL cholesterol <40 mg/dl for men and <50 mg/dl for women, raised triglycerides >150 mg/dl or specific hypolipidemic treatment, raised blood pressure >130/85 mmHg or treatment for previously diagnosed hypertension. The subsequent variables from patients included in this study were evaluated: sex, age, IDF criteria, age at psoriasis onset, disease duration. We performed a descriptive analysis of the collected data with Microsoft Excel 2010 software package, evaluating frequency values with results expressed as percentages, mean values and standard deviations. The comparison of the subgroups with/without metabolic syndrome was performed via Student’s t-test. Correlations between variables were interpreted via the Pearson correlation coefficient. Statistical significance was set at 5%, with confidence intervals at 95%.

**Results**

We evaluated 186 patients, 92 men and 94 women, out of which 91 patients met the diagnostic criteria for metabolic syndrome, with an almost equal male to female ratio (44 men: 47 women). Subjects were divided in two subgroups according to age at onset of psoriasis, with patients who reported age at onset to be under 40 years being included in the early onset subgroup, with patients without MS (p<0.0001), of 49 ± 15.14 years. When looking at age distribution among the MS group, 39.5% of patients belonged to the 60-70 years age group, followed by 24.1% of patients in the 50-60 years age group, with the mean age in the early onset subgroup of 53.45 ± 9.78 years and in the late onset subgroup of 64.66 ± 8.65 years. When regarding the age at onset of psoriasis, approximately two thirds of the patients (62.6%) reported that they first noticed psoriatic lesions after 40 years of age, whereas the rest fell into early onset psoriasis subgroup. In the early onset subgroup the mean age at onset was 28, with 8 (23.5%) patients reporting disease onset before the age of 18 ± 9.78 years. The minimum age at onset was reported to be 10 years. In the late onset group the average age was 55.24 ± 8.65 years, with a maximum age of 77 years.

Regarding the clinical form of psoriasis, 81.89% presented with plaque psoriasis, followed by palmo-plantar psoriasis (3.3%), guttate psoriasis (3.3%) and pustular psoriasis (1.1%). There was no significant difference in clinical form distribution in either subgroup concerning sex and age at onset. In terms of treatment choice, 43% of the patients in the late onset subgroup only needed topical treatment and phototherapy; the rest had clinical forms that warranted systemic treatment such as Methotrexate (42%), biological treatment (19.29%) or combination therapy (12.28%). The early onset subgroup had a different distribution regarding treatment choice. The vast majority of patients needed a systemic therapeutic approach, with either Methotrexate (76.47%), biological treatment (44.11%) or combination therapy (41.1%). Only 14.7% of patients had a clinical form where topical treatment and phototherapy were regarded as sufficient.

The mean disease duration in the MS group was 15.76 ± 12.03 years, somewhat higher than in patients without MS, 10.93 ± 8.15 years (p<0.005). Early age at onset had a strong inverse correlation with longer disease duration in the MS group (r = -0.7). Concerning the IDF criteria, early onset psoriatic patients, outside of having a waist circumference over the diagnostic limit, were in equal proportions hypertensive and/or dyslipidemic, or receiving specific treatment (61.7%). Similarly, in the late onset subgroup, the same tendency was maintained with a slight tendency towards a higher frequency of dyslipidemia.

**Discussions**

Psoriasis is chronic inflammatory skin disease that affects up to 3% of world population (3). Concrete circumstances of psoriasis onset are...
not entirely clear, but many environmental factors are presumably implicated in hastening and aggravating the disease, such as: streptococcal infection, cutaneous trauma, alcohol consumption, smoking and psychological stress. Plaque-type psoriasis is the most common clinical type and can affect patients of any age, from infancy through childhood and adulthood, with a slight tendency toward female predominance. Disease onset has been reported to peak between 15-30 years and 50-60 years. Accurate determination of age at onset can present as problematic, since most studies rely on subjective patient recall of disease onset. Furthermore, childhood onset psoriasis can resemble nummular eczema, and therefore patients may receive an erroneous diagnosis and treatment. Henseler and Christophers examined 2147 patients with psoriasis and observed a bimodal age at onset: type I that begins before the age of 40 years (deemed early onset psoriasis) and type II beginning after the age of 40 years (deemed late onset psoriasis). Several studies have reported a higher prevalence of metabolic syndrome amongst patients with psoriasis, with percentages varying between 4.3% and 40% in different studies, significantly higher than controls. The difference in prevalence resides probably in the studied population, MS definition criteria or psoriasis severity that has been studied in relation to MS only in a few studies. When looking at age distribution, most patients belonged to the 60-70 years age group. Concerning psoriasis onset, two thirds of the patients fell into the late onset subgroup. The two peaks of age could not be accurately determined because the mean age in the MS group was 60 years, which according to Henseler and Christophers it the expected age for type II psoriasis.

Similar to other studies, plaque psoriasis was the most prevalent clinical form in both subgroups. We only observed that approximately 3.3% of patients in both subgroups were diagnosed with guttate psoriasis. Some studies

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Metabolic syndrome patients (N=91)</th>
<th>Subjects with early onset psoriasis and MS (n=32) Mean ±SD Percentage out of total</th>
<th>Subjects with late onset psoriasis and MS (n=57) Mean ±SD Percentage out of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ratio (F:M)</td>
<td>47.44</td>
<td>17.15</td>
<td>30.27</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.24 ± 11.71 (p&lt;0.0001)</td>
<td>28±9.28</td>
<td>64.66±8.65</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>N/A</td>
<td>53.45±12.75</td>
<td>60±11.43</td>
</tr>
<tr>
<td>Clinical form</td>
<td>Plaque psoriasis 82% Palmo-plantar psoriasis 3.3% Guttate psoriasis 3% Pustular psoriasis 1.1%</td>
<td>Plaque psoriasis 81% Palmo-plantar psoriasis 3.3% Guttate psoriasis 3% Pustular psoriasis 1.1%</td>
<td>Plaque psoriasis 83% Palmo-plantar psoriasis 3.3% Guttate psoriasis 3% Pustular psoriasis 1.1%</td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td>Hypertension</td>
<td>N/A</td>
<td>65.62%</td>
</tr>
<tr>
<td></td>
<td>Dyslipidemia</td>
<td>N/A</td>
<td>65.62%</td>
</tr>
<tr>
<td></td>
<td>Type 2 diabetes mellitus</td>
<td>N/A</td>
<td>37.5%</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>15.76 ±12.03 (p&lt;0.005)</td>
<td>26.9±13.4</td>
<td>9.07±8.65</td>
</tr>
<tr>
<td>Treatment</td>
<td>Methotrexate</td>
<td>N/A</td>
<td>76.47%</td>
</tr>
<tr>
<td></td>
<td>Biologic treatment</td>
<td>N/A</td>
<td>44.11%</td>
</tr>
<tr>
<td></td>
<td>Topical treatment</td>
<td>N/A</td>
<td>14.7%</td>
</tr>
<tr>
<td></td>
<td>Combination</td>
<td>N/A</td>
<td>41.1%</td>
</tr>
</tbody>
</table>

Table 1. Epidemiology of clinical features and treatment of early and late onset psoriatic patients
show that it may be more frequent in childhood onset of psoriasis, and furthermore that the clinical type of psoriasis seen in childhood remains unchanged in adulthood, although it was assumed that guttate psoriasis either resolves spontaneously or turns into plaque psoriasis. Disease severity could not be assessed due to the lack of data. However, one study shows that there is no difference in severity in adult psoriatic patients between adult onset and childhood onset psoriasis.

We found a strong inverse correlation between disease duration and early age at onset of psoriasis. Unfortunately, due to a paucity of data regarding the exact moment when a MS diagnosis was made or psoriasis severity until an MS diagnosis, we cannot accurately formulate a correlation between psoriasis duration and MS onset. There are controversial data concerning the severity and duration of the disease and MS. Some studies suggest that there is no relationship between the two but state that there may be a correlation to a greater duration psoriasis or young age at onset. The prevalence of cardiovascular risk factors that build up MS was, as expected, higher in older patients. Interestingly, both subgroups expressed the same prevalence of hypertension and dyslipidemia, over diabetes, even though early onset had a slightly longer disease duration. Despite the fact that we cannot state with certainty when an MS diagnosis was formulated for the subjects in this study, some authors suggest that the prevalence of MS is significantly higher in psoriatic patients after the age of 40, rather than at a younger age and it directly correlates with disease duration.

It is difficult to say whether it is psoriasis that comes first or metabolic syndrome, but the fact that there is no clear correlation between psoriasis severity and metabolic syndrome, there is a probability that obesity might favor psoriasis. In support of this theory, de Jager et. al suggest that childhood onset psoriasis is not a risk factor for high body mass index in adult life. Although metabolic syndrome is the prerequisite of old age, one study shows that metabolic syndrome was more frequent in a pediatric psoriatic population than in controls, even when adjusting to body mass index, and this may therefore warrant for primary cardiovascular prevention in children. The relationship between pediatric psoriasis, obesity and metabolic syndrome is less well described, but may have important implications on maintaining a healthy weight, monitoring of cardiovascular comorbidities and treatment recommendations, especially in patients with a more severe clinical form. The presence of psoriasis in childhood and adolescence may indicate higher cardiovascular risk in adulthood. Further studies are needed in order to define this relationship, to better anticipate cardiovascular risk and develop adequate preventive measures and screening methods.

Regarding the treatment, both subgroups required either systemic or topical treatment, as well as a combination of the two. We did not find
any significant difference in treatment choice in either group, with the exception of topical treatment use as sole therapy. Considering the fact that early onset psoriasis is known to be more therapy-resistant with a more aggressive clinical evolution, when compared to late onset psoriasis, it is not surprising that in the late onset group, approximately 43% of patients had a clinical form that only required topical therapy. Ours being a retrospective study and patients being already on different forms of treatment suggests that metabolic syndrome components could be modified, and therefore the number of early onset patients with MS might be underestimated. Studies show that both TNF alpha antagonist and Methotrexate have shown beneficial effects on cardiovascular risk factors \(^{14,15}\).

A series of studies has demonstrated \(^{16}\) the indisputable correlation between the presence of chronic psoriasis and the important reduction in health related quality of life (QOL). Unfortunately, our study was a retrospective one and the impact of this chronic disease on the quality of life of the included patients couldn't be evaluated through specific questionnaires.

However, the psychological impact of psoriasis should always be taken into consideration independent of the age of these patients. Psychiatric comorbidities like anxiety and especially depression are very frequent in these patients, and they are contributing to the low quality of life (most patients have a low self-esteem, sexual dysfunction, suicidal ideation, sometimes being difficult for them to find a life partner). Moreover it appears to be an association between psoriasis and some lifestyle choices that can have a negative impact on patients' general health, which can contribute directly to both medical and psychological comorbidities (cigarette smoking, alcohol abuse, excessive fast-food consumption, etc). Beside the necessary treatment of the psoriatic disease, the physician should be very attentive in evaluating the mental status of each patient at every consultation, and should seek psychiatric/psychological assistance for those who are in need of it \(^{16}\).

To sum up, we have attempted to describe the epidemiology and clinical aspects of a population of psoriatic patients from an age-related point of view in relation with metabolic syndrome. We found that metabolic syndrome has a high prevalence among psoriatic patients, with a tendency towards women. However, metabolic syndrome was more prevalent in the late onset group, predictably because of old age. Disease severity does not appear to influence metabolic syndrome onset, as does rather disease duration and younger age at psoriasis onset. Systemic therapies did not differ in the early and late onset subgroups. However topical therapy was observed in a high percentage in the late onset group, suggesting that late onset psoriasis has a less aggressive clinical form, in accordance to available literature. Hypertension and dyslipidemia were the most prevalent
cardiovascular risk factors in both subgroups, albeit early onset patients having a slightly longer disease duration. We suggest that patients with psoriasis should be screened and monitored for the diagnosis of metabolic syndrome, even at a younger age and that they should be encouraged to correct modifiable cardiovascular risk factors. More prospective studies need to be aimed to clarify the relationship between early onset psoriatic patients and metabolic syndrome and to elucidate the effects of systemic therapies on metabolic syndrome.

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