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Dermatology

# A CLINICAL STUDY ON DARIER'S DISEASE IN PATIENTS ATTENDING GOVERNMENT GENERAL HOSPITAL, KADAPA.

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**ABSTRACT** **Background:** Darier's disease is a rare congenital acantholytic disorder transmitted as an autosomal dominant trait with complete penetrance, characterized clinically by persistent eruption of greasy hyperkeratotic papules in seborrheic regions, nail abnormalities, mucous membrane changes, and histologically by acantholysis and dyskeratosis. **Objectives:** To study the clinical and epidemiological features of Darier's disease. **Materials and methods:** All patients with cutaneous features suggesting of Darier's disease attending the department of DVL, Government Medical College, Kadapa, between June 2019 to June 2020. Having received consent from the patient, detailed history, thorough general and dermatological examination and relevant investigations were done. **Results:** In the current study, Peak age of incidence was between 11-20, 50% had family history, 100% had cutaneous involvement, 83.33% had nail involvement and oral mucosa involvement in 16.66%, which are similar to the studies like Burge and Wilkinson 1992, Goh et al., 2004, Zeglaoui et al., 2004, Sevil savas et al., 2018. **Conclusion:** We presented this study to report on Darier's disease as a rare condition encountered in the differential diagnosis of dermatosis with keratotic papular lesions and emphasize its clinical diversity.

**KEYWORDS :** Darier's disease, Rare Genetic disorder, Greasy hyperkeratotic papules.

**Introduction:**

Darier's disease is an autosomal dominant inherited Geno dermatosis characterized by abnormal keratinization of the skin, and involvement of the nails and mucous membrane, however, it is not always familial.[1] It mostly develops in the first two decades of life, but the onset can also be at a later age.[2],[3] The characteristic clinical manifestation of the disease is squamous hyperkeratotic yellow-brown papules and plaques over seborrheic and flexural areas of the body.[4] Diagnosis is based on the typical clinical appearance and histological findings revealing acantholytic dyskeratosis.[4].

**Methodology:**

This was an observational study conducted in Government General Hospital, Kadapa over a period of 1 year from June 2019 to June 2020. All patients, who presented with the primary symptoms, suggestive of Darier's disease, attending OPD in department of DVL were subjected to detailed history and clinical examination. During the study period, a total of 12 cases were selected after taking their consent. There was NO conflict of interest.

**RESULTS:**

**Table no 1: Age Distribution**

| AGE | NUMBER OF CASES | PERCENTAGE |
|---|---|---|
| 11-20 | 4 | 33.33 |
| 21-30 | 3 | 25 |
| 41-50 | 1 | 8.33 |
| 51-60 | 2 | 16.66 |
| 61-70 | 1 | 8.33 |
| 71-80 | 1 | 8.33 |
| TOTAL | 12 | |

**Table no 2: Sex Distribution**

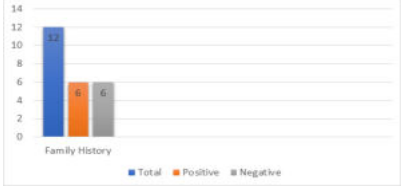
| SEX | NUMBER OF CASES | PERCENTAGE |
|---|---|---|
| **Male** | **7** | **58.33** |
| **Female** | **5** | **41.66** |
| **Total** | **12** | |

**Table no 3: Clinical Features**

| Involvement | Number of cases | Percentage |
|---|---|---|
| **Cutaneous** | **12/12** | **100%** |
| **Nail** | **10/12** | **83.33%** |
| **Mucous membrane** | **2/12** | **16.66%** |

**Table no 4: Cutaneous Changes**

| Cutaneous changes | Number of cases | Percentage |
|---|---|---|
| **Yellowish brown papules** | **12/12** | **100%** |
| **Hyperkeratotic plaques** | **2/12** | **16.66%** |
| **Palmar pits** | **7/12** | **58.33%** |
| **Guttate leukoderma** | **1/12** | **8.33%** |
| **Acrokeratosis verruciformis-like** | **4/12** | **33.33%** |




**Graph no 1: Family History**

**Figure no 1: Hyperkeratotic papules**

**Table no 5: Nail Changes**

| Nail changes | Number of cases | Percentage |
|---|---|---|
| **V shaped nicking** | **8/10** | **80%** |
| **White longitudinal lines** | **9/10** | **90%** |
| **Nail dystrophy** | **4/10** | **40%** |

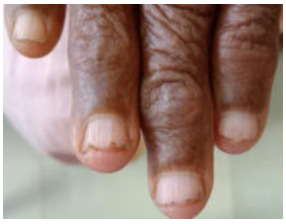


**Figure no 2: V shaped nails**

**Mucous membrane changes**

Cobble stone appearance was seen in 2 cases i.e. 16.66% of the cases.

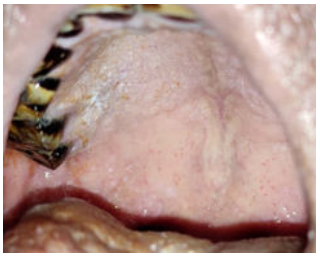


**Figure no 3: Cobble stone appearance**

**DISCUSSION:**

Darier's disease is a rare autosomal dominant inherited disease that involves skin, nails and mucous membranes. It has been reported that both genders are equally affected, and the prevalence varies between 1/36,000 and 1/100,000[2],[3]. A mutation in the ATP2A gene encoding the sarcoplasmic/ endoplasmic reticulum calcium ATPase 2 has been found in the molecular basis of Darier's disease. This mutation leads to the loss of the epidermal connection caused by acantholytic and dyskeratotic cells, such as corps ronds and grains, which are characteristic of Darier's disease [8]. Over time, the lesions unite to form plaques and vegetating masses, creating a thick and dirty appearance. Punctate keratoses and small pits in the palmoplantar area can be seen.[10],[11] In the nails, thinning, fragility, subungual keratosis and red white longitudinal lines can be present, as well as typical V-shaped splitting and longitudinal fissures on the distal part. Approximately 15% of patients have mucosal lesions in the form of white papules with a central depression (cobblestone appearance) [6], [10-12]. Although Darier's disease is inherited in an autosomal dominant pattern, non- familial cases are seen due to spontaneous mutation or incomplete penetrance [9].

**Table no 6: An overview of the patient characteristics reported in the literature and in this study**

| Sources | Number of cases | Peak age of disease onset (years) | Family history % | Nail Involvement % | Oral mucosal lesions % |
|---|---|---|---|---|---|
| Burge and Wilkinson 1992 | 163 | 11-15 | 71% | 90% | 13% |
| Goh et al.[5], 2004 | 24 | 11-20 | 21% | 50% | 8% |
| Zeglaoui et al. [6], 2004 | 12 | 12-20 | 42% | 58% | 0 |
| Sevil savas et al. [7], 2018 | 9 | 12-22 | 22% | 56% | 11% |
| Current study | 12 | 11-20 | 50% | 83.33% | 16.66% |

The presence of family history was reported as 71% in the study by Burge and Wilkinson [1], 42% by Zeglaoui et al. [6], In the current study 50% of patients had a family history. The lesions occur primarily on seborrheic areas, such as scalp, nasolabial and retroauricular folds, chest and back. Initial lesions are small, hard, skin-colored papules. Later, the papules are covered by dark-black greasy crusts. In the current study, 83.33% of the patients had nail involvement and oral mucosa involvement in 16.66% of the patients which is similar to the corresponding studies mentioned. Localized, unilateral, zosteriform, acral, segmental, and flexural variants of Darier's disease have been defined [1],[13]. Approximately 10% of patients with Darier's disease have the segmental form [14]. In this study, there was 1 patient with predominantly flexural lesions. Darier's disease is frequently accompanied by psychoneurological conditions, including mental retardation, epilepsy, psychosis, and manic Depression [6]. No psychoneurological conditions were found in our patient. Both dyskeratosis and acantholysis are seen in the pathology of Darier's disease. Acantholysis results in suprabasal cleft formation. Corps ronds are dyskeratotic cells in the stratum spinosum and stratum granulosum. They have a pyknotic nucleus and eosinophilic cytoplasm covered by a clear perinuclear halo. Grains are oval cells containing keratohyalin granules and are localized in the stratum corneum [11].

The histopathological features of our cases supported the diagnosis of Darier's disease. In this study, topical retinoids, oral retinoids and steroid therapy was administered to the patients, all patients responded well to the treatment.

**Conclusion:**

We presented this study to report on Darier's disease as a rare condition encountered in the differential diagnosis of dermatosis with keratotic papular lesions and emphasize its clinical diversity.

**Conflict of interest:** Nil

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