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ORIGINAL ARTICLE

Clinical Patterns and Risk Factors Associated With Pigmented Purpuric Dermatoses

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ABSTRACT

Objective: To investigate the clinical patterns and risk factors associated with pigmented purpuric dermatoses (PPD) in patients attended outpatient department of Indus Hospital Karachi.

Methods: A retrospective cross-sectional study was conducted at The Indus Hospital, Karachi between October 2017 to March 2020. All patients with PPD, age 16 years and above, either gender, came to dermatology outpatient department were included. Demographics, comorbids, body mass index (BMI), PPD type, clinical findings, laboratory parameters and ultrasonographic findings (USF) of both lower limbs for venous insufficiency were reviewed.

Results: Out of 65 patients, mean age was 42.6±13.9 years with male to female ratio of 1.2:1. Schamberg's disease was present in 42 (64.6%) patients. Varicose veins were present in 38 (58.5%) and features of chronic venous disease (CVD) were present in 26 (40.0%). Patients with varicosity were significantly higher in male 25 (65.8%) as compared to female 13 (34.2%), (p-value 0.022). Patients had no clinical varicosities and had no findings of CVD were significantly higher as compared to patients had clinical varicosities and had CVD present, i.e., 25 (92.6%) and 24 (63.2%) respectively, (p-value <0.001). Comparison of Schamberg's and other PPD showed statistically significant difference between clinical varicosities (p-value 0.045) and features of chronic venous disease (p-value 0.013).

Conclusion: Presence of varicosities with / without features of CVD and male sex were main risk factors associated with PPD in our population particularly in PPD other than Schamberg's disease.

Keywords: Body Mass Index, Comorbidity, Pigmented Purpuric Dermatoses, Schamberg's Disease, Venous Insufficiency.

INTRODUCTION

Pigmented purpuric dermatoses (PPD) is an uncommon group of benign disorders of cutaneous vasculature.[1] PPD is primarily localized to lower limbs. The course of disease is chronic and relapsing in majority of cases with no serious outcomes. Although rare but PPD is known to affect all races across the globe.[2] Adults are more commonly reported with male predisposition.[3] Familial cases are also reported from many ethnicities.[4] PPD has been traditionally associated with prolonged standing, exercises, occupation, various medications, food additives, autoimmune disorders and exposure to irritants but nothing has proven yet.[5]

The diagnosis and classification of PPD is usually clinical. Histopathology is supportive rather than diagnostic. The common histopathological features are superficial lymphocytic infiltration, marked hemosiderin deposition with erythrocyte extravasation and absence of vasculitis.[2] These disorders have different morphological features but share a common histopathology.[6] All types of PPD are more common in males except Majocchi's disease.[7] Schamberg's disease is the most frequently reported type both in pediatric and adult groups.[8] Frequent relapses and remissions have been reported in almost all of these diseases.[2,9]

The exact cause of PPD is still unknown, but several underlying diseases and drugs have been suggested to be associated with PPD. Commonly reported disorders are chronic venous hypertension, diabetes mellitus, hypertension, rheumatoid arthritis, chronic hepatitis B or C infection, hyperlipidemia and malignancies. Drugs which have been associated with PPD are non-steroidal anti-inflammatory drugs (NSAIDs), oral hypoglycemics,

antihypertensives and antipsychotics.[10]

Various analytical and descriptive studies have been published from different countries but data from Pakistan are lacking. Therefore, authors decided to investigate clinical patterns and risk factors associated with PPD in Pakistani population and also to correlate the relationship of various suggested aetiologic agents with PPD in our population.

METHODS

This was a retrospective cross-sectional study carried out at dermatology outpatient department of The Indus Hospital, Karachi, Pakistan between October 2017 to March 2020. Permission from the institutional ethical review committee was taken prior to conduct the study (IRB Number: IRD_IRB_2020_04_020).

All patients with a clinical diagnosis of PPD (Table 1), age 16 years and above, either gender, who attended dermatology outpatient department were included for retrospective review. But patients younger than 16 years, pregnant and lactating mothers, those having congenital vascular disorders, vascular malformations, anatomical or syndromic abnormalities of lower limbs, inherited neuropathies, malignancies and psychiatric comorbidities were excluded. So, 65 patients were selected who met the selection criteria.

Age, gender, occupation, known medical and dermatological comorbids, history of deep venous thrombosis (DVT) and previous surgeries, body mass index (BMI), type of PPD, presence or absence of clinical varicosities, features of chronic venous disease (CVD), laboratory parameters and ultrasonographic findings of both lower limbs' veins were noted down from medical records on a predesigned proforma. Reviewed laboratory parameters were blood sugars, lipid profile, uric acid, renal, thyroid and liver function tests, autoantibodies profiles, and viral hepatitis serology. PPD was defined as variable-sized, variable-shaped, well demarcated, non-blanchable, mostly asymptomatic, reddish-brown macules and patches with associated petechiae within the lesions, present predominantly over lower limbs and buttocks.

WHO definition of obesity for Asians was used to classify. BMI <18.5 kg/m^2 as underweight, BMI 18.5--22.9 kg/m^2 as healthy, BMI 23--24.9 kg/m^2 as overweight and BMI ≥25 kg/m^2 as obesity.[11]

Data were entered and analyzed by using version 26.0 of statistical package of social sciences (SPSS) software. Mean ± SD were computed for quantitative variables like, age and BMI while frequency and percentages were computed for categorical variables like, gender, employment status, PPD type, ultrasonographic findings, clinical varicosities, features of CVD, obesity and comorbidity. Stratification of PPD patients were done. First with respect to presence and absence of varicosities and then with type of PPD. These groups were compared by using Independent sample t-test for quantitative variable and Chi-Square/Fisher's Exact tests for categorical variables. p-value ≤0.05 was considered as statistically significant.

RESULTS

Of 65 patients with PPD, the mean age of patients was 42.6±13.9 years with range 16 – 77 years. There were 35 (53.8%) male and 30 (46.2%) female patients with male to female ratio of 1.2:1. In this cohort, 25 (38.5%) were employed and 40 (61.5%) were unemployed. Majority of the patients were housewives 25 (38.5%). In terms of BMI, majority of the patients were obese 51 (78.5%).

Among the type of PPD, classical Schamberg's disease was present in 42 (64.6%), transitory PPD in 5 (7.7%), itching purpura of Lowenthal in 4 (6.2%), pigmented purpuric lichenoid dermatosis of Gougerot and Blum in 4 (6.2%), eczematid-like purpura of Doucas and Kapetanakis in 2 (3.1%) and unilateral Schamberg's disease in 2 (3.1%) cases respectively. However, type of PPD was not decided in 6 (9.2%) cases due to diffuse pigmentation or mixture of features. Color Doppler ultrasound findings were reported by 58 patients only. In particular, abnormal findings were observed in 37 (63.8%) cases and normal in 21 (36.2%) cases. Abnormal findings were presence of reflux in superficial venous system of lower limbs' veins in 34 (58.6%) and damaged venous architecture in 3 (5.2%) patients.

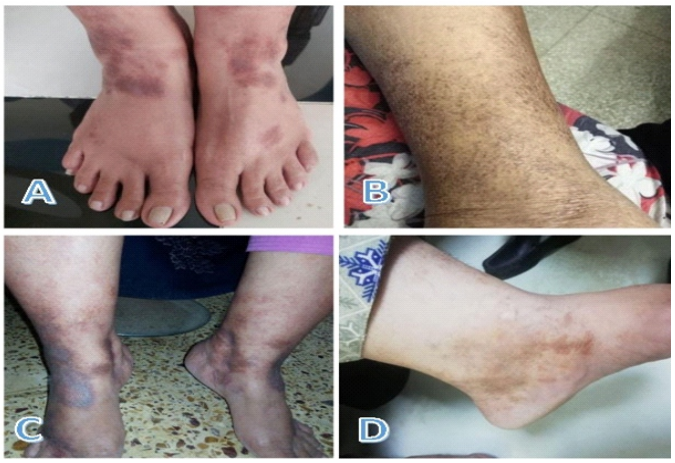

Figure 1: Different types of pigmented purpuric dermatosis. (A) Classical Schamberg's disease (B) Itching purpura of Lowenthal (C) Pigmented purpuric lichenoid dermatosis of Gougerot and Blum (D) Unilateral Schamberg's disease.

Table 1: Types of pigmented purpuric dermatoses

1.	Schamberg's disease
2.	Majocchi's disease
3.	Itching purpura of Lowenthal
4.	Lichen aureus
5.	Transitory PPD
6.	Pigmented purpuric lichenoid dermatosis of Gougerot and Blum
7.	Eczematoid-like purpura of Doucas and Kapetanakis
8.	Linear PPD
9.	Unilateral variants of PPD
10.	Granulomatous variant of PPD

Table 2: Comparison of PPD patients with and without varicosities (n=65)

Variables	Varicosities		p-value
	Absent	Present	
Age (years)	44.5±14.8	41.3±13.3	0.369 ∓
	n (%)	**n (%)**	
Gender			
Female	17 (62.9%)	13 (34.2%)	0.022 §*
Male	10 (37.04%)	25 (65.8%)	
Employment Status			
Employed	07 (25.9%)	18 (47.3%)	0.105 §
Unemployed	20 (74.1%)	20 (52.7%)	
Obesity			
Obese	21 (77.7%)	30 (78.9%)	0.910 §
Non-Obese	06 (22.2%)	08 (21.1%)	
Ultrasound Color Doppler findings			
Normal	13 (65%)	08 (31.1%)	0.001 §*
Abnormal	07 (35%)	30 (78.9%)	
Comorbidities			
No	06 (22.2%)	19 (50%)	0.023 §*
Yes	21 (77.8%)	19 (50%)	
PPD type			
Schamberg's disease	22 (81.5%)	20 (52.6%)	0.110 ł
Transitory PPD	2 (7.4%)	3 (7.9%)	
PPLDGB	1 (3.7%)	3 (7.9%)	
Itching Purpura of Lowenthal	2 (7.4%)	2 (5.3%)	
EPDK	0 (0.0%)	2 (5.3%)	
Unilateral Schamberg's disease	0 (0.0%)	2 (5.3%)	
Diffuse pigmentation	0 (0.0%)	6 (15.8%)	
Features of chronic venous disease			
Absent	25 (92.6%)	14 (36.8%)	<0.001 §*
Present	02 (7.4%)	24 (63.2%)	

EPDK: Eczematoid-like purpura of Doucas and Kapetanakis, PPD: Pigmented purpuric dermatoses, PPLDGB: Pigmented purpuric lichenoid dermatosis of Gougerot and Blum
∓ Independent T-test applied, § Chi-Square/ł Fisher Exact test applied, * p-value ≤0.05 considered as significant

Table 3: Comparison between Schamberg's disease and other PPD (n=65)

Variable	Schamberg's Disease	Other than Schamberg's Disease	p-value
Age (years)	42.5±14.5	43±13.1	0.923[Ŧ]
	n (%)	**n (%)**	
Gender			
Female	23 (52.3%)	07 (33.3%)	0.152[§]
Male	21 (47.7%)	14 (66.7%)	
Employment Status			
Employed	14 (30.9%)	11 (55%)	0.069[§]
Unemployed	30 (69.1%)	10 (45%)	
Obesity			
Yes	35 (79.5%)	16 (76.2%)	0.758[§]
No	09 (20.5%)	05 (23.8%)	
Ultrasound Colour Doppler findings			
Normal	13 (35.1%)	08 (38.1%)	0.822[§]
Abnormal	24 (64.8%)	13 (61.9%)	
Comorbidities			
No	16 (36.4%)	9 (42.9%)	0.615[§]
Yes	28 (63.6%)	12 (57.1%)	
Clinical varicosities			
No varicosities	22 (50%)	5 (23.8%)	0.045[§]*
Varicose veins present	22 (50%)	16 (76.2%)	
Features of chronic venous disease			
Absent	31 (70.5%)	08 (38.1%)	0.013[§]*
Present	13 (29.5%)	13 (61.9%)	

Ŧ Independent t -test applied, § Chi-Square test applied, * p-value ≤0.05 considered as significant

Clinically detectable varicose veins were present in 38 (58.5%) patients and absent in 27 (41.5%) patients. Feature of chronic venous disease were absent in 39 (60%) patients. While, 26 (40.0%) showed presence of specific findings which were venous stasis 20 (30.8%), venous ulcer 16 (24.6%), venous eczema 15 (23.1%), lipodermatosclerosis 10 (15.4%) and atrophie blanche 2 (3.1%) patients.

Patients had diagnosed with comorbid were 40 (61.5%) and no comorbid were 25 (38.5%). Out of these 40 patients, only 12 (30%) had single comorbid while other 28 (70%) had more than one comorbids. The most commonly reported comorbid was hypertension 30 (46.2%), followed by diabetes mellitus 18 (27.8%), hyperlipidemia 12 (18.5%), osteoarthritis 6 (9.2%), nonalcoholic fatty liver disease 5 (7.7%), and ischemic heart disease 4 (6.2%).

An insignificant difference of PPD patients with and without varicosities were found between age (p-value 0.369), occupation (p-value 0.105), obesity (p-value 0.910) and PPD type (p-value 0.110). Patients with varicosity were significantly higher in male 25 (65.8%) as compared to female 13 (34.2%), (p-value 0.022). Patients had no clinical varicosities and had no findings of CVD were significantly higher as compared to patients had clinical varicosities and had CVD present, i.e. 25 (92.6%) and 24 (63.2%) respectively, (p-value <0.0001). (Table 2)

Comparison of Schamberg's and other PPD showed statistically significant difference between clinical varicosities (p-value 0.045) and features of chronic venous disease (p-value 0.013) while, insignificant difference was found with respect to age (p-value 0.923), gender (p-value 0.152), occupation (p-value 0.069), obesity (p-value 0.758), and comorbids (p-value 0.615). (Table 3).

DISCUSSION

In this current study; Schamberg's disease was the most common variety constituting up to two-third of PPD cases. Obesity was present in almost three-quarter of patients. Clinically detectable varicose veins and subsequent detection of venous reflux on colour doppler ultrasonography was present in more than half of the patients. Majority had medical comorbids. Males were twice more commonly affected with varicosities.

Varicose veins were present in half of Schamberg's disease while in three-quarter of other PPD patients. In this present study, mean age of patients was calculated to be forty-three years with male to female ratio of 1.2:1. There was no correlation with occupation or employment status and no gender predisposition for any specific PPD type. Gönül et al. and Ozkaya et al. from Turkey reported mean age of forty nine and forty six years respectively.[12,13] Sharma & Gupta from India highlighted a slightly younger mean age of thirty four years in their analysis.[14] Kim et al. from Korea and Huang et al. from Taiwan described mean age of forty three and fifty two years in their respective studies.[15,16] Regarding gender distribution; all above mentioned authors described similar male to female ratios in their corresponding studies.[12-16] Gupta et al. proposed a possible relationship between PPD and occupations which involved prolonged standing on daily basis.[17] No impact of occupation was notified by others. All above mentioned results are in accordance with this study.

As per current study findings, Schamberg's disease was reported in sixty five percent of the cases. Unilateral involvement was detected in three percent cases only. Majocchi's disease and Lichen aureus were not found. Similar dominating percentages for Schamberg's were also reported by many other authors in their respective studies.[12-15,18] The non-existence of certain PPD types in our population could be due to genetic, geographic and environmental factors. However, Huang et al.[16] mentioned unilateral involvement in twenty one percent PPD cases in their series while others didn't report any existence of unilateral variants in their studies due to extreme rarity of this variant.[12-15]

This current study revealed about presence of abnormal USF in sixty four percent patients, detectable dilated veins in fifty nine percent, and presence of venous stasis in thirty one percent PPD cases. Males were twice more commonly affected with varicosities when compared with females. Gonul et al. apprised varicosities in twenty percent and varying degrees of ultrasonographic venous insufficiencies in seventy five percent of PPD patients.[12] Liau et al. notified venous insufficiency in six percent cases.[19] Kim et al. disclosed venous stasis in eight percent PPD patients.[15] On the contrary, Gupta et al. emphasized absence of venous insufficiency in all subjects.[17] So far, no other study highlighted these factors.

As per the present study statistics, a total of ninety three percent patients who had no clinical varicosities had no findings of CVD on cutaneous examination, $p<0.0001$. This evidence supported the concept of venous hypertension as the main pathogenic factor implicated in PPD. Persistent venous hypertension led to malfunctioning of venous valves in superficial venous system, which then caused venous reflux and subsequent formation of varicosities. All these events have contributory roles in development of PPD but their exact aetiopathogenesis has yet to be elucidated.

This study divulged presence of hypertension, diabetes mellitus and hyperlipidemia as predominant comorbids associated with PPD. This study also notified coexistence of obesity in seventy nine percent of PPD cases which no other study in the literature has documented yet. Gupta et al. from India, recently, outlined exactly same predominant comorbids in the same sequence associated with PPD.[17] Gonul et al.,[12] Kim et al.[15] and Cho et al.[20] delineated diabetes mellitus and hypertension while Dessoukey et al. notified hepatitis B or C infection as predominant comorbids.[21] Ozkaya et al. and Tato et al. disclosed hyperlipidemia as the principal culprit among patients of PPD.[13,22] On the other hand, Huang et al. described hypertension, hyperlipidemia, gout and autoimmune diseases as commonly associated factors in PPD.[16]

There is no uniform consensus over exact aetiology and predisposing elements of PPD. Gonul et al. from Turkey reported venous insufficiency and hypercholesterolemia as main predisposing factors of PPD in their study.[12] Sharma and Gupta from India correlated PPD with prolonged standing in day-to-day work and defined its strong relation with occupation.[14] Huang and associates from Taiwan mentioned that co-existing hypertension, hyperlipidemia and diabetes have some etiological association with PPD.[16] Kim and colleagues from Korea suggested some inter-relationship of PPD with cardiovascular diseases and its medications.[15] There are no prior studies published from Pakistan over this topic.

In abridgement; this present study notified that presence of venous insufficiency which can possibly lead to clinical varicosities; obesity; and comorbidities like hypertension, diabetes and hyperlipidemia were main cofactors linked with PPD. This is the first study published from Pakistan. Although PPD is not a life-threatening disorder but control of its risk factors might help in prevention of this disease in future. Therefore, various risk factors detected with PPD in this study need to be elucidated in detail via large-scale, multicenter, case-control studies.

Limitations of this study were small sample of patients, retrospective analysis, single-center study, lack of controls, non-availability of patch testing facilities, absence of histopathological data, and missing local studies for comparison.

CONCLUSION

This current study is notifying presence of varicosities with/without features of CVD particularly in PPD other than Schamberg's disease, male sex, obesity and comorbidities like hypertension, diabetes and hyperlipidemia as main risk factors associated with PPD in Pakistani population. These are mostly controllable and potentially preventable conditions. So, in future, PPD can be prevented if its exact pathogenesis will be figured out.

ETHICAL APPROVAL: The study protocol was approved by the Institutional Ethical Review Committee the Indus Hospital Karachi, Pakistan
(IRB#: IRD_IRB_2020_04_020).

AUTHORS' CONTRIBUTION: YAM:Conception & designing of the study, critical review of the literature, elaboration and writing of the manuscript, drafting of the article, approval of the final version of the manuscript.
AJ: Collection and interpretation of the data, statistical analysis of the data, elaboration and writing of the manuscript, drafting of the article, approval of the final version of the manuscript.

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