""CROSS-SECTIONAL STUDY OF DERMATOLOGIC MANIFESTATIONS IN PATIENTS WITH CHRONIC RENAL FAILURE ON HEMODIALYSIS"

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Dissertation submitted to BLDE (Deemed to be University), Vijayapura.

In partial fulfilment of the requirements for the degree of

M.D

In

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INTRODUCTION

Chronic kidney disease (CKD) is a condition in which there is a step by step deterioration of kidney functions over a period of time through five different stages. The cases diagnosed with end-stage renal disease (ESRD) in India are rising multifold with a rough estimation of about 100 per million population.[1]

Skin being the largest and one of the most important organs of the body can be used as a mirror and a window since it is easily accessible for observation and reflects the changes seen in multiple organs including the kidneys.[3]Renal failure has two stages: acute and chronic stage.[4]Chronic renal failure, also called as end stage renal disease mainly causes reduced kidney functions mainly affecting the excretion of metabolic wastes and maintenance of homeostasis. Cutaneous changes in cases of chronic renal failure are often variable.

The prevalence of chronic kidney disease is increasing multifold in all age groups but significantly in the elderly population, affecting 40% of population aged above 70 years.[5]Renal failure is a problem affecting the entire globe, but the disease has become a major concern in the developed countries.[6]

The cutaneous manifestations in patients undergoing hemodialysis can be broadly classified into specific and non-specific changes. Specific changes mainly include acquired perforating dermatosis, calcific uremic arteriolopathy, bullous dermatoses and nephrogenic fibrosing dermopathy.Non-specific skin manifestations include pruritus, xerosis, nail disorders, hair abnormalities, pigmentary changes, purpura, oral and mucosal changes, pallor and uremic frost are the major manifestations observed.[7]

Many of the features such as pruritus,xerosis, hyperpigmentation and acquired perforating dermatosis can be noticed even in patients who are not on hemodialysis therapy. “Nephrogenic fibrosing dermopathy” and “bullous dermatoses of hemodialysis” are few abnormatities which can be solely attributed to hemodialysis therapy. Prolonging the life span of the chronic kidney disease patients by hemodialysis therapy may tend to cause newer cutaneous manifestations.[8]

The advent of hemodialysis as one of the treatment for chronic renal failure (CRF) has made uremic frost and erythema papulatum uremicum the most commonly encountered cutaneous changes in the predialysis era.[8]

The frequently reported intraoral findings in CRF patients are xerostomia, macroglossia and ulcerative stomatitis.[8] Hair changes namely sparse and lustreless are commonly seen. Half-and-half nails, absent lunulae and onychomycosis are the common nail manifestations observed.[8]

From this study, we wish to establish the cutaneous changes that occur in patients undergoing hemodialysis.

Objective of the study

To study various cutaneous manifestations in chronic kidney disease patients undergoing hemodialysis.

REVIEW OF LITERATURE

Hemodialysis is one of the major treatment modalities in chronic kidney disease patients.[8] CKD is characterized by decrease in the essential functions of the kidneys for more than a period of 3 months with presence of renal damage and altered excretion of the albumin by the kidneys. To estimate the functions of the kidneys we use glomerular filtration rate(GFR) either measured or estimated [9,10].

In patients of end stage kidney disease, major modality of treatment is hemodialysis for the clearance of uremic toxins of low molecular weight. Even though hemodialysis is not very efficient in removal of uremic toxins bound to the proteins it is effective in removing small, water soluble substances and highly efficacious in removal of middle molecular weight substances[11]

CUTANEOUS MANIFESTATIONS OF HEMODIALYSIS

1. XEROSIS

   Also termed as xerosis cutis, ‘xero’ meaning dry. The patient has accentuation of skin markings with overlying fine scaling.It can be associated with skin tightening and itching. Seen in around 50-75% of patients undergoing dialysis[12,13]. The pathogenesis of development of xerosis in dialysis patients remains unknown. Mainly affects the extensors and is characterised by large dark scales, trunk isoccasionally involved. The flexors are seldom affected.

Etiopathogenesis:

a. Reduction in size and function of eccrine sweat glands leading to compromised eccrine secretion leading to epithelial dehydration.[14]
b. Reduced water content in the epidermis.[15]
c. Uraemia disturbs the corneocyte maturation
d. The decrease in the natural moisturising factor (NMF)
e. Deficiencies in skin barrier lipids, ceramides

Treatment

a. Ample usage of emollients, moisturisers and humectants applied twice daily and immediately after bathing to maintain hydration.
b. Low potency steroids including desonide and hydrocortisone.[16]

2. PRURITUS

Pruritus is also one of the most frequently encountered and troublesome cutaneous manifestation of CRF.[2, 11]

The likely cause is due to impaired renal excretion of metabolic wastes mainly the histamine and also allergic sensitization to various dialyzer membrane components.[8] The prevalence among dialysis patients is around 50-90%[2]. Pruritus also presents with secondary changes such as excoriations, lichen simplex chronicus(LSC), prurigo nodularis.

Pruritus has a negative effect in the patient's quality of life, sleep, emotional state and social relationships. It can also contribute to development of infections.

ETIOLOGY:

Pathophysiology of pruritus in dialysis patients is not understood completely, several factors are proposed in its development.

a. Xerosis causes sweat gland atrophy and dehydration of the epidermis[14]
b. Increase in Th1, Th2 cell ratio, Th1 activates cytokines and inflammatory cells and Th2 has anti-inflammatory properties.Thus the imbalance leads to pruritus.
c. Increase in μ receptor agonists.
d. Impaired clearance of pruritogens that are poorly dialyzable substances due to larger molecular size.[17]
e. Increased temperature can aggravate pruritus
f. Hyperparathyroidism, hypervitaminosis A
g. Raised histamine and serotonin levels
h. Mast cell hyperplasia and its degranulation[18]
i. Increased BUN, calcium, phosphorus, aluminum
j. Anemia, erythropoietindeficiency, raised ferritin levels, low transferrin

MANAGEMENT

a. Treatment of xerosis with emollients, moisturizers and humectants
b. Topical corticosteroids, topical tacrolimus[19]
c. Topical capsaicin leads to depletion of cutaneous ion channels and lasting desensitization to pain and pruritusand also decreases the levels of substance P[20]
d. Topical Menthol causes cooling sensation
e. Oral anti histamines
f. Antagonization of μ opioid receptors like naloxone, naltrexone[21,22]
g. Tricyclic anti-depressants like gabapentin and pregabalin [23]
h. Oil of evening primrose[24]

i. UVB therapy suppress the histamine release, photoproducts have an antipruritic effect.[25]

3. SKIN COLOUR CHANGES

I . PALLOR

Anemia of chronic renal disease is seen in 60% of patients undergoing dialysis.[8] Causes being

a. Renal compromise thus producing deficient erythropoietin (responsible for red cell production)
b. Uremia (red cell deformity)
c. Folate, vitamin B12 and iron deficiency
d. Anemia of chronic disease

II. PIGMENTARY CHANGES

β-melanocyte levels are poorly excreted by the damaged kidneysleading to diffuse hyperpigmentation.[26]

Two types of pigmentary changes that are generally observed are:

a. Hyperpigmentation

b. Yellowish tinge of the skin.

Etiology

a. Prominent hyperpigmentation over the sun-exposed areas is due to increased melanogenesis and deposition of melanin.
b. The yellowish tinge to the skin is due to carotenoids and lipochromes which are present in the epidermis and subcutaneous tissue.[8]

III. ECCHYMOSIS

Characterized by unusual bruising to minimal trauma.[27,28]

a. Usage of heparin in the procedure of dialysis.

b. Skin aging causes loss of elasticity

c. Uremia

4. NAIL CHANGES

I. Half and half nails

Also known as Lindsay nails. The typical nail change seen in renal failure patients. Seen in 40% of the patients undergoing dialysis[29]. A distal dark/ hyperpigmented band and proximal white band. Seen more commonly on the fingernails than the toenails

Causes

a. Increased β-melanocyte concentration in the distal half

b. Proximal white band is due to edema of the nail bed[29]

II. Muehrcke's lines

They are white bands parallel to the lunulae, with regions of normal or pink discoloration between the bands. They represent apparent leukonychia.

Local edema in the nail beds causes pressure on the underlying vasculature. Associated with hypoalbuminemia. [30]

III. Beau's lines

Transverse grooves on the nail plate indicating temporary arrest in the nail growth. The distance between the grooves and the nail fold is indicative of

the duration of the disease. The depth and width are indicative of the severity. [30]

5. HAIR ABNORMALITIES

Some features commonly noted in patients undergoing hemodialysis.

a. Alopecia

b. Sparse body hair

c. Hair fragility[31]

6. ORAL MUCOSAL CHANGES

a. Tongue sign

Macroglossia causes prominence of teeth markings, observed in 92% of the renal failure patients also termed as the tongue sign

b. Xerostomia

Reduced salivary flow due to atrophy and fibrosis of salivary glands leads to xerostomia causing difficulties in swallowing, tasting.

c. Ulcerative stomatitis

Accumulation of ammonia released due to nitrogenous wastes can lead to ulcerative stomatitis.[32]

SPECIFIC MANIFESTATIONS

1. Acquired perforating dermatosis

   Also called the trans epidermal eliminating disorders. Characterised by elimination of altered dermal collagen, elastin and degenerated keratin through the follicular wall and epidermis.

I. Reactive perforating collagenosis (RPC)

   The extrusion of altered collagen is termed as trans epidermal elimination disorder. Affects both genders equally.

   It can be secondary to trauma, folliculitis, insect bite reaction.

Clinical features

Small papules with hyperpigmented central umbilication of size5 to 10mm are seen. The lesions undergo spontaneous regression and leave behind small superficial scars with post inflammatory hyperpigmentation. Koebnerization is commonly seen. The adult variant is commonly associated with diabetes mellitus and alsochronic renal failure.[33]

Histopathology

Classical lesions show a shallow vertically positioned, cup shaped invagination of the epidermis forming a channel, lined by acanthotic epithelium along the sides. The base constitutes attenuated keratinocytes, with an eroded focus.[33,34]

II. Perforating folliculitis

Caused due to end result of abnormal follicular keratinisation most likely to irritation or use of chemicals.

A portion of curled hair can be seen within the area of perforation with a foreign body granuloma surrounding it.

Clinical features

Fairly uncommon complaint, seen in 2nd to 4th decade of the life. Erythematous follicular papules with central keratotic plugs. The lesions are localised over the extensors and buttocks.

Histopathology

a. Compact orthokeratosis and parakeratosis in the hair follicle
b. Degenerated basophilic staining made of granular nuclear deposits.
c. Perforation through the follicular epithelium.[35]

III. Kyrle's disease

Exaggerated form of perforating folliculitis associated with chronic renal failure, keratosis pilaris and prurigo nodularis.

Etiopathogenesis

a. Disturbance in the epidermal keratinisation characterized by dyskeratotic foci and accelerated keratinisation.
b. Keratotic plugs are parakeratotic areas. The rate of differentiation and keratinisation exceeds the amount of cell proliferation, the parakeratotic column proceeds deeper as the disease progresses.
c. Perforation is a feature of abnormal keratinisation. Rapid proliferation forms a plug which acts as a foreign body.

Clinical features

Multiple papules coalescing to form plaques and patches are found on the extremities. The lesions are mostly extrafollicular.

Dome shaped papules around 2 to 8mm with a central keratotic plug, with few excoriations are seen. Koebnerization produces linear lesions.

Histopathology

a. Follicular and extrafollicular plugs with no elastin and collagen
b. Some plugs may contain basophilic degenerated material.
c. Granulomatous inflammation with foci of suppuration[36,37]

IV. Elastosis perforansserpiginosa

Characteristic of the trans epidermal elimination disorders. The upper dermis consists of thickened and altered elastic fibres. Male predisposition is seen, affecting young adults.

Clinical features

Mostly localized to single anatomical site and most commonly over nape of neck, face and upper extremities. Lesions are around 2 to 5mm. Lesions are arranged in annular or serpinginous groups. This condition is associated with Down's syndrome, EhlersDanlos syndrome (EDS), osteogenesis imperfecta, pseudoxanthoma elasticum(PXE) and Marfan's syndrome. It is associated with renal failure.

Histopathology

A narrow transepidermal channel which is straight, wavy or corkscrew shape and thick, coarse elastic fibres are seen. Mixed cell infiltrate is seen occasionally.[38]

V. Acquired perforating dermatoses

Commonly associated with renal disease and diabetes mellitus, can also be called as perforating disorder secondary to chronic renal disease and/or diabetes mellitus, perforating folliculitis secondary to haemodialysis, Kyrle's-like lesions and uremic follicular hyperkeratosis.

Clinical features

Pruritic lesions,characterized by hyperkeratotic papules and nodules resembling kyrle's disease to reactive perforating collagenosis like umbilicated papules, nodules, and plaques to erythematous, follicular papules and nodules resembling perforating folliculitis. Annular plaques and erythematous pustules have been described, with histological features of reactive perforating collagenosis and perforating folliculitis, respectively. The most commonly over extensor surfaces of the extremities,can also affect trunk and head.

Histopathology

When oriented vertically, collagen bundles that stain positive with Masson trichrome stain are present within the perforation. Follicular association resembles perforating folliculitis. Chronic rubbing can produce secondary features like prurigo nodularis causing confusion in diagnosis.[38,39]

Treatment of perforating dermatoses

Lesions tend to improve with improvement of renal functions

a. Topical retinoids
b. Oral retinoids
c. Vitamin D3 analogue[40]
d. Emollients
e. Allopurinol[41]
f. Intralesional steroids
g. Narrow band UVB[42]

2. BULLOUS DISEASE

Renal disease can be associated with blistering diseases. These include porphyria cutanea tarda (PCT), pseudoporphyria and bullous disease of dialysis.[43,44,45]

Pathogenesis

a. Renal failure causes reduced elimination of porphyrins causingaccumulation in the skin and resulting in skin fragility and blistering.
b. Uraemia impairs the activity of Uroporphyrinogen decarboxylase.

c. Photoactive drugs like furosemide, tetracycline accumulate due to reduced clearance in renal failure patients.
d. Iron overload secondary to transfusion of blood

Management

a. Phlebotomy reduces the iron levels and aids in new
b. uroporphyrinogen decarboxylase formation.
c. IV erythropoietin
d. Chloroquine clears the porphyrins.
e. Deferoxamine lowers serum porphyrin.[43,44,45]

3. CALCIPHYLAXIS

Also termed as calcific uremic arteriolopathy

Life threatening thrombocclusive disease characterised by calcium deposition in skin and subcutaneous tissue including vessels and the surrounding tissue.[43] Commonly seen in renal failure patients. The prevalence in hemodialysis patients is around 4%.

Can be associated with[46,47,48]

a. Renal failure
b. Hyperparathyroidism
c. Hepatic failure
d. Malignancy
e. Obesity
f. Warfarin
g. Steroid usage
h. Diabetes

Pathophysiology

Multifactorial with involvement of RANK ligand and osteoprotogenerin.

Predisposing factors

Renal failure, abnormal calcium homeostasis, obesity, hepatobiliary disease and malignant conditions.

Other causes implicated are diabetes mellitus, coagulation abnormalities, chronic steroid usage.

Clinical presentation

Purpuric, necrotic, ulcerating, calcified plaques on the lower abdomen and thighs. In the lower extremities livedo is more evident than calcification. Ulcers are deep, irregular, stellate and deep.

Prognosis

Prognosis is variable and can progress to secondary sepsis. The mortality is as high as 80%.

Investigations

Deep biopsy of the indurated plaque to look for calcification of subcutaneous fat and vessel involvement. Serum calcium, blood glucose, HbA1c, liver function tests (LFT). Netlike pattern of calcification is seen.[46,47,48]

Management

a. Intravenous sodium thiosulphate, improves the symptoms quickly and short term outcome is better.

b. Long term oral sodium thiosulfate is given to avoid remission.

Other treatments include cinacalcet, phosphate binders, parathyroidectomy, anticoagulants.[48,49]

4. NEPHROGENIC SYSTEMIC FIBROSIS

This disorder is a scleromyxedema like illness seen in patients undergoing hemodialysis. The condition has no sex or age predilection. Associated with renal dysfunction. [50]

Etiopathogenesis

a. Usage of gadolinium contrast in CKD patients [51]
b. Inflammatory cascade secondary to vascular surgical procedure [52]

Clinical features

Symmetrical thickening of skin over the extremities, mostly ankle to mid thigh, sparing the face. The area is woody, erythematous and has a peau de orange appearance. Papules and nodules are present. Vesiculobullous lesions are not observed. There can be limited joint mobility due to thickening of the skin. Other systems can be involved including skeletal muscle, heart, lungs, kidneys.[53,54,55]

PATHOLOGY

Numerous spindled fibroblasts extending into the subcutaneous septae and subjacent fascia. Thickened collagen bundles are present. XIIIa factor is positive in stellate fibroblastic cells and CD68 positive multinucleated giant cells.

TREATMENT

a. Topical calcitriol under occlusion
b. Oral prednisolone
c. Measures to improve renal function
d. Photodynamic therapy[56]
e. Rapamycin
f. Intravenous Immunoglobin[57,58]

5. CALCINOSIS CUTIS

Skin condition characterised by deposition of calcium in the skin. Described initially by Virchow. The types of calcinosis cutis are

a. Metastatic
b. Dystrophic
c. Idiopathic
d. Iatrogenic

The most commonly seen calcinosis cutis is metastatic calcinosis, this is due to increased ration of calcium- phosphorus.[59]

Around 4% of renal failure patients are affected[60,61] and 1% patients on hemodialysis[62]

Associated diseases

a. Renal failure
b. Hyperparathyroidism
c. Hepatic failure
d. Malignancy[63]
e. Obesity

f. Warfarin

g. Corticosteroid use

h. Diabetes

i. Connective tissue disease

j. Protein C and S deficiency[64,65,66]

Pathogenesis

The cause of calcinosis cutis is multifactorial in hemodialysis patients.

a. Impaired renal clearance of substances leading to accumulation of phosphorus, giving rise to hyperphosphatemia

b. Hyperphosphatemia can trigger the rise of serum calcium levels

c. Renal failure causes increased hypercalcemia

d. Raised parathyroid hormone contributes in causing abnormal calcification

e. Thus the calcium and phosphate that is mobilised is deposited in skin at various sites[67]

Clinical features

Chalky white plaques and papules, hard in consistency are deposited over the large joints lie knee, elbow and around the fingers.

There maybe extrusion of chalky white substance that extrude through the epidermis.

This material can be viewed under light microscopy or polarised microscopy, for further confirmation biopsy sample stained with Von Kossa stain can be used

The patients are generally asymptomatic but may occasionally present with ischemic pain.[67]

Histopathology

Calcium occurs as small granules when located in the dermis and as large deposits in the subcutaneous tissue.

Foreign body response is triggered secondary to calcium deposits mainly the large ones with giant cells, inflammatory infiltrate, fibrosis.

The deposits of calcium stain deep blue on hematoxylin and eosin stain and black with Von Kossa.[67]

Treatment

Medical

a. Dietary measures:
b. Restrict the intake of foods rich in calcium and phosphate, avoid consumption of ketogenic diet that causes accumulation of ketoacids, oxidation of fattyacids resulting in a drop in the pH and thus increasing the chances of crystallisation
c. Intralesional corticosteroid therapy inhibits the fibrinogenesis and prevents inflammation
d. Parenteral sodium thiosulfate reduce the bone turnover[68]
e. Calcium channel blockers like oral diltiazem decreases the mineral content in the calcified tissues.[68]

Surgical

Indications for surgical management

a. Excessive pain
b. Recurrent infection
c. Ulcerations
d. Contractures and limited joint movement

Complication

If calcinosis cutis is left untreated the patient candevelop

a. Pain
b. Ulcerations
c. Secondary infections
d. Restricted mobility
e. Contractures
f. Mechanical compromise
g. Vascular compromise

6. GYNAECOMASTIA

Can occur in the early phase of dialysis treatment and is a refeeding phenomenon after the start of the treatment.

Occurs rarely due to hemodialysis

In patients of chronic kidney disease there is suppression of the pituitary and testicular functions, following treatment there can be transient gynaecomastia[69]

7. INFECTIONS

The patients of hemodialysis have highly susceptible to fungal, bacterial, viral and parasitic infections.

There is poor wound healing and delayed response to treatment in many cases.[8]

8. ANGINA BULLOSA HEMORRHAGICA (ABH)

Sub-epithelial mucosal hemorrhagic blister in the oral cavity, etiology of which is unknown. Clinically, it presents as acute, spontaneous, asymptomatic hemorrhagic vesicle/bullae.

Histopathology reveals subepithelial blister containing RBCs with superficial perivascular lymphocytic infiltrate. There are few case reports ABH in association with chronic renal failure on hemodialysis.[70]

MATERIALS AND METHODS

A hospital based cross-sectional study of the patients with chronic renal failure undergoing hemodialysis in Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapura from a period of November 2019 to May 2021. Approval was obtained from the institutional ethical committee prior to conduct of the study.

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Inclusion criteria:

1. All cases of chronic renal failure of all age groups and sexes undergoing hemodialysis therapy in dialysis unit at Shri BM Patil Medical College, Vijayapura.

Exclusion criteria:

1. Patients with acute renal failure.
2. Patients who have undergone a renal transplant.

Methodology

The patients' age, sex, specific and nonspecific manifestations and medications were noted along with the cutaneous diseases. A detailed history about the duration of CRF and dialysis, duration of skin ailment and improvement following dialysis was noted. Investigations in this regard such as routineinvestigations, skin biopsy, culture and sensitivity for bacterial infections, Gram's stain, potassium hydroxide mount and fungal culture was done if indicated.

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) was used. For categorical data, the number and percentage was used in the data summaries and data was analysed by Chi square test for association, comparison of means using t test, ANOVA and diagrammatic presentation

OBSERVATION AND RESULTS

The study population included 94 patients undergoing hemodialysis.

AGE

The age of the patients in this study ranged between 23 to 73 years. Mean age was 47.

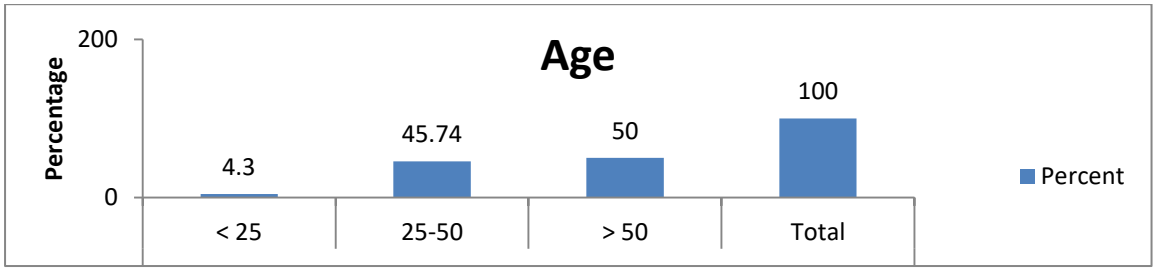
Fifty cases were above the age group of 50 years. Only 4 patients were below 25 years of age.

The pattern of age distribution is presented in Table 1 and Figure 1.

Table 1. Age distribution of study population

Age	Percentage of patients
< 25 years	4.3 (4)
25-50 years	45.74 (43)
> 50 years	50.0 (47)
Total	100.0 (94)

Figure 1. Age distribution of study population



SEX:

Out of 94 patients, 66% males and 34%females. The sex distribution is presented in table 2 and figure 2.

Table 2. Sex distribution of study group

Sex	Percentage of patients
Female	34.0 (32)
Male	66.0 (62)
Total	100.0

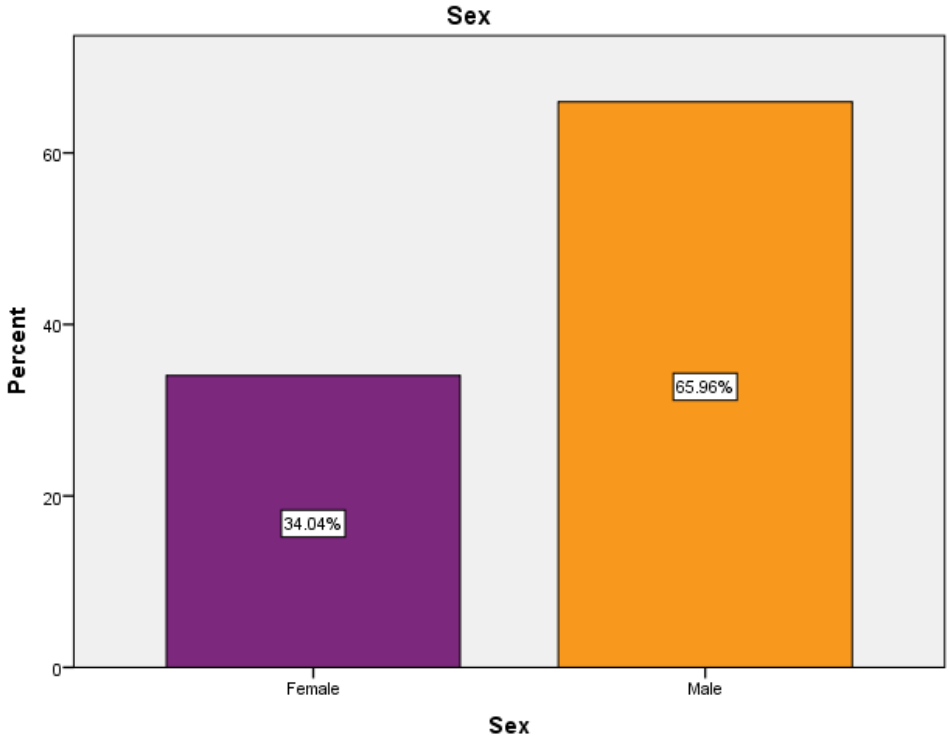


Figure 2. Sex distribution of study group

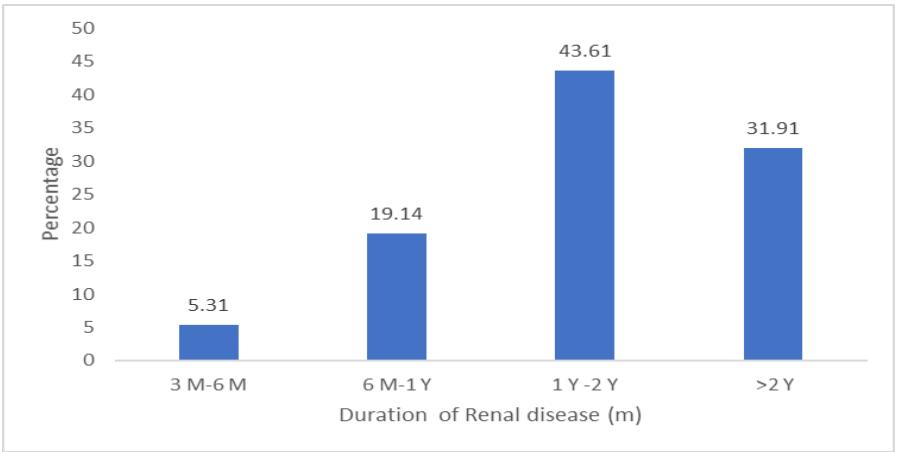
DURATION OF RENAL DISEASE

The duration of illness ranged from 3 months to 13 years. Majority of the patients underwent dialysis for more than one year. Nineteen percent of patients for 6 months to 1 year and 5 patients with duration of renal disease of less than 6 months. The data regarding the duration of renal disease is presented in table 3 and figure 3.

Table 3. Duration of renal disease in study population

Duration of Renal disease	Percentage
3-6months	5.31 (5)
6months -1year	19.14 (18)
1-2years	43.61 (41)
>2years	31.91 (30)
Total	100.0 (94)

Figure 3. Duration of renal disease in study population



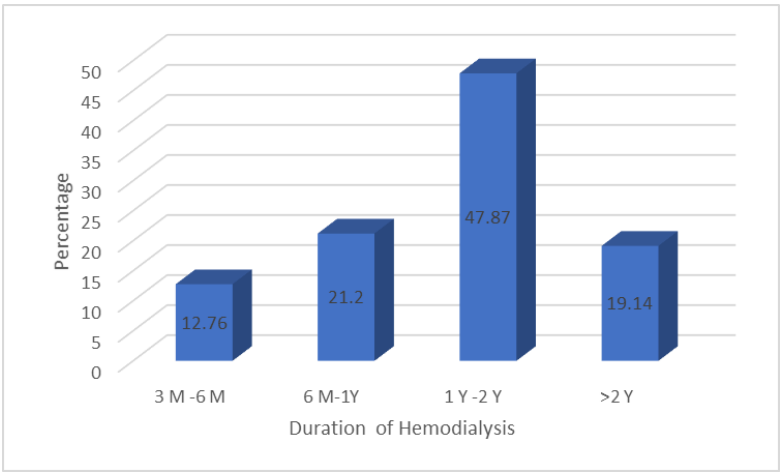
DURATION OF HEMODIALYSIS

Nineteen percent of the patients had undergone dialysis for more than 2 years, 47.87%(45) patients had undergone dialysis for 1 to 2 years, 20 patients between 6 months to 1 year and 12 patients for less than 6 months. Data regarding duration of hemodialysis is presented in table 4 and figure 4.

Table 4. Duration of hemodialysis in study group

Duration of Hemodialysis	Percentage of patients
3-6 months	12.76 (12)
6 months -1year	21.20 (20)
1-2 years	47.87 (45)
>2 years	19.14 (18)
Total	100.0 (94)

Figure 4. Duration of hemodialysis in study group



FREQUENCY OF DIALYSIS PER WEEK

Majority of study population (92.6%) received hemodialysis twice a week and 7.4% thrice per week.(Data represented in table 5 and figure 5)

Table 5. Frequency of dialysis per week

Cycles/week	Percent
Thrice	7.4 (7)
Twice	92.6 (87)
Total	100.0 (94)

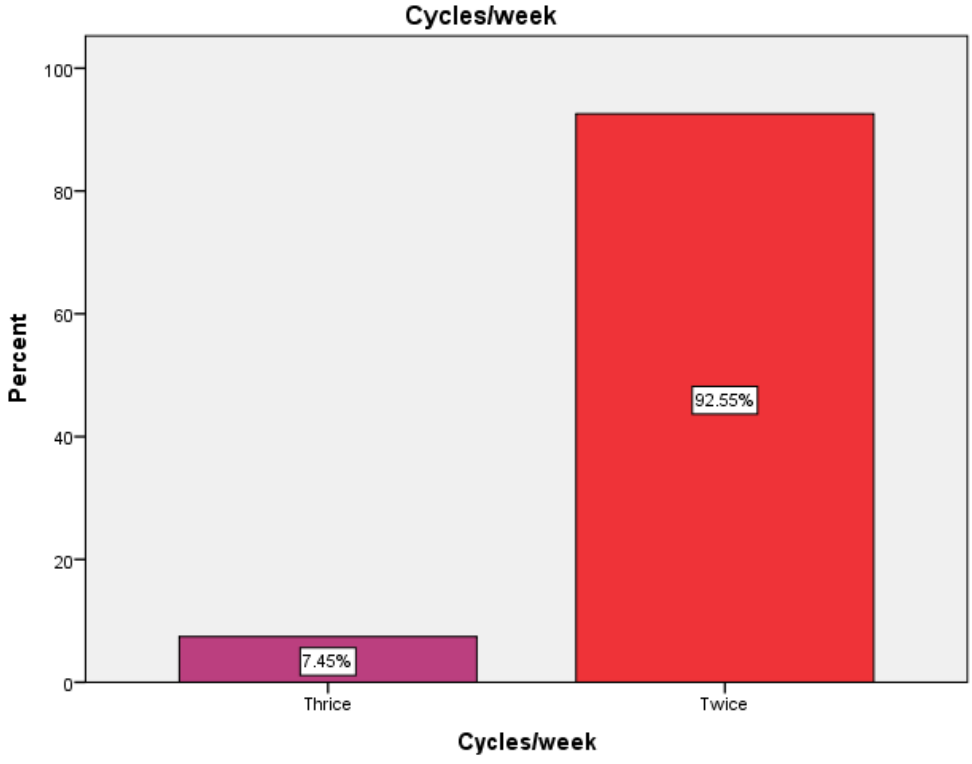


Figure 5. Frequency of dialysis per week

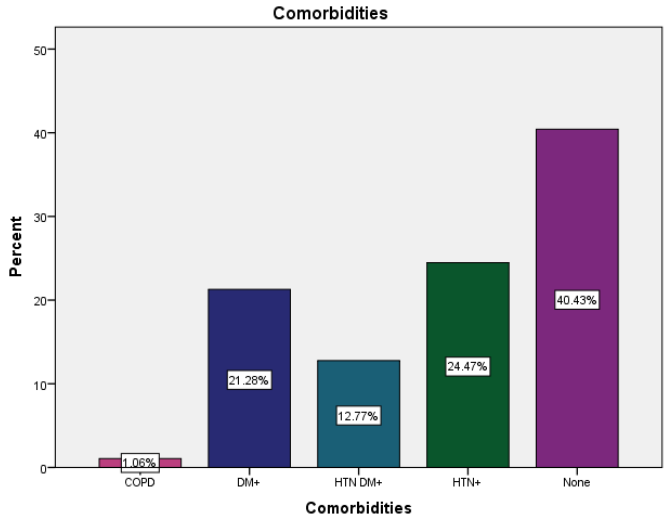
ASSOCIATED COMORBIDITIES:

Out of 94 patients 40.4% had no associated comorbidities. 21.3% patients had only diabetes and 24.5% patients had only hypertension, 12.8% of the patients had both diabetes and hypertension. 1 patient had COPD. Associated comorbidities are represented in Table6 and Figure6

Table 6. Comorbidities in study population

	Percentage
Chronic obstructive pulmonary disease	1.1 (1)
Diabetes mellitus	21.3 (20)
Hypertension and diabetes mellitus	12.8 (12)
Hypertension	24.5 (23)
None	40.4 (38)
Total	100.0 (94)

Figure 6.Comorbidities in study population



PREVALANCE OF NON-SPECIFIC CUTANEOUS MANIFESTATIONS

1. PRURITUS

   Eighty(85.10%) out of 94 patients suffered from pruritus. Excoriations were seen in 54 patients. Lichen simplex chronicus, prurigo nodularis were seen in few of the patients.

   Pruritus was most common in patients who underwent dialysis for a period of 1 to 2 years (40 patients, 50%), followed by patients who were undergoing dialysis for more than 2 years, (14 patients, 17.5%). In patients undergoing dialysis for less than 1 year, 26 (32.5%) patients undergoing dialysis for less than 1 year also had pruritus Pruritus was seen in association with diabetes and xerosis in 26 patients and 72 patients respectively. All the patients with Kyrle's disease had associated pruritus. Excoriations were seen in 54 patients, Lichen simplex chronicus (9.6%), prurigo nodularis(14.9%), generalised pruritus(1.1%), excoriations with generalisedpruritus(1.1%), excoriations with lichen simplex chronicus(LSC)(1.1%) were observed in this study.

   Table 7. Pruritus in study population

Pruritus	Percentage
Excoriations	57.4 (54)
Prurigo Nodularis	14.9 (14)
Lichen Simplex Chronicus	9.6 (9)
Excoriations, Lichen Simplex Chronicus	1.1 (1)
Excoriations, Pruritus	1.1 (1)
None	14.9 (14)

2. SKIN COLOUR CHANGES

56 (59.57%)patients presented with skin colour changes, of which pallor was the most common (38 patients, 40.4%) , followed by ecchymosis (15 patients,16%). Hyperpigmentation and yellowish tinge was seen in few patients.

Table 8. Skin colour changes in study group

Skin colour change	Percent
Pallor	40.4 (38)
Ecchymosis	16.0 (15)
Hyperpigmentation	3.2 (3)
Ecchymosis and pallor	1.1 (1)
Yellowish tinge	1.1 (1)
None	38.3 (36)
Total	100.0 (94)

3. XEROSIS

Xerosis was seen in 84% (79) patientsof the study population. Data represented in Table 9 and Graph 6. Xerosis was most commonly seen on the bilateral lower extremities followed by upper extremities.

Xerosis was higher in patients undergoing dialysis for less than 2 years.

Patients receiving dialysis for more than 2 years had lesser incidence in xerosis (16 (20.20%) patients. This implies that dialysis may improve xerosis in the CKD patients. Represented in table 9 and figure 7

Table 9. Frequency of xerosis

		Percent
	Present	84.0 (79)
	Absent	16.0 (15)
	Total	100.0 (94)

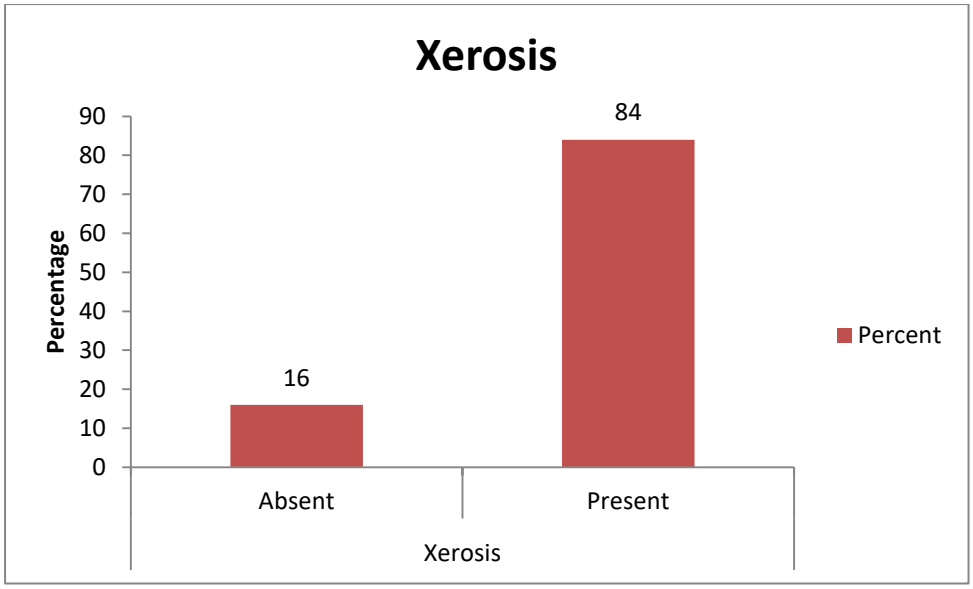


Figure 7. Frequency of xerosis

NAIL CHANGES

Nail changes	Percentage
Half and half nails	12.8 (12)
Onycholysis	11.7 (11)
Beau's lines	9.6 (9)
Pitting, onycholysis	6.4 (6)
Longitudinal ridges	5.3 (5)
Onychomycosis	3.2 (3)
Subungual hyperkeratosis	2.1(2)
Onycholysis, Subungual hyperkeratosis	2.1(2)
Onychoschizia	1.1 (1)
Onycholysis	1.1 (1)
Koilonychia, onycholysis, onychorrhexis	1.1 (1)
None	43.6 (41)
Total	100 (94)

53 (56.38%) patients had nail changes most common being half and half nails seen in 12 of them. Other nail changes seen wereBeau's lines (9%), onycholysis(11%). Few patients presented with onychorrhexis, subungual hyperkeratosis, onychomycosis. Some patients also had multiple nail changes. Data presented in table 10 and figure 8.

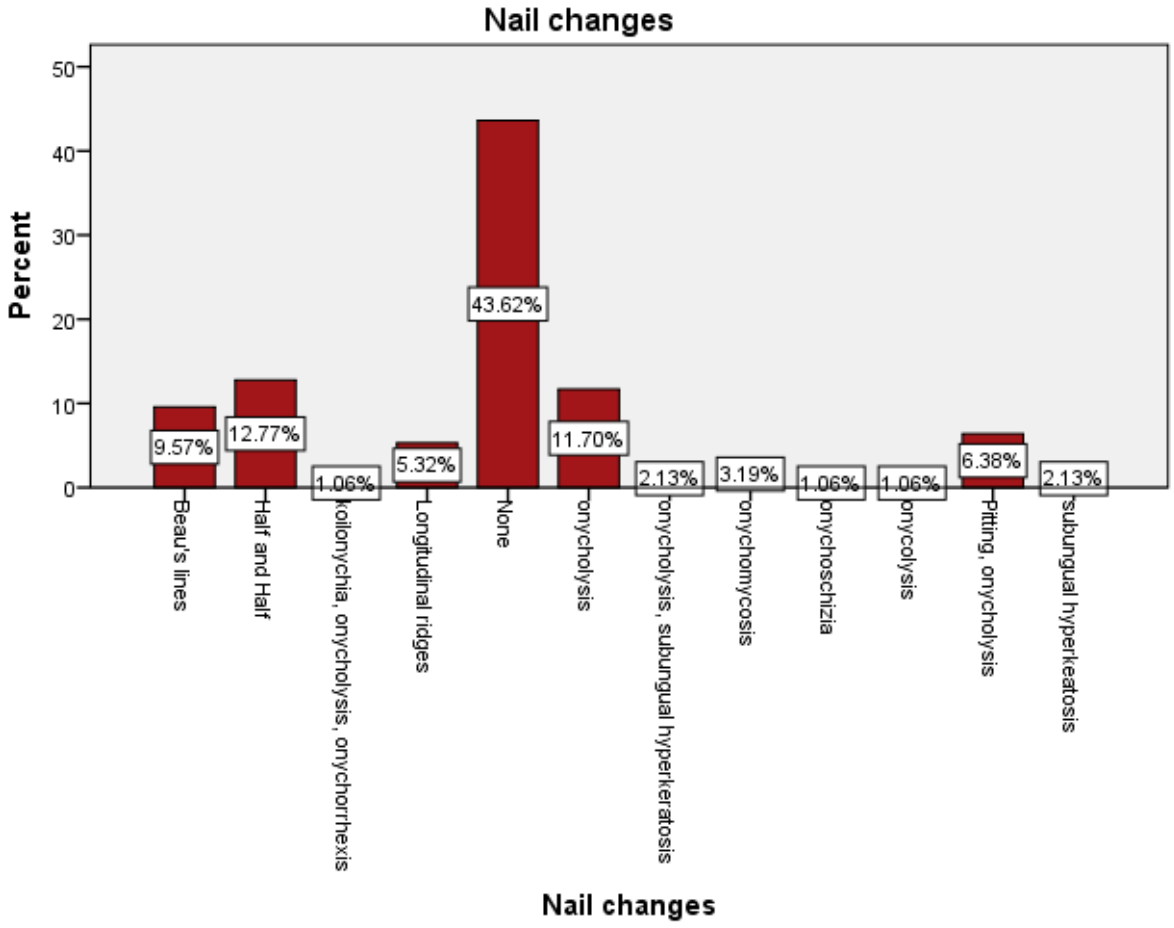


Figure8.Nail changes in study population

5. HAIR CHANGES

Out of 94 patients, 23 patients had hair changes. Most commonly seen was sparse body hair seen in 21.3% of the patients, 2 patients had androgenic alopecia and 1 patient had alopecia areata. Data represented in figure 9 and table 11

Table 11. Hair changes in study population

Hair changes	Percentage
Sparse body hair	21.3 (20)
Androgenic alopecia	1.1 (1)
Female pattern baldness	1.1 (1)
Alopecia areata	1.1 (1)
No hair abnormality	75.5 (71)
Total	100 (94)

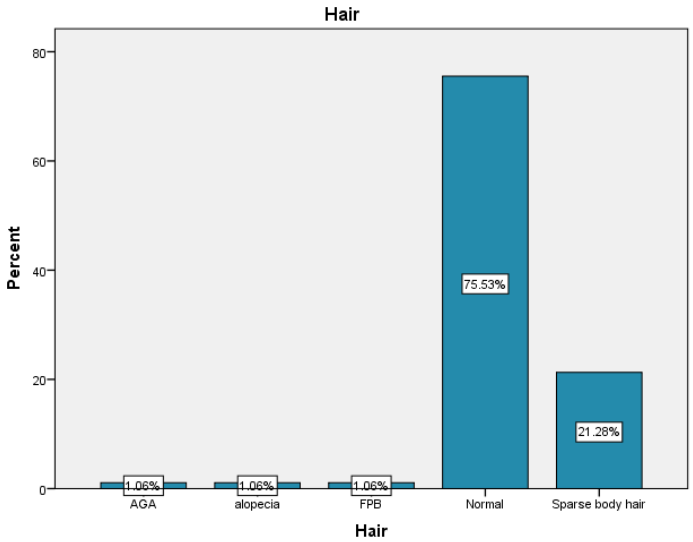


Figure9.Hair changes in study population

6. ORAL MUCOSAL CHANGES

Out of 94 patients, 34 (36.17%) patients showed changes in the oral cavity, most common was depapillated tongue (12.8%), macroglossia(8.5%), oral candidiasis(6.4%), tongue sign(4.3%), xerostomia(3.2%), black hairy tongue(1.1%). Data presented in table 12.

Table 12. Oral mucosal changes in study group

Oral mucosal changes	Percentage
Depapillated tongue	12.8 (12)
Macroglossia	8.5 (8)
Oral candidiasis	6.4 (6)
Tongue sign	4.3 (4)
Xerostomia	3.2 (3)
Black hairy tongue	1.1 (1)
Normal	63.8 (60)
Total	100 (94)

7. ACQUIRED PERFORATING DERMATOSES

Kyrle's disease was seen in 6.4% of the patients. Out of these 3(50%) patients had associated diabetes mellitus.

4 out of the 6 (66.6%) patients underwent dialysis for less than a period of 1 year and 2 underwent dialysis for more than 1 year.

All the 6 patients with acquired perforating dermatosis had associated xerosis and pruritus. Data presented in table 13 and figure 10

Table 13. Frequency of acquired perforating dermatoses

	Percentage
Kyrle's disease	6.4 (6)
Absent	93.6 (88)
Total	100.0

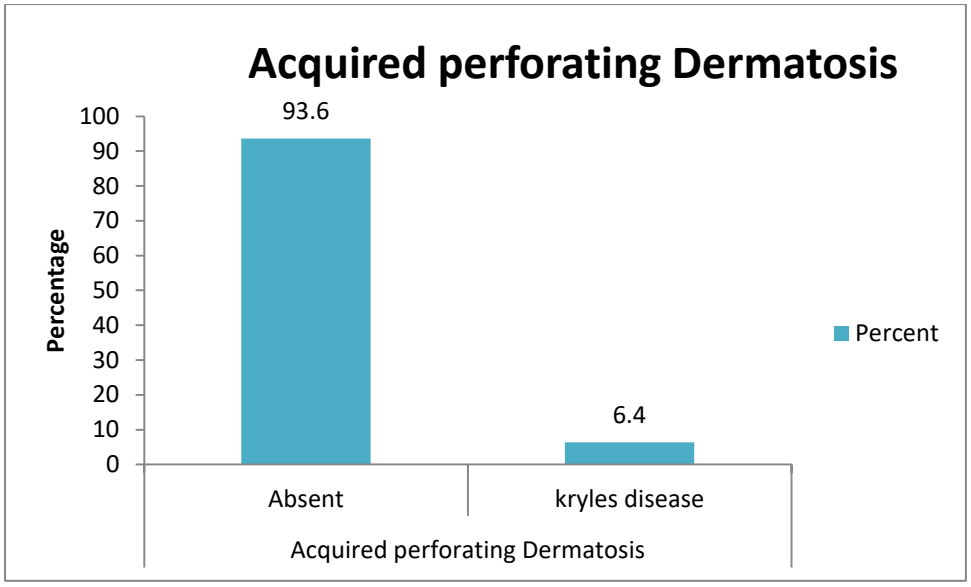


Figure 10. Frequency of Acquired perforating dermatoses

8. OTHER NON-SPECIFIC DERMATOSES

Few of the miscellaneous findings noted in this study was 1 case of angina bullosa hemorrhagica, herpes zoster(1.1%), hypertrophic scar (1.1%) and keloid (1.1%) at the site of fistula and tinea cruris infection (7, 7.4%). Data presented in table 14 and figure 11.

Table 14. Other non- specific dermatoses

	Percentage
Tinea cruris	7.4 (7)
Angioma bullosa hemorrhagica	1.1 (1)
Eczema	1.1 (1)
Herpes zoster	1.1 (1)
Hypertrophic scar	1.1 (1)
Keloid	1.1 (1)

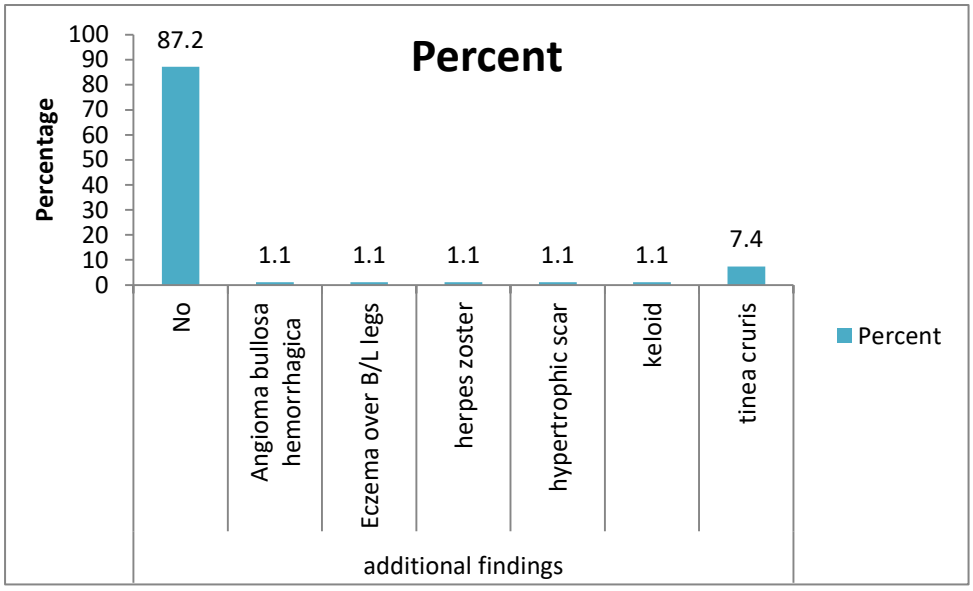


Figure 11. Other non- specific dermatoses

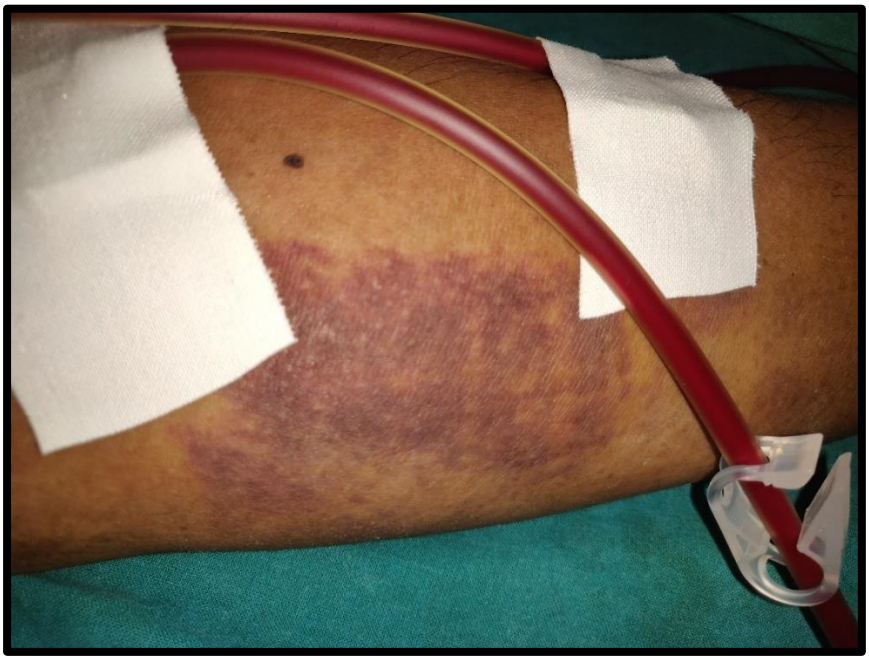


Figure 12. Ecchymotic patches over forearm

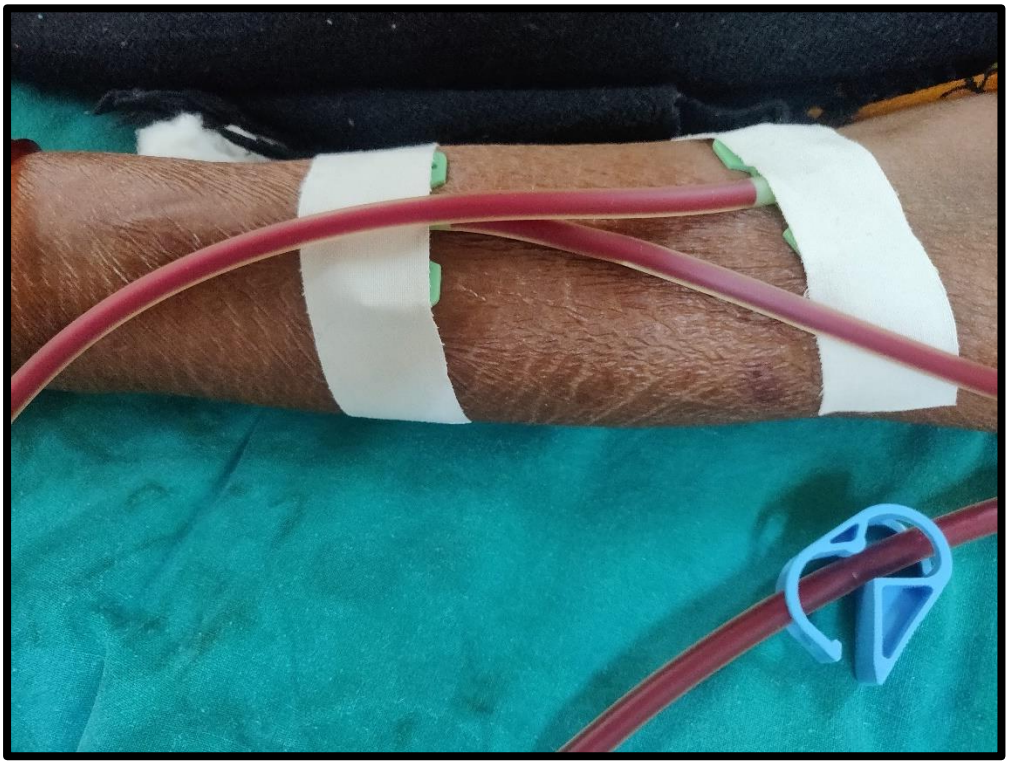


Figure 13. Diffuse xerosis over extremity

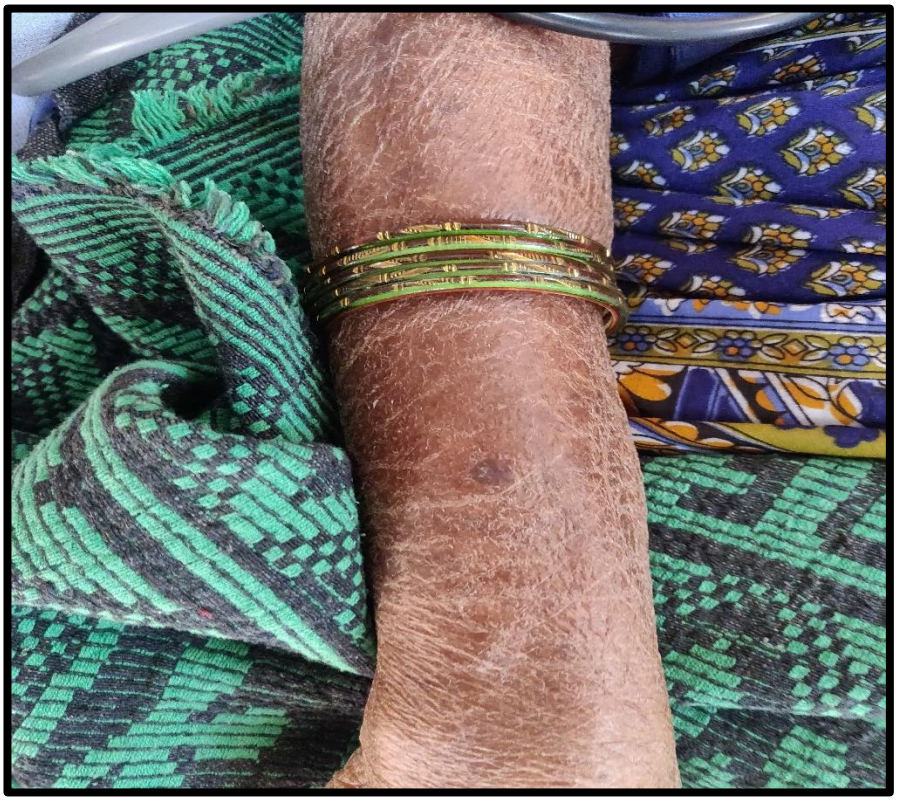


Figure14. Diffuse xerosis over upper extremity

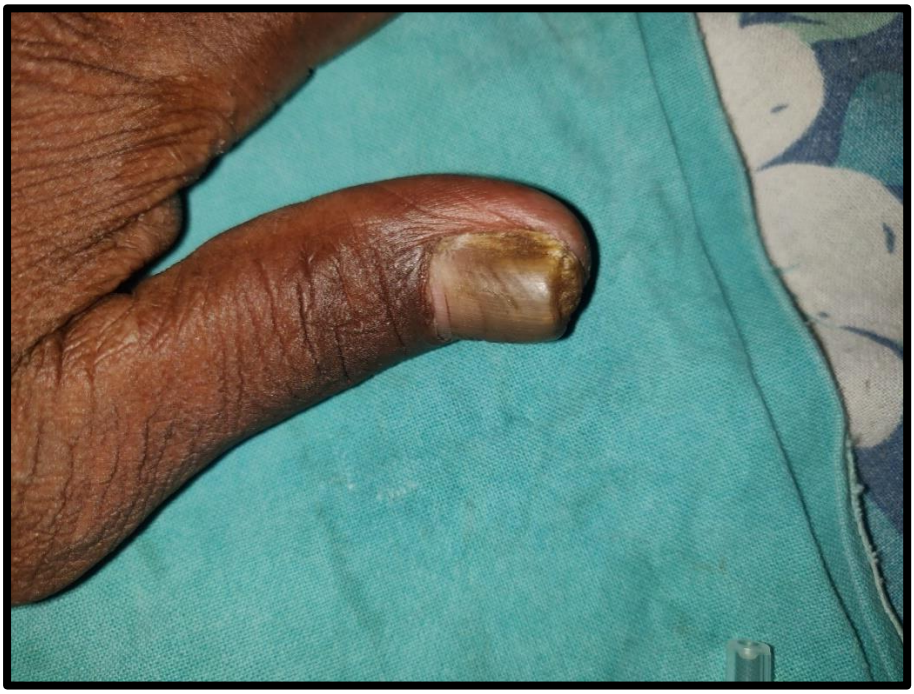


Figure 15. Onychomycosis of the left thumb nail

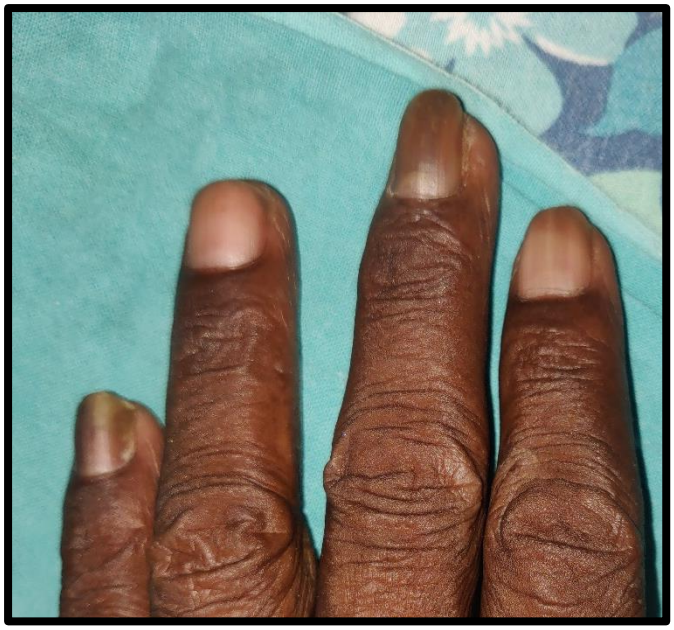


Figure 16. Onychomycosis over the left middle finger

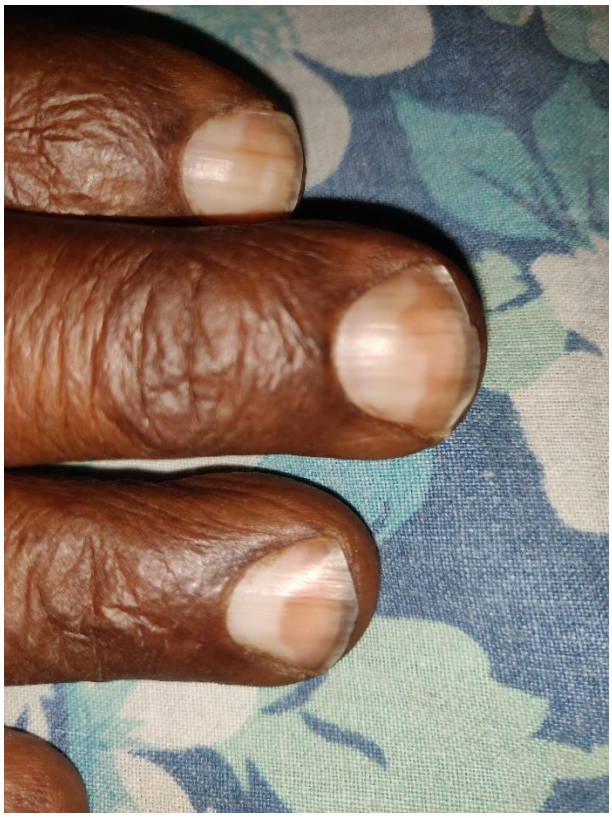


Figure 17. Half and half nails with xerosis of the dorsum of hand

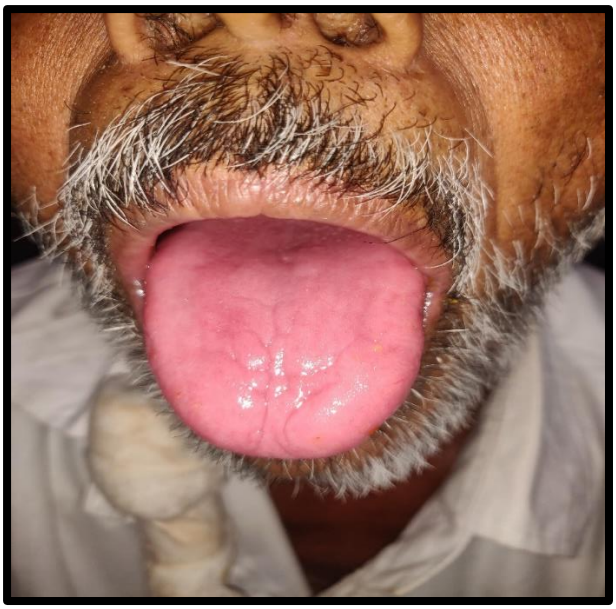


Figure 18. Macroglossia with bald tongue

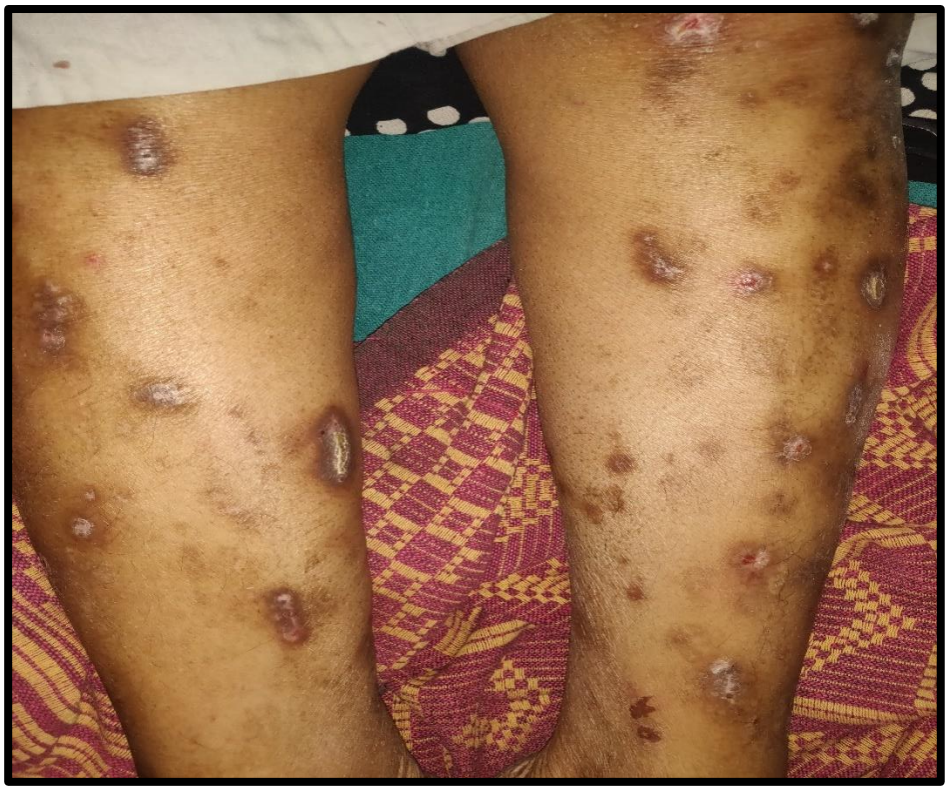


Figure 19. Prurigo nodularis over bilateral lower extremities

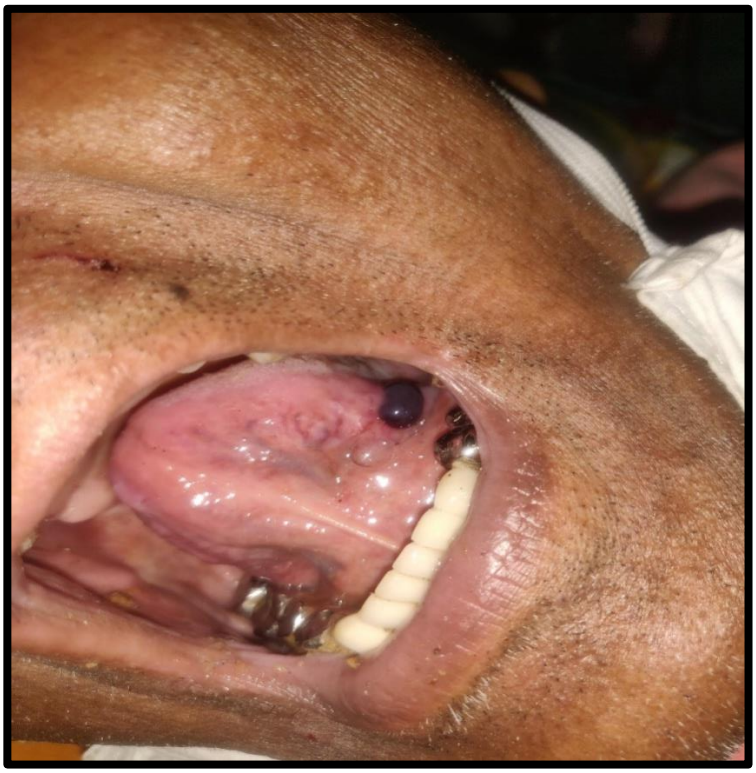


Figure 20. Angina bullosa hemorrhagica over the lateral border of tongue

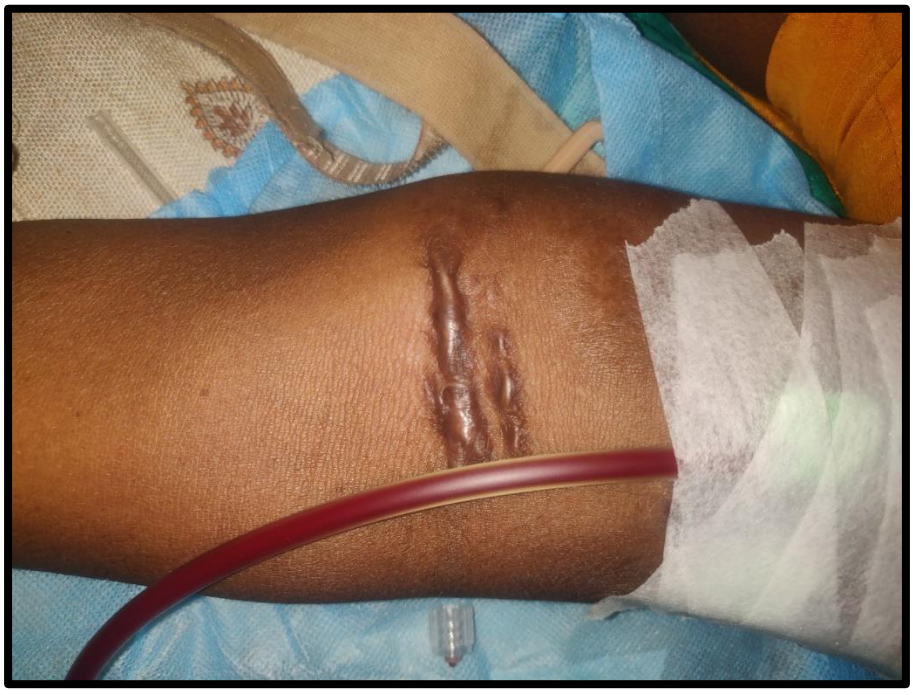


Figure 21. Keloid over the Fistula site

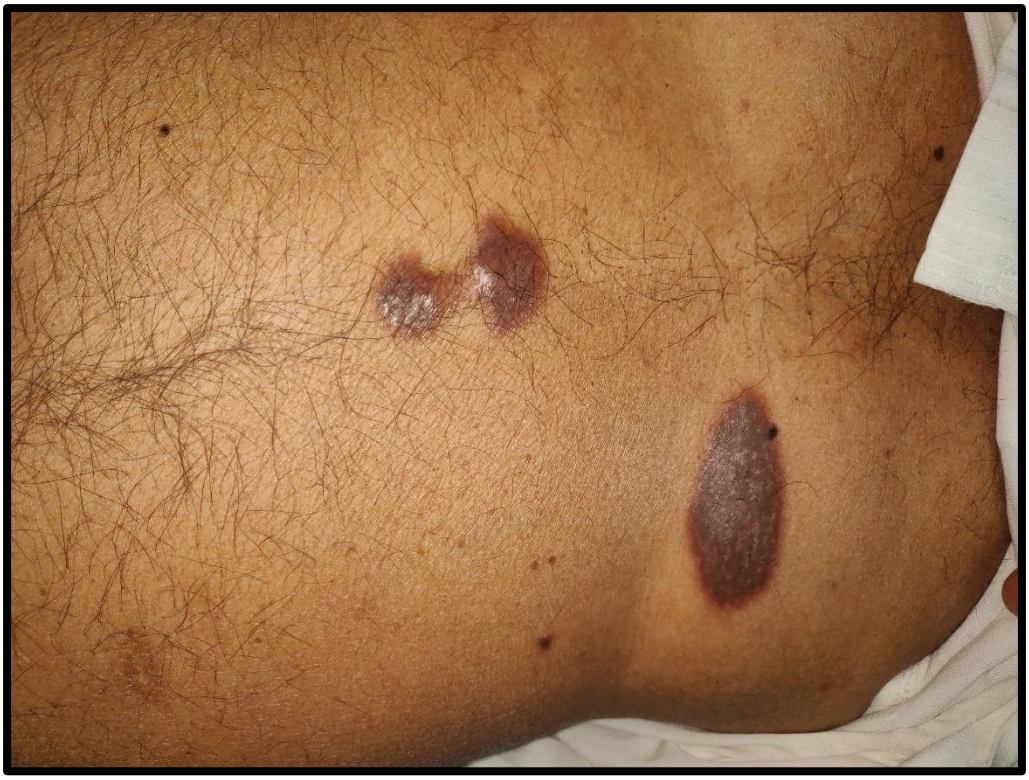


Figure 22. Hypertrophic scars over the chest and abdomen

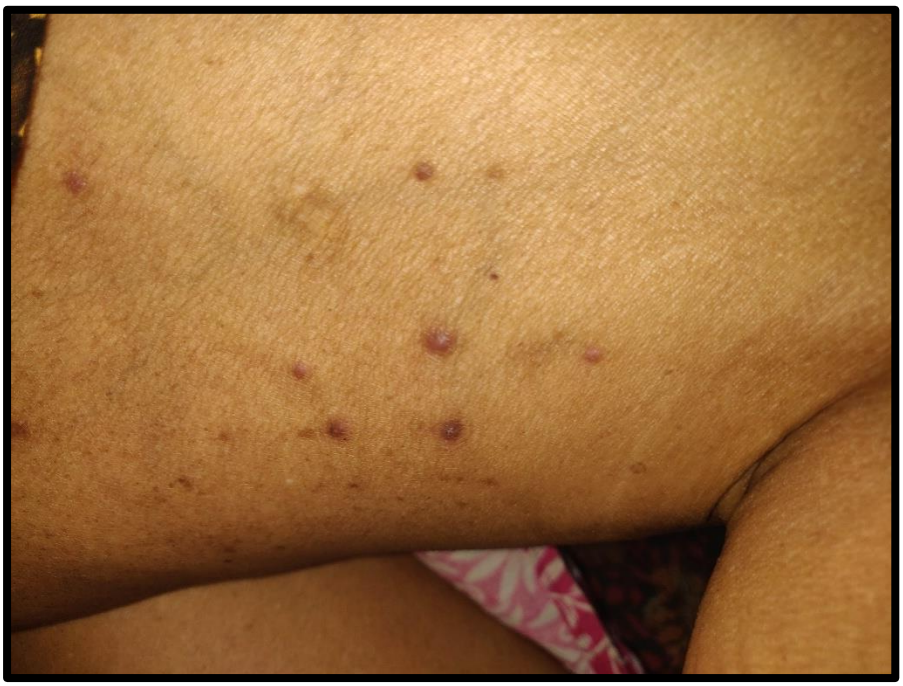


Figure23. Kyrle’s disease over the thigh

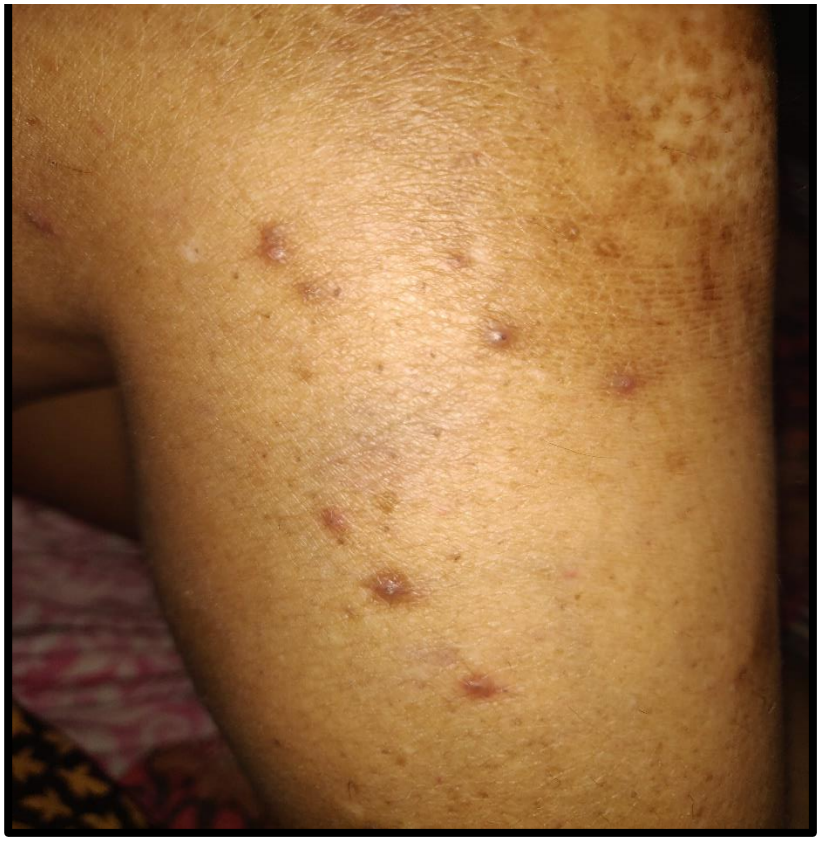


Figure 24. Kyrle’s disease over lower limb

DISCUSSION

Hemodialysis is one of the major treatment modalities in chronic kidney disease patients.[8]

The cutaneous manifestations in patients undergoing hemodialysis can be broadly classified into specific and non-specific changes. Specific changes mainly include acquired perforating dermatosis, calcific uremic arteriolopathy, bullous diseases and nephrogenic fibrosing dermopathy and non-specific skin manifestations include pruritus, xerosis, nail disorders, hair disorders, pigmentary changes, purpura, oral changes, pallor and uremic frost.[7]

Pruritus was the most common finding in this study documented in 85.1% (80) patients, of which 28 were females and 58 were males. The studies by Sanad et al[71]and Mourad et al[72] reported pruritus in 52% and 51.6%patients respectively, findings were lesser than our study Pruritus was most commonly noticed in patients who underwent dialysis for a period of less than 1 year (64.3%). The incidence of pruritus decreased as the duration of dialysis increased mostly due to the clearance of pruritogenic substances by hemodialysis.

Pruritus was associated with diabetes and xerosis in 26 and 72 patients respectively. In a study by Udaykumar et al pruritus was found to be very severe in diabetic patients[8]. All the patients with Kyrle's disease had associated pruritus.

Xerosis (figure 12,13) was the second most common finding noted in our study population. With a prevalence of 84%.Xerosis was most commonly seen on the lower extremities followed by upper extremities.

Xerosis decreased as the duration of dialysis increased. The findings were in par with study by Udaykumar et al who observed xerosis in 79% of the patients. Reduced size of sweat glands, excessive ultrafiltration and high doses of diuretics can be the causes for xerosis.[8]

Xerosis was the most common finding in study by RafeekM et al[73], Sanad et al[71] ,

Udaykumar et al[8], but it was the second most common finding in our study. However the incidence of pruritus was similar to our study.

Diffuse hyperpigmentation and yellowish tinge were noted in 3.2% and 1.1% of our patients respectively. Our study findings were much lesser than previous studies by Pico et al[2] and Kolla et al[1] which reported pigmentation in 70% and 40% of the patients respectively. Mourad et al [72] reported hyperpigmentation in 20% of the study population.

Diffuse hyperpigmentation is due to increased beta MSH(Melanocyte Stimulating Hormone).The reason for low incidence of hyperpigmentation in our study maybe due to the ethnicity of the population belonging to Fitzpatrick skin types IV and V.

Ecchymosis (figure 11) was observed in 15 patients (15.9%) of the study group. The findings were less than a study by Sanad et al[71] that reported ecchymosis in 36% of the population.Defects in primary hemostasis such as increased vascular fragility, abnormal platelet function, and the use of heparin during dialysis are the main causes of ecchymosis in CKD patients on HD.

Pallor was seen in 56 (59.57%) patients of the study population. Findings were in par with studiesdone by Udaykumar et al[8] and Deshmukh et al[16]who observed pallor in 60% and 68% respectively of the patients and findings were greater than a study by Sanad et al[71], reported pallor in 34% of the patients. Cause of pallor can be due to deficient erythropoietin production due to kidney impairment, malnutrition, anemia of chronic disease.

Nail changes were observed in 53 (56.38%) patients.The most common nail change observed was half and half nails (figure 16)(12, 22.6%). Other nail changes seen were Beau's lines

(9%), onycholysis(11%), onychorrhexis, subungual hyperkeratosis, onychomycosis (figure 14,15). Some patients had a combination of nail changes.Study by Deshmukh et al[16] noticed nail changes in 60% of the study population, Beau's lines and subungual hyperkeratosis were the commonest findings followed by half and half nails which was in par with our study.

Mucosal changes were seen in 53 patients. Most common was depapillated tongue (12.8%), macroglossia(8.5%) (figure 17) , oral candidiasis(6.4%), tongue sign(4.3%), xerostomia(3.2%), black hairy tongue(1.1%). In a study by Udaykumar et al 35% of the patients had changes in oral mucosa which wassimilar to our study whereas Kolla et al[1] reported oral mucosal changes in 27.3% of the patients which was lesser than our study findings.

Acquired perforating dermatoses (figure 22,23) was seen in 6.4% of the patients.Findings were slightly more than Sultan et al [74] who reported Kyrle's disease in 3% of the CRF patients on HD. However, Deshmukh et al[16] and Udayakumar et al[8] reported Kyrle's disease in 17.14 and 21%, respectively, in their patients. 3(50%) out of these patients had associated diabetes mellitus.In a study by Udaykumar et al[8] the perforating dermatoses was significantly more in diabetics. 4 out of the 6 (66.6%) patients underwent dialysis for less than a period of 1 year and 2 patients underwent dialysis for more than 1 year.This is in par with a study reported by Udaykumar et al[8] who reported 90% of the patients with acquired perforating dermatosis underwent dialysis for less than 1 year. The exact cause for Kyrle’s disease in patients undergoing hemodialysis for a period of less than one year is not clear, it can be attributed to the elevated creatinine levels and the severity of renal damage. Hemodialysis tend to improve the renal functions over a period of time and the incidence of Kyrle’s disease decreases.

The pathogenesis of the disease is not known, but it may occur as a result of dermal

connective tissue dysplasia and decay. Suspected causes include an inflammatory skin reaction secondary to the presence of uremic toxins, uric acid deposits, or scratching-induced trauma[75]. Microvascular deposition of calcium may interrupt blood flow to connective tissue in the dermal layer, causing death and necrosis[76]

Few of the miscellaneous findings noted in this study were 1 case of angina bullosa hemorrhagica, hypertrophic scar (1.1%) (figure 21) and keloid at the site of fistula (1.1%) (figure 20).

Skin infections were noted in 8 (8.51%)caseswhich included 7 cases of dermatophytosis and 1 case of herpes zoster. 5 out of the 8 cases had associated diabetes mellitus.The prevalence of skin infections was much lesser than a study compared to Pico et al[2] who noticed skin infections in 25% of the patients.

Angina bullosa hemorrhagica (figure 19) was seen in one patient. Shashikumar et al[70] observed this finding in one patient of chronic renal failure undergoing hemodialysis. The etiology remains unknown.

No cases of calcinosis cutis, calciphylaxis, Nephrogenic systemic fibrosis, porphyria or uremic frost were noted in this study.

CONCLUSION

This is a cross-sectional study to observe the cutaneous manifestations in chronic renal failure patients undergoing hemodialysis. The sample size of the study population was 94.

Non-specific changes like pruritus, xerosis, pallor, nail changes like half and half nails, mucosal changes like tongue sign were noticed in the patients undergoing hemodialysis.

Pruritus was the most common finding in our study, followed by xerosis. The incidence of pruritus and xerosis decreased with increasing duration of dialysis which maybe attributed to clearance of pruritogenic substances by hemodialysis.

Specific change like Kyrle's disease was seen in 6% of the study population. The finding was more common in patients undergoing dialysis for a period of less than one year.

One case of angioma bullosa hemorrhagica was noted in this study.

Other specific changes like calcinosis cutis, calciphylaxis, nephrogenic systemic fibrosis were not observed in our study.

Prompt diagnosis and early treatment helps alleviate many of the cutaneous manifestations posed due to hemodialysis.

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ANNEXURE 1

ETHICAL CLEARANCE CERTIFICATE

IEC/NO-131/2019
22-11-2019

B.L.D.E. (DEEMED TO BE UNIVERSITY)

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 13-11-2019 at 3-15 pm to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A Cross-Sectional study of Dermatologic manifestations in patients of chronic renal failure on hemodialysis at a tertiary care centre.

Name of PG student: Dr. Indira Potthuri, Department of Dermatology,

Name of Guide/Co-investigator: Dr. Arun C. Inamadar, Professor And Head Department of Dermatology,

DR RAGHVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College, BIJAPUR-586103

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

APPENDIX – III

B.L.D.E. (Deemed to be University) SHRI B.M PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586 103

RESEARCH INFORMED CONSENT FOR

TITLE OF THE PROJECT :- A Cross-sectional study of Dermatologic manifestations in patients of chronic renal failure on hemodialysis at a tertiary care centre**.**

PG GUIDE :- DR. ARUN C.INAMADAR

PG STUDENT :- DR. INDIRA POTTHURI

PURPOSE OF RESEARCH: -

I have been informed that this project will assess the cutaneous manifestations of chronic kidneyfailure patients undergoing hemodialysis at Shri BM Patil Medical College and research centre, Vijayapura.

BENEFITS:-

I understand that my participation in this study will help the investigator to know the cutaneous changes in chronic renal failure patients undergoing hemodialysis.

PROCEDURE:-

I understand that relevant history will be taken and proper head to toe examination will be done looking for any cutaneous manifestations secondary to hemodialysis.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time concerned. Dr. Indira Potthuri is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in this study at any time without prejudice. I also understand that Dr. Indira Potthuri may terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician, if this is appropriate.

INJURY STATEMENT:-

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that …….(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

_____ _____

Participant / guardian Date

_____ _____

Witness to signature Date

KEY TO MASTERCHART

ABBREVATION	FULL FORM
Y	Years
m	Months
M	Male
F	Female
DM	Diabetes Mellitus
HTN	Hypertension
COPD	Chronic Obstructive pulmonary disease
PN	Prurigo nodularis
LSC	Lichen simplex chronicus

ANNEXURE IV

MASTER CHART

	Name	Age/Sex	Duration	Duration c	Cycles/we	Comorbidi	Pruritus	Skin colou	Xerosis	Nail chang	Hair	Oral Muco	Acquired p	Bullous dis	Metastatic	Nephroger	infections	additional findings
1	Rubina	44y/F	6 y	6 m	Twice	DM+	PN	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
2	Asif	34y/M	6 m	3 m	Twice	None	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
3	Basappa	70y/M	6 m	3 m	Twice	None	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
4	Arun Chall	60y/M	2 y	1 y	Twice	HTN DM+	PN	None	Absent	None	Sparse boc	Normal	Absent	Absent	Absent	Absent		
5	Syrabanu	40y/F	6 m	3 m	Twice	DM+	PN	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
6	Vijaylaksh	21y/F	5 y	3 y	Twice	None	Excoriatio	Pallor	Present	None	Sparse boc	Normal	Absent	Absent	Absent	Absent		
7	Mahadevi	29y/F	2 y	1 y	Twice	None	Excoriatio	None	Absent	None	Normal	Normal	Absent	Absent	Absent	Absent		
8	basavraj	46y/M	1.5 y	1 y	Twice	None	None	Ecchymosi	Present	onycholysi	Sparse boc	Normal	Absent	Absent	Absent	Absent		
9	Basamma	43y/F	5 y	2 y	Twice	None	Excoriatio	Ecchymosi	Present	onycholysi	FPB	Normal	Absent	Absent	Absent	Absent		
10	Sumangala	53y/F	2 y	1 y	Twice	None	Excoriatio	None	Present, ic	None	Normal	Normal	Absent	Absent	Absent	Absent		
11	shakuntala	35y/F	6 m	4 m	Twice	DM+	Excoriatio	Ecchymosi	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
12	Ishwar	38y/M	6 m	4m	Twice	None	Excoriatio	Pallor	Present	Pitting, on	Normal	Normal	Absent	Absent	Absent	Absent		
13	Avvamma	60y/F	1y	6m	Twice	DM+	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
14	Ganghadh	71y/M	5m	5m	Twice	DM+	Excoriatio	Pallor	present	onychosch	Normal	Normal	Absent	Absent	Absent	Absent	tinea cruris	
15	Seetaram	70y/M	1y	6m	Twice	HTN DM+	PN	Pallor	Present	none	Normal	Normal	Absent	Absent	Absent	absent		
16	shivasanga	42y/M	6m	3m	Twice	None	None	None	present	None	Normal	Normal	Absent	Absent	Absent	Absent		
17	Baburai	43y/F	4y	1y	Twice	HTN DM+	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
18	Savanna	61y/F	6m	4m	Twice	COPD	None	None	Present	onycholysi	Sparse boc	Xerostomi	Absent	Absent	Absent	Absent	tinea cruris	
19	Devappa	46y/M	2y	1y	Twice	DM+	None	None	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
20	Shivakka	50y/F	8m	6m	Twice	None	Excoriatio	Pallor	Present	Subungual	Sparse boc	Normal	Absent	Absent	Absent	Absent		
21	dattaraya	61y/F	2y	1y	Twice	DM+	Excoriatio	Ecchymosi	present	Half and H	Normal	oral candi	Absent	Absent	Absent	Absent		
22	Hanmanth	58y/M	3m	3m	Twice	None	Pruritus	Ecchymosi	present	Beau's line	Sparse boc	Depapilate	Absent	Absent	Absent	Absent	herpes zoster	
23	Sugalaww	60y/F	8y	7y	Twice	None	Excoriatio	none	present	Half and H	Sparse boc	Depapilate	Absent	Absent	Absent	Absent		
24	devandra	40y/M	1y	8m	Twice	None	none	none	None	Beau's line	Normal	Normal	Absent	Absent	Absent	Absent	tinea cruris	
25	basawwa	67y/F	7m	6m	Twice	HTN DM+	excoriatio	Pallor	present	Pitting, on	Normal	Normal	Absent	Absent	Absent	Absent		
26	dundappa	39y/M	4m	2m	Twice	DM+	excoriatio	Pallor	present	None	Normal	Normal	Absent	Absent	Absent	Absent		
27	anil laman	45y/M	4y	4y	Twice	HTN+	None	None	present	onycholysi	Sparse boc	Normal	Absent	Absent	Absent	Absent		
28																		

29	dundubai	60y/M	1y	7m	Twice	HTN DM+	None	None	present	Half and H	Normal	Normal	Absent	Absent	Absent	Absent		
30	asha	25y/F	2y	2y	Twice	HTN+	excoriatio	None	None	None	Normal	Normal	Absent	Absent	Absent	Absent		
31	shrishail	50y/M	1y	1y	twice	DM+	excoriatio	none	present	Beau's line	normal	normal	Absent	Absent	Absent	Absent		
32	sasikala	50y/F	4y	4y	Twice	HTN+	excoriatio	Hyperpigm	Present	Pitting, on	Normal	Normal	Absent	Absent	Absent	Absent		
33	Mallinath	54y/M	1y	1y	Twice	HTN+	excoriatio	Pallor	Present	Half and H	Normal	Normal	Absent	Absent	Absent	Absent		
34	SM Patil	60y/M	9y	8y	Thrice	DM+	Excoriatio	None	None	Beau's line	Normal	Depapilate	absent	Absent	Absent	Absent	tinea cruris	
35	Jayashree	50y/M	2y	2y	Twice	HTN+	excoriatio	Ecchymosi	Present	None	Sparse boc	Macroglos	Absent	Absent	Absent	Absent		
36	Ramling	52y/M	2y	2y	Twice	None	None	Ecchymosi	present	onycholysi	Normal	Normal	Absent	Absent	Absent	Absent		
37	Shreedhar	50y/M	2y	2y	Twice	None	prurigo no	Pallor	present	None	Normal	Normal	absent	Absent	Absent	Absent	Eczema over B/L legs	
38	Mallamma	60y/M	6m	6m	Twice	None	excoriatio	None	present	None	Normal	Normal	Absent	Absent	Absent	Absent	tinea cruris	
39	Parikswam	73y/M	6y	3y	Twice	HTN DM+	excoratior	Ecchymosi	present	Beau's line	Normal	Normal	Absent	Absent	Absent	Absent		
40	Sushila	56y/F	1y	1y	Twice	DM+	prurigo no	None	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
41	Lakshmi	65y/f	1y	1y	Thrice	None	prurigo no	None	present	None	Sparse boc	Depapilate	Absent	Absent	Absent	Absent		
42	Ismail	62y/M	2y	1y	Twice	None	excoriatio	None	None	onycholysi	Normal	Normal	Absent	Absent	Absent	Absent		
43	tarabai	64y/F	6y	6m	Twice	None	None	None	Present	None	Normal	Normal	Absent	Absent	Absent	Absent	tinea cruris	
44	Lalitha	54y/F	1y	1y	Twice	DM+	LSC	None	Present	None	Normal	Normal	Absent	Absent	Absent	Absent		
45	Mallamma	31y/F	7y	7y	Twice	None	prurigo no	None	Present	None	Sparse boc	Normal	Absent	Absent	Absent	Absent		
46	vinod	40y/M	6y	6y	Twice	HTN DM+	LSC	None	Present	None	Sparse boc	Normal	Absent	Absent	Absent	Absent		
47	Maleppa	60y/M	2y	2y	Twice	HTN DM+	prurigo no	Pallor	Present	koilonychi	Sparse boc	Depapilate	absent	Absent	Absent	Absent		
48	Balavantar	65y/M	1y	1y	Twice	DM+	excoriatio	Pallor	Present	Longitudin	Normal	Macroglos	Absent	Absent	Absent	Absent		
49	Mohamme	62y/M	2y	2y	Twice	HTN+	Excoriatio	Pallor	Present	None	Normal	Depapilate	Absent	Absent	Absent	Absent		
50	Laxman	73y/M	1y	1y	Twice	HTN+	Excoriatio	None	Present	Half and H	Normal	Normal	Absent	Absent	Absent	Absent		
51	Sadashiv	35y/M	3y	3y	Twice	DM+	Prurigo no	None	Present	Beau's line	Normal	Normal	kryles dise	Absent	Absent	Absent		
52	Appasab	65y/M	3y	1y	Twice	HTN+	excoriatio	None	Present	Beau's line	Normal	Normal	Absent	Absent	Absent	Absent		
53	Vinod	34y/M	2y	2y	Twice	HTN DM+	Excoriatio	None	Present	Pitting, on	Normal	Normal	kryles dise	Absent	Absent	Absent		
54	Shahed	51y/M	7y	5y	Twice	HTN	None	Hyperpigm	present	Half and H	Sparse boc	Macroglos	Absent	Absent	Absent	Absent		
55	Shivappa	64y/M	13y	7y	Thrice	HTN+	Excoriatio	None	Present	Onycholys	Sparse boc	oral candi	kryles dise	Absent	Absent	Absent		
56	Shridevi	45y/F	8y	8m	thrice	HTN+	LSC	None	Present	Longitudin	Sparse boc	Xerostomi	Absent	Absent	Absent	Absent		

58	Suman	57y/M	1y5m	1y5m	Twice	DM+	Excoriatio	None	Present	onychomy	Normal	tounge sig	absent	Absent	Absent	Absent	
59	Sushila	35y/F	5y	5y	Twice	HTN+	excoriatio	Hyperpigm	Present	None	Normal	Normal	Absent	Absent	Absent	Absent	
60	Sabbura	40y/M	6y	4y	thrice	HTN+	LSC	Pallor	Present	Onychomy	Normal	Macroglos	Absent	Absent	Absent	Absent	tinea cruris
61	Nagappa	23y/M	1y	6m	Twice	DM+	Excoriatio	pallor	present	Half and H	Normal	Depapilate	Absent	Absent	Absent	Absent	
62	Nirmala	65y/F	1y	6m	Twice	DM+	Excoriatio	Pallor	Present	Subungual	Normal	Xerostomi	Absent	Absent	Absent	Absent	
63	Sridharam	43y/F	2y	1y 6m	Twice	DM+	Excoriatio	Ecchymosi	present	Beau's line	AGA	oral candic	Absent	Absent	Absent	Absent	
64	Shakira	25y/F	1y	6m	Twice	HTN+	prurigo no	Ecchymosi	Present	Longitudin	Normal	tounge sig	kryles dise	Absent	Absent	Absent	
65	Shivalingar	42y/M	6m	6m	Twice	None	Excoriatio	Pallor	present	None	Normal	Normal	Absent	Absent	Absent	Absent	
66	Sundaram	47y/F	5y	1y	Twice	DM+	Excoriatio	Ecchymosi	Present	Longitudin	Normal	Normal	Absent	Absent	Absent	Absent	
67	baburao	34y/M	6m	6m	Twice	HTN+	excoriatio	Ecchymosi	Present	onycholysi	Sparse boc	Normal	Absent	Absent	Absent	Absent	
68	kashinath	72y/M	1y	1y	Twice	HTN+	Excoriatio	Pallor	Present	onycholysi	Normal	black hairy	absent	Absent	Absent	Absent	
69	Appasab	65y/M	1y	1y	Twice	HTN+	Excoriatio	Pallor	Present	Half and H	alopecia	oral candic	Absent	Absent	Absent	Absent	
70	Sarojini	40y/F	1y	1y	Twice	HTN DM+	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	absent	Absent	Absent	
71	Basavraj	48y/M	1y	1y	Twice	None	None	None	None	None	Normal	Normal	Absent	Absent	Absent	Absent	
72	Rasulabel	60y/F	1y	1y	Twice	None	None	None	None	None	Normal	Normal	Absent	Absent	Absent	Absent	
73	Nirmala	40y/F	8m	8m	Twice	None	Excoriatio	Pallor	None	onychomy	Normal	Depapilate	Absent	Absent	Absent	Absent	
74	Shridevi	45y/F	1y	1y	Twice	None	None	None	None	onycholysi	Normal	Normal	Absent	Absent	Absent	Absent	
75	Digamba	36y/M	8m	8m	Twice	None	None	Pallor	None	Half and H	Normal	Depapilate	Absent	Absent	Absent	Absent	
76	Malathi	39y/F	4y	4y	Twice	None	Excoriatio	Pallor	Present	Pitting, on	Normal	Depapilate	Absent	Absent	Absent	Absent	
77	Prema	28y/M	2y	2y	Twice	None	Excoriatio	Pallor	Present	None	Normal	Depapilate	Absent	Absent	Absent	Absent	
78	Rajeev	50y/M	1y	1y	Twice	None	Excoriatio	Pallor	Present	Onycolysis	Normal	Depapilate	Absent	Absent	Absent	Absent	
79	Mehaboob	40y/M	2y	2y	twice	None	Excoriatio	Pallor	Present	None	Normal	tounge sig	Absent	Absent	Absent	Absent	
80	Shrinath	64y/M	6m	6m	Twice	None	Excoriatio	Pallor	Present	onycholysi	Normal	Macroglos	Absent	Absent	Absent	Absent	
81	Rudragouc	55y/M	5m	5m	Twice	HTN+	LSC	Ecchymosi	None	Half and H	Normal	oral candic	Absent	Absent	Absent	Absent	
82	Alok	23y/M	2y	2y	Twice	DM+	prurigo no	Pallor	Present	onycholysi	Sparse boc	Normal	Absent	Absent	Absent	Absent	
83	Sanjeev	25y/M	1y	1y	Twice	HTN+	Excoriatio	Ecchymosi	Present	Longitudin	Normal	Macroglos	Absent	Absent	Absent	Absent	
84	Laxmi	24y/F	2y	1y	thrice	HTN DM+	LSC	Ecchymosi	None	None	Normal	Normal	Absent	Absent	Absent	Absent	
85	Sushanth	28y/M	4y	2y	Twice	HTN+	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent	
86	Vinod	30y/M	3y	2y	Twice	HTN+	excoriatio	Pallor	present	None	Normal	Normal	Absent	Absent	Absent	Absent	
87	Sandhya	50y/F	2y	2y	Twice	None	LSC	None	Present	None	Normal	Normal	Absent	Absent	Absent	Absent	
88	Mulla	54y/M	2y	1y 6m	Twice	None	excoriatio	None	Present	None	Normal	Macroglos	Absent	Absent	Absent	Absent	keloid
89	Bouramma	35y/F	1y	1y	Twice	None	Excoriatio	Pallor	Present	None	Normal	Normal	Absent	Absent	Absent	Absent	
90	Ashaf	27y/M	7y	7y	Thrice	None	Excoriatio	Pallor	Present	Half and H	Sparse boc	tounge sig	kryles dise	Absent	Absent	Absent	
91	Rafiq i	55y/M	1y	6m	Twice	HTN+	Excoriatio	ecchymosi	Present	onycholysi	Normal	Macroglos	Absent	Absent	Absent	Absent	
92	Yashwanth	55y/M	7m	7m	Twice	HTN DM+	prurigo no	yellowish t	None	None	Normal	Normal	Absent	Absent	Absent	Absent	
93	Mallappa	32y/M	1y	1y	Twice	None	excoriatio	Pallor	Present	Half and H	Normal	Normal	Absent	Absent	Absent	Absent	
94	Mahadev	34y/M	1y	6m	Twice	None	LSC	None	None	Pitting, on	Normal	Normal	Absent	Absent	Absent	Absent	