

Descriptive assay of the clinico-morphological characteristics of dermatoses presenting with reticulate pigmentation

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ABSTRACT

Background: Reticulate pigmentation is characterized by freckle-like lesions configured to form a net-like or chicken-wire configuration with varying degrees of pigmentation. It intermingles with similar terms such as *mottled pigmentation* and *dyschromia* and poses difficulty in classification. Both genetic and acquired dermatoses may present with reticulate patterns yet may vary in morphology as well as the age of onset and presentation. **Materials and methods:** This was a hospital-based, descriptive, observational study conducted on thirty-two patients over a period of fifteen months at the dermatology OPD. Patients presented with reticulate pigmentary dermatoses were enrolled in the study after giving written informed consent. A detailed history and clinical examination were performed, and findings were recorded on a standard predesigned proforma. The data was analyzed with appropriate statistical tests. **Results:** In our study, a total of thirty-two patients with reticulate pigmentary dermatoses were enrolled, fourteen males and eighteen females, yielding a male-to-female ratio of 1:1.28. The most common age group affected was 41–50 years (28.12%). The onset of lesions was in young to middle adulthood (56.25%), followed by childhood and teenage years (34.37%). The most common disorder found was erythema ab igne (15.62%), while livedoid vasculopathy, Dowling–Degos disease, and confluent reticulate papillomatosis each constituted 9.37% of cases. **Conclusion:** This study assisted to incorporate the spectrum of RPD and to assess its frequency, morphological patterns, and prognosis. Owing to the paucity of research studies on RPD, the present study will be helpful in exploring future treatment modalities, thereby decreasing the enigma and concerns associated with RPD.

Key words: Reticulate pigmentary dermatoses, Net-like lesions, Dyschromia

INTRODUCTION

Reticulate dermatoses are clinically described as a wide range of dermatological conditions with a net-like arrangement of skin lesions. One of its subset, reticulate pigmentation, denotes a group of diseases characterized by the presence of hyper- and/or hypopigmented macules with varying sizes and degrees of pigmentation [1]. However, a group of disorders with reticulate pigmentation still poses a problem regarding its categorization due to numerous conditions under the umbrella term exhibiting patterns other than reticulate yet demonstrating close similarity with terms such as *dyschromia* and

poikilodermatous disorders. To overcome this, some authors use the broader term *mottled pigmentation*, that is, mixed, hyper- and/or hypopigmented macules in a blotchy pattern, to encompass all aforementioned conditions [2,3].

Moreover, the term *reticulate pigmentary dermatoses* (RPD) may also be preferred to incorporate a heterogenous group of disorders characterized by hyperpigmented, freckle-like macules with varying sizes and amounts of pigmentation coalescing at the margin to form a net-like/reticular pattern, sometimes associated with scattered, hypopigmented macules between hyperpigmented lesions [4,5].

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Among various reticulate pigmentary dermatoses, prototype or true reticulate pigmentary disorders have the morphology of classic freckle-like hyperpigmentation and consist of reticulate acropigmentation of Kitamura (RAPK), reticulate acropigmentation of Dohi (RAPD), and Dowling–Degos disease (DDD). Some acquired dermatoses such as lichen planus pigmentosus, livedo reticularis, and prurigo pigmentosa may also present with mixed hyper- or hypopigmented macules with a reticular pattern. This typical reticulate pattern may also be associated with autoimmune disorders such as scleroderma, lupus erythematosus, and certain metabolic, infectious, and vascular conditions [6].

Most of the true reticulate pigmentary disorders are genetically inherited and occur in infancy and early childhood, with a possible exception of DDD and RAPK, in which lesions may begin during adolescence or adult/middle age. Although genetic mutations have been identified in various true reticulate pigmentary disorders, genetic predispositions, alterations, and susceptibilities have not been elucidated comprehensively [7].

Different reticulate pigmentary dermatoses may be classified on the basis of their origin, onset, distribution, and mode of inheritance, as these features may provide a distinguishing clue between true and other acquired conditions presenting with a reticulate pattern. Yet, often, an overlap in multiple features exists due to the absence of a remarkable morphological pattern of isolated dermatoses.

In purview of the absolute scarcity of larger studies of the spectrum of dermatoses displaying the reticulate pattern and limited epidemiological data in central India, the present study may be helpful in determining the spectrum of various pigmentary patterns and in ascertaining a better clarification of closely related true and acquired dermatoses exhibiting reticulate pigmentation.

Objective

The present study aimed to assess the frequency, distribution, and clinico-morphological patterns of dermatoses presenting with reticulate pigmentation.

METHODOLOGY

A hospital-based, descriptive, observational study was conducted on thirty-two patients over a period of twelve

months at the dermatology outpatient department. Patients presenting with clinical features suggestive of reticulate pigmentary lesions were enrolled in the study after giving written informed consent.

Inclusion Criteria

Patients with genetic reticulate pigmentary disorders as well as acquired dermatoses leading to mixed hyper- to hypopigmentary macules primarily or secondarily were included in the study. We enrolled disorders displaying hyper- and/or hypopigmented macules with a reticulate pattern and encompassed them under reticulate pigmentary dermatoses (RPD).

Exclusion Criteria

Patients with a reticulate pattern secondary to infections, drugs, malignancy, and syndromes were excluded due to their reticulate pattern being auxiliary and having a non-dominant mode of presentation.

A detailed history, including the age at onset, the duration and progression of lesions, and site-wise distribution along with the history of concomitant cutaneous or systemic illnesses was taken. A history of sun exposure, friction, atopy, and hereditary associations in siblings or first-degree family members were also recorded. A history of exposure to chemicals or drugs was obtained as well.

A complete clinical examination was performed, and the morphology of the lesions—color, shape, distribution, size, pigmentary density, and associated secondary changes—was evaluated. Associated changes in the teeth, nails, hairs, and orogenital mucosa, as well as Fitzpatrick skin types, were also examined and recorded on a standard predesigned proforma.

All routine investigations, including HbA1c, thyroid function test, lipid and metabolic profiles, liver and renal function tests, and peripheral smear for atypical cell, were performed. Dermoscopy and skin biopsy were done in doubtful cases. The data was compiled in an Excel sheet and analyzed with SPSS Statistics.

RESULTS

In our study, thirty-two patients out of all patients visiting the dermatology OPD over a period of fifteen months had reticulate pigmentary lesions, with a frequency of study-specific dermatoses of 0.09%.

Among the enrolled patients, female cases (18) outweighed male (14), with a male-to-female ratio of 1:1.28. The mean age of the patients was 31.63 ± 15.24 years, with an almost equal proportion of young adults belonging to the 21–40 year age group and middle-aged adults belonging to the 41–60 year age group. Cases of the extreme age group constituted 18.75% (Fig. 1).

The onset of the lesions was in young to middle adulthood (56.25%), followed by childhood and teenage years (34.37%). Similarly to the age of presentation, the onset of the lesions was the least (9.37%) in polar ages. The onset of the lesions was insidious in 66.6% and abrupt in the remaining 33.62% of cases of RPD. The average duration of the lesions was 1–5 years in almost half of all cases of RPD, with an equal proportion of cases (16.12%) falling into less than six months, as well as 6–12 months, with a mean duration of 5.97 ± 6.17 years.

The progression of RPDs did not follow the typical spread in the majority of cases and was proximal to distal acral or vice versa in 43.75% of the cases from the commencement of the lesions till complete evolution. Due to the changing pattern of RPDs, our study provided a definite difference between the age of onset and the age of presentation with a special reference to site-specific changes.

An advancing rate of progression of pigmented lesions had a marginal edge on steady lesions so was true in the pattern of density of RPDs, in which discrete lesions had a precedence over confluent ones. The average size of the lesions ranged from 3–5 mm in 65.62% of all RPD cases, with pin-point lesions constituting only around one-fifth of all cases. The intensity of pigmentation was higher in the flexures when compared to the trunk or face (Table 1).

We adopted the classification proposed by Sinha [2] and Sardana [3] to further classify various RPDs, and

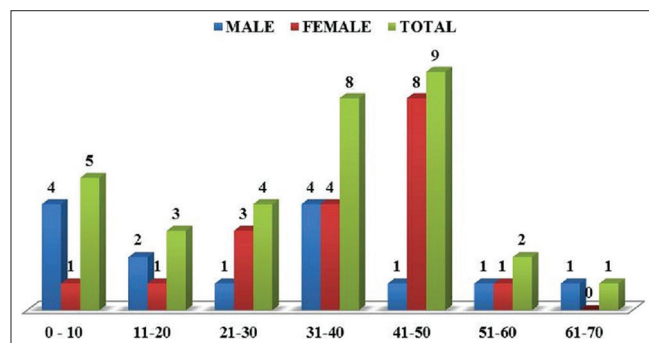


Figure 1: Age and sex distribution of RPDs.

found true RPD in seven cases, genetic disorders with secondary reticulate pigmentation in two cases, dermatoses with reticulate pigmentation in fifteen cases, and autoimmune and miscellaneous conditions in two and six cases, respectively (Table 2).

As per the overall site-specific involvement of RPD, the upper limbs constituted 46.87%, closely followed by the lower limbs in 40.62%, the trunk in 31.25%, and the back in 21.87%. The face and neck were involved in 15.62%. The site-specific onset of the lesions differed from that of site-wise distribution at the time of presentation and was attributed to the progressive nature of disorders in around half of them (Table 2).

The most common disorder found in this study was erythema ab igne (15.62%). Livedoid vasculopathy, Dowling–Degos disease, and confluent and reticulated papillomatosis each constituted 9.37%. Among the most common dermatoses in the studied population, truncal involvement was observed by large in 60% of all cases of erythema ab igne, while upper and lower limb involvement was observed in 40% of the cases each. The legs were exclusively affected in three out of four cases (75%) of livedoid vasculopathy, while the

Table 1: Morphological patterns of the reticulate pigmentary dermatoses

| Feature | n (%) |
|---------------------------------|-------------|
| Age of onset | |
| Since birth | 2 (6.25%) |
| Childhood (till 12 yrs. of age) | 5 (15.62%) |
| Teenage | 6 (18.75%) |
| Adulthood | 18 (56.25%) |
| Old age | 1 (3.12%) |
| Duration of lesions | |
| < 6 months | 5 (15.62%) |
| 6–12 months | 5 (15.62%) |
| 1–5 yrs. | 16 (50%) |
| > 5 yrs. | 6 (18.75%) |
| Manner of progression | |
| Acral | 14 (43.75%) |
| Centripetal | 7 (21.87%) |
| Centrifugal | 11 (34.37%) |
| Course of lesions | |
| Static | 14 (43.7%) |
| Progressive | 18 (56.25%) |
| Size of lesions | |
| < 1 mm | 7 (21.87%) |
| 1–3 mm | 2 (6.25%) |
| 3–5 mm | 21 (65.62%) |
| > 5 mm | 2 (6.25%) |
| Density of pigment | |
| Confluent | 15 (46.87%) |
| Discrete | 17 (53.12%) |

Table 2: Site-wise distribution of the reticulate dermatoses

| | Disorder | Area of distribution |
|---|---|--|
| True (genetic) RPD | Dowling–Degos disease = 3 (9.37%) | Neck, axilla, hands = 1 Forearms and hands = 2 |
| | Reticulate acropigmentation of Dohi = 2 (6.25%) | Dorsum of hands = 1 Dorsum of feet and legs = 1 |
| | Reticulate acropigmentation of Kitamura = 2 (6.25%) | Dorsum of Hands = 1 Dorsa of hands and feet = 1 |
| Genetic disorders with secondary reticulate pigmentation | Epidermolysis bullosa with mottled pigmentation = 1 (3.12%) | Arms, forearms, abdomen = 1 |
| | Cutis marmorata telangiectatica congenita = 1 (3.12%) | Face, legs, abdomen = 1 |
| Dermatoses presenting with de novo or secondary reticulate pigmentation | Confluent and reticulate papillomatosis = 3 (9.37%) | Neck, axilla, inframammary area, trunk = 2 Back = 1 |
| | Prurigo pigmentosa = 1 (3.12%) | Trunk and thighs = 1 |
| | Dyschromic amyloidosis = 2 (6.25%) | Shoulders and upper back = 1 Arms and back = 1 |
| | Cutis marmorata = 2 (6.25%) | Face and upper limbs = 1 Trunk and legs = 1 |
| | Livedo reticularis = 2 (6.25%) | Lower legs = 2 |
| | Livedoid vasculopathy = 3 (9.37%) | Face and feet = 1 Legs = 2 |
| | Lichen planus pigmentosus = 2 (6.25%) | Trunk = 1 Trunk and upper limbs = 1 |
| Autoimmune disorders with mottled pigmentation | Systemic sclerosis = 2 (6.25%) | Back, forearms, legs = 2 |
| | Miscellaneous conditions | Erythema ab igne = 5 (15.62%) |
| Atrophoderma vermiculatum = 1 (3.12%) | | Cheeks = 1 |

upper limbs were predominant sites in all three cases of Dowling–Degos disease. Confluent and reticulated papillomatosis involved the trunk in 66.6% and the back in 33.3% of cases.

Among the various RPDs, systemic involvement was seen in the total seven patients (21.87%). Individually, one case of dyschromic amyloidosis was associated with hypertension and diabetes, two cases of livedoid vasculopathy, and one of livedo reticularis were associated with varicose veins. Asymmetry of the limbs and hip dysplasia were the anomalies found in cutis marmorata telangiectatica congenita. Among the autoimmune dermatoses, interstitial lung disease was present in both cases of systemic sclerosis.

DISCUSSION

The net-like configuration of reticulate pigmentary dermatoses, although peculiar, is not essentially found in all true and acquired subtypes, therefore leads to problems in primarily recognizing them according to the dominant morphology. Also, the variable pigmentation pattern among each subtype and related conditions such as mottled pigmentation and dyschromia adds further hurdles due to the different

phenotypical expressions of a similar gene defect, hence the terms are often used interchangeably, leading to difficulty in defining each disorder and finding appropriate demographic data.

Based on our experience from the present study and literature research, the term *reticulate pigmentary dermatoses* (RPD) was found to be expedient to explicate dermatoses enrolled in our study, which presented with hyperpigmented macules with varying sizes and amounts of pigmentation, arranged in a net-like pattern with or without hypopigmented macules.

Considering the female predominance and erythema ab igne being the most common individual RPD in our study, similar sex preponderance was seen in the study done on patients with erythema ab igne by Murat Ozturk et al. [8], who observed a male-to-female ratio of 1:2. In terms of true RPD, the present study mirrored the case series conducted by Chandramohan et al. [9], in which the male-to-female ratio was 1:2.

The most common age group affected (41–50 years) and the mean age of cases (31.63 years) in the present study differed from the study by Namitha et al. [10] on a case series of five cases of dyschromia, in which the most common age group affected was 21–30 years

(60%), with a mean age of 19.2 years. This negates the preconceived belief of the early age onset of RPDs, although the assertive number of acquired RPDs with a relatively later presentation cannot be overlooked.

The most common age of onset (adulthood: 56.25%) and the mean duration (5.97 years) belonging to our study slightly differed from the study conducted by Katoulis et al. [11] on fifty patients with poikiloderma of Civatte, among which the mean age at diagnosis was 47.8 years for females and 61.7 years for males, with a mean duration from onset to diagnosis of 6.2 years. Our assumption concerning the onset of lesions would have been earlier if the study involved only true RPDs with a possible exception of some secondary disorders complying an early advent.

In our study, acral progression of the lesions was found in approx. 2/5 of the cases, and the association with systemic illnesses was found in approx. 1/5 of all RPD cases. A comparison could not be done due to a lack of specific data in the literature and in view of the limited sample size. Similarly, other variables such as the rate, size, and density of RPDs were the first to be described comprehensively in the present study.

Individual Dermatoses and Distribution

Erythema ab igne

It is an acquired dermatosis characterized by erythematous to violaceous patches with a reticular configuration usually on the sites of exposure to heat or thermal radiation. It accounted for 5 (15.62%) cases in our study, with 4 out of 5 patients in the age group of 41–50 years. The trunk (60%) and thighs (40%) were the most common sites affected (Fig. 2a). This observation was synonymous with the study by Raza et al. [12], in which 0.3% of 4563 registered patients were diagnosed with erythema ab igne and 42.8% of the cases fell into the 41–50 year age group.

Livedo vasculopathy and livedo reticularis

Livedo vasculopathy is a disorder characterized by painful, purpuric lesions predominantly on the gaiter area of the lower limbs, while livedo reticularis predominantly presents with blotchy, reddish-blue to purple, net-like discolorations on the legs. In our study, livedo vasculopathy was present in 3 (9.37%) patients, with 2 cases (66.6%) in 2–3 decades of life, while livedo reticularis was noted on the legs in 2 (6.25%) cases (Fig. 2b). In a study conducted by Emily et al. [13] on seventy patients with livedoid vasculopathy, 47% of the cases presented between 21–40 years of age.

Confluent and reticulate papillomatosis (CRP)

CRP is a benign acquired keratinization disorder characterized by scaly, brownish, centrally confluent, reticulate macules that coalesce to form patches. In the present study, CRP was found in 9.37% of the cases, with 66.6% belonging to the 21–30 year age group and a male-to-female ratio of 2:1. In an analogous study conducted by Shashikumar et al. [14] on thirty patients with CRP, the mean age at the onset of eruptions was 17–48 years and the male-to-female ratio was 1:1.5.

Dowling–Degos disease

Among all reticulate disorders, DDD was found in 9.37% of our cases, among which 2 patients (66.6%) were females and 1 (33.33%) was male (Figs. 3a and 3b). None showed systemic abnormalities. These findings differed from the study by Agut Busquet et al. [15] on fifteen patients with DDD, revealing males in 53% of the cases and females in 47%, with 20% of the cases being hypertensive.

Reticulate acropigmentation of Kitamura (RAPK)

RAPK is an autosomal dominant disorder characterized by reticulate, atrophic, freckle-like hyperpigmentation most commonly on acral areas. In the present study, RAPK was found in 2 patients, a mother and daughter from the same family (Fig. 2c). The lesions involved the



Figure 2: (a) Erythema ab igne: erythematous, reticular pattern on the extensor aspect of the forearm. (b) Primary livedo reticularis: erythematous-to-pigmented, blotchy lesions on the leg. (c) Reticulate acropigmentation of Kitamura: hyperpigmented macules on the bilateral hands. (d) Dyschromic amyloidosis: mixed, hypo- to hyperpigmented lesions on the arms.

face, hands, and feet. A study conducted by Kocaturk et al. [16] reported a familial case of acropigmentation of Kitamura in a 53-year-old female and her daughter with a similar presentation. We also witnessed the circumstantial shift of disorders within the same spectrum with changes in the site-specific distribution of disease in 3 out of 5 patients with DDD and RAPK collectively.

Reticulate acropigmentation of Dohi (RAPD)

RAPD was found in 6.25% of the cases who presented with hypopigmented macules on the dorsal extremities (Figs. 4a and 4b). A similar observation was seen by Peng et al. [17] in a study on 25 patients with dyschromatosis symmetrica hereditaria, with the typical sites being the extremities in 48% of the cases.

Dyschromic amyloidosis

In the present study, dyschromic amyloidosis, a rare form of typical reticulate hyperpigmentation interspersed with hypopigmented-to-depigmented macules was present in 2 (6.25 %) cases, with a female preponderance and the involvement of the arms and back in both cases (Fig. 2d). This was analogous to

a case study on amyloidosis cutis dyschromica by Yang et al. [18] on two female siblings, who both presented with diffuse, mottled hyperpigmentation and hypopigmentation involving the trunk, upper limbs, and thighs.

Lichen planus pigmentosus

The trunk (100%) and upper limbs (50%) were the predominant sites in 2 enrolled cases of lichen planus pigmentosus with an equal sex dominance and a reticular variant in both. A case report of lichen planus presenting as reticulate pigmentation by Sinha et al. [19] involving a 61-year-old male patient had a network-like pattern of pigmentation on the trunk and limbs.

Prurigo pigmentosa

In our study, we found a single case of prurigo pigmentosa, which is a rare entity, also known as Nagashima disease [20]. The distribution of hyperpigmented, reticular lesions was generalized, involving predominantly the trunk and limbs for four months in our only patient with prurigo pigmentosa. Similar features were recorded in a case series by Schevchenko et al. [21] on two patients, who presented with erythematous and hyperpigmented, reticulate eruption on the back, trunk, and shoulders apparent for two weeks and three months, respectively.

Cutis marmorata telangiectatica congenita (CMTC)

We found a single case of CMTC, in a male child (Fig. 5) who presented with erythematous, net-like lesions on the face, abdomen, and thighs, while Kienast et al. [22], in a prospective study of 27 cases, reported leg involvement in 74% of the cases and the face in 15%.

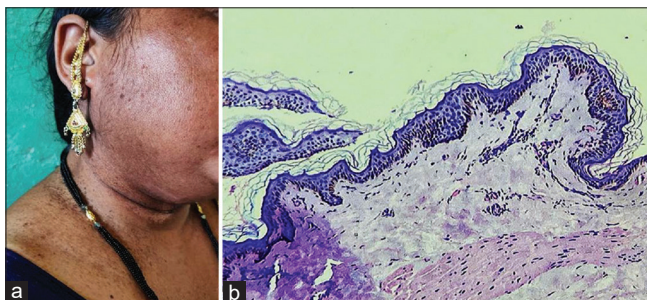


Figure 3: Dowling–Degos disease: (a) hyperpigmented macular lesions on the face, neck, and shoulders; (b) photomicrograph of DDD showing atrophic epidermis and flattened rete ridges with an antler-like appearance without pigment incontinence (H&E, 40x).



Figure 4: (a and b) Reticulate acropigmentation of Dohi: a) admixture of mottled pigmentation on the bilateral feet; b) photomicrograph of RAPD showing focal thinning of the epidermis, dilated follicular infundibula with a keratin cyst, and basal layer hyperpigmentation (H&E, 40x).



Figure 5: Cutis marmorata telangiectatica congenita: net-like, erythematous, telangiectatic lesions on the face in a child.



Figure 6: Epidermolysis bullosa simplex: bullae with crusts on the face and hands with mottled pigmentation on the abdomen.

Epidermolysis bullosa simplex with mottled pigmentation (EBS)

We found one case of EBS (3.12%) in a male child, who presented with bullae and crusted lesions on the face, limbs, and abdomen along with mottling on the abdomen (Fig. 6). A case of EBS with mottled pigmentation reported by Browning et al. [23] presented with hyperpigmentation involving the axilla, forearms, anterior shin, and dorsa of the feet in a seven-year-old boy.

Reticulate pigmentary dermatoses found in our study, although progressive, were expected to have a favorable outcome in the majority. A detailed evaluation of the patients assisted in more precise understanding of morphology, patterns, onset, and possible progression potential, whose analysis had been substantially missing in individual case reports or case series so far.

A positive family history in some RPDs served as an aid in genetic counseling. Studying some of the acquired reticulate dermatoses, such as dyschromic amyloidosis, erythema ab igne, lichen planus pigmentosus, revealed possible etiological and predisposing factors imperative to the pathogenesis of the diseases.

CONCLUSION

In this study, we attempted to rationally classify all reticulate pigmentary dermatoses and analyze each condition clinically and demographically, which helped

us to predict their prevalence, various demographic and morphological features, and management strategy. Through these cases and this literature review, it was our initial effort to incorporate the spectrum of RPDs and, from the epitome of morphological uncertainty, we hoped to delineate the unique clinical, histological, and genetic features of such a diverse group of dermatoses.

This study also helped to predict the impending recurrences and other systemic features accompanying reticulate dermatoses that could prepare the patient and the treating physician to expect a realistic diagnostic and therapeutic outcome. These observations may also be noticeable for equivalent succeeding cases to further explore any remote association. This short literature was an attempt to fill the existing lacunae in the research of RPD and to discover future modalities to provide aesthetic confidence to patients with treatable RPD and to decrease the associated enigma and concerns associated with these dermatoses.

Study Limitations

The major limitations of this study were a relative unavailability of comparative research data on reticulate pigmentary disorders, a lack of clearance regarding inconclusive histopathological findings in differentiating overlapping disorders of the same group, and restricted resources in conducting higher and specific diagnostic interventions, such as immunofluorescence.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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