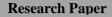
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Metabolic Syndrome and Clinical Characteristic Profiles among Psoriasis Patients In Nigeria

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ABSTRACT:- Several studies have suggested a relationship between psoriasis and metabolic syndrome. The common denominator in their pathogenesis being abdominal obesity which has been linked with insulin resistance and elaboration of various proinflammatorycytokines. This study seeks to evaluate the relationship between metabolic syndrome and its various characteristic profiles at early and late onset psoriasis in North-Central Nigeria. The study consisted of 32 psoriatic patients and 32 age and sex matched control group. A proforma was designed to capture their demographic data, Psoriasis Area Severity Index (PASI score), percentage Body Surface Area involvement and, clinical types of psoriasis. Patients' and controls' blood pressures, waist circumference, Body Mass Index were assessed. The prevalence of metabolic syndrome among psoriatic patients (Late onset) and controls were 21.9% and 3.1% respectively. Mean age for early onset and late onset psoriasis with metabolic syndrome and without metabolic syndrome was 29.2±6.7; 49.3± 7.8 and 60.7 ± 10.1 years respectively and it was statistically significant (p=0.011). The waist circumference among psoriatic patients was significantly higher (P=0.041) when compared with controls. There was a higher prevalence of metabolic syndrome in patients at late onset who were more predisposed to metabolic disorders such as hypertension, obesity and dyslipidemia.

Keywords: - Blood lipids, blood pressure, early onset of psoriasis, late onset of psoriasis, metabolic syndrome, obesity, PASI score.

I. INTRODUCTION

There is a plethoral of population based studies recently been published about metabolic syndrome and psoriasis that have shown an increased risk of metabolic syndrome in these patients, independent of severity (1-4). Metabolic syndrome (MS) is a constellation of risk factors including glucose intolerance, hypertension, central obesity and atherogenic dyslipidemia, which confers a higher risk of cardiovascular disease than the individual components (5). The pathophysiology of metabolic syndrome is attributed to insulin resistance while quite a number of systemic inflammatory markers like adiponectic, leptin, resistin, T-helper cell-1 (Th-1), T-helper cell 17 (Th-17) and tumour necrosis factor (TNF) have been observed to be elevated in metabolic syndrome (6-10).

Psoriasis is a chronic inflammatory disorder of the skin and in some patients the joints may be involved. Psoriasis may begin at any age, but it is most likely to appear between the ages of 15-30 years (11). Possession of certain Human Leucocyte Antigen (HLA), particularly HLA-CW6, is associated with a positive family history. This finding led Hensseler and Christophers to propose that two different forms of psoriasis exist: type I psoriasis (early onset) with age of onset before 40 years and HLA-associated and type II (late onset) with age of onset after 40years without HLA-association (11). The inflammatory process in psoriasis is evident histopathologically by the lymphocytic infiltration in the dermis and neutrophilic infiltration in the epidermis (12-14). There is an observable increase in inflammatory markers such Th-1, Th-17 cytokines, interleukin-6 and tumour necrosis factor (TNF) in psoriasis; the last 2 markers have been implicated to play a role in both psoriasis and metabolic syndrome (15).

An increased mortality from cardiovascular disease in patients with severe psoriasis has been documented and psoriasis confers an independent risk of myocardial infarction especially in young psoriatic patients (5,16). Major factors that may contribute to this untoward cardiovascular risk profile include cigarette smoking, obesity, physical activity, hyperhomocysternaemia and psychological stress, which have a higher prevalence among patients with psoriasis (5). Studies have shown a direct correlation between severity of psoriasis and the prevalence of obesity, dyslipidemia, hypertension and hyperhomocysternaemia in psoriatic patients (5, 18). This suggests the direct role skin involvement (degree of inflammation) in psoriasis play in determining these risk factors (19).

This study seeks to evaluate the relationship between metabolic syndrome and the two clinical characteristic profiles(early- and late onset) of psoriasis in Nigeria.

II. MATERIALS/METHODS

This was a hospital based retrospective study, which was conducted over a period of three (3) years (January 2013 to December 2015), at the Dermatology unit of the Department of Internal Medicine, University of Abuja Teaching Hospital, Gwagwalada-Abuja. The dermatology unit sees averagely ten (10) to sixteen (16) new dermatology patients weekly. During these years of review, a total of one thousand, six hundred and eighty new dermatology patients were seen and their case files retrieved. Those who were diagnosed clinically and supported histologically and treated for psoriasis either as outpatient or in patients were noted.

A proforma was designed to capture their demographic data; age; sex, occupational level, educational status and tribe. Others were; history of smoking, alcohol abuse, exposure to smoke from firewood, kerosene or generator.

Onset and duration of psoriasis, clinical type of psoriasis, associated medical conditions, percentage basal area of involvement (<10% is regarded localized and > 10% is regarded generalized), psoriasis area severity index (PASI) score. Also, blood pressure measurement of \geq 140/90mmHg was considered as abnormal. Similarly, Body mass index (BMI) (weight/ (height)² greater than 30 Kg/M²was abnormal; waist circumference (cm) landmark being posterior superior iliac spine round the abdomen for men \leq 102cm was normal and \leq 88cm was normal for women (24,37, 40).

Other values recorded with normal values in parenthesis include: fasting blood sugar (FBS) (3.2-6.1mmol/L or 60mg/dL-110mg/dL). Fasting serum lipid: Total Cholesterol (TC) (\leq 5.20mmol/L), High Density Lipoprotein (HDL) (>0.9mmol/L), Triglycerides (TG) (0.40-1.52mmol/L) and, Low Density Lipoprotein (LDL) (< 4.19 mmol/dL) (37, 40). Metabolic syndrome was diagnosed in the presence of any three or more of abnormalities in blood pressure (either of systolic or diastolic); obesity or waist circumference; either of TC, HDL, TG or LDL and or FBS.

The result of the HIV, hepatitis B surface antigen and hepatitis C antibody were all noted. A sex and age matched control group were retrieved from the hospital data for those who came for routine medical checkup and other skin dermatoses.

Data generated were transferred to SPSS 20.0 version and analyzed using descriptive analysis, frequencies, mean, t test, standard deviation, confidence intervals, odds ratio and logistic regression analysis. Mann Whitney U test was used for variables that were not normally distributed.

III. RESULTS

The study consisted of 32 cases and 32 controls that were both age and sex matched. The ratio of male to female and the mean age \pm standard Deviation (SD) in the cases and control was 1.3: 1; 1: 1.5 and 39.8 \pm 15.2 and 38.6 \pm 12.0 years respectively. The prevalence of psoriasis among the newly diagnosed dermatological patients over the last three years was (32/1680) that is 1.9%. A total of 18/32 cases had early onset psoriasis and they comprised nine (9) males and nine (9) females while 14/32 cases had late onset psoriasis and the comprised nine (9) males and five (5) females. Mean age \pm SD of onset of psoriasis was 39.8 \pm 15.2 years. Additionally, mean age \pm SD of onset of psoriasis for those of the early onset was 29.2 \pm 6.7 years while that of those with late onset psoriasis with and without metabolic syndrome was 49.3 \pm 7.8 and 60.7 \pm 10.1 years respectively and their mean differences were statistically significant (p=0.011). MS was observed only in patients with late onset psoriasis.

Table1: Characteristic profile of clinical/metabolic values of psoriatic patients and control						
	Subject (n=32					
	Mean ± SD	Mean ±SD	OR (95%CI)	P value		
Age in years (Mean ± SD)	39.8±15.2	38.6±12.0		0.727 ^a		
BMI (kg/M^2) (Mean ± SD)	26.5±6.5	26.0 ± 7.4		0.732 ^a		
SBP (mmHg) (Mean ± SD)	122.2±17.6	122.2±12.4		0.999 ^a		
DBP (mmHg) (Mean ± SD)	78.1 ± 12.0	77.5±10.5		0.829 ^a		
WC (cm) (Mean ± SD)	89.2±16.5	81.5±12.7		0.041 ^a *		
TC (mmol/L) (Mean ± SD)	4.5 ± 1.5	4.2 ± 1.2		0.308 ^a		
HDL (mmol/L) (Mean ± SD)	1.1±0.5	1.1±0.4		0.999 ^a		
TG (mmol/L) (Mean ± SD)	1.2 ± 0.8	1.2±0.8		0.999 ^a		
LDL (mmol/L) (Mean ± SD)	3.1±1.3	2.6±1.2		0.115 ^a		
FBS (mmol/L) (Mean ± SD)	4.7 ± 0.6	4.7±0.7		0.999 ^a		
Sex: Male/Female (n)	18/14	13/19	0.532 (0.197-1.436)	0.159 ^b		
BMI: Normal/Abnormal (n)	24/8	24/8	1.000 (0.323- 3.101)	0.613 ^b		
WC: Normal/Abnormal (n)	22/10	28/4	3.182 (0.897-11.524)	0.06 ^b		
BP status: Normal/Abnormal (n)	23/9	25/7	1.398 (0.478-4.363)	0.387 ^b		
TC: Normal/Abnormal (n)	24/8	27/5	1.800 (0.518-6.253)	0.268 ^b		
HDL: Normal/Abnormal (n)	17/15	24/8	2.647 (0.918-7.636)	0.058 ^b		
TG: Normal/Abnormal (n)	29/3	27/5	0.559 (0.122- 2.565)	0.354 ^b		
LDL: Normal/Abnormal (n)	24/8	28/4	2.533 (0.624-8.720)	0.169 ^b		
FBS: Normal/Abnormal (n)	28/4	30/2	2.143 (0.363-12.629)	0.336 ^b		

IV.	TABLES AND FIGURES	
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a- t test p value

b- Fisher's exact p Value

Table 1 indicates that the clinical and metabolic characteristics of the subjects with psoriasis and control without psoriasis were statistically similar with the exception of their waist circumference that showed a significant difference with p=0.041.. Odds ratio >1 shows that the clinical and metabolic characteristics were higher in subjects with psoriasis than those without psoriasis; whereas odds ratio equal to one or less than one shows equal risk or the control being more susceptible respectively.

psoriasis						
	I	MS		Fisher's		
	Absent	Present			exact	
	n (%)	n (%)	n (%)	OR (95%CI)	P value	
Subject	25 (78.1)	7 (21.9)	32 (100.0)			
Control	31 (96.9)	1 (3.1)	32 (100.0)	8.68 (1.001-75.307)	0.027*	
Time of onset						
Early onset (15-39years)	18 (72.0)	0 (0.0)	18 (56.2)			
Late onset (🗆 40years)	7 (28.0)	7 (100.0)	14 (43.8)			
Total	25 (100)	7 (100.0)	32 (100.0)	-	0.0001*	

Table 2: Prevalence of Metabolic syndrome in psoriatic and non-psoriatic patients and the onset of
ngoriogia

Table 2 shows that the prevalence of metabolic syndrome in the subject (21.9%) is significantly higher than that of the control (3.1%). The odds ratio of 8.68 (1.001-75.307) 95% confidence interval; indicates that the risk of having metabolic syndrome was higher in psoriatic patients. Metabolic syndrome was observed in late onset psoriasis only. This table shows there is a statistically significant association between the time of onset of psoriasis and metabolic syndrome (p=0.0001).

	<u>Metabolic S</u> Absent (n=25) Pr	P value			
Duration of eruption (in years) Mean ±SD	4.1±4.5	9.1 ±8.4	0.042* ^b		
· · · · ·					
BSA (%) (Mean ±SD)	21.9± 19.4	23.9±21.6	0.656 ^a		
PASI (Mean ±SD)	17.8 ± 16.6	27.1±29.1	0.420 ^a		
SBP (mmHg)	116.8±11.1	141.4±8.9	0.0001* ^b		
DBP (mmHg)	73.2±8.0	95.7±5.3	0.0001^{*b}		
BMI (kg/m ²)	24.8±4.7	32.3±8.9	$0.005^{*^{b}}$		
WC (cm)	84.1±12.6	107.4±16.9	0.0004^{*b}		
TC (Mean ±SD)	4.4 ±1.5	5.4±1.2	0.119 ^b		
HDL (Mean ±SD)	1.0±0.4	1.3±0.7	0.159 ^b		
TG (Mean ±SD)	1.0±0.5	1.8±1.6	0.040* ^b		
LDL (Mean ±SD)	2.9±1.2	3.6±1.6	0.245 ^b		
FBS (Mean ±SD)	4.5 ±0.5	5.3±0.7	0.002* ^b		
Age in years (Mean ±SD)	38.0 ± 16.3	49.3 ±7.8	0.205 ^b		
Age of onset: Early onset/Late onset	18/7	0/7	0.001* ^c		
Sex: Male/Female	14/11	4/3	0.999 °		

Table3: Comparison between Psoriatic patients with metabolic syndrome and Psoriasis without metabolic
syndrome

a- Mann Whitney U

b- t test

c- Fisher's exact test

*-significant

The table 3 above infers that mean \pm SD difference in psoriasis patients with metabolic syndrome in terms of age at recruitment into the study; clinical and metabolic characteristics were all higher than that of those without metabolic syndrome. However, the mean differences in their duration of eruption, SBP, DBP, WC, BMI TG and FBS were statistically significant (p: 0.042; 0.0001; 0.0001; 0.0004; 0.005; 0.040; and 0.002 respectively). Notably, there was statistically significant difference in the age of onset of psoriasis in those with or without metabolic syndrome (p=0.001) but there was sex match in the two groups. PASI score in patients with metabolic syndrome ranges from 2-72 with a mean score of 27.1±29.1 against a range of 4-55 and a mean score of 17.8± 16.6. However, the difference was not statistically significant. Observed also was the difference between the mean \pm SD of the body surface area of patients with or without metabolic syndrome which was not statistically significant, the range was 3-70 for those with MS and 9-70 for those with MS.

Table 4: Psoriatic patients with metabolic syndrome and Psoriasis without metabolic syndrome with
recourse to their time of onset of psoriasis

	Early onset Metabolic Syndrome Absent Present (n=0) (n=18)	Late onset Metabolic Syndrome Absent Present (n=7) (n=7) Mean± SD Mean± SD		ANOVA P value
Age in years	mean± SD 29.2±6.7	60.7±10.1	49.3±7.8	0.011*
BMI (kg/M ²)	23.9±4.1	27.4±5.4	32.3±9.0	0.204
SBP (mmHg)	113.9±10.9	124.3±7.8	141.4±9.0	0.003*
DBP (mmHg)	70.6±7.3	80.0±5.8	95.7±5.3	0.002*
Waist circumference (cm)	80.8±11.4	92.4±12.1	107.4±16.9	0.080
TC (mmol/L)	4.2±1.8	4.6±0.8	5.4±1.2	0.168
HDL (mmol/L)	1.0±0.4	1.1±0.4	1.3±0.7	0.524
TG (mmol/L)	0.9±0.5	1.2±0.3	1.8±1.2	0.224
LDL (mmol/L)	2.9±1.4	2.8±0.7	3.6±1.2	0.249
Fasting Blood Sugar (mmol/L)	4.6±0.4	4.4±0.5	5.3±0.7	0.017*
Severity Score	3.06±1.1	2.9±0.4	3.1±1.3	0.752

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PASI ^a : D 10 Mean± SD (range) >10 Mean± SD (range)	5.2±3.1 (0.4-8.7) 34.3±13.7 (16.0-55.0)	0.800±0.0 (0.8) 28.9±11.5(14.6- 41.2)	6.7±4.2 (2.0-10.0) 42.5±30.8 (15.8- 72.0)	<0.0001* <0.0001*
BSA ^b : D 10% Mean± SD (range) >10% Mean± SD (range)	6.7±3.1 (3-10) 30.1±20.6 (11-70)	8.0±2.8 (4-10) 38.3±16.1 (20-50)	9.5±0.7 (9.10) 29.6±23.6 (12-70)	>0.05 0.821

*significant

a- Eta squared =0.582 i.e. 58.2% Measure of Association

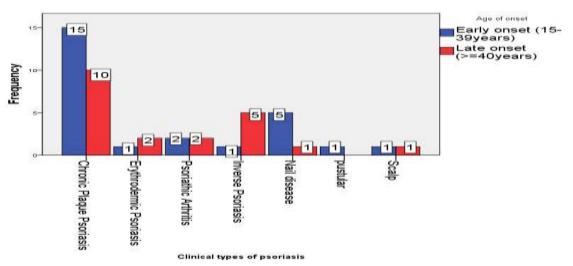
b- Eta squared =0.353 i.e. 35.3% Measure of Association

Table 4 above is a summary of association between the time of onset of psoriasis and clinical/ metabolic characteristics of psoriatic patients with/without metabolic syndrome. Whereas the mean age of onset of psoriasis for those with early onset was 29.2 ± 6.7 years, the mean age of onset of psoriatic patients with metabolic syndrome and without metabolic syndrome was 49.3 ± 7.8 and 60.7 ± 10.1 years respectively and their mean differences were statistically significant (p=0.011). Other variables that were significant (p<0.05) are: SBP, DBP, and FBS, PASI ≤ 10 ; PASI > 10 (p=0.003, 0.002, 0.017, <0.0001; <0.0001 respectively).

Table 5: Logistic regression output showing predictive factors for both psoriatic patients and non-
psoriatic patients

poor and participations					
	В	Sig.	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Metabolic syndrome	-2.500	0.280	0.082	0.001	7.655
Sex	.874	0.253	2.396	0.536	10.706
BMI	3.472	0.015*	32.208	1.939	535.030
WC	131	0.004*	0.877	0.802	0.960
BP	2.337	0.077	10.346	0.775	138.078
ТС	-2.262	0.295	0.104	0.002	7.170
HDL	-1.707	0.036*	0.181	0.037	0.896
TGS	1.334	0.312	3.797	0.286	50.327
LDL	.265	0.903	1.303	0.018	92.017
FBS	-19.131	0.999	0.000	0.000	
Constant	9.451	0.012	12723.088		

The regression output in table 5 shows that only BMI, WC and HDL were predictive factors. Remarkably, is the high odds ratio observed in BMI and blood pressure status in psoriatic patients with/without metabolic syndrome. Moreover, BMI, WC and HDL were predictors (p: 0.015; 0.004; 0.036 respectively)





V. DISCUSSION

Psoriasis has been recognized as a systemic disease associated with multiple comorbidities (20, 21). Researchers had focused their attention on comorbidities in psoriasis which includes; type 2 diabetes, atherosclerosis, hypertension, myocardial infarction, depression and obesity (22,23,24). The prevalence of metabolic syndrome among psoriatic patients varies according to the study and the adopted criteria of metabolic syndrome. Gisondi and his group using the National Cholesterol Education Programme (NCEP) ATP III criteria studied 338 patients with Chronic plaque psoriasis and 334 patients with other skin diseases, a higher prevalence of metabolic syndrome was observed in the first group (30.1% and 20.6% respectively) (5). Sommer et al (19) using a modified version of the WHO criteria reported that metabolic syndrome in patients with psoriasis was twice as common as in a control group. Love et al (24) using the revised NCEP ATP III criteria found the prevalence of metabolic syndrome to be 40% among psoriatic patients as against 23% among control group. Meanwhile Lakshmi et al (25) using the NCEP ATP III criteria did not find any statistical association between metabolic syndrome and psoriasis after controlling for age and gender. Also, Kim et al (26) studied 490 patients with psoriasis and 682 controls and found no statistical significant difference in metabolic syndrome between patients with psoriasis and controls (p=0.2). These differences might be due to differences in race and genetic make-up. (25-26). On the contrary, Also, Mebazaa et al (38) studied 164 psoriasis patients and 216 controls and showed a slightly higher prevalence of MS in psoriatic patients (35.5%) as compared to controls (30.8%).

Our study showed a prevalence of 21.9% of metabolic syndrome in psoriasis patients (all of them from late onset of psoriatic patients' \geq 40years) and 3.1% in the control group. None of the early onset psoriatic patients (15-39years) had metabolic syndrome. This is the pattern observed in most studies (5, 26-27). This would be due to the fact that individual components of MS are more common in older populations (25). However, we observed that late onset psoriatic patients with metabolic syndrome were younger (mean age 49.3 years) than those without MS (mean age 60.7 years). This is not in agreement with Sumner et al (19) conclusion that the prevalence of MS increases with age, as well as Kim et al (26) who observed that psoriatic patients with MS were significantly older than those without. More studies (from Nigeria?) are required to validate this trend. Commonly reported lipid abnormalities in patients with psoriasis include: elevated Low Density Lipoprotein (LDL), Total Cholesterol (TC) and Triglyceride (TG) levels (28) as well as decreased High Density Lipoprotein (HDL) levels (29, 30). The study published by Tekin et al shows that oxidized Low Density Lipoprotein is accumulated in psoriatic skin lesions. It is worth noting that, both in psoriasis and atherosclerosis, HDL becomes dysfunctional and has proinflammatory properties (31).

Also, CD $209^+/CD$ 163^+ dermal macrophages which are capable of engulfing oxidized lipids have been identified in psoriatic tissue and it has been demonstrated that TPH-1 macrophages stimulated by component of minimally oxidized LDL express IL-1, 6, 15, 17, 23, VEGF and cathelicidin, all of which are involved in the pathogenesis of psoriasis (31, 32, 33).

Our findings did not show any statistically significant differences among the lipid metabolites either in early onset psoriasis or late onset psoriasis. However, the mean of various lipid metabolites in psoriatic patients with MS were higher than those without MS. This is in contrast with other studies (25, 34-35) and Furthermore, a comparison of psoriasis cohort with metabolic syndrome in our study showed statistically significant differences in mean \pm SD for Fasting blood sugar, waist circumference; body mass index, systolic and diastolic blood pressure when compared with those psoriatic patients without metabolic syndrome (p=0.002, 0.0004, 0.005, 0.0001 and 0.0001 respectively). This findings was consistent with Lakshmi et al (25) who found that fasting blood sugar level was significantly higher among psoriatic patients with metabolic syndrome (p<0.0001) but no significant relationship with other components of metabolic syndrome such as obesity, hypertension and dyslipidemia.

Regarding the relationship between MS and severity of psoriasis based on PASI scores and BSA involvement, most studies did not find a significant difference (5, 25, 27, 37, 38). In contrast, Kim et al (26)was able to demonstrate a significant difference in the prevalence of MS and severe forms of psoriasis (p=0.048). This is similar to our study. For we observed that individuals with late onset psoriasis and metabolic syndrome had severe form of psoriasis with (PASI>10) when compared to thosewithout metabolic syndrome (PASI>10) and (p=0.0001).

Some of the limitations in this study are: first, it was conducted in a tertiary care setting where patients have the tendency to present in a more severe form of the disease. Secondly, the retrospective nature of the study entails that most of the measurements for the risk factors were obtained from medical records; this might have introduced some bias. Since psoriasis is a chronic disease, it would be good to follow up the early-onset psoriasis patients to find out when and if they developed MS in the course of the disease.

In conclusion, we found a higher prevalence of metabolic syndrome in late onset psoriasis. The tendency to have cardiovascular event is high if not properly investigated and managed. We therefore suggest that management of

metabolic syndrome be fully integrated in our treatment protocol for all our psoriasis patients in order not to miss any one.

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