Research Paper

A Clinical Study Of Cutaneous Manifestations In Chronic Renal Failure

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ABSTRACT:

BACKGROUND:

Skin -mirror of internal disease and diagnosting the systemic disease by cutaneous manifestations has always fascinated clinicians . Chronic renal failure is a common medical problem due to its increased incidence.

Key words: pruritis, xerosis, gynecomastia

AIMS AND OBJECTIVES:

To study the cutaneous manifestations and their incidence in patients with chronic renal failure.

MATERIALS AND METHODS:

Seventy five patients with CRF who attended the Department of Dermatology and Nephrology of our Institute were enrolled.

RESULTS:

Among 75 patients, 69% were males and 31% were females with M:F ratio of 2.2:1. The common symptom was pruritus (82%), common cutaneous finding was pigmentary change (53%) and xerosis (44%). Acquired perforating dermatosis specific to chronic renal failure was seen in 9.3%. Significant number (20%)had gynecomastia. Hair changes, nail changes and oral mucosal changes were seen in 21.3%, 30.6%,28% respectively. Brown arc was the most common nail change followed by half and half nails. Oral mucosal lesions was present in 28% with stomatitis . Fungal infection (20%) with tinea versicolor was the commonest presentation followed by viral infections (12%) and bacterial infection (5.3%).

CONCLUSION:

Recognition and management of the dermatological manifestations vastly reduces the morbidity and also improve the cutaneous outcome in these patients.

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INTRODUCTION:

Skin is the mirror of internal disease and the ability to diagnose systemic disease by cutaneous manifestations has always fascinated clinicians .(1) The kidneys and the skin are two important organs whose supply far exceeds their demand; the former for maintaining the milieu and the later for rendering man's homeothermic property. It is no wonder that pathology

of one is reflected on the other. This fact and many others form the basis for skin manifestations in renal disease.

50%–100% of patients with end-stage renal disease (ESRD) have at least one associated cutaneous change.(2)Cutaneous manifestations in renal failure range from asymptomatic to life-threatening forms. Clinical manifestations can occur before or after initiation of dialysis and are divided as Specific and non-specific types. (3)

MATERIAL AND METHODS:

After obtaining institutional ethics committee approval, a cross sectional study was conducted in 75 patients who attended the Department of Dermatology and Nephrology of the Institute from August 2023 to June 2024.

Before the collection of data, counselling and information regarding the study and the procedure were given to all the patients enrolled in the study.

Individual study participant's gave written informed consent.

A detailed clinical history, nature of onset , duration and progression of the symptoms were taken. History regarding renal disease ,its etiology, treatment taken (including dialysis) were taken in detail. History of any associated co-morbidities were also recorded. A detailed physical examination and dermatological examination were done in all our patients for;

a) Specific lesions of Chronic renal failure
b) Presence of cutaneous infections
c) Skin lesions due to effect of treatment
d) Other co-existing skin lesions

Pruritus, xerosis, pigmentation disorders, and half and half nails (Lindsay's nails) were classified as non-specific and APDs, bullous dermatoses, calcifying disorders, and nephrogenic systemic fibrosis as specific manifestations of Chronic renal failure.(3)

All patients were thoroughly investigated with complete hemogram, urine microscopy, standard biochemical investigations like blood urea, serum creatinine, serum electrolytes, blood sugar, serum calcium, serum phosphate and liver function test. Doubtful lesions were confirmed by biopsy.

Data were entered in Microsoft Excel and analyzed with SPSS version 16.0.

RESULTS:

The total number of 75 patients were included in the study. Of the 75 patients, 52(69%) were males and 23 (31%) were females.Male to female ratio was 2.2.:1

The age of the patients ranged from 18 years to 62 years with average age around 40 years. The youngest male and female patients were of 18 years and 22 years while the oldest were 62 years and 50 years respectively.

Severity of renal failure was graded as mild, moderate and severe or end stage renal failure.

I-INCIDENCE OF SPECIFIC LESIONS OF CHRONIC RENAL FAILURE:Pruritus was seen in 62 patients out of which males were (47) and females (15), with an incidence of 82%. Severity of pruritus was graded as mild, moderate and severe. It was severe in 8 patients, moderate in 30 patients and mild in 24 patients.

Xerosis or dryness of the skin (Fig:1) was seen in 33 patients, with an incidence of 44%. Dry scaly skin predominantly was seen in the extremities

Fig: 1- Xerosis of the lower extremities

Three kinds of pigmentary changes were seen.

a) Sallow grey skin of uraemia could be seen only as a yellowish hue of skin or as pallor. This was the predominant pigmentary change seen in 20 patients with an incidence of 26%.
b) Diffuse hyperpigmentation of the exposed parts of skin was seen in 12 patients.
c) Hypermelanotic macules on palms were seen in 7 patients. Total number of patients with pigmentary changes were 39, with an incidence of 52%.

Perforating Dermatosis:

This was seen in 10 patients. Clinical and histological criteria were followed for the diagnosis of the individual dermatosis.

Kyrle's disease(Fig:2)was seen in 4 patients. Clinical criteria used for diagnosis were

a) Hyperkeratotic papular scattered eruption in generalised distribution
b) Lesions which were follicular and extrafollicular
c) Lesions which coalesced into hyperkeratotic verrucous plaques
d) Lesions which did not involve mucous membrane , palmar or plantar surfaces

Histopathological criteria were

a)A keratotic plug which filled an epidermal invagination
b)Parakeratosis in parts of the plug
c)Basophilic cellular debris not staining with elastic tissue stains within the plug
d)Abnormal parakeratotic keratinization of all the epiderrmal cells including the basal cells present in atleast one region deep to the plug.

Routine H&E stains as well as special stains like Verhoeff Von Gieson stain were used for histopathological study. An interesting observation on this study was 3 out of the 4 patients with kyrle's disease were diabetics.

Perforating folliculitis was seen in 3 patients.

Clinical criteria used for diagnosis were,

a) Elevated erythematous follicular papule with central plugs of keratinous material

b) Lesions involving the extremities with the predilection of the hairy areas of arms, thighs and legs
c) Usually asymptomatic, sometimes mildly pruritic

Histopathological criteria were

a) Widely dilated hair follicle plugged by a thick mass of orthokeratotic and parakeratotic material
b) A curled up hair which was usually cut cross
c) Follicular epithelium showing disruption with areas of perforation, above the level of the sebaceous gland
d) At sites of perforation , dermis showed an inflammatory infiltrate containing degenerated collagen and degenerated elastic fibres without an increase in elastic fibres.

Routine H&E stain and special stain of Verhoeff Von Gieson showed the degenerated collagen fibres eliminated through the perforation in the hair follicle.

Fig:2 Kyrle's Disease

Purpura was seen in 7 patients with an incidence of 9.3%. It more commonly occurred on the lower limb.

Gynecomastia (Fig:3)was seen in 15 patients with an incidence of 20%.

Fig:3- Gynecomastia

HAIR, NAIL AND MUCOSAL CHANGES:

ORAL MUCOSAL CHANGES: Oral mucosal changes(Fig:4) were seen in 21 patients with an incidence of 28%. Stomatitis was seen in 10 patients, angular stomatitis in 2 patients, ulcers over labial margins in 2 patients.

Fig:4- Stomatitis

HAIR ABNORMALITIES:

Sparse scalp hair was reported in 16 patients with an incidence of 21.3%

NAIL CHANGES:

Specific nail changes was seen in 23 patients with an incidence of 30.6%.Half and Half nails(Fig:5) were seen in 7 patients, Brown arcs in 16 patients, shiny nails was seen in 5 patients.

Fig:5- Half and half nails

Table 1: SPECIFIC SKIN LESIONS:

Specific Skin Lesions	Males	Females	Total Number	Percentage
Pruritus	47	16	62	82%
Xerosis	23	10	33	44%
Pigmentary changes	15	5	20	52%
Bullous Dermatosis	-	-	-	-
Metastatic Calcification	-	-	-	-

Perforating Dermatosis	6	1	7	9.3%
Purpura	3	4	7	9.3%
Gynecomastia	15	-	15	20%
Uremic Frost	-	-	-	-
Oral Mucosal Changes	14	7	21	28%
Hair Abnormalities	10	6	16	21.3%
Nail changes	18	11	23	30.6%

II-CUTANEOUS INFECTIONS:

Of the 75 patients , 31 patients presented with cutaneous infection and infestations with an incidence of 41.3%.

Fungal infections:

Pityriasis versicolor (Fig:6)was seen in 9 patients. Tinea curis in 5 patients and generalised dermatophytosis in 2 patients. Scraping for direct microscopic visualisation with 10% KOH was done in all cases along with innoculation of specimen into culture medium. Direct microscopic visualisation was positive in all cases , whereas culture was positive in 2 cases. The infecting agent grown was Trichophyton rubrum.

Fig-6: Pityriasis Versicolor

Viral infections:

Herpes simplex labialis was seen in 6 patients. Herpes zoster was seen in 1 patient. TZANCK smear was done and multinucleate giant cells were seen.Verruca vulgaris was seen in one patient.Chicken pox was seen in one female patient on hemodialysis.

Bacterial infections:

Furunculosis was seen in 1 patient and infected leg ulcers in 3 patients with diabetes.

Parasitic infestations: Scabies (Fig:7) was seen in 3 patients. Mite was demonstrated by KOH.

Fig:7- Scabies

Table-2 :CUTANEOUS INFECTIONS:

	Fungal infections	**Viral infections**	**Bacterial infections**	**Parasitic infections**
Tinea Versicolor	9	-	-	-
Dermatophytosis	6	-	-	-
Herpes Simplex	-	6	-	-
Chicken Pox	-	1	-	-
Herpes Zoster	-	1	-	-
Verruca Vulgaris	-	1	-	-
Furunculosis	-	-	1	-
Infected Ulcers	-	-	3	-
Scabies	-	-	-	3
Total	15	9	4	3
Percentage	20%	12%	5.3%	4%

Total Number :31
Incidence :41.3%

III- SKIN CHANGES DUE TO TREATMENT OF RENAL FAILURE:

Eczematous leisons at arteriovenous fistula site(Fig:8) was seen in 2 patients and abcess in 1 patient. Pruritus due to dialysis was reported in 12 patients.

Fig 8**:** Eczematous lesions at arteriovenous fistula

Table-3 :DIALYSIS INDUCED SKIN LESIONS

	Pruritus	**Bullous Dermatosis**	**Vascular malformations**	**A-V fistula infections**
Male	8	-	-	3
Female	4	-	-	0
Total Number	12	-	-	3
Percentage	16%	-	-	2.6%

IV-ASSOCIATED SKIN LESIONS

These were classified into those lesions which could contribute to the etiology of the renal failures and those which did not have any clinical significance.

Skin lesions which contributed to the etiology of renal failure:

A) Malar rash due to SLE in 4 patients.

B) Hide bound skin due to MCTD(Fig:9) in 1 patient.

Fig:9- Scleroderma

Other associated skin lesions:

Lichenified skin changes over legs- 5 patients

Ichthyosis vulgaris(Fig:11)-5 patients

Phrynoderma - 4 patients

Vitiligo-(Fig:10)- 4 patients

Fig:10- Vitiligo

Fig:11- Ichthyosis Vulgaris

Table -4:SKIN LESIONS WHICH CONTRIBUTED TO AETIOLOGY OF CRF

	Skin lesions of SLE	**Scleroderma MCTD**
Male	1	0
Female	3	1
Total Number	4	1
Percentage	5.3%	1.3%

Total Number : 6
Incidence : 8%

DISCUSSION:

Diabetes mellitus documented as the most common cause of ESRD which was consistent with the literature. (4)

Dermatological manifestations in ESRD are varied and can impair the quality of life. Prompt diagnosis may help to ensure treatment which, in turn, can reduce the disease associated morbidity.

Pruritus is considered as one of the most common and difficult to treat manifestations when it is associated with CRF and renal transplant as the definite treatment for ESRD reduced its severity(5)There is no statistically significant association between pruritus and gender.

The frequency of pruritus noted by us (82%) was concordant to the reported frequency of 40%–90%. (6,7,8)The underlying causes may be due to uremia, hypermagnesemia, hypercalcemia, hyperphosphatemia, hypervitaminosis A and also a role of secondary hyperparathyroidism is postulated. Compared to one study in which pruritus was graded as mild, moderate and severe by equal number of patients, this study showed that majority of patients had moderate to mild pruritus and severe pruritus was experienced only by 13% of patients.(9)

It can be due to the inability of hemodialysis to clear the blood off the pruritogenic middle molecular weight substances (molecular weight range 300-1200), like β2 microglobulin, advanced glycosylation end products, and parathyroid hormones. (10)The efficacy of oral cholestyramine, opioid naltrexone, oral ondansetron and topical capsaicin cream, and UVB phototherapy has been documented. (11)

Xerosis was seen in 44% of patients.. Data from several studies recorded prevalence of xerosis ranging from 46% to 90%. (12,3,14) Majority of our xerotic patients were known cases of diabetes mellitus. The management for xerosis is nonspecific and more challenging. Emollients can reduce scaling, and creams containing endocannabinoids (N-acetylethanolamine and N-palmitoylethanolamine) are found to be effective. (15).Atrophy of the sweat glands and loss of integrity of the superficial layer of epidermis due to decreased water content can cause xerosis. Alteration in metabolism of Vitamin A and use of diuretics are implicated in the dryness of skin (16,17)

Diffuse hyperpigmentation on sun exposed areas occurs as a result of increase in melanin in the basal layer and superficial dermis as the kidneys fail to excrete beta-melanocyte stimulating hormone. (18)

Perforating dermatosis was encountered in 10 patients clinically. Using clinical and histopathological criteria, kyrle's disease was found in 4 patients, perforating folliculitis in 3 patients, non specific histopathological finding in 3 patients. In A study by Udayakumar et al. (2)and Sultan et al. (19) prevalence of APD was reported as 21% and 10%, respectively. APD can present as hyperpigmented and hyperkeratotic follicular papule due to trans-epidermal limination of altered dermal substances.

Purpura was seen in 7 patients giving rise to an incidence of 9.3%. Elevated levels of guanidinosuccinic acid in uraemia could interfere with activation of platelet factor III by adenosine diphosphate and contribute to the impaired platelet function causing purpura.(20)There are also studies stating purpura can be caused by increased vascular fragility, use of anticoagulant for dialysis and capillary leak.

Gynecomastia was seen in 15 patients giving rise to an incidence of 20%. This occurs due to suppression of testosterone production and testicular damage secondary to uraemia.

Hair abnormality was seen in 22% of the patients. This was consistent with a study conducted by Supriya P et al(21). Decreased sebum production and decreased hemoglobin due to erythropoietin insufficiency in CRF can be a contributing factor.

Nail changes - Half and Half nails was reported in 20 to 35% of the patients.Similar findings were seen in a study by Supriya P et al (21) where the incidence was found to be 20%.

A nail exhibiting a whitish or a normal proximal half and a distinctly abnormal brownish distal portion was taken as criteria for Half and Half nail. Brown arc was diagnosed by the presence of a brown arch distally at the point of separation of the nail from its bed.

Mucosal changes was seen in 21 patients giving rise to an incidence of 28%.Uremic stomatitis was the most common mucosal change, seen in 10 patients. Leucokeratosis seen as whitish plaques in the oral mucosa was noticed in 2 patients. Glossitis and cheilitis in ESRD may be attributed to nutritional deficiency diseases due to riboflavin , iron and zinc deficiencies(22)

The percentages of cutaneous infections in our study was 41.4% . This is consistent with an Indian study (2)and an Egyptian study (19)in which it was 55% and 40%, respectively. Fungal infections had an incidence of 20% with pityriasis versicolor seen in 9 , tinea cruris in 4 and generalised dermatophytosis in 2 patients. Inflammation caused by the use of nonsterile dialysate and non biocompatible membranes (4)during hemodialysis can cause increase susceptibility to infections due to decreased T and B lymphocyte function and decreased natural killer cell activity. (23)

Viral infections are seen in 12% of patients. Bacterial infections in 5.3% of patients and parasitic infestations in 4% of patients.

Other associated skin lesions seen in our study are Lichenified skin changes over legs- 5 patients(6.6%), Ichthyosis vulgaris- 5 patients(6.6%), Phrynoderma - 4 patients(5.3%),Vitiligo- 4 patients(5.3%). Other dermatoses like calcinosis cutis, bullous dermatoses of hemodialysis and nephrogenic fibrosing dermopathy are reported in other studies.(23-25)

CONCLUSION:

In this study, xerosis, pallor, dyspigmentation, and pruritus were the commonest cutaneous manifestations observed.. Of these, xerosis and acquired perforating dermatosis were more prevalent in diabetics. Of the cutaneous infections manifesting in CKD , in our study fungal infections were more common.Correlation of other manifestations with their etiologies was difficult due to small sample size. Nail changes were more prevalent in patients who received hemodialysis for a longer period of time.

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