A STUDY OF CUTANEOUS MANIFESTATIONS IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS

Dissertation submitted in partial

fulfilment of the university regulations for

M.D. DEGREE in

DERMATOLOGY, VENEREOLOGY AND LEPROSY

(BRANCH XX)

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THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI – TAMIL NADU

CERTIFICATE FROM THE DEAN

This is to certify that this dissertation entitled "**A STUDY OF CUTANEOUS MANIFESTATIONS IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS"** submitted by **DR.N.HAAMEEM SUBAITHA JALVA** to The Tamil Nadu Dr. M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D.[DERMATOLOGY, VENEREOLOGY AND LEPROSY] and is a bonafide research work carried out by her under direct supervision and guidance. This work has not previously formed the basis for the award of any degree or diploma.

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DECLARATION

I, **DR.N.HAAMEEM SUBAITHA JALVA** solemnly declare that the dissertation titled **"A STUDY OF CUTANEOUS MANIFESTATIONS IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS"** is a bonafide work done by me at Government Rajaji Hospital during 2016–2019 under the guidance and supervision of **Prof. Dr. G. GEETHARANI M.D., D.D.,** Professor and Head of the Department of Dermatology, Madurai Medical College, Madurai. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree and diploma to any university, board either in India or abroad. The dissertation is submitted to The Tamilnadu Dr.M.G.R. Medical University, towards partial fulfilment of requirement for the award of **M.D.Degree in Dermatology, Venereology and Leprosy (BRANCH –XX).**

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CONTENTS

INTRODUCTION

INTRODUCTION

Acute and Chronic kidney disease are common and they reflect an ongoing rise in prevalence of diabetes and hypertension which are the two most common causes of renal failure. Cutaneous manifestation of renal disease occur frequently in the setting of chronic kidney disease.

The skin is the most visible and easily accessible organ of body and is an important diagnostic window to diseases affecting the internal organ systems including the renal system.[1]

There are various ways in which the skin is affected in Chronic kidney disease. Numerous specific and non-specific skin abnormalities are observed in these patients, which are caused either by the disease or by the treatment and is due to a range of factors from metabolic disturbances to immunosuppressive drugs.[2]

With the advent of dialysis, there is increase in the life expectancy of these patients, giving time for more and more newer cutaneous changes to manifest.[3]

The dermatological complications can impair the quality of life significantly in affected individuals , therefore early diagnosis and treatment can greatly reduce the associated morbidity.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in the glomerular filtration rate (GFR).

The term end-stage renal disease represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys results in the uremic syndrome. This syndrome leads to death unless the toxins are removed by renal replacement therapy, using dialysis or kidney transplantation.

CRITERIA FOR DIAGNOSIS OF CKD:

Either of the following present for more than 3 months:

1. MARKERS OF KIDNEY DAMAGE: (one or more)
    i. Albuminuria >30mg/g
    ii. Urine sediment abnormalities
    iii. Electrolyte and other abnormalities due to tubular disorders
    iv. Abnormalities detected by histology
    v. Structural abnormalities detected by imaging
    vi. History of kidney transplantation
2. DECREASED GFR:

    GFR<60ml/min/m^2BSA

RISK FACTORS :

Risk factors for CKD include small for gestation birth weight, childhood obesity, hypertension, diabetes mellitus, autoimmune disease, advanced age, African ancestry , a family history of kidney disease ,a previous episode of acute kidney injury and the presence of proteinuria, abnormal urinary sediment, or structural abnormalities of the urinary tract.

ETIOLOGY OF CKD: [4]

1. Metabolic disorders
    i. Diabetes mellitus
    ii. Obesity
    iii. Amyloidosis
2. Hypertension
3. Renal vascular disorders
    i. Atherosclerosis
    ii. Nephrosclerosis-hypertension
4. Immunologic disorders
    i. Glomerulonephritis
    ii. Polyarteritis nodosa
    iii. Lupus erythematosus
5. Infections

i. Pyelonephritis

ii. Tuberculosis

6. Primary tubular disorders

    i. Nephrotoxins (analgesics, heavy metals)

7. Urinary tract obstruction

    i. Renal calculi

    ii. Hypertrophy of prostate

    iii. Urethral constriction

8. Congenital disorders

    i. Polycystic disease

    ii. Congenital absence of kidney tissue (renal hypoplasia)

PATHOPHYSIOLOGY OF UREMIA:

Manifestations of uremic syndrome are

(1) those consequent to accumulation of toxins that normally undergo renal excretion, including products of protein metabolism.

(2) those consequent to loss of other kidney functions, such as fluid and electrolyte homeostasis and hormone regulation

(3) progressive systemic inflammation and its vascular and nutritional consequences.

CLINICAL MANIFESTATIONS OF CKD:[5]

SYMPTOMS:

Fatigue, anorexia, breathlessness, nausea, vomiting, pruritus, dry skin, hiccoughs, bone pain, nocturia, muscle cramps, drowsiness, amenorrhoea , decreased libido

SIGNS:

Pallor, pigmentation, increased respiratory rate, hypertension, increased jugular venous pulsation, pedal edema, pulsus paradoxus (pericardial tamponade), xerosis, brown nails, paresthesia, absent reflexes.

SYSTEMIC EFFECTS OF UREMIA:

Almost every system is affected by uremia. These include cardiovascular, pulmonary, hematologic, neuromuscular, gastrointestinal abnormalities, endocrine and metabolic disturbances and the most clinching dermatologic abnormalities.

CUTANEOUS MANIFESTATIONS OF UREMIA:

1. **PRURITUS**:

   Pruritus is one of the most common cutaneous symptoms of CKD. It is not present in acute renal failure and it does not necessarily subside with dialysis, although it may improve with kidney transplantation. Its prevalence among hemodialysis patients ranges from 19 to 90%.[6]

It leads on to secondary skin lesions – excoriations, chronic prurigo or acquired perforating dermatoses.

ETIOLOGY:

Pruritus is multifactorial. The proposed causes are

i. Generalized Xerosis
ii. Impaired clearance of Pruritogens (pruritus causing agents) called "middle molecules", which are thought to be poorly dialyzable substances due to their larger molecular size. β2 microglobulin, advanced glycosylation end products and parathyroid hormones are the middle molecules that have been studied, but their role is uncertain.[7]
iii. Environmental heat can aggravate pruritus
iv. Dialysis associated neuropathy of Type-C unmyelinated nociceptive nerve fibres in the skin.[8]
v. Hyperparathyroidism – Parathormone itself or its disturbance of Calcium-phosphorus metabolism results in pruritus[9]
vi. Hypervitaminosis A[10]
vii. Increased serum histamine
viii. Increased serotonin levels[11]
ix. Endogenous opioids
x. Mast cell hyperplasia – Mast cells proliferate in renal failure and they are the storage and release site for histamine. Mast cell proliferation theory was

refuted when ultra violet light therapy was shown to decrease the number of mast cells without a corresponding decrease in pruritus[12]

xi. Types of dialysis membrane and dialysis tubing also contribute to pruritus

MANAGEMENT:

i. Regular use of emollients, humectants or moisturizers to reduce xerosis

ii. Cool environment

iii. UVB Therapy:[13]

- Suppress histamine release
- Reduce epidermal Vitamin A content
- Forms photoproducts with antipruritic effect
- Should be used in caution if transplant is considered because of risk of skin cancer

iv. PUVA Therapy:[14]

- Reduces skin phosphorus
- Reduces dermal histamine

v. Topical menthol

vi. Topical capsaicin[15] 0.025% is an irritant cream and it depletes Substance P in peripheral sensory neurons and reduces itch sensation

vii. In dialysis, lowering the Mg concentration of the dialysate[15]

viii. Parathyroidectomy

ix. Naltrexone[16](μ receptor antagonist) 50 mg/day for 4 weeks

x. Nicergoline[17](dopamine agonist) 30 mg orally qid for 2 weeks

xi. Ketotifen (Mast cell stabilizer) – 1-2 mg bd[18]

xii. Cimetidine[19]

xiii. Mexilitine[16]

xiv. Topical tacrolimus[20] – 0.1% for 2- 6 weeks

xv. Oral activated charcoal[21] -6gm daily for 8 weeks. It chelates the circulating toxins in the gut.

xvi. Heparin infusion[22] – reduces uremic solutes in blood.

xvii. Erythropoietin[23]- reduction of plasma histamine concentration

xviii. Oral oil of evening primrose[24]

xix. Gabapentin or Pregabalin for burning or painful itch

xx. A transcutaneous electrical needle stimulation[25]

2. **XEROSIS**:

It manifests as dry skin, sometimes with fine scaling. Significant xerosis occurs in 50-75%[26] of the dialysis population for unknown reasons. The extensor surfaces of legs and arms are more severely affected with large dark scales whereas over the abdomen the scales are smaller and finer. The flexor surfaces, the axillae , the ante-cubital fossa and popliteal fossa are relatively spared. Xerosis generally appears before initiation of dialysis therapy. It seems to be little influenced by dialysis.

ETIOPATHOGENESIS:

i. Decrease in size of eccrine sweat glands resulting in decreased sweat volume[27]

ii. Hypervitaminosis A contributes to xerosis[28]

iii. Reduced water content in the epidermis

iv. Secondary hyperparathyroidism

v. Uremia induced alteration in corneocyte maturation

PATHOLOGY:

i. Reduction in size of eccrine sweat gland[27]

ii. Atrophy of sebaceous glands

MANAGEMENT:

i. No specific treatment

ii. Emollients, moisturizers and humectants can provide symptomatic relief

3.PIGMENTARY CHANGES:

1. PALLOR:

It is due to anaemia in CKD patients. The cause of anaemia may be any one of the following:[29]

i. Relative deficiency of erythropoietin

ii. Diminished red blood cell survival

iii. Iron deficiency

iv. Hyperparathyroidism/ bone marrow fibrosis

v. Chronic inflammation

vi. Folate / Vitamin B12 deficiency

vii. Hemoglobinopathy

viii. Comorbid conditions: Hypo/hyperthyroidism, Pregnancy, HIV-associate disease, autoimmune disease, immunosuppressive drugs

2. DIFFUSE HYPERPIGMENTATION:[30]

It occurs in ESRD due to increase in β Melanocyte Stimulating Hormone which is poorly dialyzable and results in increased melanogenesis and deposition of melanin

3. YELLOW DISCOLORATION:

Deposition of urochromes or pigmented metabolites and carotene in the epidermis and subcutaneous tissue results in yellow discoloration

4. HYPERPIGMENTED MACULES ON PALMS AND SOLES:[6]

It has been reported in many uremic patients. Cause is unknown.

4.PERFORATING DERMATOSES:

The acquired perforating dermatoses have been variously labeled based on the precise clinicopathological presentation as follows:

1. Reactive perforating collagenosis(RPC)
2. Perforating folliculitis
3. Kyrle disease
4. Elastosis perforans serpiginosa
5. Acquired perforating dematoses. [31]

The perforating disorders share the common characteristic of transepidermal elimination (TEE). This is characterized by the elimination of altered dermal collagen and elastin admixed with degenerate keratin through the follicular wall and/or the epidermis.

Pruritus is always present and up to 11% of dialysis patients may be affected.

The cutaneous lesions consist of hyperpigmented papules, plaques and nodules up to 1 cm in diameter with a central keratinous plug. The extensor surfaces of the limbs are more commonly affected but the trunk and face may be involved as well.

1. REACTIVE PERFORATING COLLAGENOSIS (RPC):

RPC is a rare perforating disorder in which altered collagen is extruded by means of TEE. True, classic RPC is a genodermatosis that is inherited as an autosomal dominant or recessive trait.[32]

ETIOPATHOGENESIS:

Precipitating factors:

1. Trauma
2. Arthropod bite
3. Folliculitis
4. Exposure to cold

RPC occurs early in life, and both genders are equally affected.

CLINICAL FEATURES:

The primary clinical lesion is a small papule which enlarges to the size of 5 to 10 mm with a hyperkeratotic central umbilication. The lesion often appears eroded. These lesions spontaneously regress, leaving superficial scars with postinflammatory pigmentary alteration. Koebnerization is common.

An adult, acquired type of RPC has been described in association with diabetes mellitus and chronic renal failure.[33]

HISTOPATHOLOGY:

The classic lesion shows a shallow, vertically oriented, cup-shaped invagination of the epidermis, forming a short channel.

The channel is lined by acanthotic epithelium along the sides. At the base of the invagination, there is an attenuated layer of keratinocytes, that in some foci appear eroded.

Within the channel, there is densely packed degenerated basophilic staining material and altered collagen bundles.

Vertically oriented perforating bundles of collagen are present interposed between the keratinocytes of the attenuated bases of the invagination . It is important that a Masson's trichrome stain be done to confirm that the fibers are collagen[34]

2. PERFORATING FOLLICULITIS:

Perforating folliculitis is a perforating disorder that is first described by Mehregan and Coskey [35]

ETIOPATHOGENESIS:

Perforating folliculitis is the end result of abnormal follicular keratinization which most likely is caused by irritation, either chemical or physical, and even chronic rubbing.

A portion of a curled-up hair is often seen close to or within the area of perforation surrounded by a foreign body granuloma[36]

CLINICAL FEATURES:

This is a relatively uncommon disorder that usually is observed in the second to fourth decades of life

It is characterized by erythematous follicular papules with central keratotic plugs.

The lesions are 2 to 8 mm in diameter and tend to be localized to the extensor surfaces of the extremities and the buttocks.

The key to making this diagnosis is the clinical and the histologic identification of a follicular unit as the primary site for the inflammatory process.

HISTOPATHOLOGY[37]:

The main pathologic abnormalities consist of

(a) a dilated follicular infundibulum that is filled with compact ortho and parakeratotic cornified cells

(b) degenerated basophilic staining material, comprised of granular nuclear debris from nuclear neutrophils, other inflammatory cells, and degenerated collagen bundles

(c) perforations through the follicular epithelium

(d) associated perifollicular inflammatory cell infiltrate composed of lymphocytes, histiocytes, and neutrophils.

Additionally, altered collagen and eosinophilically altered elastic fibers are found adjacent to the sites of perforation. When serial sections through the specimen are examined, a remnant of the hair shaft can sometimes be found.

3. KYRLE'S DISEASE:

Kyrle's disease is a rare disorder, described by Kyrle in 1916[38]. There is controversy as to whether it represents a distinct entity or an exaggerated form of perforating folliculitis[39], or actually comprises a group of disorders with similar epidermal– dermal reaction patterns associated with diabetes chronic renal failure, prurigo nodularis, and even keratosis pilaris.

ETIOPATHOGENESIS:

i. The primary event is a disturbance of epidermal keratinization characterized by the formation of dyskeratotic foci and acceleration of the process of keratinization.

ii. This leads to the formation of keratotic plugs with areas of parakeratosis[40]. Because the rapid rate of differentiation and keratinization exceeds the rate of cell proliferation, the parakeratotic column slowly extends deeper into the abnormal epidermis, leading in most cases to perforation of the parakeratotic column into the dermis.

iii. Perforation is not the cause of Kyrle's disease, as originally thought[41], but rather represents the consequence or final event of the abnormally sped-up keratinization. This rapid production of abnormal keratin forms a plug which acts as a foreign body, penetrating the epidermis and inciting a granulomatous inflammatory reaction.

CLINICAL FEATURES:

This eruption presents with a large number of papules, few coalescing into plaques, numbering in the hundreds and often distributed on the extremities. Although some may appear to involve the follicular units, these lesions are more likely to be extrafollicular.

The typical patient is young to middle aged and often has a history of diabetes mellitus. The papules are dome shaped, 2 to 8 mm in diameter, with a central keratotic plug. Excoriations are found in the vicinity of these lesions. Linear lesions related to possible koebnerization have been described.

HISTOPATHOLOGY:

The essential histopathologic findings include

(a) a follicular or extrafollicular cornified plug with focal parakeratosis embedded in an epidermal invagination,

(b) basophilic degenerated material identified in small collections throughout the plug with absence of demonstrable collagen and elastin,

(c) abnormal vacuolated and/or dyskeratotic keratinization of the epithelial cells extending to the basal cell zone,

(d) irregular epithelial hyperplasia

(e) an inflammatory component that is typically granulomatous with small foci of suppuration

In most instances, it is important to perform elastic tissue stains and even trichrome stains to exclude perforating elastic fibers, as in elastosis perforans serpiginosa, or collagen fibers, as in RPC[42].

4. ELASTOSIS PERFORANS SERPIGINOSA:

EPS is the most distinctive of the perforating disorders as it demonstrates the best example of TEE. In EPS, increased numbers of thickened elastic fibers are present in the upper dermis, and altered elastic fibers are extruded through the epidermis. It is a rare disorder that affects young individuals, with a peak incidence in the second decade. Men are affected more often than women.

CLINICAL FEATURES:

EPS is primarily a papular eruption localized to one anatomic site and most commonly affecting the nape of the neck, the face, or the upper extremities. The papules are typically 2 to 5 mm in diameter. These papules are arranged in arcuate or serpiginous groups and may coalesce.

Of particular importance is the association of EPS with systemic diseases. The important associations include Down's syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta, PXE, and Marfan's syndrome. In addition, on rare occasions, EPS is observed in association with Rothmund-Thompson syndrome or other connective tissue disorders and as a secondary complication of penicillamine administration.

Few cases of EPS with renal failure have been reported.[43]

HISTOPATHOLOGY:

The essential findings include a narrow transepidermal channel that may be straight, wavy, or of corkscrew shape and thick, coarse elastic fibers in the channel admixed with granular basophilic staining debris. A mixed inflammatory cell infiltrate accompanies the fibers in the channel. Also observed are abnormal elastic fibers in the upper dermis in the vicinity of the channel. In this zone, the elastic fibers are increased in size and number. As these fibers enter the lower portion of the channel, they maintain their normal staining characteristics, but as they approach the epidermal surface, they may not stain as expected with elastic stains.

5. ACQUIRED PERFORATING DERMATOSES:

The term acquired perforating dermatosis was suggested by Rapini et al. to describe a pathologic process encompassing the various forms of TEE seen in patients with renal disease and/or diabetes mellitus[31].

Differences in clinical and histologic features, such as the presence of koebnerization, or histologic evidence of follicular involvement with or without collagen fibers in the epidermis have variably led to diagnoses of Kyrle's disease, "acquired" RPC, or perforating folliculitis[45,46,47].

Other terms that have been used include perforating disorder secondary to chronic renal failure and/or diabetes mellitus, perforating folliculitis of hemodialysis, Kyrle-like lesions and uremic follicular hyperkeratosis[48,49,50,51].

CLINICAL FEATURES:

Clinically, lesions are pruritic and range from hyperkeratotic papules and nodules resembling Kyrle's disease to RPC-like umbilicated papules, nodules, and plaques to erythematous, follicular papules and nodules mimicking perforating folliculitis[31,44,51]. Annular plaques and erythematous pustules have been described, with histologic features of RPC and perforating folliculitis, respectively[51]. The most common location is the extensor surfaces of the extremities, but the trunk and head can also be involved[51]

HISTOPATHOLOGY:

The histologic features of APD are variable

When vertically oriented, Masson trichrome–positive collagen bundles are present within a perforation, the findings are suggestive of RPC.

When perforation is associated with a follicle, the findings resemble perforating folliculitis.

However, chronic rubbing can lead to superimposed features of prurigo nodularis, thus distorting the follicle and making it unrecognizable.

TEE in the absence of follicular involvement, without demonstrable collagen or elastin, is reminiscent of Kyrle's disease.

Perforation associated with elastic van Gieson (EVG)-positive elastic fibers within a transepidermal canal, as seen in EPS, has also been described [43,51].

MANAGEMENT OF PERFORATING DERMATOSES:

1. No treatment is of proven benefit.
2. Spontaneous improvement if renal function improves[52]
3. Allopurinol
4. Topical retinoids
5. Oral isotretinoin
6. Methotrexate
7. Rifampicin
8. Emollient creams
9. Intralesional steroids
10. Topical steroids under occlusion[31,47]

11. Narrow-band UVB
12. PUVA
13. Photodynamic therapy
14. Amitriptyline
15. Topical tacalcitol

5.CALCINOSIS CUTIS:

This term refers to a group of disorders in which deposits of calcium are found in the skin.[53] It was initially described by Virchow in 1855. Calcinosis cutis occurring in ESRD and patients on hemodialysis is a type of metastatic calcification due to increased Calcium – Phosphate ratio. It occurs in 1% of patients on hemodialysis.

PATHOGENESIS:

Cause of Calcinosis cutis in ESRD is multifactorial. These include

1. Hyperphosphataemia due to decreased renal clearance occurs early.
2. Hypocalcemia which occurs either as a result of hyperphosphataemia or is worsened by renal failure.
3. Parathyroid hormone is produced in excess as a compensatory measure.
4. Hyperparathyroidism causes an increase in calcium and phosphate mobilization and an elevated solubility product and subsequently the formation and precipitation of calcium salts.

CLINICAL FEATURES:

Rock hard papules, nodules and plaques typically occur around large joints[54] and over fingertips. These may exude a chalky discharge through the epidermis. This occurs in sub-acute fashion without livedo or ischaemic pain.

HISTOPATHOLOGY:

The calcium occurs as massive deposits when located in the subcutaneous fat and usually as granules and small deposits when located in the dermis. Large deposits of calcium evoke a foreign body reaction with giant cells, inflammatory infiltrate, and fibrosis may be present around them[55]. Calcium deposits are recognized easily in histologic sections, because they stain deep blue with H&E. They stain black with the von Kossa stain for calcium phosphate.

TREATMENT:

MEDICAL:

i. Dietary measures: Restriction of dietary phosphates and calcium, consumption of ketogenic diet including free fatty acids, which causes accumulation of keto acids, metabolic products of fatty acids that result in decreased pH and thus preventing crystallization.
ii. Magnesium or aluminium antacids may be effective phosphate binders in patients with hyperphosphataemia. However use in patients with renal insufficiency may result in magnesium or aluminium toxicity.
iii. Probenecid causes increased renal phosphate clearance and Colchicine act by reducing inflammation associated with pruritus
iv. Intralesional corticosteroid has anti-inflammatory and antifibrotic activity.

v. Warfarin

vi. Sodium etidronate and diphosphonates reduce bone turnover and inhibit the growth of ectopic hydroxyapatite crystals

vii. Calcium channel blockers – Diltiazem (120mg/day) causes reduction in mineral content of calcified tissues.

SURGICAL: Excision

Indications:

- Pain
- Recurrent infections
- Ulcerations
- Functional impairment

Complications:

Pain, paraesthesia, ulceration, infection, cosmetic disfigurement, restricted mobility, mechanical compromise, vascular occlusion resulting in gangrene.

6.CALCIPHYLAXIS:

Synonym: Calcific uremic arteriolopathy

Calciphylaxis is a serious, life-threatening thrombo-occlusive disorder characterized by calcium deposition in the skin and subcutis both within vessels and in the surrounding tissues most commonly seen in the setting of renal failure. It is estimated

to have an incidence of 4.5 per million per year[56]. The prevalence in chronic renal failure is reported to be approximately 1%[57,58} and in haemodialysis patients 4%[59].

Associated diseases:

1. Renal failure
2. Hyperparathyroidism
3. Hepatic failure
4. Malignancy[60]
5. Obesity
6. Warfarin
7. Corticosteroid use
8. Diabetes
9. Connective tissue disease
10. Protein S and protein C deficiency[61-63]

PATHOPHYSIOLOGY:

Pathophysiology is multifactorial. The final common pathway might be via receptor activator of nuclear factor κB (RANK), RANK ligand and osteoprotogenerin, which appear to regulate extraskeletal mineralization[64].

Parathyroid hormone, aluminum, corticosteroids, liver disease and various forms of inflammation can activate this system, which may have a role in calciphylaxis.

Matrix Gla protein and fetuin A, which inhibit extraosseous calcification, are also important[65,66]. A role for warfarin could be explained by inhibition of vitamin K-dependent γ-carboxylation of matrix Gla protein.

PREDISPOSING FACTORS:

Renal failure, abnormalities of systemic calcium homeostasis, obesity, hepatobiliary disease and malignancy are recognized predisposing factors for calciphylaxis. Other possible factors include diabetes, warfarin, coagulation abnormalities ,steroid use and elevated aluminium levels.

PATHOLOGY:

(a) calcification of soft tissue and small vessels

(b) nonspecific intimal proliferation of small vessels, often resulting in luminal narrowing

(c) variable fibrin thrombi

(d) frequent ischemic necrosis of skin and subcutis

The small vessels involved by this process cannot be identified as either arterial or venous. Foreign body giant cell reaction to calcium and mixed inflammatory cell infiltrates that are neutrophil-rich may be seen.

CLINICAL PRESENTATION

The presentation is quite variable. The first description by Selye *et al.* in 1961 in rats[67] was followed in 1968 by a case report typical of calciphylaxis in end-stage renal failure[68].

The typical presentation is with purpuric, necrotic, ulcerating, calcified plaques on the lower abdomen or thighs. On the lower legs, calcification may be less obvious clinically but livedo is characteristic. In some cases the cutaneous involvement is little, with more diffuse subcutaneous calcification, which may have a better prognosis.

Calciphylaxis has also been reported on the penis[69] , breasts[70] , tongue[71] and occasionally internal organs[72]. The ulcers are irregular, stellate and deep. Surrounding livedo is evidence of the local vascular thrombosis.

DISEASE COURSE AND PROGNOSIS

The progression of calciphylaxis is variable, but secondary sepsis is common. Although calcification of cardiac, gastrointestinal and other systemic arteries may be demonstrated, an ischaemic process similar to the skin is not seen internally[73] . The mortality is very high up to 80% and the median survival is <3 months. Even in those cases where treatment seems to improve the cutaneous features, the mortality is still >60% [74].

INVESTIGATIONS

A single deep biopsy of an indurated plaque is needed to demonstrate calcification of subcutaneous fat and the involvement of vessels. Assessment of systemic calcium homeostasis, levels of glucose and HbA1c, liver function tests and coagulation screen should also be checked. X-rays of soft tissues may reveal 'netlike' patterns of calcification[75] or diffuse calcification of small to medium-sized arterioles out into the dermis[76]

MANAGEMENT

1. Intravenous sodium thiosulphate. This certainly does seem to improve symptoms quickly (generally within a week) and the short-term outcome appears to be better although the long-term impact is uncertain.

2. Long-term oral sodium thiosulphate has been reported to be effective at maintaining remission[77]
3. Correction of abnormal calcium homeostasis is sensible but may not affect outcome.
4. Cinacalcet [78-81].
5. Phosphate binder sevelamer[82]
6. Parathyroidectomy is of questionable benefit survival
7. Anticoagulation is logical but controversial and it is important to exclude warfarin

Or heparin necrosis before recommending this.

8. Thrombolysis

7.BULLOUS DISEASE

Various blistering disorders can be seen in patients with renal disease. These include Porphyria cutanea tarda(PCT), Pseudoporphyria and the Bullous disease of dialysis.[83]

PATHOGENESIS:

1. Azotemia causes reduced activity of Uroporphyrinogen decarboxylase
2. Renal failure causes relatively slower than normal clearance of Porphyrins which accumulates in the skin and results in skin fragility and blistering. Blood porphyrin levels are normal or near normal [84, 85]

3. Reduced clearance of photoactive drugs like frusemide, tetracycline, nabumentone, nalidixic acid, phenytoin in renal failure patents.[84]
4. Iron overload from blood transfusion
5. Increased incidence of Hepatitis C in dialysis population.

MANAGEMENT:

i. Phlebotomy can reduce iron levels in the liver, allowing new hepatic uroporphyrinogen decarboxylase to be formed. However, patients with end-stage renal disease often have significant anemia and cannot tolerate phlebotomy.
ii. IV erythropoietin may both lower total body iron stores and support phlebotomy [86,87]
iii. Chloroquine effectively clears porphyrins from the liver. In patients with CRF, however, porphyrins may not be effectively cleared by hemodialysis or excreted in the urine.[88]
iv. Deferoxamine lower serum porphyrin levels in some patients. [86]
v. Others require renal transplantation to obtain complete resolution of symptoms. [86]

8.PURPURA

Purpura, petechiae , ecchymoses are due to mild thrombocytopenia or more marked platelet dysfunction and increased vascular fragility or associated poor quality of collagen. Abnormal platelet function, increased vascular fragility and the use of heparin

during dialysis are the causes of abnormal bleeding in CKD patients[30] . It is partly reversed by dialysis.

9.NEPHROGENIC SYSTEMIC FIBROSIS

It was first described by Cowper *et al*.[89] in renal dialysis patients as a scleromyxedema like illness with distinct histologic and pathologic features, in the year 2000. There is no age or sex predilection for this disease . The only known constant association is renal dysfunction[90]. This condition has affected predialysis patients, patients on hemodialysis and peritoneal dialysis, and renal transplant recipients.[91-93]

ETIOPATHOGENESIS:

1. Usage of Gadolinium contrast in CKD patients[94]
2. Vascular surgical procedure can initiate an inflammatory cascade resulting in an aberrant wound healing and therefore causing Nephrogenic systemic fibrosis.[95]
3. Recruitment of bone marrow derived CD34/procollagen I+ circulating fibroblasts[96]

CLINICAL FEATURES:

The disease causes symmetrical thickening of skin over the extremities and occasionally over trunk but spares the face. The most frequent site is the area from ankle to mid-thigh. The involved area becomes erythematous, woody and shows a peau de

orange surface change. Papular and nodular lesions can also occur but blistering is rare. Thickening of skin over joints limits its mobility.

Other systems affected include skeletal muscle, fascia, heart, lung, diaphragm and kidney.

PATHOLOGY:

Histologic findings show spindled fibroblasts that extend into subcutaneous septae and subjacent fascia . Collagen bundles are thickened and cytoplasmic processes of fibrocytes surround collagen bundles. These areas may demonstrate factor XIIIa–positive stellate fibroblastic cells and CD68-positive multinucleated giant cells.

Immunohistochemical stains show fibrocyte reactivity with CD34 in a membranous pattern and procollagen I in a cytoplasmic pattern[91,94]

TRAETMENT:

1. Improvement of renal function
2. Renal transplant
3. Topical Calcitriol under occlusion
4. Oral Prednisolone[97]
5. Extracorporeal photopheresis[98]
6. Photodynamic therapy[99]
7. Thaliomide
8. Pentoxifylline

9. Rapamycin
10. IVIg[100]

10.UREMIC FROST

It was first described by Hirschsprung[83] in 1865. It is rarely encountered nowadays due to the widespread availability of dialysis.

PATHOGENESIS

When the blood urea nitrogen (BUN) rises, urea concentrates in the sweat and deposits on the skin following evaporation.

CLINICAL FEATURES

Typically seen first in the beard area, or on other areas of the face, neck or trunk as fine white to yellow crystals. It represents a grave prognostic sign , unless treatment is emergently initiated.

11.GYNAECOMASTIA

It can occur as a complication of hemodialysis[101]. It occurs during the early stages of regular dialysis treatment and is described on the basis of 'refeeding' after the start of treatment.[102] As a consequence of CKD and protein energy malnutrition, pituitary gonadotrophic and testicular functions remain suppressed and later following treatment and increase in daily protein intake, a 'second puberty' ensues. This may lead to transient gynecomastia.

12.VASCULAR DISORDERS

i. MICROANGIOPATHY:

Severe microangiopathy has been revealed in skin biopsies from 75% of patients with chronic renal failure[103], due to reduction of VEGF(Vascular Endothelial Growth Factor)

Histopathology:

- Endothelial cell activation and / or necrosis
- Basement membrane thickening
- Reduplication of the basal lamina involving both venules and arteries

ii. SKIN NECROSIS:

Proximal skin necrosis and / or peripheral gangrene may occasionally occur in uremic patients. Proximal skin necrosis can involve the trunk, shoulders , buttocks or thigh. Lesions usually spread rapidly covering large areas and have a bad prognosis. Distal skin necrosis of the fingers and toes can lead to digital gangrene but the disease is usually self limiting.

13.POOR WOUND HEALING

It occurs due to decreased collagen turnover caused by acidosis

14.RESTLESS LEG SYNDROME

It is characterized by burning, painful paraesthesia of the dorsal or plantar surface of the feet . It is due to peripheral neuropathy.[104] Treatment is with Dopamine agonists, Gabapentin and Opioids

15.INFECTIONS

Patients with CKD have impaired cellular immunity due to a decreased T lymphocyte count[6]. This will explain the high prevalence of infections in CKD patients.

16.IATROGENIC MANIFESTATIONS:

1. Arteriovenous shunt dermatitis[105]
2. Eczema at cannulation site
3. Infection, phlebitis and haematoma at fistula site
4. Cannulation septicemia[106]
5. Pseudokaposi sarcoma
6. Premature ageing of skin and actinic keratoses

ORAL MUCOSAL CHANGES:

1. **TONGUE SIGN OF UREMIA:**[107]

   Teeth marking with macroglossia was first described by Mathews in 92% of patients with CRF.

2. **XEROSTOMIA**

   It is due to mouth breathing and dehydration.

3. **STOMATITIS**[108]

It is due to chemical burn caused by ammonia released by bacteria due to increased content in the salivary secretion.

4. **ANGULAR CHEILITIS**
5. **UREMIC FETOR**

It is an ammoniacal odour caused by high concentration of urea in the saliva and its breakdown to ammonia.

HAIR ABNORMALITIES[28]

1. Scalp hair loss
2. Loss of hair on forearms and legs
3. Drying and hair fragility – due to decreased secretion of sebum.
4. Hair discoloration

NAIL CHANGES

The following nail changes occur in patients with uremia as well as in those undergoing dialysis.

1. Half & Half nail
2. Mee's line
3. Muehrcke's line
4. Beau's line
5. Brown nail bed arc

6. Onycholysis
7. Onychomycosis
8. Koilonychia
9. Subungual hyperkeratosis
10. Splinter hemorrhage

HALF AND HALF NAIL:

Synonym: Lindsay's nail

Bean first described half and half nails in 1953. Though not pathognomonic of renal failure , they occur in 33%[109] of patients with uremia and 40% of those in dialysis. It is characterized by a dark distal band that occupies 20-60% of the nailbed and a white proximal band. The color of distal band varies from red to brown. It is more common in fingernails, although it has also ben noted in toenails.

Causes:[110]

- Brown colour due to deposition of melanin in the nail plate due to stimulation of matrix melanocytes or pink due to normal nail bed
- Increase of capillaries and thickening of their walls
- Proximal white band is due to edema of nail bed

Pigment is more visible distally than proximally because of looser attachment of distal nail plate to the nail bed. The nail changes do not correlate with serum calcium, phosphorus or bicarbonate. It is the most useful onychopathological indicator of renal failure.

MEE'S LINE:

These are single or multiple white transverse bands that run parallel to lunula. It moves with the nail growth. It is due to disturbance of nail growth at nail matrix.

MUEHRCKE'S LINE:

They are paired white bands that are parallel to the lunula in the nail bed, with pink between two white lines. It does not move with nail growth. It represents an abnormality in the vascular bed of the nail. It is commonly associated with hypoalbuminemia.

BEAU'S LINE:

They are transverse grooves which arise through temporary interference with nail formation and become visible on the nail surface some weeks after the precipitating event. The distance of the groove from the nail fold is related to the time since the onset of growth disturbance. The depth and width of the groove may be related to the severity and duration of disturbance, respectively.

BROWN NAIL BED ARC:[111]

It was described y Stewart and Raffle as a brown arch affecting the distal part of the finger nail bed, just proximal to the point of separation of the nail from its bed.

It is due to deposition of lipochromes , which are fat soluble pigments occurring in natural fat. (eg: Lutein, Carotene)

ONYCHOLYSIS:

It is distal separation of nail plate from nail bed.

DIALYSIS [112]:

Dialysis is the separation of substances in solution by means of their unequal diffusion through semipermeable membranes

TYPES OF DIALYSIS:

There are three different types of dialysis.

HEMODIALYSIS

It is the most common type of dialysis. In this process an artificial kidney (hemodialyzer) is used to remove waste and extra fluid from the blood. Then the filtered blood is returned to the body with the help of a dialysis machine.

PERITONEAL DIALYSIS

Peritoneal dialysis involves surgery to implant a catheter into the abdominal cavity. The catheter helps to filter the blood through the peritoneum. During treatment, a special fluid

called dialysate is allowed to flow into the peritoneum. The dialysate absorbs waste which is then drained from the abdomen.

CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

This therapy is used primarily for people with acute kidney injury. It's also known as hemofiltration. A machine passes the blood through tubing. A filter then removes water and waste products. The blood is returned to the body, along with replacement fluid. This procedure is performed 12 to 24 hours a day.

SKIN MANFESTATION DUE TO CKD AS WELL AS DIALYSIS:

There are certain skin manifestations which can occur not only in CKD but also in persons undergoing dialysis and the pathomechanisms of these manifestations vary in CKD and dialysis.

1. PRURITUS:
    - In hemodialysis there in increased incidence of pruritus due to reduced clearance of pruritogenic substances known as middle molecues. These are poorly dialyzable due to their low molecular weight.
    - Type of dialysis membrane and dialysis tubing also can lead on to pruritus.

2. BULLOUS DISEASE OF HEMODIALYSIS:

- Etiology of PCT in hemodialysis is not clear. But inadequate clearance of porphyria precursors by urine excretion or hemodialysis have been proposed.[84]
- Pseudoporphyria or bulous dermatosis of dialysis can occur in upto a fifth of patients undergoing hemodialysis.[84,85]
- It is indistinguishable from PCT but hypertrichosis is less common and plasma porphyrin levels are typically normal.

3. ACQUIRED PERFORATING DERMATOSES:
    - It occurs in upto 10% of patients on hemodialysis[49]
    - It is distinct from other perforating disorders like elastosis perforans serpiginosa, perforating golliculitis, Kyrle disease and reactive perforationg collagenosis.[47]
    - Proposed etiologies include dysregulation of Vit A or Vit D metabolism, diabetic microangiopathy, abnormality of collagen or elastic fibres and / or inflammation and connective tissue degradation caused by dermal deposition of substances such as calcium pyrophosphate and uric acid.[50]

4. NEPHROGENIC FIBROSING DERMOPATHY:
    - It resembles scleromyxoedema in some aspects[91] and occurred in patients with End stage renal disease, most of whom were on hemodialysis.[95]

- It is closely linked to the use of gadolinium contrast in MRI procedures.[94]

5. CALCIPHYLAXIS:
    - It occurs in 4% of patients on long term hemodialysis.[59]
    - Pahophysiology of calcium deposition in vessel walls among patients undergoing hemodialysis is not clear.

SKIN MANIFESTATIONS DUE TO DIALYSIS:

There are certain skin manifestations which occur at dialysis site as a direct result of dialysis. These are:

1. Arteriovenous shunt dermatitis[105]
2. Eczema at cannulation site
3. Infection, phlebitis and haematoma at fistula site
4. Cannulation septicemia[106]
5. Edema in the arm of A-V fistula
6. Pseudokaposi sarcoma

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

1. To evaluate the prevalence of dermatological problems in chronic kidney disease patients on hemodialysis or peritoneal dialysis

2. To identify and analyse the varied presentations of dermatoses in those patients

MATERIALS AND METHODS

MATERIALS AND METHODS

This cross-sectional study was carried out in department of Nephrology, Government Rajaji hospital, Madurai medical college, Madurai for a period of one year from May 2017 to May 2018 . Approval was obtained from institutional ethical committee prior to conduct of the study.

Eighty chronic kidney disease patients admitted in nephrology ward for hemodialysis or peritoneal dialysis with symptomatic or asymptomatic cutaneous manifestations were included in the study

PATIENT SELECTION:

Inclusion criteria:

1.Chronic kidney disease patients on dialysis with skin manifestations including nail and hair abnormalities.

Exclusion criteria:

1.Post renal transplant patients on dialysis

2.Immunocompromised patients

3.Patients with Chronic Liver Disease

4.Patients who did not give consent for the study

A pre designed proforma was used to collect the clinical details of the patients. The name, age, sex, address, inpatient number were all noted.Detailed patients' history were elicited and dermatological examination were done in good light. The skin, hair, nails, mucosa were examined thoroughly for all skin lesions including specific lesions of chronic renal failure. Photographs were taken for all patients after informed consent.

All patients were thoroughly investigated with routine hematologic and biochemical investigations . Scraping of skin for microscopic examination with 10% KOH , Tzanck smear, pus culture sensitivity and skin biopsy were done whenever necessary..

Statistical Tools

The information collected regarding all the cases included in the study were recorded in a Master Chart. Data analysis was done with the help of computer by using SPSS 16 software.

Using this software, percentages, means, standard deviations were calculated and 'p' value was calculated from Student 't' test for raw data and chi square test for consolidated data to test the significance of difference between variables.

A 'p' value less than 0.05 is taken as significant relationship.

OBSERVATIONS AND RESULTS

OBSERVATIONS AND RESULTS

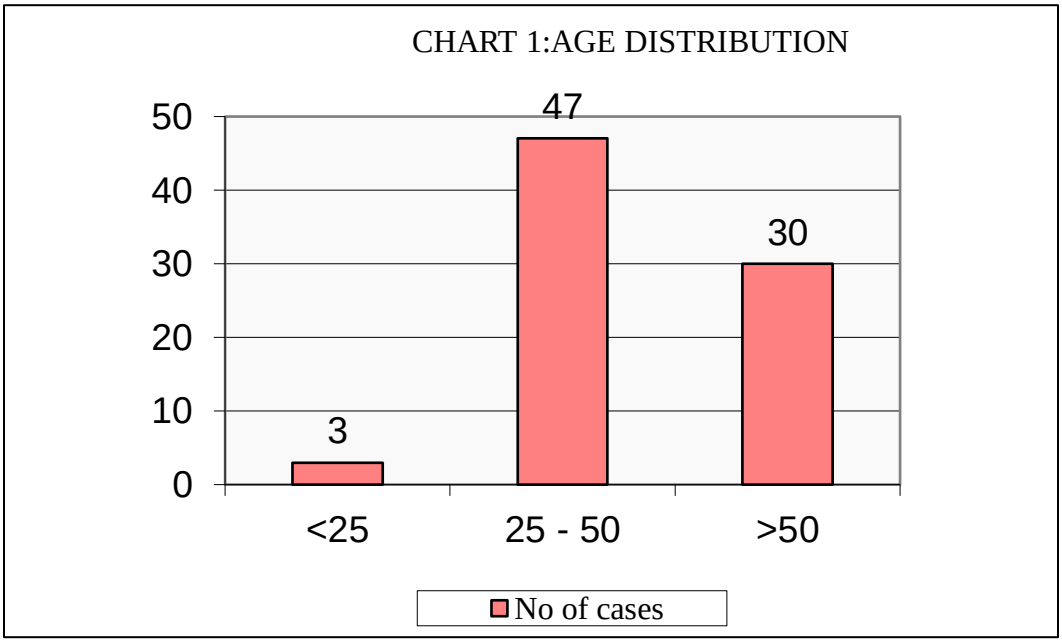
The total number of patients studied with Chronic kidney disease on dialysis was 80.

AGE PREVALENCE: The age of the patients varied from 15 to 70 with a mean of 47.25 years. 58.75% of cases were in the age group between 25 to 50; 37.5% were above 50 years of age and 3.75% were less than 25 years of age.

TABLE 1: AGE DISTRIBUTION

AGE	No of cases	%
<25	3	3.75
25 - 50	47	58.75
>50	30	37.50
TOTAL	80	100.00

CHART 1:AGE DISTRIBUTION

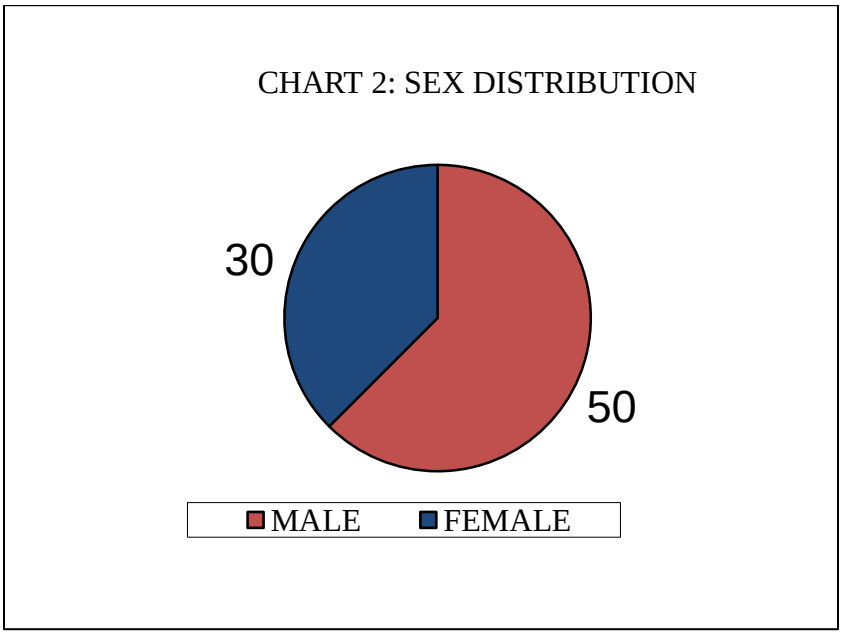


SEX PREVALENCE:

Out of 80 patients, 50(62.5%) were males and 30 (37.5%) were females.

TABLE 2: SEX DISTRIBUTION

SEX	No of cases	%
MALE	50	62.50
FEMALE	30	37.50
TOTAL	80	100.00

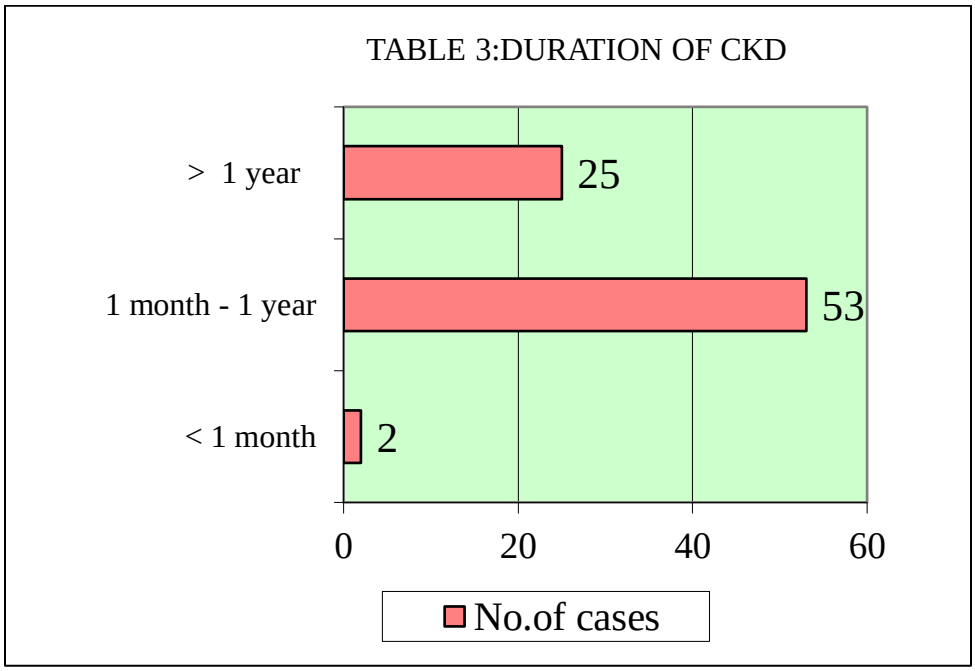


DURATION OF CKD :

The duration of illness from the time of diagnosis ranged from 10 days to 7 years. In 53 cases (66.25%) the duration after diagnosis was between 1 month to 1 year; in 25 cases (31.25%) it was more than 1 year and in 2 cases (2.5%) the duration after diagnosis was less than 1 month.

TABLE 3: DURATION OF CKD

Duration of illness	No of cases	%
< 1 month	2	2.50
1 month - 1 year	53	66.25
> 1 year	25	31.25
TOTAL	80	100.00



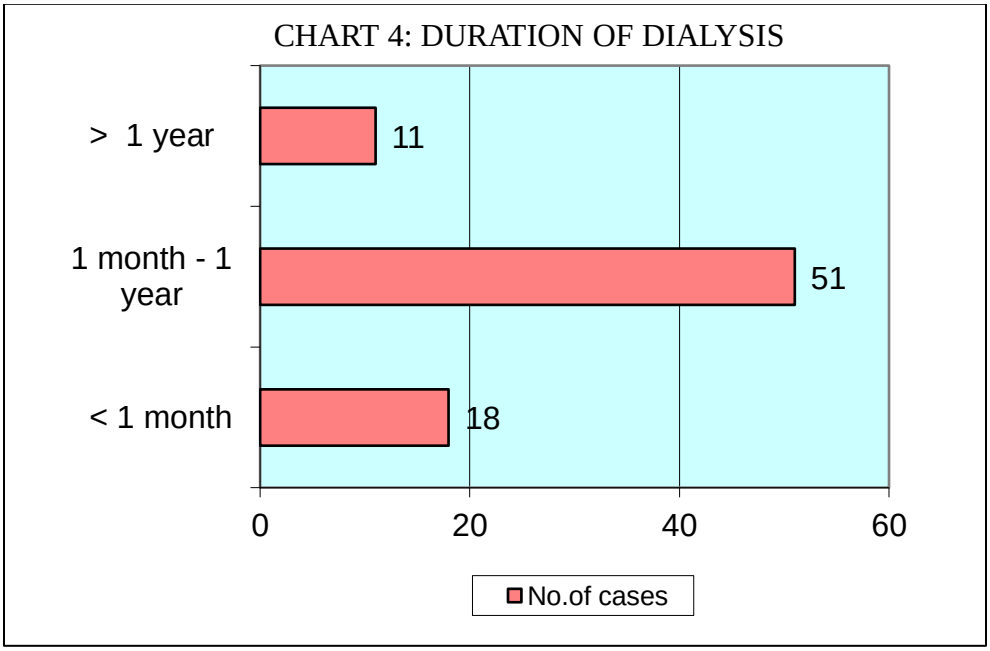
DURATION OF DIALYSIS:

The duration of dialysis ranged from 2 days to 2 years. The duration was less than 1 month in 18 patients (22.5%) , between 1 month to 1 year for 51 patients (63.75%) and more than one year for 11 patients (13.75%)

TABLE 4: DURATION OF DIALYSIS

Duration of dialysis	No of cases	%
< 1 month	18	22.50
1 month - 1 year	51	63.75
≥ 1 year	11	13.75
TOTAL	80	100.00

CHART 4: DURATION OF DIALYSIS



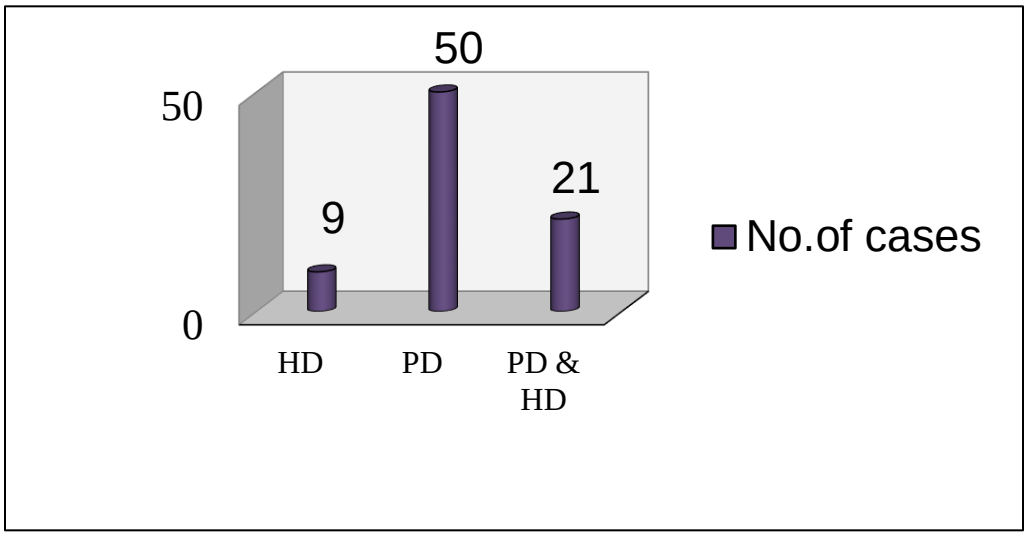
TYPE OF DIALYSIS:

Of the 80 patients, 50 patients (62.5%) had undergone only Peritoneal dialysis, 9 patients(11.25%) had undergone only Haemodialysis and 21 patients (26.25%) had undergone both Peritoneal and Hemodialysis.

TABLE 5: TYPE OF DIALYSIS

Types Of Dialysis	No of cases	%
HD	9	11.25
PD	50	62.50
PD & HD	21	26.25
TOTAL	80	100.00

CHART 5: TYPE OF DIALYSIS



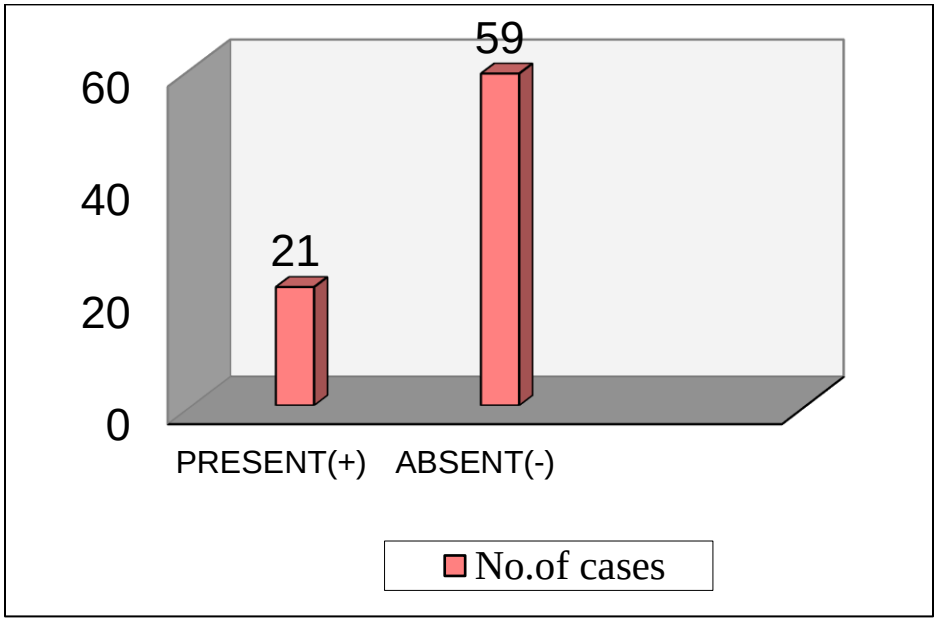
ASSOCIATED DIABETES MELLITUS:

Of the 80 patients, 21 patients (26.25%) were diabetic and the rest (73.75%) were non diabetic.

TABLE 6: ASSOCIATED DM

Diabetes	No of cases	%
PRESENT(+)	21	26.25
ABSENT(-)	59	73.75
TOTAL	80	100.00

CHART 6: ASSOCIATED DM



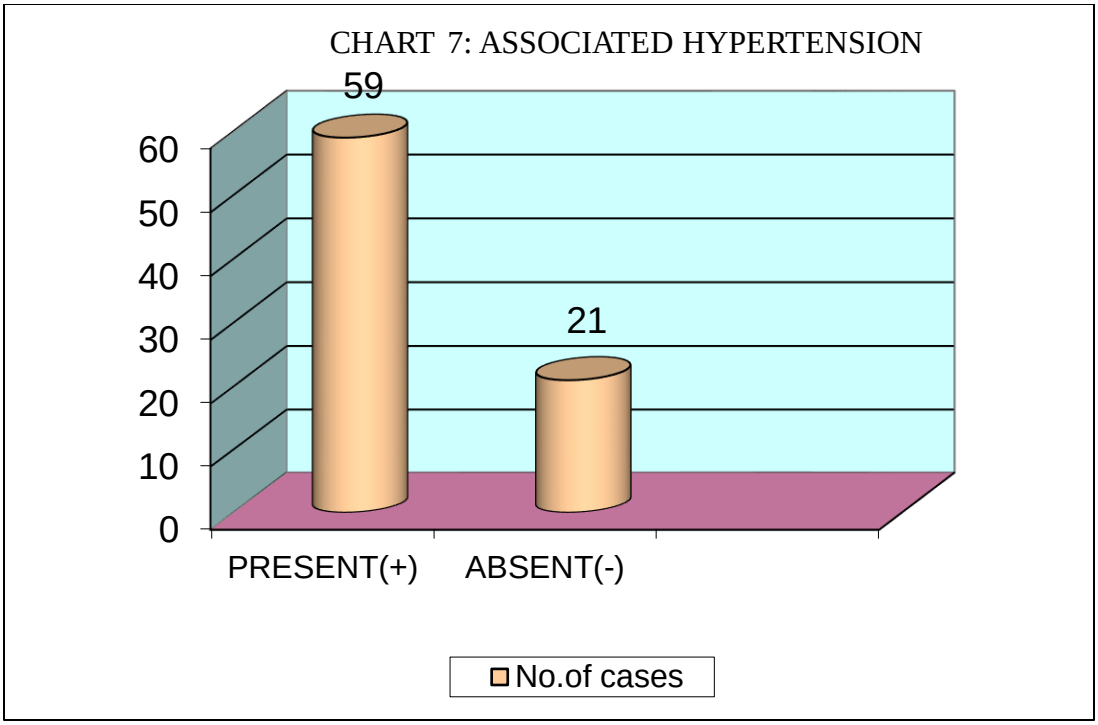
ASSOCIATED HYPERTENSION:

Out of 80 patients, 59 patients (73.75%) were hypertensive against 21 patients (26.25%) who were normotensive.

TABLE 7: ASSOCIATED HYPERTENSION

Hypertension	No of cases	%
PRESENT(+)	59	73.75
ABSENT(-)	21	26.25
TOTAL	80	100.00

CHART 7: ASSOCIATED HYPERTENSION



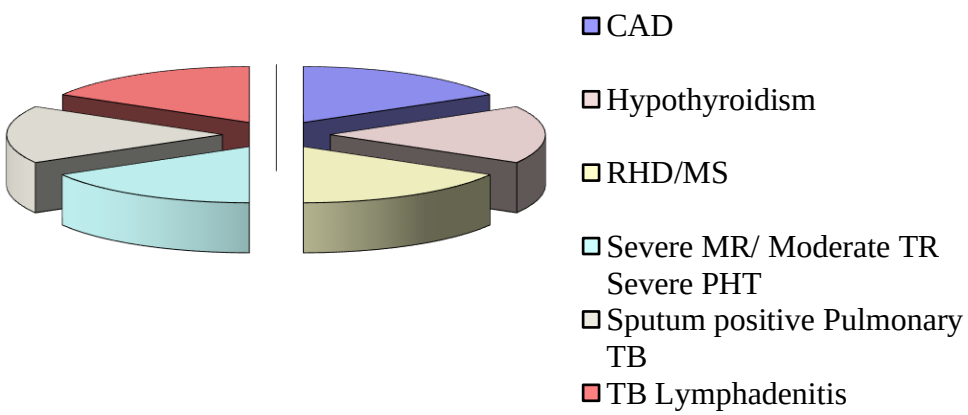
OTHER ASSOCIATED DISEASES:

One patient(1.25%) each had Coronary Artery Disease (CAD), Hypothyroidism, Mitral stenosis, Mitral regurgitation/ Tricuspid regurgitation with Pulmonay hypertension, pulmonary Tuberculosis, Tuberculous lymphadenitis.

TABLE 8: OTHER ASSOCIATED DISEASES

Others	No of cases	%
CAD	1	1.25
Hypothyroidism	1	1.25
Mitral Stenosis	1	1.25
Severe MR/ Moderate TR Severe PHT	1	1.25
Sputum positive Pulmonary TB	1	1.25
TB Lymphadenitis	1	1.25
TOTAL	6	7.50

CHART 8: OTHER ASSOCIATED DISEASES

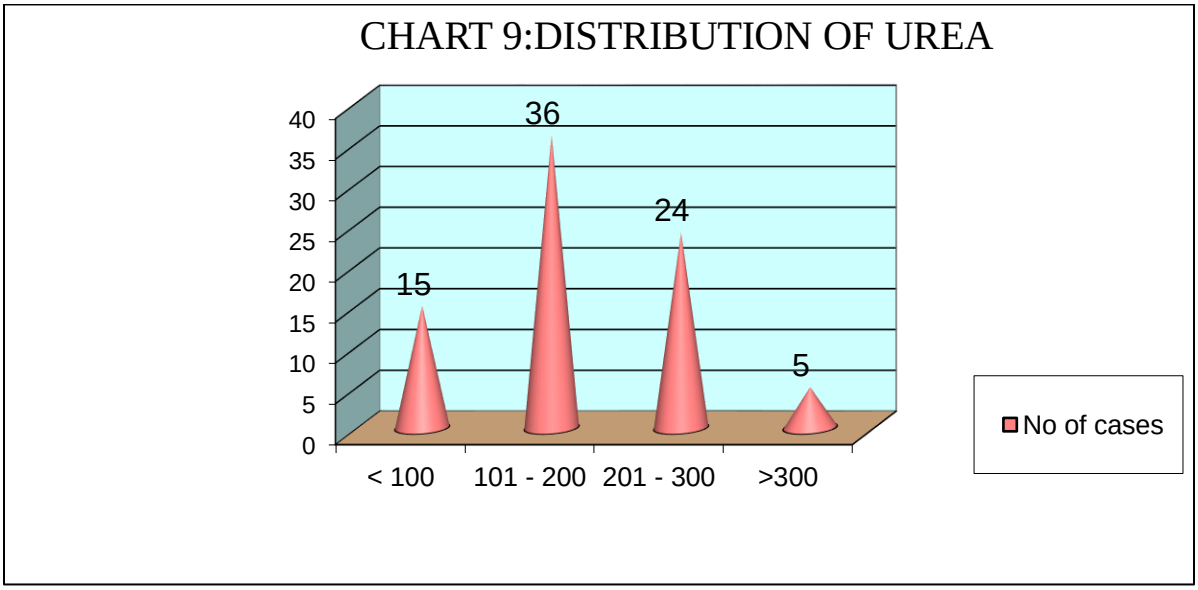


DISTRIBUTION OF SERUM UREA:

The serum urea level of patients ranged from 58 to 333 mg/dl. Of these 15 patients (18.75%) had serum urea level of less than 100. It was between 101-200 for 36 patients (45%) , 200- 300 for 24 patients (30%) and more than 300mg/dl for 5 patients.

TABLE 9: DISTRIBUTION OF SERUM UREA

Urea	No of cases	%
< 100	15	18.75
101 - 200	36	45.00
201 - 300	24	30.00
>300	5	6.25
TOTAL	80	100.00

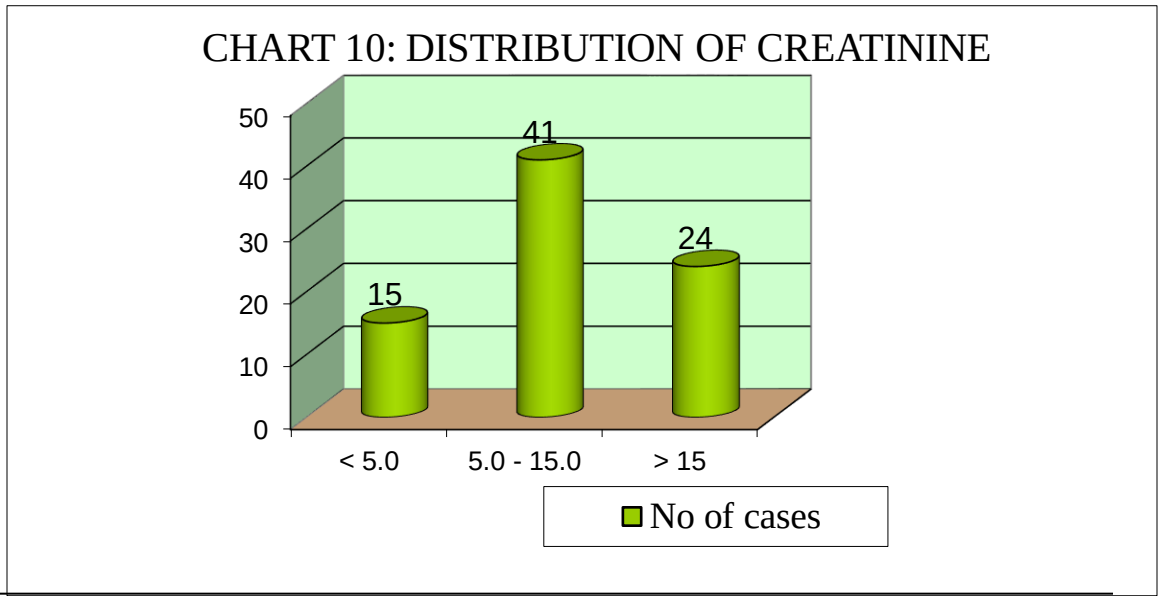


DISTRIBUTION OF SERUM CREATININE:

The Serum creatinine values of our patients ranged from 3.8 to 23.5 mg/dl. It was less than 5 mg/dl in 15 cases (18.75%), between 5-15 for 41 patients (51.25%) and more than 15mg/dl for 24 patients(30%).

TABLE 10: DISTRIBUTION OF SERUM CREATININE

Creatinine	No of cases	%
< 5.0	15	18.75
5.0 - 15.0	41	51.25
> 15	24	30.00
TOTAL	80	100.00



PREVALENCE OF SPECIFIC CUTANEOUS MANIFESTATIONS OF CKD AMONG PATIENTS UNDERGOING DIALYSIS:

1. PRURITUS:

   Out of 80 patients, 25 males (31.25%) and 22 females (27.5%) suffered from pruritus. The total prevalence in both sexes was 58.75% (47 cases).

2. XEROSIS:

   Xerosis was present in 37 patients (46.25%). It was noted in 27 males (33.75%) and 10 females (12.5%).

3. PALLOR:

   Of the 80 patients, 30 males (37.5%) and 14 females (17.5%) had visible pallor and the total incidence is 55% (44 patients)

4. PIGMENTARY CHANGES:

   Diffuse hyperpigmentation was noted in 3 patients (3.75%) totally. Of these, there were 2 females (2.5%) and 1 male.

5. YELLOW SKIN:

   Yellow pigmentation of skin was present in 1 female (1.25%)

6. PURPURA:

   It was noted in 1 male (1.25%) and 1 female (1.25%).

7. ACQUIRED PERFORATING DERMATOSES:

It was observed in 10 patients (12.5%) totally. Of these 7 were males (8.75%) and 3 were females (3.75%).

8. ECZEMA AT FISTULA SITE:

It was present in 2 patients (2.5%) totally, one each in both sexes.

PREVALENCE OF SKIN INFECTIONS:

Total incidence of skin infections is 10% (8 patients) . Of these 1 male patient had pyoderma (1.25%), 2 patients had Tinea corporis (2.5%), 2 patients had Herpes Labialis (2.5%), 2 patients had Herpes Zoster(2.5%) and 1 patient had Scabies(1.25%).

OTHER CUTANEOUS MANIFESTATIONS:

Two patients (2.75%) had Lymphedema of upperlimb, Cellulitis, Lichenoid dermatitis, Peeling of skin over palms and soles were seen in one patient(1.25%) each.

TABLE 11 : PREVALENCE OF SPECIFIC CUTANEOUS MANIFESTATIONS OF CKD AMONG PATIENTS UNDERGOING DIALYSIS

	MALE		FEMALE		TOTAL	
	No Of CASES	%	No Of CASES	%	No Of CASES	%
Pruritus	25	31.25	22	27.50	47	58.75
Xerosis	27	33.75	10	12.50	37	46.25
Pallor	30	37.50	14	17.50	44	55.00
Pigmentation	1	1.25	2	2.50	3	3.75
Yellow skin	0	0.00	1	1.25	1	1.25
Purpura	1	1.25	1	1.25	2	2.50
Acquired Perforating Disorder	7	8.75	3	3.75	10	12.50
Eczema at fistula site	1	1.25	1	1.25	2	2.50

CHART 11 : PREVALENCE OF SPECIFIC CUTANEOUS MANIFESTATIONS OF CKD AMONG DIALYSIS PATIENTS

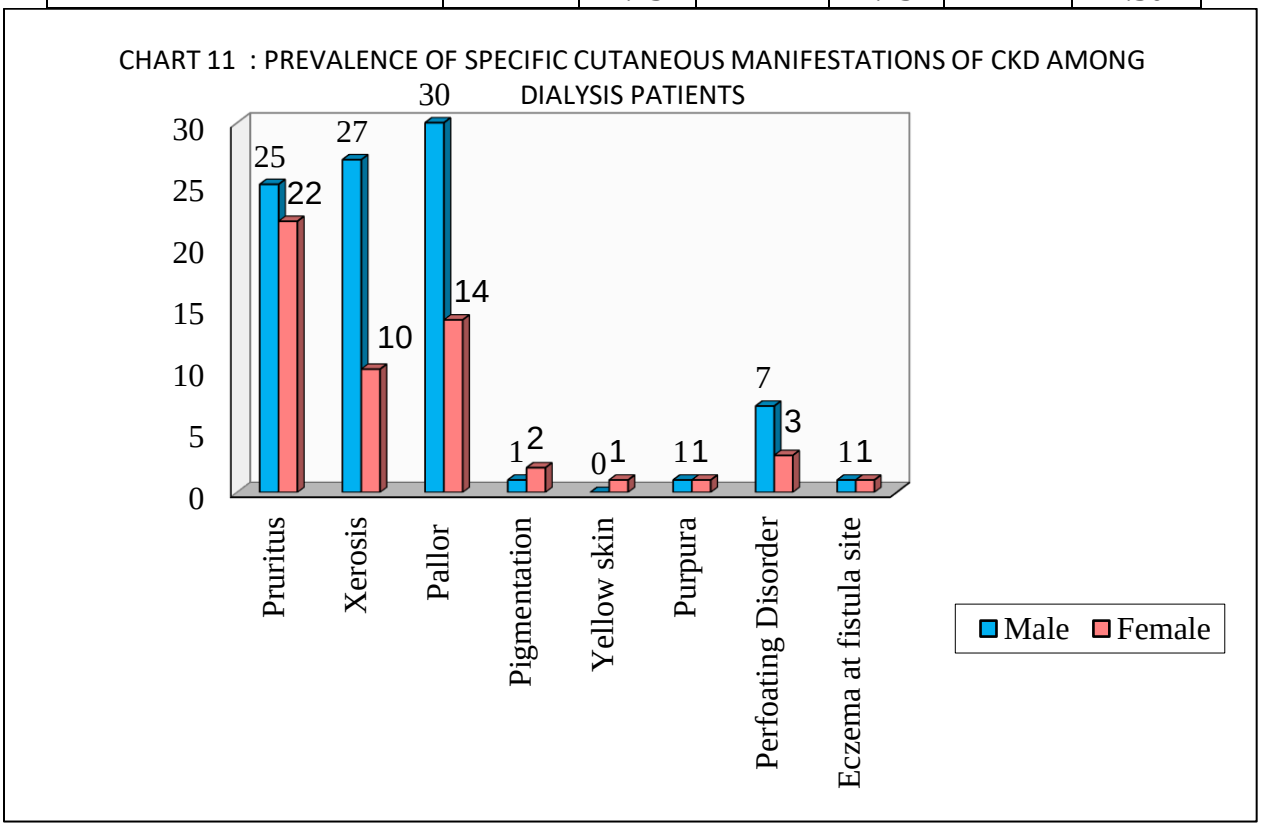


TABLE 12: PREVALENCE OF INFECTIONS

	MALE		FEMALE		TOTAL	
	No Of CASES	%	No Of CASES	%	No Of CASES	%
Bacterial infection	1	1.25	0	0.00	1	1.25
Fungal infection	1	1.25	1	1.25	2	2.50
Viral infection	2	2.50	2	2.50	4	5.00
Scabies	1	1.25	0	0.00	1	1.25
TOTAL	5	6.25	3	3.75	8	10.00

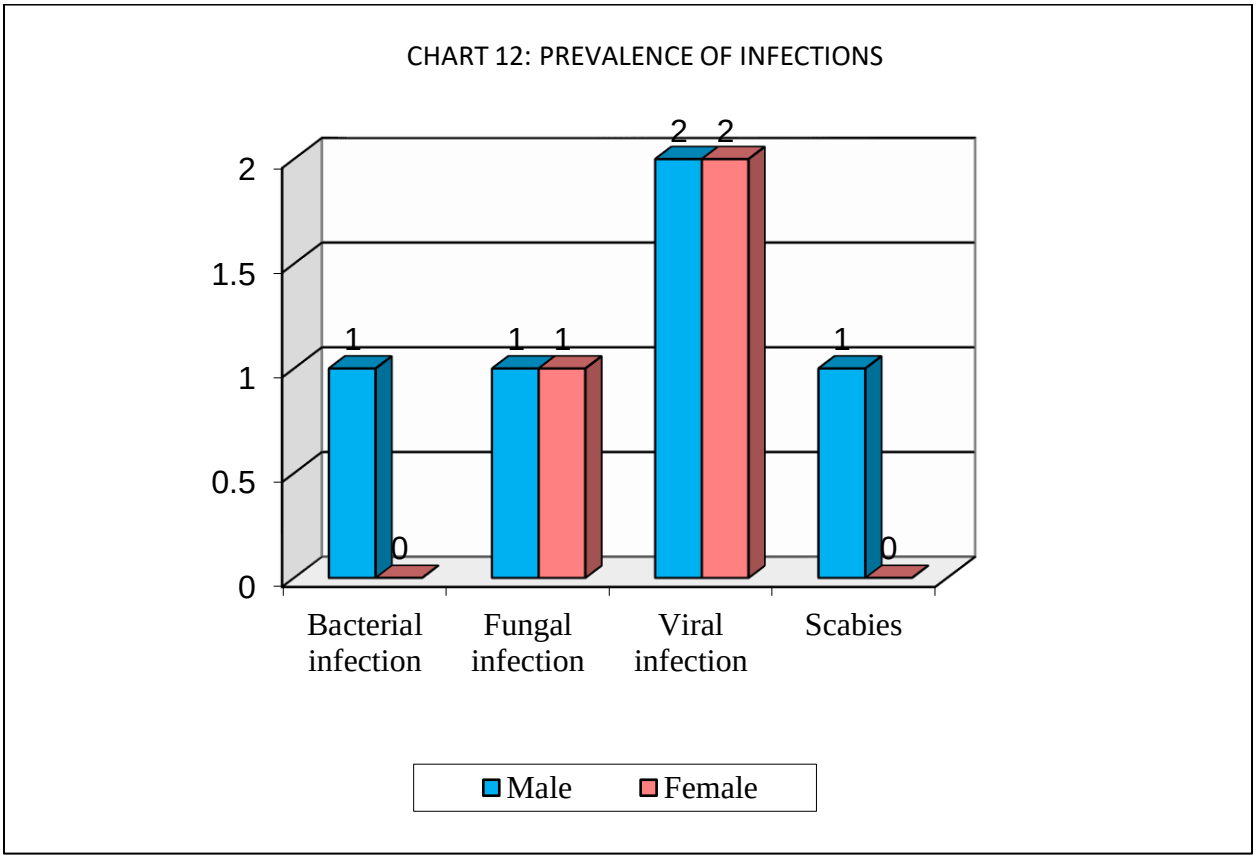
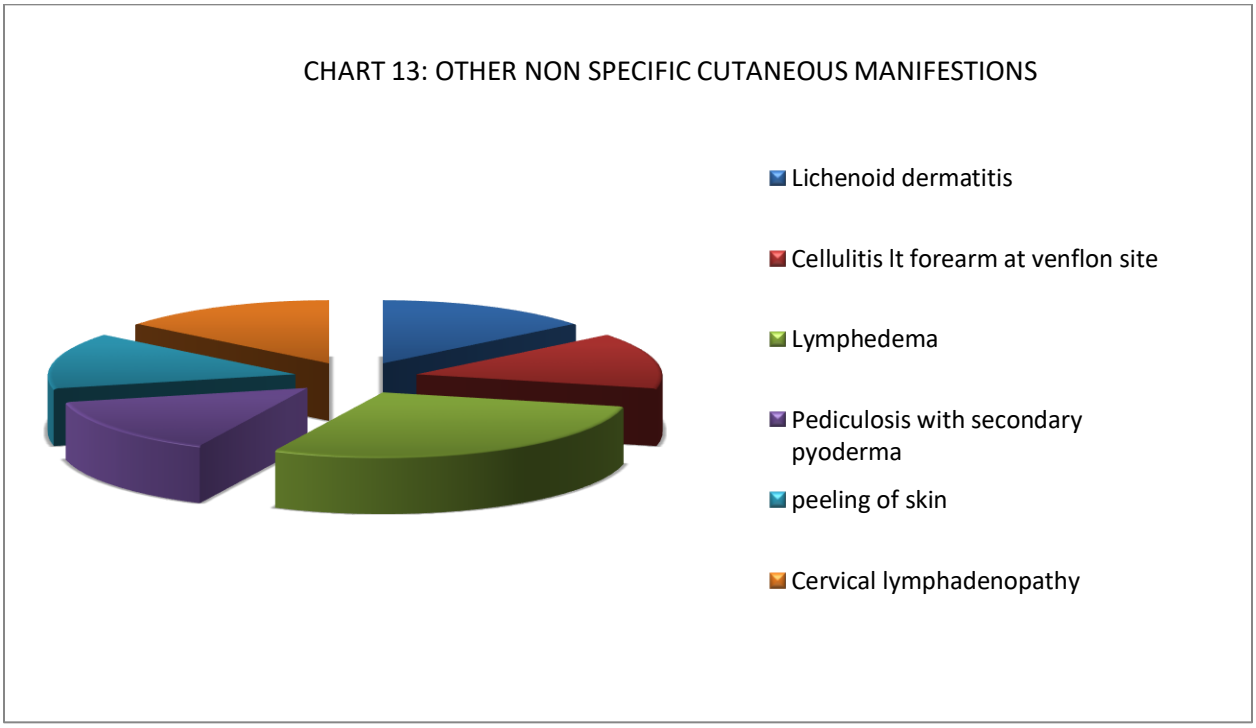


TABLE 13: OTHER NON SPECIFIC CUTANEOUS MANIFESTIONS

Others cutaneous manifestations	No of cases	%
Lichenoid dermatitis	1	1.25
Cellulitis lt forearm at venflon site	1	1.25
Lymphedema	2	2.50
Pediculosis with secondary pyoderma	1	1.25
peeling of skin	1	1.25
Cervical lymphadenopathy	1	1.25
TOTAL	7	8.75



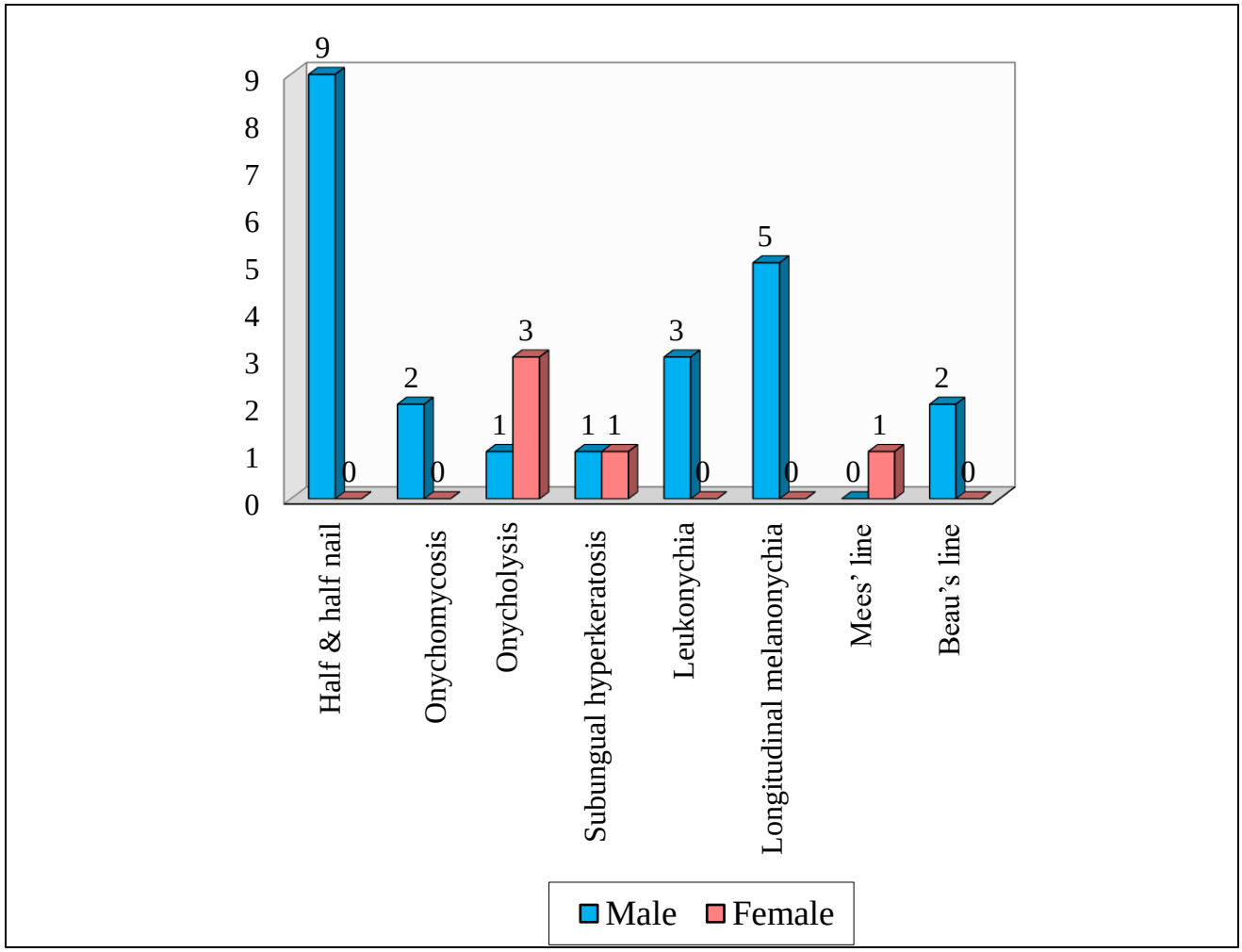
PREVALENCE OF NAIL CHANGES:

Of the 80 patients, 28 patients(35%) showed nail changes. 9 male(11.25%) patients had Half & half nail, 2 patients (2.5%) had onychomycosis, 4 patients(5%) had Onycholysis , 5 patients(6.25%) showed Longitudinal melanonychia, 2 each(2.5%) showed Subungual hyperkeratosis and Beau's line and one had Mee's line(1.25%).

TABLE 14: PREVALENCE OF NAIL CHANGES

	MALE		FEMALE		TOTAL	
	No Of CASES	%	No Of CASES	%	No Of CASES	%
Half & half nail	9	11.25	0	0.00	9	11.25
Onychomycosis	2	2.50	0	0.00	2	2.50
Onycholysis	1	1.25	3	3.75	4	5.00
Subungual hyperkeratosis	1	1.25	1	1.25	2	2.50
Mees' line	0	0.00	1	1.25	1	1.25
Beau's line	2	2.50	0	0.00	2	2.50
Leukonychia	3	3.75	0	0.00	3	3.75
Longitunidal melanonychia	5	6.25	0	0.00	5	6.25
TOTAL	23	28.75	5	6.25	28	35.00

CHART 14: PREVALENCE OF NAIL CHANGES



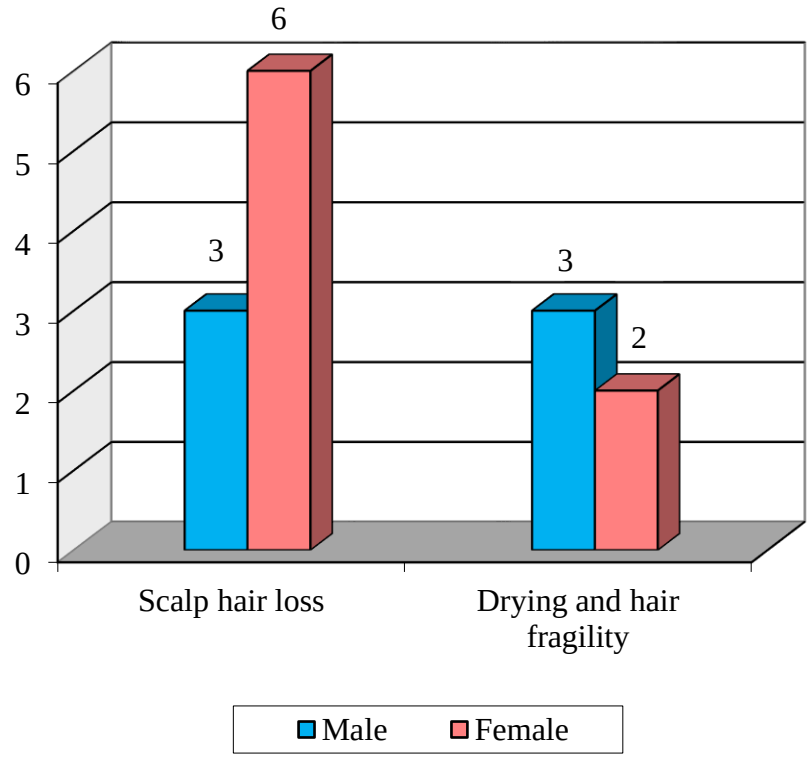
PREVALENCE OF HAIR CHANGES:

Out of 80 patients, hair changes were noted in 13 patients (16.25%). 3 males (3.75%) and 6 females (7.5%) showed scalp hair loss. 3 males(3.75%) and 1 female (1.25%) had drying of hair and hair fragility.

TABLE 15: PREVALENCE OF HAIR CHANGES

	MALE		FEMALE		TOTAL	
	No Of CASES	%	No Of CASES	%	No Of CASES	%
Scalp hair loss	3	3.75	6	7.50	9	11.25
Drying and hair fragility	3	3.75	1	1.25	4	5.00
TOTAL	6	7.50	7	8.75	13	16.25

CHART 15: PREVALENCE OF HAIR CHANGES



PREVALENCE OF MUCOSAL CHANGES:

Out of 80, 13 patients (16.25%) showed mucosal changes. 8 males (10%) and 3 females (3.75%) showed Macroglossia with teeth marking (Tongue sign of uremia). Uremic fetor was observed in 2 male patients(2.5%).

TABLE 16: PREVALENCE OF MUCOSAL CHANGES

	MALE		FEMALE		TOTAL	
	No Of CASES	%	No Of CASES	%	No Of CASES	%
Macroglossia with teeth marking	8	10.00	3	3.75	11	13.75
Uremic fetor	2	2.50	0	0.00	2	2.50
TOTAL	10	12.50	3	3.75	13	16.25

CHART 16: PREVALENCE OF MUCOSAL CHANGES

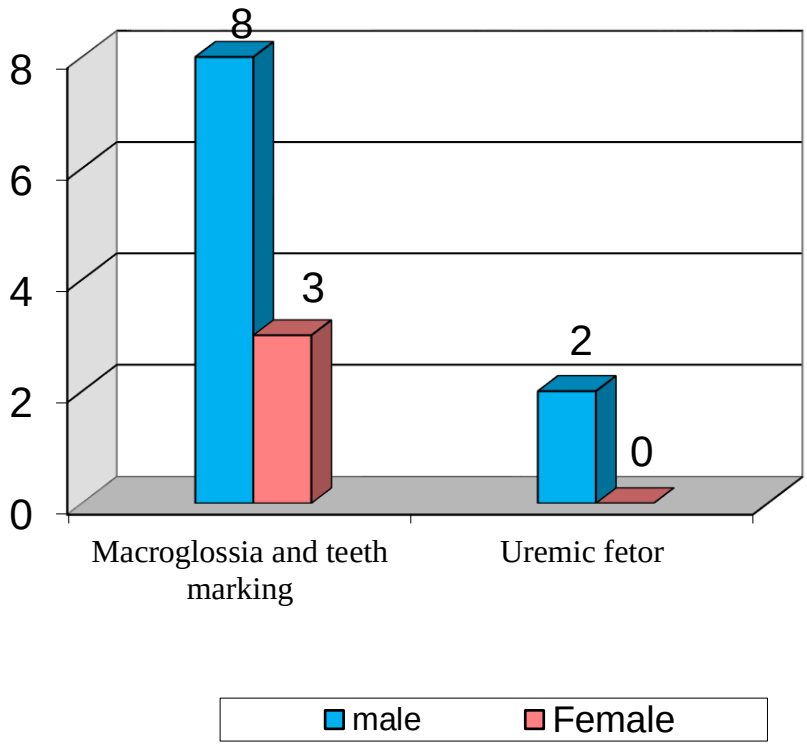


TABLE 17:DURATION OF CKD AND DIALYSIS WITH RESPECT TO SPECIFIC CUTANEOUS MANIFESTATIONS

CLINICAL MANIFESATION	DURATION OF CKD						DURATION OF DIALYSIS					
	< 6 MON		6MON-1YEAR		>1 YEAR		< 6 MON		6MON-1YEAR		>1 YEAR	
	NO.	%	NO.	%	NO.	%	NO	%	NO	%	NO.	%
PRURITUS	12	25.53	10	21.28	25	53.19	29	61.7	8	17.02	10	21.28
ACQUIRED PERFORATING DERMATOSES	6	60.00	0	0.00	4	40.00	8	80.00	1	10.00	1	10.00
XEROSIS	10	27.02	8	21.62	19	51.35	25	67.56	5	13.51	7	18.91

CHART 17: SKIN DISEASE VS DURATION OF CKD

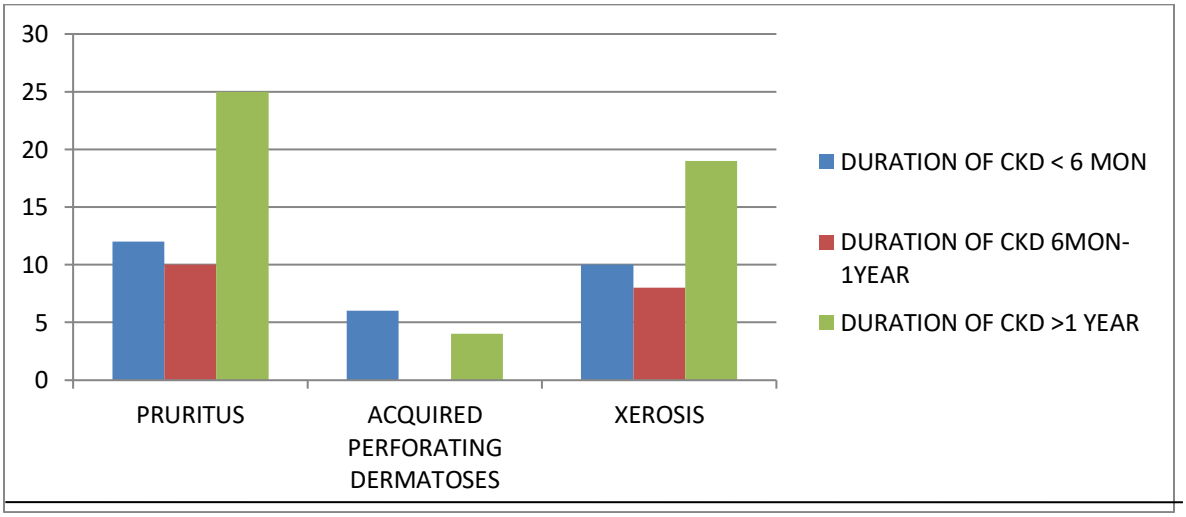
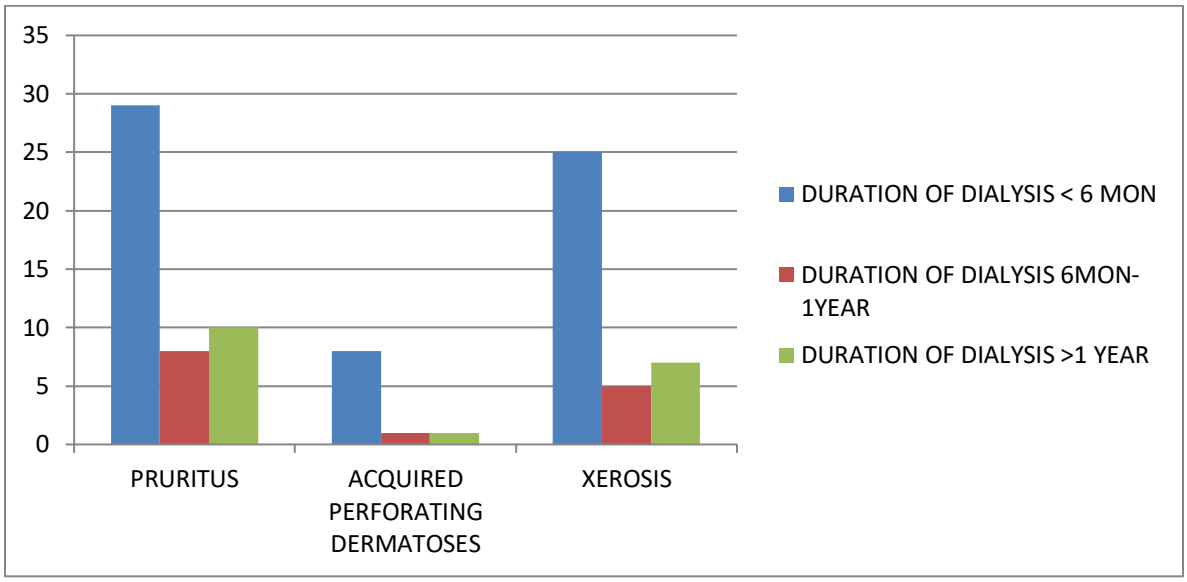


CHART 18: SKIN DISEASE VS DURATION OF DIALYSIS

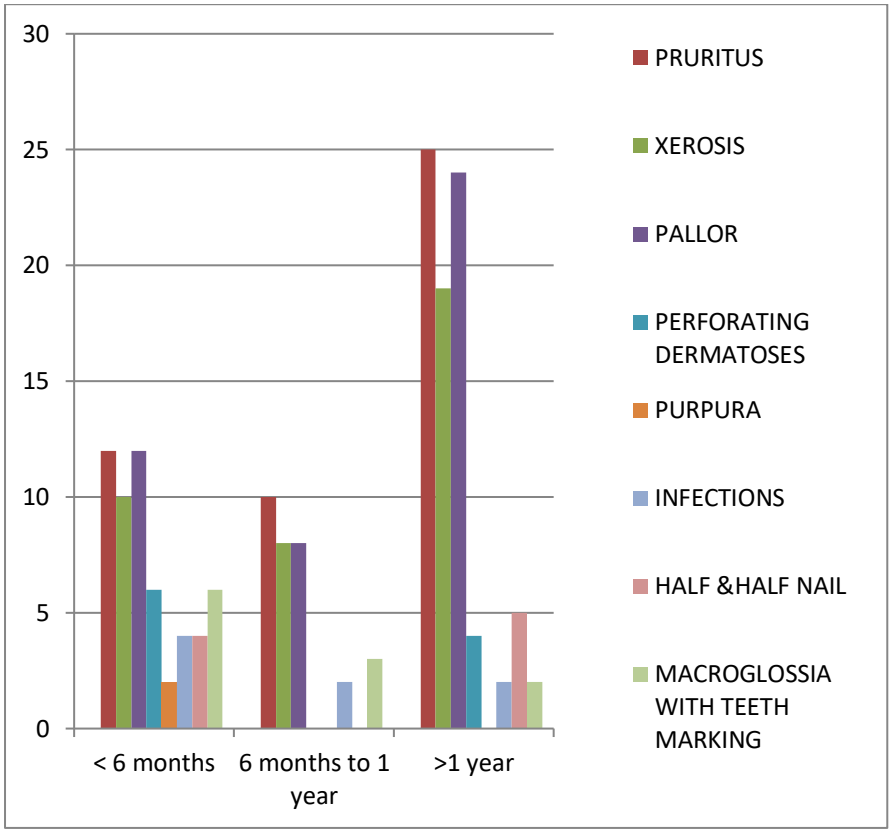


Of the 47 patients with pruritus, 12 patients (25.53%) were diagnosed as CKD for a period of less than 6 months, 10 patients (21.28%) were diagnosed within a period of 6 months to 1 year and 25 patients(53.19%) were diagnosed more than 1 year back. 29 patients (61.7%) were on dialysis for a period of less than 6 months, 8 patients(17.02%) were on dialysis for more than 6 months but less than 1 year, while the remaining 10 patients (21.28%) were on dialysis for more than a year.

Out of 10 patients with Acquired perforating dermatoses, 6 patients (60%) were diagnosed as CKD less than 6 months back while 4 patients (40%) were diagnosed more than 1 year back. 80% (8 patients) were on dialysis for a period of less than 6 months , 10% (1 patient) each were on dialysis for a period between 6 months & 1 year and more than 1 year.

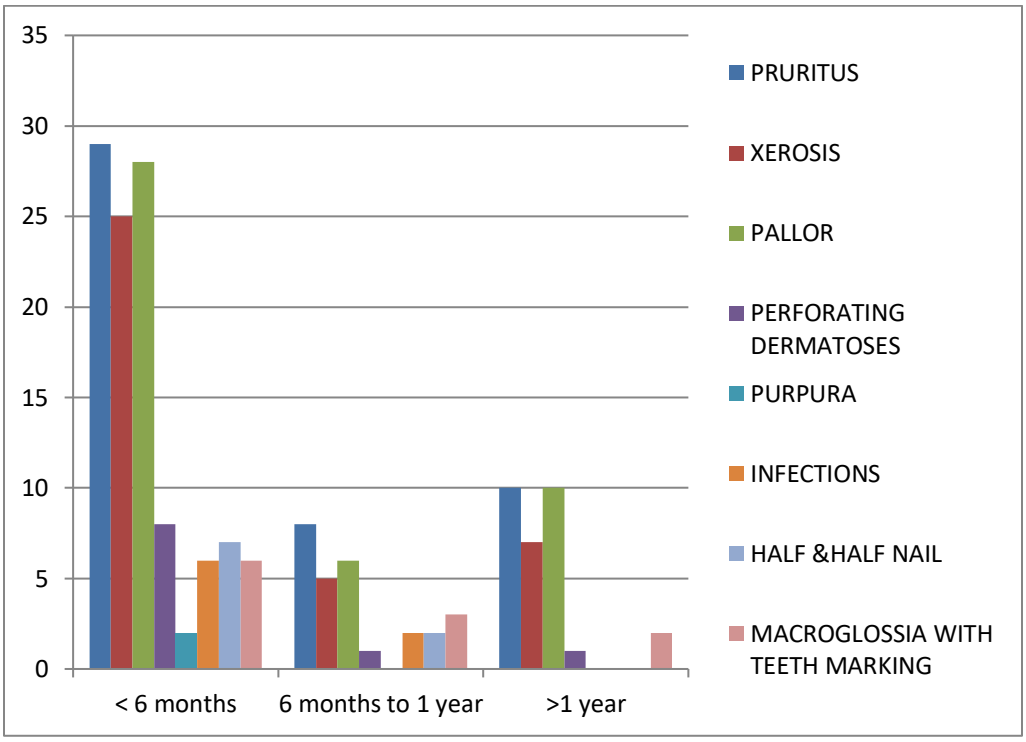
Of the 37 patients with xerosis, 10 (27.02%), 8(21.62%) and 19 patients(51.35%) each were diagnosed as CKD for a period of less than 6 months, 6 months to 1 year and more than a year respectively. 25(67.56%), 5(13.51%) and 7 patients (18.91%) each were on dialysis for less than 6 months, 6 months to 1 year and more than a year respectively.

CHART 19: SPECIFIC SKIN MANIFESTATIONS WITH RESPECT TO DURATION OF CKD



There is increase in prevalence of skin manifestations like pruritus, xerosis and pallor with increasing duration of dialysis . Within 6 months of diagnosis of CKD, the skin manifestations like pruritus ,xerosis ,pallor, perforating dermatoses, purpura, infections, Half and half nails and macroglossia with teeth marking were present in 12,10,12,6,2,4,4 and 6 patients respectively. Whereas with more than 1 year duration from diagnosis of CKD the no. of patients were 25, 9 , 24, 4, 0, 2, 5 and 2 patients respectively.

CHART 20: SPECIFIC SKIN MANIFESTATIONS WITH RESPECT TO DURATION OF DIALYSIS



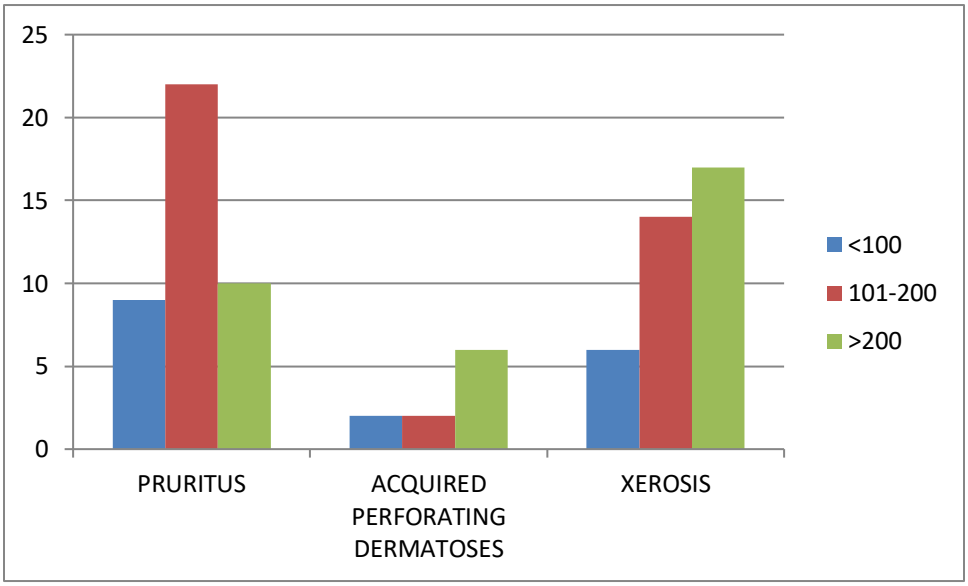
In CKD patients undergoing dialysis for less than 6 months duration, the skin manifestations like pruritus ,xerosis ,pallor, perforating dermatoses, purpura, infections, Half and half nails and macroglossia with teeth marking were present in 29, 25, 28,8 ,6 ,7 and 6 patients respectively. Whereas with more than 1 year of dialysis the no. of patients were 10 , 7 ,10 , 1, 0, 0 and 2 patients respectively.

This implies that there may be improvement in these skin conditions with increase in duration of dialysis

TABLE 18: SKIN MANIFESTATION VS SERUM UREA LEVELS

CLINICAL MANIFESATION	SERUM UREA					
	<100		101-200		>200	
	NO. OF CASES	%	NO. OF CASES	%	NO. OF CASES	%
PRURITUS	9	19.14	22	46.81	10	21.28
ACQUIRED PERFORATING DERMATOSES	2	20	2	20	6	20
XEROSIS	6	16.21	14	37.83	17	45.94

CHART 21: SKIN MANIFESTATION VS SERUM UREA LEVELS



Of the 47 patients with pruritus, 9 (19.14%), 22 (46.81%) and 10 patients(21.28%) had serum urea level of less than 100mgs% , 100- 200mgs% and >200 mgs% respectively. While 2 patients(20%) each and 6 patients (60%) of patients with perforating dermatoses had urea level in the above cutoff respectively. Out of 37 patients with xerosis, 6(16.21%), 14 (37.83%) and 17 (45.94%) each had urea levels in the above cutoff respectively.

DISCUSSION

DISCUSSION

SEX DISTRIBUTION:

The study population consisted of 80 patients of CKD with 50 males and 30 females. There is a male preponderance of 62.5% in this study.

AGE DISTRIBUTION:

The age of the patients varied from 15 to 70 years. 58.75% of cases were in the age group between 25 to 50; 37.5% were above 50 years of age and 3.75% were less than 25 years of age. The mean age of patients in this study is 47.25 years which is in par with the literature.[5]

DURATION OF CKD AND DIALYSIS:

The exact duration of CKD could not be made out in most of the patients but the duration of CKD since the time of diagnosis ranges from 10 days to 7 years with a mean duration of 17.25 months. The diagnosis of CKD was made based on elevated renal parameters for more than 3 months or based on the ultrasonographic evidence of contracted kidneys. The duration of dialysis ranges from 2 days to 2 years with a mean duration of 4.85 months.

ASSOCIATED COMORBIDITIES:

In this study, 59 patients (73.75%) were hypertensive , 21 patients (26.25%) were diabetic and 18 patients(22.5%) were both diabetic and hypertensive . One patient each(1.25%) had Coronary Artery Disease (CAD), Hypothyroidism, Mitral stenosis, Mitral regurgitation/ Tricuspid regurgitation with Pulmonary hypertension, pulmonary Tuberculosis, Tuberculous lymphadenitis.

TYPE OF DIALYSIS:

Most of the patients (62.5%) in our institution had undergone peritoneal dialysis alone and hence most of the skin manifestations were common among the peritoneal dialysis group. This is followed by 26.25% who had undergone both peritoneal and hemodialysis and the rest (11.25%) had undergone only hemodialysis.

DISTRIBUTION OF SERUM UREA AND CREATININE:

The serum urea level of patients ranged from 58 to 333 mg/dl with a mean value of 169.77 . Of these only 15 patients (18.75%) had serum urea level of less than 100. The remaining 65 patients had serum urea value of more than 100. It was between 101-200 for 36 patients (45%) , 200- 300 for 24 patients (30%) and more than 300mg/dl for 5 patients.

The Serum creatinine values of our patients ranged from 3.8 to 23.5 mg/dl with a mean value of 11.53. It was less than 5 mg/dl in only 15 cases (18.75%), between 5-15 for 41 patients (51.25%) and more than 15mg/dl for 24 patients(30%).

CUTANEOUS MANIFESTATIONS:

SKIN CHANGES:

PRURITUS:

- Pruritus is the most common cutaneous manifestation noted in this study seen in 47 patients constituting about 58.75%. The sex-wise distribution is 25 males(31.25%) and 22 females (27.5%).
- Its prevalence among peritoneal dialysis group is 58% [P value - 0.98] while among those on hemodialysis is 55.55%. Its prevalence among those who had undergone both peritoneal dialysis and hemodialysis is 61.9%. In other studies prevalence of pruritus among hemodialysis ranges from 53%[3] to 63%[6].
- 25 patients(53.19%) with pruritus had disease duration of more than or equal to 1 year while rest 22 patients(46.81%) had duration of CKD less than one year.
- 38 patients (80.86%) with pruritus were on dialysis for less than one year while 9 patients(19.14%) with pruritus were on dialysis for more than or equal to 1 year. This is in contrast to the observations by Pico et al [6] who noticed pruritus in 30% patients with duration of dialysis less than one year and 45% in those receiving dialysis for > 1 year.
- 27 patients (57.44%) out of 47 patients had pruritus before starting dialysis and it remained unchanged after dialysis while 20 patients(42.56%) with pruritus had onset after starting dialysis .In one study[113] pruritus remain unchanged in 73.9% after dialysis while it worsened in 17.39%. Onset after dialysis may be due

to impaired clearance of pruritogenic middle molecules due to their molecular weight[7] or due to dialysis associated neuropathy.

- 12 patients(25.53%) with pruritus were suffering from diabetes mellitus. In a study by Udayakumar et al [3] pruritus was found to be very severe in diabetic patients.
- Among 47 patients with pruritus 23 patients (48.93%) had associated xerosis.
- 6 patients(12.77%) with pruritus had associated Acquired perforating dermatoses.

PALLOR:

- Pallor of the skin due to anaemia was observed in 55% of patients.This is in par with Udayakumar et al, who noticed pallor in 60% of patients. [3] The haemoglobin level of patients range from 3.4 g% to 15.8 g% with a mean value of 7.09. The haemoglobin level was less than 8 g% in 66 patients (82.5%). This is the second commonest cutaneous manifestation noted in my study.

XEROSIS:

- Xerosis of skin was noted in 37 patients (46.25%). 23 patients with xerosis has associated pruritus [P value – 0.593]. This is in par with literature[6] which states that there is a positive correlation with the severity of xerosis and the degree of pruritus. It was predominantly seen over extensor aspect of forearms, legs and thighs.

- Prevalence of xerosis increases with increasing duration since the diagnosis of CKD with 51.35% of patients were diagnosed as CKD more than one year back while only 10 patients (27.02%) had xerosis within six months of diagnosis of CKD.
- Also, 67.56% (25 patients) of those with xerosis were on dialysis for less than 6 months while 18.91%(7 patients) were on dialysis for more than one year. This implies that dialysis may improve xerosis in CKD patients.
- Prevalence of xerosis increases with increasing serum urea levels with , 6 patients(16.21%), 14 patients (37.83%) and 17 patients(45.94%) each had urea levels of less than 100, 100 to 200 and more than 200mgs% respectively.

ACQUIRED PERFORATING DERMATOSES:

- Acquired perforating dermatosis was observed in 12.5% (10 patients comprised of 7 males and 3 females) which is in par with the prevalence reported in literature(4.5- 17 %) [3,6] .
- 5 patients (50%) had associated diabetes mellitus. In a study by Udayakumar et al[3] it is given that perforating disorders were significantly more prevalent in diabetic populations. Onset of skin lesions were before the diagnosis of CKD in 4 patients with diabetes mellitus but it is before CKD in only one patient without concomitant diabetes mellitus.

- Eight(80%) of these ten patients were on peritoneal dialysis [P value- 0.337] , while two(20%) were on hemodialysis. This is in par with Pico et al[6] who noticed increased prevalence of perforating disorders in peritoneal dialysis patients.
- Eight (80%) out of ten patients were on dialysis for less than 6 months. This goes in par with study by Udayakumar et al who reported that 19 out of 21 patients were on dialysis for less than 6 months.
- Two of these 10 patients (20%) had onset of this skin disease after dialysis whereas the rest 8 patients(80%) had the disease before starting dialysis.
- Six patients (60%) with perforating dermatoses had associated pruritus while three (30%) of them has associated xerosis.
- Six patients (60%) out of 10 patients with perforating dermatoses had serum urea level above 200mgs%. So, probably the chances of acquiring perforating dermatoses increases with increase in serum urea levels.

PIGMENTATION:

- Diffuse pigmentation and yellowish discoloration of skin was noted in 3.75% and 1.25% of patients respectively. This was less compared to study by Pico et al[6], who described pigmentary changes in 70 % of patients. This may be due to the darker skin type of our patients.

PURPURA:

- Purpura was observed in two patients (2.5%) with negative history of intake of drugs known to cause bleeding and with normal platelet count . This finding in our patients could be due to increased vascular fragility observed in CKD patients[30]. It was seen in 9 patients in one study[3].

SKIN INFECTIONS:

- Skin infections were noted in 8 patients (10%). These include pyoderma, Tinea corporis, Herpes labialis, Herpes zoster and Scabies. Out of these 8 patients only one patient who had multiple pyodermas was suffering from concomitant diabetes mellitus. Remaining patients (7patients) were non-diabetic. So the cause of infection in these patients could be due to decreased T cell count causing impairment of immunity in these patients.
- Prevalence of skin infections in our patients is much less compared to study by Pico et al[6] who noticed Tinea pedis in 25% of patient.

OTHER MANIFESTATIONS:

- Other specific skin manifestations noted include eczema at fistula site and lymphedema of upperlimb in two patients(2.75%), and one patient (1.25%) with cellulitis.

- Non- specific skin manifestations seen in our patients include one patient(1.25%) each with lichenoid dermatitis & peeling of skin over palms and soles.

- We haven't seen any case of Calcinosis cutis , Calciphylaxis, Nephrogenic systemic fibrosis , Pseudoporphyria or Uremic frost.Cancerous or precancerous lesions were also not seen in my study.

- Calcinosis cutis was reported in one patient out of 100 patients in one study [6]. Calciphylaxis and pseudoporphyria were not seen in studies by Pico et al[6] and Udayakumar et al[3].

- Nephrogenic systemic fibrosis was reported to occur in patients who had exposure to gadolinium contrast in olden days but is rarely seen nowadays.[3,113]

- Uremic frost which occurs due to deposition of urea crystals was a frequent finding in pre- dialysis era, but it seen rarely nowadays due to the wide availability of dialysis[3].

NAIL CHANGES:

The nail changes were observed in 28 patients (35%) out of 80 patients. The most common nail change noted was Half and half nails which was seen in 9 patients(11.25%). Prevalence of this nail change in previous studies range from 21%[3] in

one study to 39%[6] in another.The prevalence in general population has been reported to be 1.4%.[6,3]

Other changes observed include Onychomycosis (2.5%) , Onycholysis (5%), Longitudinal melanonychia (6.25%) , Leukonychia(3.75%), Subungual hyperkeratosis(2.5%), Beau's line(2.5%) and Mees' line(1.25%). Muehrcke's lines, Splinter haemorrhages and Brown nail bed arcs were not seen in my study.

HAIR CHANGES:

Hair changes were observed in 13 patients (16.25%) in my study. These include Scalp hair loss in 9 patients (11.25%) , Dry and fragile hair in 4 patients (5%). In a study by Udayakumar et al, about 57 patients had hair changes which include sparse body hair, diffuse alopecia and dry, lustreless hair. Dry and fragile skin are due to reduced sebum secretion.[28]

ORAL MUCOSAL CHANGES:

In our study oral mucosal changes were observed in 13 patients(16.25%) . Oral mucosal changes have been reported in up to 90% of patients with CKD.[3] Macroglossia with teeth marking (Tongue sign of uremia) was seen in 13.75% of patients. This was first described by Mathew in 92% of patients with CKD.[107] It was observed in 35% of patients in one study.[3]

Uremic fetor of breath was observed in 2 patients (2.5 %) and both these patients had serum urea level of more than 200. It was seen in 8% of patients in a study by Udayakumar et al[3].

SUMMARY

SUMMARY

- This study of Cutaneous manifestations in Chronic Kidney Disease patients on dialysis comprised of 80 patients with 50 males and 30 females with a Male:Female ratio of 1.7:1 .
- The age of the patients varied from 15 to 70 years with a mean age of 47.25 years.
- The duration of CKD since the time of diagnosis in our patients ranged from 10 days to 7 years with a mean duration of 17.25 months.
- The duration of dialysis ranged from 2 days to 2 years with a mean duration of 4.85 months.
- 59 patients (73.75%) in my study were hypertensive and 21 patients (26.25%) were diabetic.
- Of the 80 patients, 50 patients (62.5%) had undergone only Peritoneal dialysis, 9 patients(11.25%) had undergone only Haemodialysis and 21 patients (26.25%) had undergone both Peritoneal and Hemodialysis.
- The serum urea level of patients ranged from 58 to 333 mg/dl with a mean value of 169.77.
- The serum creatinine values of patients ranged from 3.8 to 23.5 mg/dl with a mean value of 11.53.

- Pruritus was the most common cutaneous manifestation seen in about 47 patients (58.75%) . 25 patients(53.19%) with pruritus had disease duration of more than or equal to 1 year while 9 patients(19.14%) with pruritus were on dialysis for more than or equal to 1 year. 27 patients (57.44%) out of 47 patients had pruritus before starting dialysis.23 patients(48.93%) with pruritus had associated xerosis while 12 patients(25.53%) had associated diabetes mellitus . 6 patients (12.77%) with pruritus had associated perforating dermatoses.
- This is followed by pallor seen in 44 patients (55.0%) and xerosis in 37 patients (46.25%) . Prevalence of xerosis increased with increase in serum urea levels and it decreased with increasing duration of dialysis.
- Acquired perforating dermatoses was present in 10 patients(12.5%). It was more common in peritoneal dialysis patients (8 out of 10) and in 80% of patients the skin lesions started long before the commencement of dialysis indicating that it is not dialysis related in these patients but primarily renal disease related. 50% had associated diabetes and the skin lesions manifested before the diagnosis of CKD in these diabetic patients (4 out of 5 patients). 60% of patients with perforating dermatoses had serum urea level above 200mgs% impling that the chance of acquiring this disease increases with increase in blood urea levels.
- Other cutaneous manifestations noted include skin infections (10.0%), hyperpigmentation(3.75%), yellowish discoloration of skin(1.25%), Purpura(2.5%) and Eczema at fistula site (2.5%), lymphedema of upperlimb (2.5%) and cellulitis of upper limb (1.25%).

- Nail changes were seen in 28 patients (35 %), most common being Half & half nail (11.25%), followed by Longitudinal melanonychia (6.25%) , Onycholysis(5%) , Leukonychia (3.75%), Onychomycosis (2.5%), Subungual hyperkeratoses (2.5%), Mee's line(1.25%) and Beau's line(1.25%).
- Hair changes were seen in 13 patients (16.25%), which include Diffuse scalp hair loss (11.25%) & Dry and fragile hair (5%).
- Oral mucosal changes were seen in 13 patients (16.25%) of which Macroglossia with teeth marking (Tongue Sign of Uremia) was seen in 13.75% and Uremic fetor in 2.5%.
- There is no statistically significant correlation [P value < 0.5] between the type of dialysis and pruritus or acquired perforating dermatoses noted in this study.
- Calcinosis cutis, Calciphylaxis, Nephrogenic systemic fibrosis , pseudoporphyria and uremic frost were not seen in our study.

CONCLUSION

CONCLUSION

In this cross-sectional study of cutaneous manifestations in Chronic Kidney Disease patients on dialysis, hypertension and diabetes were the most common etiologies of CKD. The specific manifestations of CKD like pruritus, pallor, xerosis, acquired perforating dermatoses, purpura, eczema at arterio-venous fistula site, half and half nail, macroglossia with teeth marking, uremic fetor were observed in our study. But Calcinosis cutis, Calciphylaxis, Pseudoporphyria and Nephrogenic Systemic Fibrosis were not seen. Skin manifestations were common in patients undergoing Peritoneal dialysis than Hemodialysis. The mean duration of CKD was 17.25 months while that of dialysis was 4.85 months. Xerosis and perforating dermatoses showed correlation with increasing serum urea levels though not statistically significant. Pruritus and xerosis showed positive correlation with duration of CKD and negative correlation with the duration of dialysis ie., less prevalent in those undergoing diaysis for longer duration.

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113. Clinicoepidemiological study of skin manifestations in patients of chronic renal failure on hemodialysis Indian Dermatology Online Journal - January-March 2013 - Volume 4 - Issue 1

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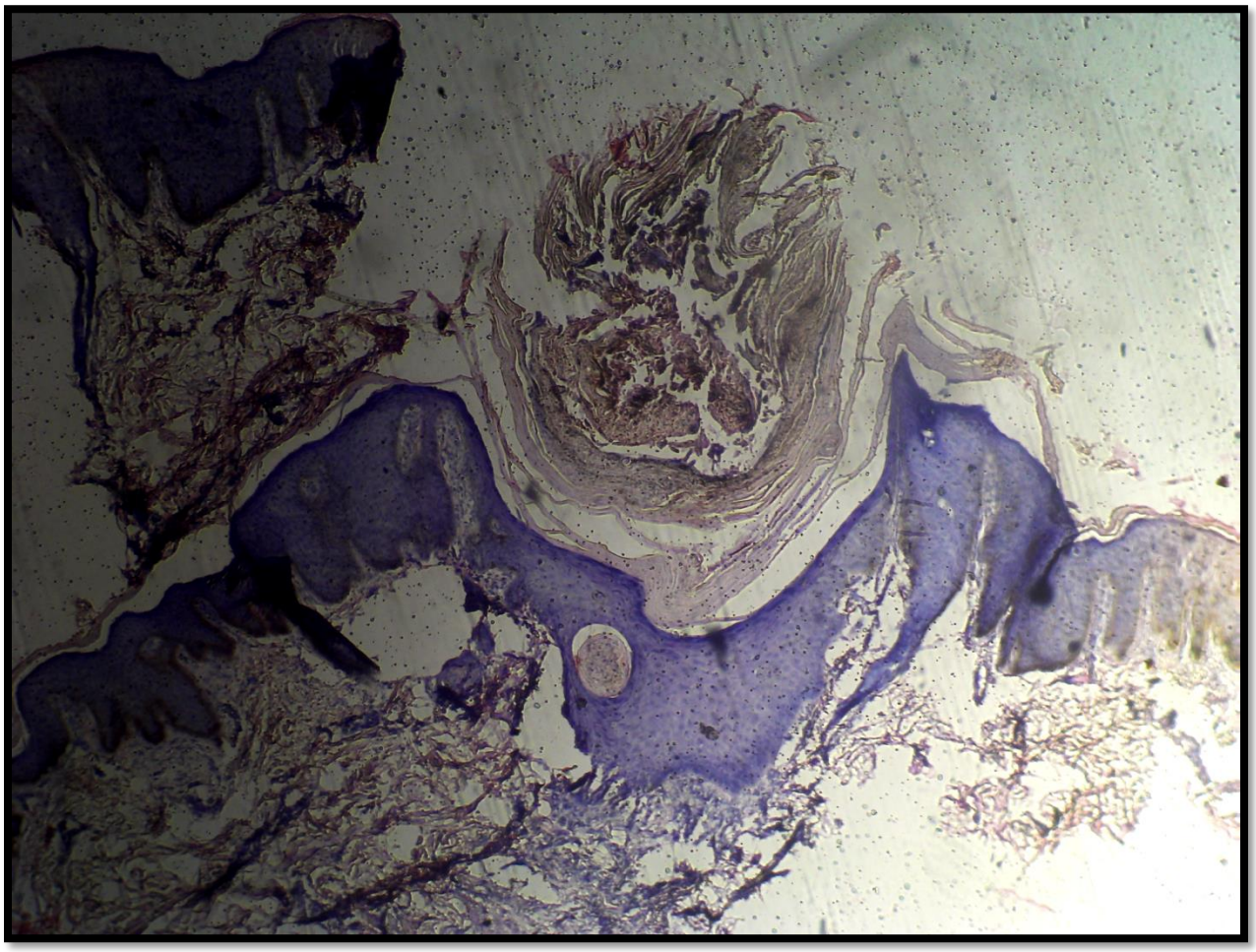
CLINICAL PICTURES

XEROSIS CUTIS

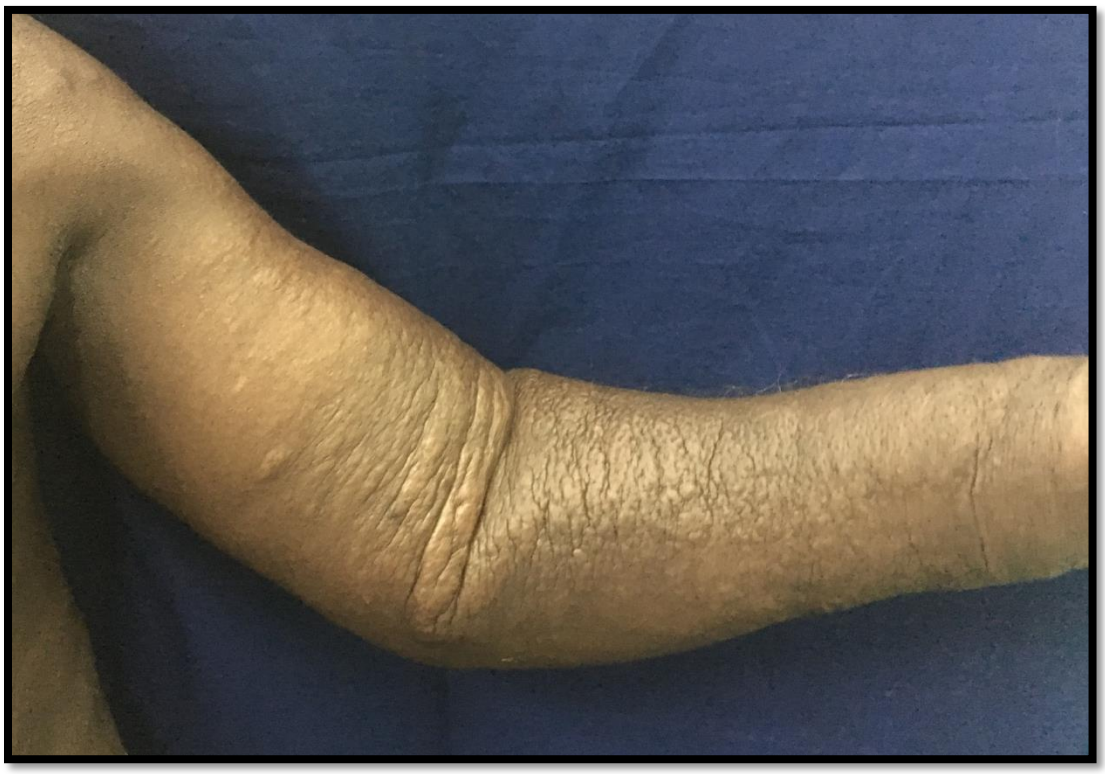
ACQUIRED PERFORATING DERMATOSES

HISTOPATHOLOGY OF ACQUIRED PERFORATING DERMATOSES



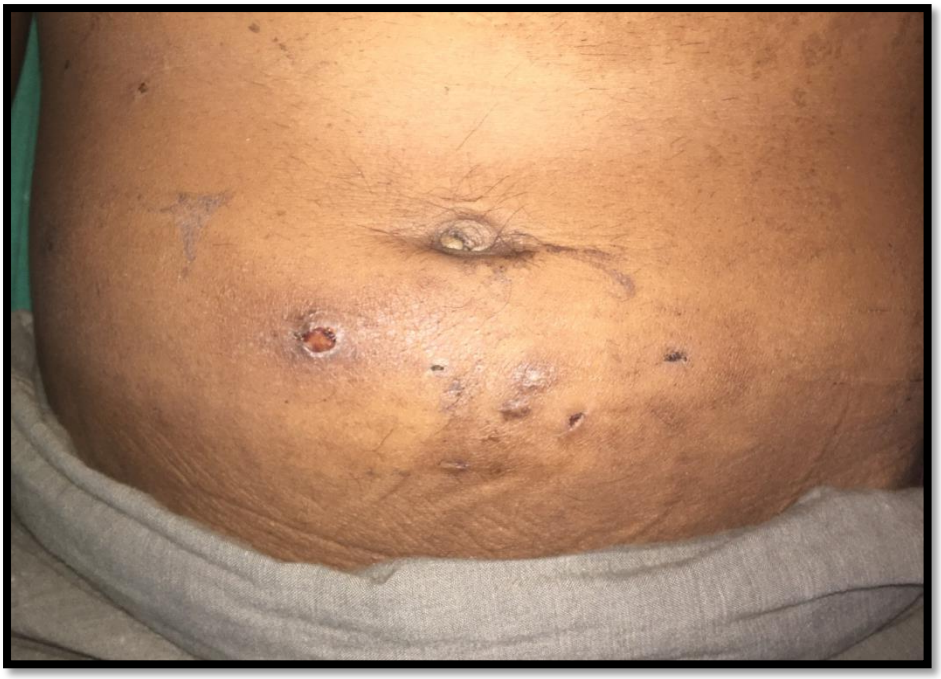
The picture shows epidermal cup shaped invagination filled with eosinophilic keratin plug.

LYMPHEDEMA SECONDARY TO ARTERIO-VENOUS SHUNT



PURPURA

INFECTION AT DIALYSIS SITE



BACTERIAL INFECTIONS

FUNGAL INFECTIONS

VIRAL INFECTIONS

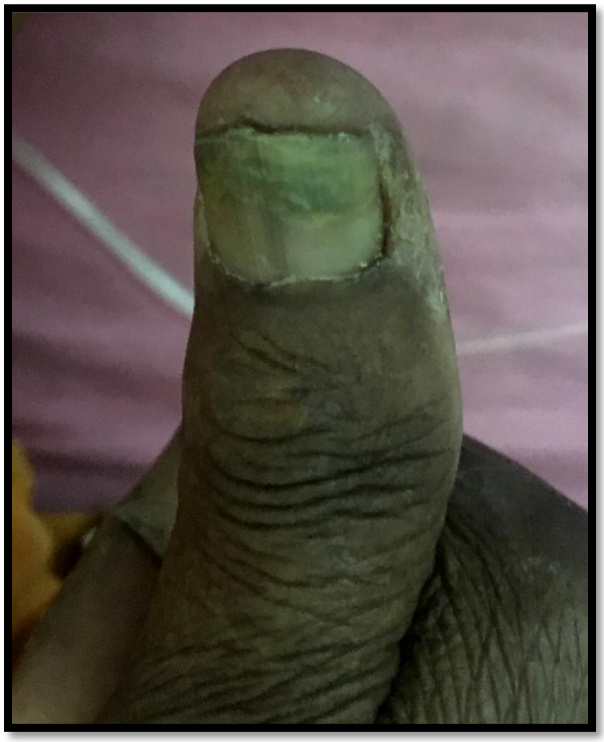
HERPES LABIALIS

HERPES ZOSTER

NAIL CHANGES

HALF AND HALF NAILS

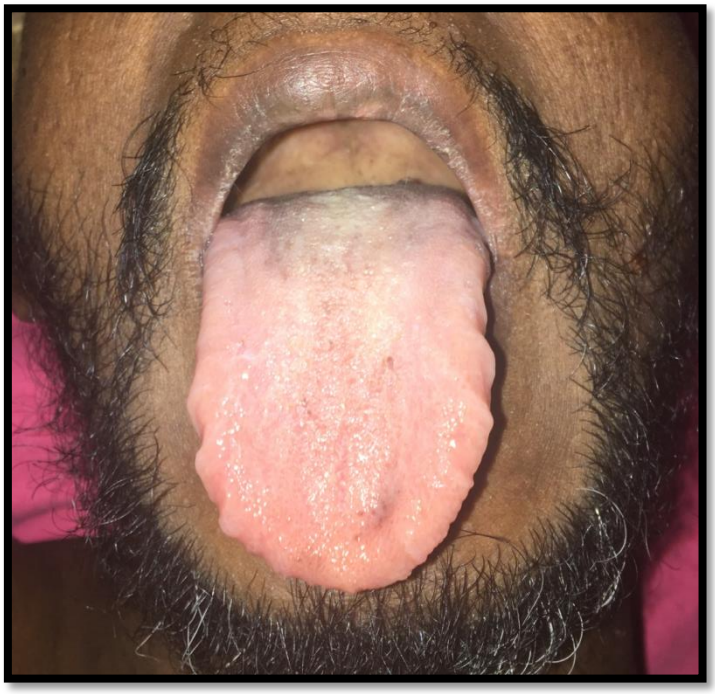
ONYCHOMYCOSIS

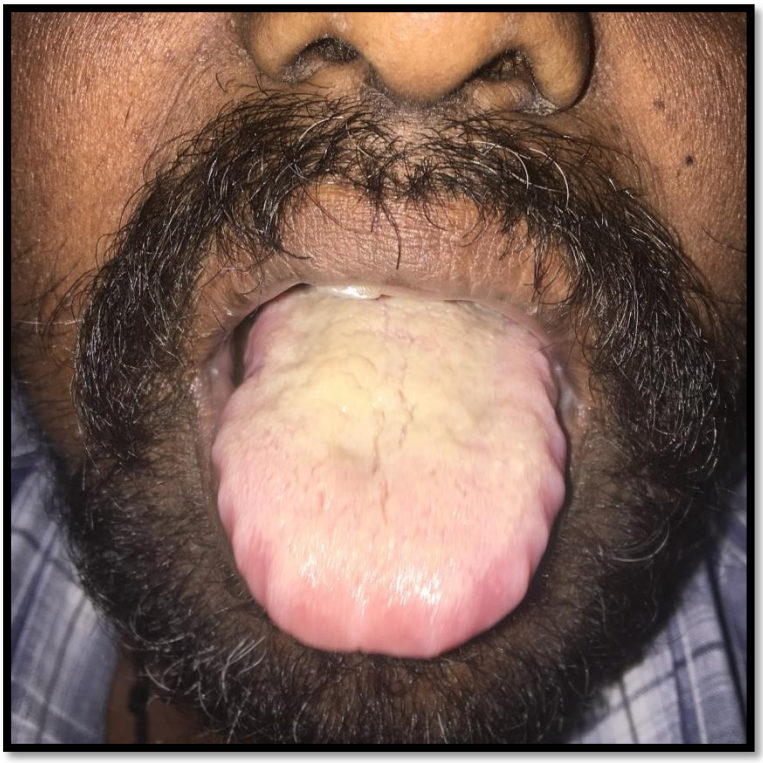


LEUKONYCHIA

ORAL MUCOSAL CHANGES

MACROGLOSSIA WITH TEETH MARKING





PROFORMA

A STUDY OF CUTANEOUS MANIFESTATIONS IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS

Name : Age/Sex: IP.NO :

Address :

Diagnosis:

Etiology of CKD:

Duration of illness:

Duration of dialysis:

Concomitant diseases:

Diabetes ☐ HbsAg:

Hypertension ☐ Anti-HCV:

Others HIV:

Medication:

Prior cutaneous illness, if any:

Duration of cutaneous illness:

Onset of skin changes in relation to diagnosis of CKD & starting dialysis:

EXAMINATION:

Built:

Icterus ☐ Cyanosis ☐ Clubbing ☐ Pedal edema ☐

Generalised lymphadenopathy ☐

BP:

PR:

CVS: RS: P/A: CNS:

Dermatological examination:

SKIN:

1. Pruritus ☐
2. Xerosis ☐
3. Pallor ☐
4. Pigmentation ☐

5. Yellow skin
6. Purpura ☐
7. Acquired Perfoating Disorder ☐
8. Uremic frost ☐
9. Pseudo Kaposi's sarcoma ☐
10. Eczema at fistula site ☐

11. Infection:

    Bacterial ☐

    Fungal ☐

    Viral ☐

12. Pseudoporphyria ☐
13. Nephrogenic systemic fibrosis ☐
14. Calcinosis cutis ☐
15. Calciphylaxis ☐
16. Others ☐

NAIL:

1. Half & half nail ☐
2. Koilonychia ☐
3. Onychomycosis ☐
4. Onycholysis ☐
5. Subungual hyperkeratosis ☐
6. Muehrcke's line ☐
7. Mees' line ☐

8. Beau's line ☐
9. Splinter hemorrhage ☐
10. Other ☐

HAIR:

1. Scalp hair loss ☐
2. Whole body hair loss ☐
3. Drying and hair fragility ☐
4. Hirsuitism ☐
5. Others ☐

MUCOUS MEMBRANE:

1. Macroglossia and teeth marking ☐
2. Xerostomia ☐
3. Ulcerative stomatitis ☐
4. Angular cheilitis ☐
5. Uremic fetor ☐
6. Others ☐

INVESTIGATIONS (relevant):

1. Renal Parameters: Urea -

Creatinine -

2. Haemoglobin :

3. Blood sugar: FBS -

PPBS -

4.Skin biopsy:

5.Bacterial infections

- Culture & sensitivity

- Gram's stain

6.Fungal infections

- KOH mount

- Fungal Culture

7.Other

CONSENT FORM

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு: சிறுநீரக கோளாறுக்காக கூழ்மப்பிரிப்பு செய்யும் நோயாளிகளிடம் உள்ள தோல் நோய் அறிகுறிகள்

பெயர்: தேதி:

வயது: உள் நோயாளி எண்:

பால்: ஆராய்ச்சி
சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது.

எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது முழு மனதுடன் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில் தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் பின்வாங்கலாம் என்றும் அதனால் எந்த பாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழுசுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

MASTER CHART

S.NO	Name	Age	Sex	Duration of illness	Duration of dialysis	Type of dialysis	Diabetes	Hypertension	Others	Duration of illness	Onset of skin changes in relation to diagnosis of CKD & starting dialysis	Pruritus	Xerosis	Pallor	Pigmentation	Yellow skin	Purpura	Acquired Perfoating Disorder	Eczema at fistula site	Infections	Others, if any	Half & half nail		Onychomycosis Onycholysis	Subungual hyperkeratosis	Mees' line	Beau's line	Longitudinal melanonychia	Leukonychia	Others	Scalp hair loss	Drying and hair fragility	Macroglossia and teeth marking	Uremic fetor	Others	Urea	Creatinine	Hemoglobin	RBS
1	SRINIVASAN	35	M	2 Years	6 months	PD & HD	+	+		2 weeks	after dialysis								pyoderma			+											+			199	23.5	6.5	109
2	VELMURUGAN	39	M	6 months	3 weeks	HD	-	+						+											+											132	8.6	6	123
3	BAVANI	56	F	5 Years	2 years	HD	+	+			before dialysis	+		+																						98	6.5	5.2	221
4	KARUNANIDHI	40	M	1 year	1 month	HD	+	+	Sputum positive Pulmonary TB				+	+																						85	9.4	5.8	115
5	MARISAMY	50	M	1.5years	1 year	HD	-	+		6 months	after dialysis	+		+							Lymphedema lt UL																	
6	AMSU	32	F	7 Years	3 months	PD & HD	-	-	Severe MR/ Moderate TR Severe PHT		before dialysis	+	+	+		+																					184	15.5	5.6	60
7	ALAGAR	47	M	1 year	1 year	PD & HD	-	+																						+				+			247	16.4	7.4	130
8	CHINNARAJA	42	M	3months	1 month	PD	+	-		2 months	before dialysis		+	+				+															+			145	20.3	6.68	101
9	LAKSHMI	35	F	1 year	3 months	PD	-	+			before dialysis	+	+																							221	12.4	126	
10	MURUGAN	59	M	6 months	1 month	PD	-	+		2 months	before dialysis	+	+	+									+													218	20	6.4	93
	GANESAN	57	M	1 year	3 weeks	PD	+	+	Hypothyroid on Thyroxine					+								+														136	12.6	4.1	159
12	ALAGANAPATHY	37	M	7 months	2 weeks	PD	-	+																					+							58	8.8	11.5	63
13	BALAKRISHNAN	33	M	4 months	4 months	PD	-	+			after dialysis	+	+	+																+						132	7	6.5	121
14	BACKIYALAKSHM	45	F	4 Years	6 months	PD & HD	-	-	RHD/MS											Herpes zoster																143	9.1	7.2	94
15	GURUSAMY	54	M	10days	2 days	PD	+	+					+									+									N.D.	+		+		285	12	8.3	FBS-96 PPBS-171
16	SHANTHI	42	F	3 Months	2 months	PD	-	+		3 months	before dialysis	+																							156	5.7	8.2	154
17	MARIMUTHU	25	M	2 Years	6 months	PD & HD	-	+		3 months	after dialysis	+	+	+															+							58	4.7	7.1	96
18	PANDIYAN	48	M	2 years	3 months	PD	+	-		1.5 years	before dialysis	+			palms						Allergic contact dermatitis															63	3.8	9.2	FBS-60 PPBS-290
19	VASUMATHI	51	F	6 months	3 months	PD	-	-		3 days	after dialysis		+							Herpes labialis															204	15.1	6.5	121
20	KALEESWARI	28	F	6 months	3 weeks	PD & HD	-	+	TB Lymphadenitis				+	+							Cervical L.N								+				+			149	10.6	6.1	97
21	PANDI	68	M	6 months	1 month	PD	-	+		3 months	before dialysis	+	+	+																						310	17.2	6.1	122
22	POORNIMA	37	F	1 year	5 months	PD & HD	+	+			after dialysis	+																								225	7.9	8.4	154
23	SUYARAJYAM	70	M	3 years	6 months	HD	-	-		3 years	before dialysis	+	+								Lymphedema Lt UL															96	6.5	8.5	104
24	AISHWARIYA	15	F	1 week	1 week	PD	-	-						+							Pediculosis															261	8.1	6.1	124
25	KARUPPIAH	64	M	2 Years	1 month	PD	-	+					+									+		+											183	8.9	7.5	82
26	MAHESHWARI	36	F	11 years	2 years	HD	-	-					+	+																						131	8.5	4.2	93
27	MOKKAMAYAN	50	M	10 Months	1 week	PD	-	+		2 months	before dialysis	+																								194	12.7	8.5	96
28	BALAMURGAN	23	M	3 Months	2 months	PD & HD	-	+					+	+						Herpes labialis																204	20.5	5.2	122
29	KALA	48	F	2 Years	1 year	PD & HD	-	-			after dialysis	+		+																						86	4.5	6.1	95
30	CHINNASAMY	43	M	3 Months	2 weeks	PD	+	+					+	+																				+		253	20.3	5.6	127
31	GANAPATHY	50	M	2years	1 year	PD	+	+			after dialysis	+	+	+															+					+		130	9.9	5.4	166
32	PAAPATHI	65	F	1 month	20 days	PD	-	-		6 months	before dialysis	+					+							+											102	9.7	6.6	90
33	THANGAVEL	60	M	2 Months	2 days	PD	-	+												Herpes zoster																84	5.2	7.6	86
34	VASUMATHI	52	F	4 years	1 year	PD	-	-		6 Months	after dialysis	+	+	+																						124	4.1	6.2	69
35	DHANAM	52	F	5years	1year	PD	+	-		3 months	after dialysis	+	+	+				+							+						+			+		221	14.9	5.5	FBS-179 PPBS-268

36	JAGADEESWARI	43	F	6 months	2 months	PD	-	+		2 months	before dialysis	+											Rt Thumb						Pitting & N. D	+					198	11.8	6.3	126
37	MANIKANDAN	29	M	1 month	2 days	PD	-	+		1 month	before dialysis	+	+																							66	2.4	9.6	94
38	MARIAMMAL	56	F	8 months	3 months	PD	-	-			before dialysis	+	+																							75	3.8	7.1	106
39	MURUGESAN	55	M	1 month	15 days	PD	+	+		1 year	before dialysis	+		+				+				+										+				206	17.9	6.4	149
40	RAMASAMY	64	M	6 months	2 weeks	HD	-	+			before dialysis	+	+	+													+									205	9.2	6.5	50
41	ERIYAKARUPPAN	60	M	2 YEARS	6 months	PD	+	+		2 months	after dialysis	+	+														+									127	8.4	10.1	235
42	POONGOTHAI	55	F	1 year	1 year	PD	-	+		2 months	after dialysis	+	+	+																						115	7	6.5	130
43	URUNATHASAM	28	M	1 year	6 months	PD	-	-		3 months	after dialysis	+	+																							141	6.5	9.2	63
44	SUBRAMANI S	62	M	3 Months	2 months	PD & HD	-	+			before dialysis	+	+				+				Cellultis lt forearm	+											+			273	17.3	10.8	91
45	SUDHA	49	F	2 Years	2 months	PD	-	+		2 months	before dialysis	+																								105	7.2	9.5	114
46	AZHAGAN	64	M	1 year	2 months	PD & HD	+	+			before dialysis	+	+	+																					aptho us ulcer	198	8.8	6.1	98
47	LAKSHMANAN	50	M	2 years	1 month	PD	-	+		2 months	before dialysis	+	+	+																						210	9.6	5.3	70
48	DHANARAJ	32	M	6 months	3 months	PD	-	+		2 months	after dialysis	+		+														+								156	5.5	7.5	69
49	TAMILSELVAM	59	M	6 months	4 months	PD	-	-											Tinea corporis																		114	4.8	15.8	60
50	BASKARAN	57	M	2 Years	6 months	PD	-	-			after dialysis	+		+																						143	7.5	5.4	84
51	SIVAKUMAR	44	M	1 month	1 month	PD	-	+					+									+														247	16.3	8.5	85
52	SIVAKUMAR P	49	M	1 month	1 week	PD	-	+		1 year	before dialysis	+	+	+				+					+				+									308	12.9	5.7	93
53	ANCHAVARNAM	42	F	1 month	4 days	PD	-	+		1 month	before dialysis	+						+																		333	20.4	8.1	81
54	MALATHI	39	F	7 Years	5 years	PD & HD	-	+		5 years	before dialysis	+	+		+																		+			139	10.6	5.6	85
55	THANGAMUTHU	72	M	3 Months	2 months	PD & HD	-	+		2 months	before dialysis	+	+																							216	13.3	7.6	74
56	DHAMAYANTHI	68	F	7 months	3 months	PD	-	+			after dialysis	+																								187	9.4	9.2	97
57	PALANISAMY	55	M	1 year	3 months	PD	+	+		1 year	before dialysis	+		+				+																		292	19.5	7.8	108
58	BASTEN	38	M	1 year	6 months	PD	-	+		1 week	after dialysis			+							peeling of skin+															286	20.8	3.4	96
59	BALAJI	37	M	7 months	3 months	PD	-	+					+	+																						376	15.1	6	157
60	VELUSAMY	45	M	1 month	10 days	PD	-	-						+																						220	20.7	6.1	107
61	KANNAN	43	M	3 months	1 month	PD	-	+					+	+																						130	15.4	4.6	124
62	GOPALKRISHNAN	45	M	8 months	8 months	PD	-	+						+																						137	12.6	5.6	93
63	ANDICHI	54	F	2 years	8 months	PD	+	+		5 months	after dialysis	+		+																						110	10.5	6.5	135
64	CHANDRA	52	F	2 months	2 months	PD	-	+						+										+												242	22.2	4.6	194
65	VIJAYA	46	F	9 Months	6 months	PD & HD	+	+			after dialysis	+																								126	4.9	8.9	224
66	ALAGIRI	45	M	2 Years	2 months	PD & HD	-	-					+	+																						235	19	6.5	118
67	ANDICHAMY	48	M	3 Years	2 months	PD	-	+					+	+																						150	15.2	6.8	71
68	PANJU	55	F	1 month	15 days	PD	-	-			before dialysis	+		+																						75	5	6.4	120
69	PARAMAN	60	M	1 year	6 months	HD	+	+						+								+														94	9.5	5.8	273
70	ANDAL	48	F	3 Months	3 months	PD & HD	+	+											fistula site infection							+										133	11.5	8.5	131
71	ELANGOVAN	46	M	2 months	2 months	PD & HD	-	+		2 months	before dialysis							+															shiny nails				98	17.1	7.4	121
72	PANDI	34	M	2 months	2 weeks	PD	-	+		2 months	before dialysis	+																								254	21	9.1	77
73	LATHA	43	F	1 year	1 month	PD	+	+		1 year	before dialysis			+				+																		68	3.9	6.5	333
74	PARAMASIVAM	55	M	1 year	4 months	PD	-	+						+								+														154	6.8	5.6	92
75	SENTHIL	41	M	4 Years	1 year	PD & HD	-	+			after dialysis	+	+	+				Fistula site infection																		203	16.5	6.5	104
76	JAGADEESWARI	43	F	4 Years	6 months	PD & HD	-	+		2 months	after dialysis	+																								184	14.3	9.1	133
77	MANIMEGALAI	47	F	2 Years	4 months	PD & HD	+	+	CAD		before dialysis	+		+	+																					140	9.7	4.3	227
78	SEKAR	52	M	1 year	6 months	PD	-	+		1 year	before dialysis							+																		112	7.8	9.4	245
79	SEETHA	40	F	1 year	4 months	HD	-	-			after dialysis	+							Tinea corporis																	98	4.5	8.4	97
80	BOOMI	43	M	4 months	4 months	PD & HD	-	-		3 months	after dialysis	+						+		Scabies																216	16.3	5.4	58

KEY TO MASTER CHART

PD	-	Peritoneal dialysis
HD	-	Hemodialysis
ND	-	Nail dystrophy

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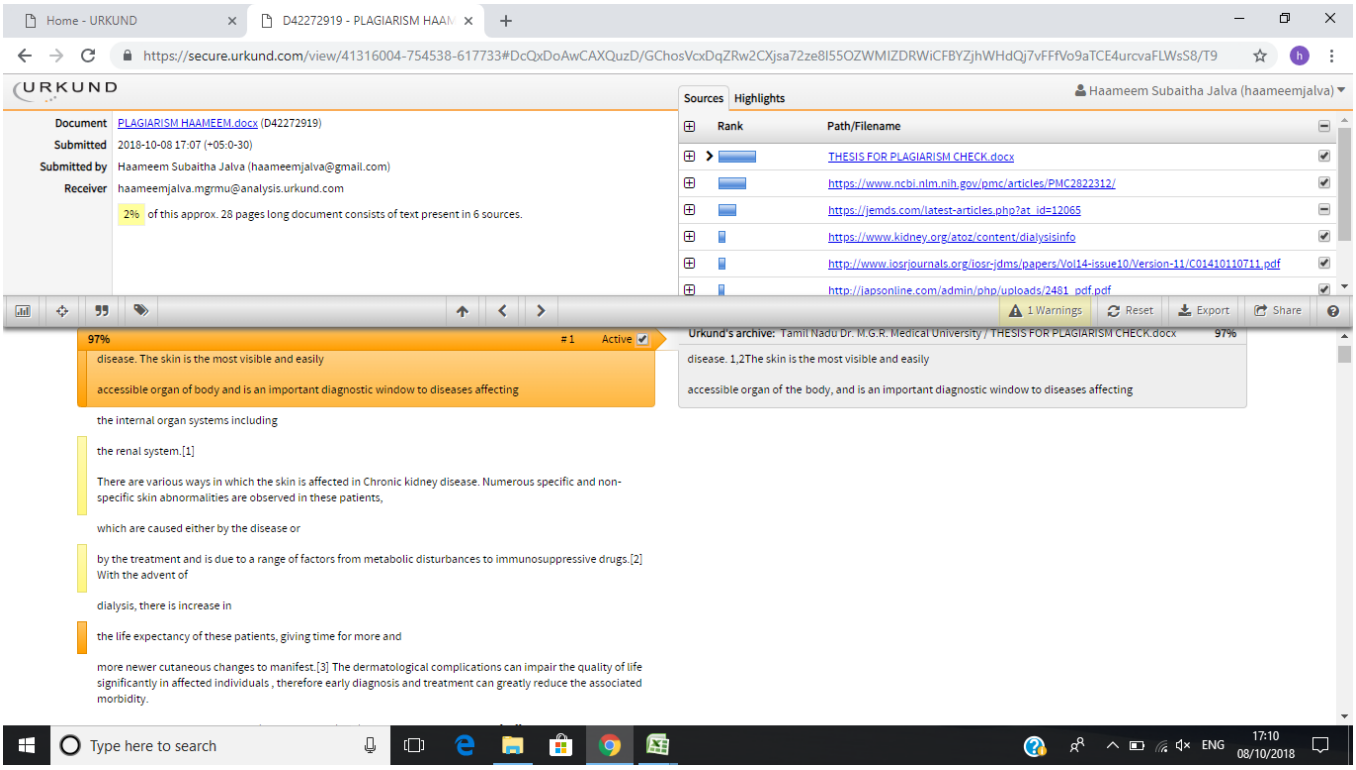
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Active
disease. The skin is the most visible and easily
accessible organ of body and is an important diagnostic window to diseases affecting
the internal organ systems including
the renal system.[1]
There are various ways in which the skin is affected in Chronic kidney disease. Numerous specific and non-specific skin abnormalities are observed in these patients,
which are caused either by the disease or
by the treatment and is due to a range of factors from metabolic disturbances to immunosuppressive drugs.[2] With the advent of
dialysis, there is increase in
the life expectancy of these patients, giving time for more and
more newer cutaneous changes to manifest.[3] The dermatological complications can impair the quality of life significantly in affected individuals , therefore early diagnosis and treatment can greatly reduce the associated morbidity.
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CERTIFICATE – II

This is to certify that this dissertation work titled **A STUDY OF CUTANEOUS MANIFESTATIONS IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS** of the candidate **DR.N.HAAMEEM SUBAITHA JALVA** with registration Number **201630101** for the award of **M.D. Degree** in the branch of **Dermatology, Venereology and Leprosy** . I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **TWO** percentage of plagiarism in the dissertation.

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Name of the Candidate	:	Dr.N.Haameem Subaitha Jalva
Course	:	PG in MD., DVL
Period of Study	:	2016 - 2019
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A study of cutaneous manifestations in chronic kidney disease patients on dialysis
Ethical Committee as on	:	11.09.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

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