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Pattern of comorbidities in psoriasis patients from western India and the relation between disease severity and systemic comoridities: cross sectional study at a tertiary care centre

[1]Shruti Kulkarni ,[1] Priyanka Sondarva,[2]Neela Bhuptani

[1]*Resident Doctor , Dept. Of D.V.L. (SKIN), P. D. U. Govt. Medical College and Hospital, Rajkot, India*
[2] *Professor and Head, Dept. Of D.V.L. (SKIN), P. D. U. Govt. Medical College and Hospital, Rajkot, India*

ABSTRACT

Background: Various studies have shown association of much physical and psychosocial comorbidity with psoriasis. **Aims & Objectives:** To note pattern of various comorbidities in psoriasis patients and the association of systemic comorbidities with severity of psoriasis. **Materials & methods:** Cross sectional study of 200 psoriasis patients was done.Detailed history and examination done. Investigations included complete blood count, CRP, ESR, urine routine and microscopic examination, LFT, RFT, S .calcium, lipid profile, blood sugar estimation, S. protein, TFT, ultrasound abdomen. In case of joint involvement- X-ray of involved joint, Rheumatoid factor and S. uric acid were done. General Health Questionnaire 12 for psychiatric morbidity, CASPAR criteria for psoriatic arthritis, ATP III criteria for metabolic syndrome, cardiovascular criteria based on BMI , NCEP for lipid levels, AGA diagnostic criteria for non-alcoholic fatty liver disease, were used for calculation. Statistical analysis was done by Chi-Square Test. **Results:** most common comorbidities noted were:- abdominal obesity (71%), increased BMI (70%), dyslipidemia (40%); hypertension (28%); diabetes mellitus (25%); metabolic syndrome (21.5%); Increased cardiovascular risk (81.5% based on BMI; 71% based on waist circumference) was noted. Significant association between disease severity and increased BMI, psoriatic arthritis, psychiatric comorbidity was noted. **Conclusion:** Screening of all patients for comorbidities and prompt treatment is necessary to break the vicious cycle of comorbidities worsening psoriasis and vice-versa, as well as for therapeutic implications.

Keywords: psoriasis, comorbidities, cardiovascular, metabolic syndrome, psoriatic arthritis

Introduction

Psoriasis, an immune-mediated skin disease, has various systemic and cutaneous comorbidities, as shown by previous studies. These comorbidities are found to be more in patients with moderate to severe psoriatic skin disease [1].Some of the concomitant medications for comorbidities may worsen psoriasis; conversely, systemic treatment of psoriasis with certain drugs may impact the comorbid conditions. This necessitates a multidisciplinary approach, with coordination between dermatologists and other specialists, to minimize co-medication and morbidity[2].Thus, it is necessary for a dermatologist to be aware of comorbidities prevalent in psoriasis patients and the significance of timely screening. However, there are only few Indian studies on the various comorbidities prevalent in psoriasis and there are no recommended guidelines for screening in Indian population.

**Correspondence*
Dr. Priyanka Sondarva
Resident Doctor , Dept. Of D.V.L. (SKIN), P. D. U. Govt. Medical College and Hospital, Rajkot, India
E Mail: sondarvapiya26@gmail.com

Materials and methods

An observational, prospective, cross-sectional study of 200 patients of psoriasis with comorbidities, aged above 18 years, attending outpatient department of PDU Government Medical College & Hospital, Rajkot was done over a period of 2 years, from November 2013 to October 2015.With informed consent, detailed history was taken including duration of the disease, joint pain, smoking, alcohol intake, tobacco

consumption, concomitant illnesses, concomitant drug intake and family history of psoriasis. Thorough clinical examination was done and the severity of disease was calculated by psoriasis area severity index (PASI) score, presence of nail, or joint involvement. Biometric data such as weight, height, waist circumference were noted. Waist circumference was measured at the highest level of the iliac crest[3]]. Investigations included complete blood count (hemoglobin, total count, differential count, platelet count), C reactive protein, erythrocyte sedimentation rate, urine routine and microscopic examination, liver function tests, renal function tests, serum total protein and albumin, serum calcium, lipid profile, blood sugar estimation, thyroid function tests, ultrasound abdomen.. In clinically difficult cases, biopsy was done for diagnosis. Specific investigations included: electrocardiogram (ECG) in patients with history of cardiovascular risk factors; chest X ray and pulmonary function tests with history of respiratory complaints and referred to physician if abnormal; X-ray of involved joint, Rheumatoid factor, and S. uric acid with history of joint pains[4].The statistical analysis was done by Chi-Square Test.

Various scores and criteria used for the study are as follows:

1) PASI calculation[5]: Four sites of affection, the head (h), upper limbs (u), trunk (t) and lower limbs (l), were scored by using three parameters: erythema (E), infiltration (I) and desquamation (D), each of which was graded on a severity scale of 0-4, where 0 = nil, 1 = mild, 2 = moderate, 3 = severe and 4 = very severe.

The area-wise percentage involvement of the involved sites was calculated as: 1 ≤ 10% area; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; and 6 = more than 90%.

The final formula for PASI score: PASI = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + Iu + Du) Au + 0.3 (Et + It + Dt) At + 0.4 (El + Il + Dl) A1

Mild psoriasis was classified as a PASI between 0 and 7, moderate between 8 and 12 and severe>12.[3]

2) Body mass index (BMI) was calculated using the formula: Weight (kg) /Height (m^2). According to Indian guidelines, a BMI from 23 to 24.9 is overweight, ≥ 25 is moderate obesity, and ≥ 30 is severe obesity. Cut-off values for waist circumference for Indian men and women were 90cm and 80 cm, respectively[3].

3) Cardiovascular risk was estimated based on BMI (as recommended by WHO Expert Consultation Group in Asian population[6]

4) Metabolic syndrome (MS) can be identified by presence of three or more of the Adult Panel III (ATP III) criteria[3].

1. Elevated waist circumference - Men: ≥90 cm; **Women**: ≥80 cm (for Asians)
2. Reduced HDL- Men: <40 mg/dl; Women: <50 mg/dl
3. Elevated blood pressure- ≥130/85 mm Hg
4. Elevated fasting glucose- ≥100 mg/dl
5. Elevated triglycerides- ≥150 mg/dl

5) The diagxnosis of psoriatic arthritis (PsA) was based on the classification criteria of psoriatic arthritis (CASPAR) criteria[4]. Number of tender and/or swollen joints were counted and the pattern of arthritis was recorded according to Moll and Wright's classification criteria. Spondylitis was diagnosed when at least one of the following was present in a patient with inflammatory back pain, with or without peripheral joint disease/ Tenderness on the spine or sacroiliac joint / sacroiliitis on pelvis X-ray / spinal syndesmophytes on X-ray[4].

6) The National Cholesterol Education Program Blood Lipid guidelines for optimal blood lipid levels were used[3].

7) GENERAL HEALTH QUESTIONNAIRE -12 (for General Psychiatric Morbidity) was used to detect psychiatric morbidity- SCORE ≥ 2 is considered significant[7].

8) NAFLD (non-alcoholic fatty liver disease) diagnostic criteria: (as per American Association for the Study of Liver Diseases, American College of Gastroenterology, and the Amerivcan Gastroenterological Association 2012)[8].

Table 1: Cardiovascular risk was estimated based on BMI (as recommended by WHO Expert Consultation Group in Asian population)

BMI	Risk
18.5—23 kg/m2	Acceptable risk
23—27.5 kg/m2	Increased risk
>27.5 kg/m2	High risk

Results

Various systemic comorbidities observed in our study are as in [Table 2].Cardiovascular risk was increased in 81.5% cases based on BMI and in 71% cases based on increased waist circumference. Most of the patients 44% cases had long duration of disease (>5yrs). No significant association was found between Metabolic Syndrome and duration of the disease. Maximum patients (77.5%) had mild disease (PASI <8). No association was found between MS, its components (individually) and severity of the disease [Table 3]. Amongst patients with respiratory comorbidity (5 cases),2 cases of chronic obstructive pulmonary disease (COPD) and 1 case of bronchial asthma had history of smoking. Of the 11 patients with thyroid disorder, 4 cases were previously known hyperthyroids and 5 cases were already known hypothyroids on treatment. All of them had mild psoriasis (PASI<8) except two hypothyroid cases having severe disease (PASI-15 and 13.5).Of the 4% cases with alcohol addiction, 1.5% cases had fatty liver. Fatty liver (with no history of alcoholism) was observed in 4.5% cases [0.5% case was on oral methotrexate treatment and 4% cases had NAFLD]. Amongst patients with NAFLD, 2 patients had hypertension and 1 case had MS. One case (0.5%) of each renal stones (without any associated nephropathy) and chronic renal failure were noted. The patient with chronic renal failure also had diabetes mellitus (DM), hypertension (HTN), diabetic retinopathy and diabetic neuropathy.1 out of 2 cases with human immunodeficiency virus (HIV) infection in our study with PASI-6 had crusted lesions [figure 1] whose diagnosis was confirmed by biopsy. Recurrent exacerbations of psoriasis were seen in patient of Down syndrome with the age of onset at 29 years, less compared to the mean age of onset seen in females i.e., 47.48%.Psoriatic arthritis was seen in 6% cases and asymmetrical oligoarthritis was the most common pattern observed [figure 2 & 3].Amongst systemic comorbidities associated, we found significant association between severity of the disease and increased BMI, psoriatic arthritis, psychiatric comorbidity; while no significant association with rest of the comorbidities [Table 4].Various associated cutaneous disorders (infectious and non-infectious) noted are in our study are Tinea unguium(1.5%), Intertrigo(0.5%), Pitted keratolysis(0.5%), Tinea corporis(1.5%), verruca vugaris(2%), Herpes labialis(0.5%), Pityriasis versicolor(0.5%), Phototoxic reaction, Vitiligo(1.5%), Acute urticaria, LSEA, Seborrheic keratoses, Dermatosis papulosa nigra, Bullous pemphigoid, Acne(1%), Xanthelesma(1%).

Discussion

A recent meta-analysis indicates elevated risk of cardiovascular events in psoriatic patients in relation to non-psoriatic controls [9]. Also, Asian-Indians have a higher predisposition to obesity, metabolic syndrome, diabetes, and cardiovascular disorders as compared to western populations. Psychological comorbidity in psoriasis leads to addiction to alcohol, smoking and tobacco chewing. Both alcohol and smoking in turn worsen psoriasis. Also alcohol intake releases proinflammatory cytokines like TNF-alpha, exacerbating psoriasis and causing alcoholic hepatitis[10].In our study, HTN, abdominal obesity and ischemic heart disease (IHD) were more common while DM, family history of DM, alcohol addiction and tobacco chewing were more common in Periera et al study[6].The increased cardiovascular risk due to increased BMI as well as due to increased waist circumference, in our study was comparable to Periera et al study findings[6].Abdominal obesity prevalence varies across different populations. Love TJ et al [11] found that, abdominal obesity was most common component of metabolic syndrome associated with psoriasis followed by hypertriglyceridemia and low levels of HDL cholesterol. Abdominal obesity was more in males contradicting the findings of Love TJ et al which was probably due to higher male: female ratio in our study. Several studies have shown that psoriasis is associated with atherogenic dyslipidemia. The association with dyslipidemia was less in our study compared to Pierera et al[6].MS is a strong predictor of cardiovascular disease, that confers a cardiovascular risk higher than the individual components[5]. We found no significant relationship between the duration of the disease and the presence of MS similar to findings in study by Madanagobalane S et al[3].In present study, PASI score ranged from 0.2 to 34.6 with mean and median of 4.8 and 1.5, respectively. While, in study by Madanagobalane S et al[3], PASI score ranged from 0.6 to 45.6 with mean and median of 6.2 and 82. Maximum number of patients (77.5% cases) who presented to our OPD had mild disease (PASI <8). Out of 45 (22.5%) patients, who had moderate and severe psoriasis, 6 patients had MS. We found no significant association between MS and extent of involvement as well as between the severity of the disease and various components of MS, against the findings of Madagobalane S et al[3].The presence of psychological distress in our study group (11%) was comparable to that in group of Kumar et al (16%)[12].Around 79% patients with severe psoriasis

have negative impact on their lives. Competition, increased cosmetic awareness and the stresses of day-to-day life make psoriasis patients feel inferior and less competent as compared to the normal population, which leads to anxiety and depression, which get further precipitated by the frequent relapses and chronicity of the disease[12].Psoriasis in HIV is known to have increased exacerbations, increased association with PsA and may present with atypical lesions like papules, crusted and hyperkeratotic lesions[13]. Unstable psoriasis associated with Down's syndrome has been reported by our study comparable to Mariyath et al[14].Many studies have shown increased association of COPD with psoriasis. Since both psoriasis and bronchial asthma are chronic immune-mediated inflammatory diseases, increased prevalence of asthma with psoriasis has been seen[15].Moderate to severe psoriasis is also a risk factor for chronic kidney disease (CKD). There is nearly a two-fold risk of moderate to advanced CKD among psoriasis patients and a greater than four-fold risk of end stage renal disease, independent of other comorbidities. The risk of CKD associated psoriasis is greater than the risk of CKD associated with diabetes and hypertension.The cause for CRF in our patient could not be ascertained to particular cause as the patient also had HTN and DM with microvascular complications. Thyroid hormones increase EGF and may cause uncontrolled and relapsing psoriasis[16]. Arican et al found the serum TT4 and FT3 levels were significantly higher in psoriatics than in the control group and also they had higher PASI scores .But we did not find severe disease with hyperthyroidism, probably as they were under treatment. NAFLD, considered as hepatic manifestation of the metabolic syndrome, is associated with risk of cardiovascular disease and methotrexate-induced hepatotoxicity. In an Indian study, the occurrence of NAFLD was higher in psoriasis patients than in controls[17]. NAFLD patients in the psoriasis group were more likely to have metabolic syndrome and diabetes than those with psoriasis alone, which was not seen in our study. 6% cases had PsA comparable with Indian prevalence of 1-9%. Variations with findings from Kumar et al[4] study were probably due to smaller sample size of PsA (n=12) in our study. Significant association was not found between disease severity and increased BMI; psoriatic arthritis and psychiatric comorbidity only probably because 77.5% (i.e., more than ¾ th) of the sample belonged to mild psoriasis group.

Cutaneous comorbidities: Xanthelesma usually represents a localized cutaneous phenomenon, but may signify a systemic hyperlipidemia, as seen in one of our case. Seborrheic keratosis can be a cutaneous marker of internal malignancy, though in our case it was not eruptive seborrheic keratosis. Various studies have shown increased association of psoriasis with malignancy including cutaneous tumors and solid organ tumors. Hence according to AHA recommendations, age appropriate screening for various malignancies is necessary in all patients. Itching associated with LSEA, urticaria and eczema can aggravate psoriasis due to koebnerisation and reduce the efficacy of treatment. Amongst the cutaneous autoimmune conditions, various studies have shown association of vitiligo [figure 4] and bullous pemphigoid with psoriasis, though the strength of association is not known yet.

Conclusion

The above findings of various comorbidities associated with psoriasis indicate that a dermatologist should always screen for the coexistent comorbidities as the management of psoriasis depends on comorbidities and vice-versa. Till the screening guidelines are available, the dermatologist has to rely upon relevant history, clinical examination and investigations, for the detection of comorbidities at the earliest. Paucity in Indian data regarding the subject needs to be addressed by conducting more epidemiological studies with larger sample size, which will help in formulating screening guidelines for Indian population.

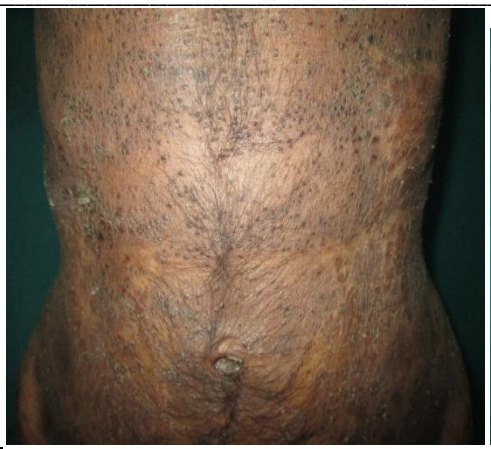

Fig 1: Psoariasis presenting as crusted papules in HIV Infection

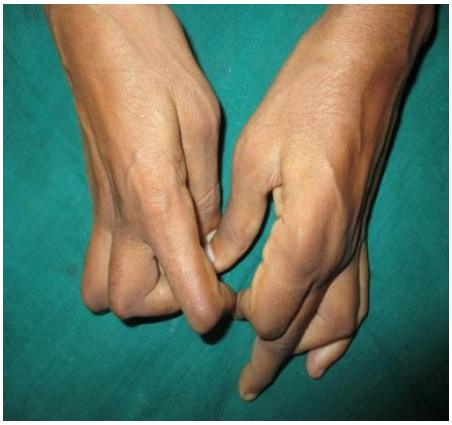

Fig 2: Arthritis mutilans

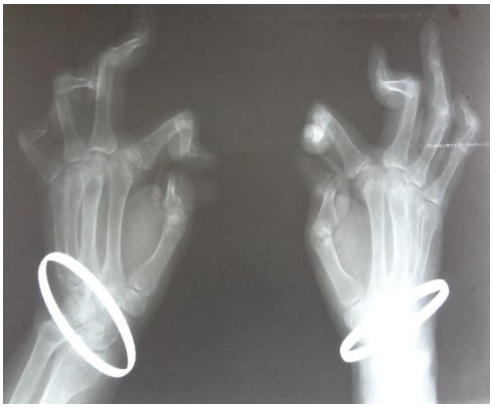

Fig 3: X Ray(AP view both hands)multiple deformities noted involving pip, dip, mcp jts

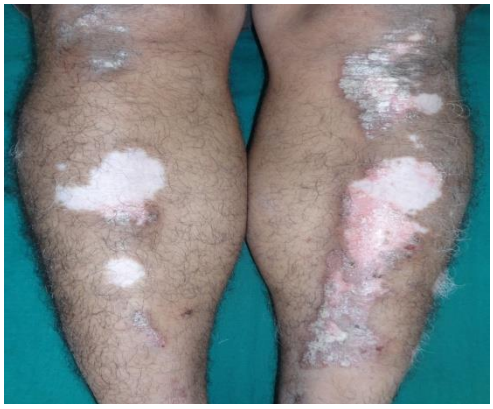

Fig 4: Psoriatic plaques on vitiligo patches

Table 2: Distribution of patients based on various co- morbidities observed in our study

Systemic comorbidity	*Present study % (n=200)*
Metabolic syndrome	21.5
HTN	28
DM	25
IHD	5
Dyslipidemia	40
Morbid obesity	25
Obesity	36.5
Overweight	8.5
Hyperthyroidism	2.5
Hypothyroidism	3
COPD, Bronchial asthma	2.5
Psychiatric comorbidity	11
Alcohol dependence	4
Chronic renal failure, renal stones	1
Down's syndrome	0.5
Psoriatic arthropathy	6
HIV	1
Tuberculosis	0
Fatty liver/ cirrhosis liver*	1.5

NAFLD **	4
Ca breast	0.5
Hepatitis B	0.5

*H/O chronic alcoholism present

**NAFLD: non-alcoholic fatty liver disease

Table 3: Relation between disease severity and metabolic syndrome, its components

Metabolic syndrome and its components	*Present study (2015)% (n=200)*				*Madanagobalane S et al[3] (2012)% (n=118)*			
	PASI >12 Severe	***PASI 8–12 Mod-erate***	***PASI <8 Mild***	***P value***	***PASI >12 Severe***	***PASI 8–12 Mod-erate***	***PASI <8 Mild***	***P value***
Metabolic syndrome	5	1	37	0.138	8	6	38	0.499
Waist circumference ≥90 cm (M) or ≥80 cm (F)	17	16	109	0.449	3	7	37	0.018
Triglyceridemia ≥150 mg/dl	4	5	29	0.977	7	4	30	0.043
HDL <40 mg/dl (M) or <50 mg/dl (F)	3	1	27	0.352	10	12	54	0.176
Blood pressure ≥130/85 mmHg	6	7	45	0.980	2	8	26	0.018
Fasting plasma glucose ≥100 mg/dl	6	6	45	0.955	9	9	54	1.000

Table 4: Relation between disease severity and various systemic comorbidities

systemic comorbidity	*present study (2015) no. (n=200)*			
	PASI >12 severe	***PASI 8–12 moderate***	***PASI <8 mild***	***P value***
DM	4	6	40	0.95
HTN	3	6	47	0.484
IHD	1	1	8	0.85
Dyslipidemia	6	9	65	0.712
Increased BMI	18	21	101	0.038
Psychiatric comorbidity	6	4	12	0.027
Psoriatic arthritis	5	0	7	0.004
NAFLD	2	1	5	0.612
COPD	0	0	3	0.908
Bronchial asthma	1	1	0	0.49
Hyperthyroidism	0	0	5	0.93
Hypothyroidism	2	0	4	0.287

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