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Clinicoepidemiological Study Of Renocutaneous Disorder A Prospective Study

KEYWORDS: Chronic Kidney Disease, uremic pruritus, Calcific uremic arteriolopathy, Nephrogenic systemic Fibrosis

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ABSTRACT *Introduction: The majority of dermatological disorders in Chronic Kidney Disease are relatively benign and few rare skin diseases have potential to cause severe morbidity and mortality like uremic pruritus , calcific uremic arteriolopathy and nephrogenic systemic fibrosis. Early recognition of these severe skin disorders and prompt initiation of treatment can dramatically alter the course and even save a patient's life. The pathogenesis of cutaneous manifestations in CKD is multifactorial.*

Objectives: The present study was carried out to know the prevalence of cutaneous manifestations in relation to kidney diseases and in relation to age, sex and basic disease, systemic disorders like Diabetes, Hypertension , SLE ,Sclero-derma , Amyloidosis etc.

Study design: 50 Clinically diagnosed cases of renal disease with cutaneous manifestations attending to dermatology and nephrology departments were included in this study. In all the patients the type of underlying renal disease , dura-tion of the disease, stage of renal disease was identified and the type of cutaneous manifestations were studied.

Results : A total of 50 patients were studied. Majority patients with cutaneous lesions had chronic kidney disease than acute renal disease. The study compared cutaneous manifestations in CKD in relation to age, sex, type and duration of kidney disease and type of cutaneous lesions. All the 50 patients showed at least one cutaneous manifestation.

Conclusion: The cutaneous manifestations were proportional to the severity of chronic kidney disease. Non-infectious skin manifestations like xerosis, Pruritus and anemia and nail changes like koilonychias, half and half nail were more common than infections.

INTRODUCTION

The majority of dermatological disorders in CKD are relatively benign a few rare skin diseases have the potential to cause serious morbidity and mortality. Early recognition of severe skin diseases like calcific uremic arteriolopathy,nephrogenic systemic fibrosis can alter the course of the disease and may even save the patients life and prompt initiation of treatment can dramatically alter their course.[1] Uremic pruritus, is an ongoing therapeutic challenge in patients with CKD. Finally, acquired perforating dermatosis (Kyrle disease) and porphyria cutaneatarda are very rare.[2-3-4]

A wide variety of skin diseases occur in patients with chronic kidney disease (Table 1)[2-3-4]. These diseases are sometimes related to the underlying renal illness but are more frequently directly or indirectly associated with 'uremia' in its broadest sense. With an almost 100% prevalence in dialysis population.Skin disorders are frequently the subject of patients' complaints.[5] Skin diseases have a considerable negative effect on a patients quality of life. They can induce serious discomfort, anxiety, depression and sleep disorders and have an overall negative effect on mental and physical health.

Based on recent guide lines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)], in which stages of CKD are defined according to the estimated eGFR.[6] Table 1

TABLE 1 CLASSIFICATION OF CHRONIC KIDNEY DISEASE (CKD)

Stage	GFR, mL/min per 1.73 m2
0	>90a
1	>90b
2	60-89
3	30-59
4	15-29
5	<15

A with risk factors for CKD

Bwith demonstrated kidney damage (e.g., persistent proteinuria, abnormal urine sediment, abnormal blood and urine chemistry, abnormal imaging studies)

TABLE 2 RECOMMENED EQUATIONS FOR ESTIMATION OF GLOMERULAR FILTRATION RATE (GFR) USING SERUM CRETININE CONCENTRATION (PCr), AGE, SEX, RACE AND BODY WEIGHT

Equation from the Modification of Diet in Renal Disease study a Estimated GFR (mL/min per 1.73 m2 = 1.86X(PCr) -1.154 X (age) -0.203

Multiply by 0.742 for women
Multiply by 1.21 for s.

2. Cockroft – Gault equation.
Estimated creatinine clearance (mL/min) (140-ageXbody weight, kg)

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= 72XPCr (mg/dL)
Multiply by 0.85 for women

a Equation is available in hand-held calculators and in tabular form.

Adopted from AS Leveyer al : Am J Kidney Dis 39 (Suppl 1) : S1, 2002, with permission

MATERIALS AND METHODS

The present study was a prospective observational study . A total of 50 patients with kidney disease having cutaneous lesions were enrolled for the study attending Dermatology and Nephrology departments in Govt General hospital. Predesigned and pretested proforma were filled after taking informed consent, photographs and relevant investigations.

The kidney disease patients with cutaneous manifestations were taken for the study. A detailed history was taken with particular reference to duration, initial site of appearance of lesions, extension of lesions, and symptoms, history of renal disease and duration of symptoms, duration of skin aliments, changes with relation to renal disease. History of underlying systemic conditions like Diabetes, Hypertension, TB, connective tissue disorder etc was obtained. Clinical photographs were taken at the beginning of study and when cutaneous manifestations were encountered.

All the patients were subjected to thorough clinical examination noting the site, number and morphological pattern of skin lesions, other associated conditions were recorded. The severity of chronic kidney disease was graded into stage 1-5 based on GFR (Cockroft-Gault equation)[6].(Table 2)

Mild (stage 1, 2), moderate (stage 3), severe (stage 4, 5).

All patients were followed up regularly.

RESULTS

Of the 50 patients studied 25 were male and 20 were female and 5 were children. Age ranged from 1 year to 75 years. Maximum cases 12(24%) were in the age group of 40-50 years.5 cases (10%) belonged to paediatric age group.(Table 3)

29 cases belonged to underlying primary renal diseases (like chronic glomerulonephritis, interstitialnephritis, analgesicnephropathy, FSGS, Adult PCKD, Acute nephritis) and 21 cases belongs to systemic disease with renal involvement (like DM,HTN,SLE,TB,HSP.)

In this study out of 50 patients 40 patients had chronic kidney disease and remaining 10 patients belonged to acute renal involvement. (LE with acute renal failure 5 cases and non-LE with acute renal failure 5 cases.)

The duration of chronic kidney disease varied from 1 to 5 years in maximum number of patients (56%) with cutaneous manifestations. (Table 4)

Among the cutaneous manifestations in CKD patients, xerosis(Fig 1) was observed in 70% of cases followed by Anaemia (65%)(Fig 2), pruritus (53%), pigmentary alterations (20%)(Fig 2), purpura (5%) and prurigonodularis (2.5%) and infections (20%).Severity of xerosis was assessed by modified version of the grading by Marton.[7]Severexerosis was observed with stage IV and V of CKD.Nail changes were observed in 40% of patients with CKD which include koilonychias,half and half nails(Fig 3),white nails and onychomycosis.[8]

Hair changes were seen in 15%.
Sparse body hair-10%
Sparse scalp hair-5%

TABLE 3: DERMOGRAPHIC PROFILE OF PATIENTS

Characteristic	Subgroups	NO. of cases	TOTAL
Age group	<10 years	4	50
	10-20	6	
	20-30	8	
	30-40	7	
	40-50	12	
	50-60	9	
	>60	4	

SEX	NO. of cases	TOTAL
MALE	25	50
FEMALE	20	
CHILDREN	5	

TABLE 4: CLINICAL PROFILE

Characteristic	Subgroup	NO. of cases	Total
Cutaneous	Xerosis	28	50
	Anemia	26	
	Pruritus	16	
	Pigmentary changes	8	
	Purpura	2	
	PN	1	
	Eczema	2	
	Infections	8	
	LP	1	
	Diabetic dermopathy	1	
NAIL	Koilonychia	7	
	Half and half nail	5	
	White nail	3	
	Onychomycosis	1	
HAIR	Sparse body hair	4	
	Sparse scalp hair	2	

TABLE 5

Kidney disease				
	Chronic	<1 year	4	40
		1-5	23	
		5-10	12	
		10-20	1	
	Acute	< 1 week	1	
		1-2 weeks	4	
		3-12weeks	5	

Etiology	Primary	29
	Systemic	21

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DISCUSSION

Chronic kidney disease is recognized as a public health problem and mild to moderate chronic kidney disease is very common in unselected populations. Skin manifestations in acute renal failure are rare, on contrary skin manifestations are more common in chronic kidney disease.[9] Generally cross section population studies in a number of countries suggest an overall prevalence of Chronic kidney disease stage 1-5 >10%. [5]

Reported Community prevalence of various stages of chronic kidney disease is typically of the order (oxford desk reference nephrology 2009)[5]

stage 1 : 3%
stage 2 ; 3%
stage 3 : 5%
stage 4 : 0.2%
stage 5 : 0.1%

Although serum urea and creatinine concentrations are used to measure the excretory capacity of the kidneys, accumulation of these two molecules themselves do not account for the many symptoms and signs that characterize the uremic syndrome in advanced renal failure. Hundreds of toxins that accumulate in renal failure have been implicated in the uremic syndrome. These include water-soluble, hydrophobic, protein-bound, charge, and uncharged compounds. Compounds with a molecular mass between 500 and 1500 Da, the so-called middle molecules, are also retained and contribute to morbidity and mortality. It is thus evident that the plasma concentrations of urea and creatinine should be viewed as being readily measured, but incomplete, surrogate markers for these compounds, and monitoring the levels of urea and creatinine in the patient with impaired kidney function represents a vast over simplification of the uremic state.

Furthermore, plasma levels of many hormones, including PTH, insulin, glucagon, sex hormones, and prolactin, change with renal failure as a result of urinary retention, decreased degradation, or abnormal regulation. Finally, progressive renal impairment is associated with worsening systemic inflammation. Cutaneous examination of patients with CKD has shown that 50-100% of patients have at least one dermatologic condition. A high prevalence of cutaneous disorders is expected, since most patients with CKD have an underlying disease process with cutaneous manifestations. In addition, uremia and conditions associated with renal replacement therapy are fraught with numerous and, often, relatively unique cutaneous disorders.

The study included 50 patients who were clinically diagnosed with cutaneous manifestations, ranging from age 1yr- 70 yrs ,which showed higher preponderance in males (1.25:1).Majority of the patients were middle aged 40-50 yrs . In children the ratio is 1.5:1. The duration of Chronic kidney disease is 1-5 yrs in majority of the patients.The ratio of primary to secondary diseases in the etiology of CKD was 3.6:2.6 with preponderance of chronic glomerulonephritis in primary and diabetes mellitus in secondary diseases.

`Out of 50 patients with kidney disease with cutaneous manifestations .40 were with chronic kidney disease, 5 were with acute nephritis (Non – LE) and 5 were with systemic disease with acute nephritis (LE) (TABLE 5).

In our study xerosis is found in 70% (28 patients) which correlates well with the studies of Uday kumar et al[2] who reported a prevalence of 79%, Bhagavat et al 1[10] who reported a prevalence of 66%, and Morton et al[7] who reported a prevalence of 46 – 90%. But Tawade et al[11] reported 46% and Guru charan singh et al[12] reported 90% of xerosis among chronic kidney disease patients.

In the present study anemia was the second predominant skin manifestation noted in 26 patients (65%). The previous studies conducted by Bhagavat et al[10](2003) showed the prevelance of 76.5% and 97% by Uday Kumar et al[2] (2006). The less prevalence of anemia in the present study compared to previous studies may be due to the fact that most of the patients were on Erythropoietin and more no of patients in our study were in 3-5 stage of Chronic kidney disease as compared to stage 5 of chronic kidney disease in the above mentioned studies.

In the present study Pruritus was recorded in 16 patients (52%) which is in accordance with findings of Tawade et al [11] who reported a prevalence of 34%, Uday kumar et al[2] who reported a prevalence of 53% and Bhagavat et al[10] 19.6% in their series.

In the present study hyperpigmentation of sun exposed was noted in 8 patients (20%) which is in accordance with Uday Kumar et al[2] who reported 26%, Bhagavat et al[10] 25.5%, Morton et al[7] 20-22% and Pico et al [13] 22% in their studies.

Purpura was seen in 2 patients (5%) in present study which is in accordance with findings of Uday Kumar et al[2] 9%, all these patients had underlying systemic disease.

Prurigo nodularis was seen in 1 patient (2.5%) in the present study. The previous study by Uday Kumar et a[4] showed the prevalence of (8%). The less prevalence of prurigo nodularis in present study compared to previous study may be due to more no.of patients in our study being in 3-5 stage of chronic kidney disease as compared to stage 5 of chronic kidney disease in above mentioned study.

In the present study infections (Bacterial, Fungal, viral) were recorded in 8 patients (20%). The previous study by Uday Kurmar et al[2] showed the prevalence of (40%). The less prevalence of infections in present study compared to previous study may be due to more number of patients in our study being in 3-5 stage of chronic kidney disease as compared to stage 5 of chronic kidney disease in above mentioned study. In the present study various nail changes were seen in 16 patients (40%) which is in accordance with previous studies reported by Uday Kumar et al[2] 48% , Bhagavath et al[10] 42% and Tawade et al[11] 16-50.6%.

Hair changes were seen in 6 patients (15%) in present study. The previous studies showed the prevalence of 30% by Uday Kumar et al[2] and 30% by Guru charan singh et al[12]. The less prevalence of hair changes in present study compared with previous study may be due to more number of patients in our study being in stage3- 5 of chronic kidney disease as compared to stage5 of chronic kidney disease in above mentioned studies . Miscellaneous conditions: Other cutaneous lesions observed in the present study were lichen planus in 2.5%, diabetic dermopathy in 2.5%. No comparative studies were available for above conditions. (Chart 1)

Skin changes were rare in acute renal failure[5]. The manifestation of acute renal failure include anemia 7 (14%), Macular rash 6 (12%), Purpura 2 (4%), and Vasculitis 2 (4%)

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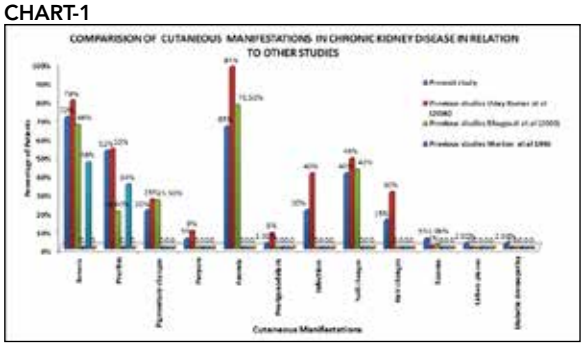
CHART-1



CONCLUSION

The Study was conducted on renal disease patients with cutaneous lesions attending to Departments of Dermatology and Nephrology, Government General Hospital , over a period of 1 year. 50 cases of renal disease with cutaneous manifestations were included in the study, all showing at least one cutaneous manifestation. Male predominance is observed in both adults and children. Most of patients were in the age group of 40-50 years. Majority of patients with cutaneous lesions had stage 3-5 CKD (80%) who showed array of cutaneous manifestations, Xerosis being the commonest (70%). Among primary CKD, Chronic Glomerulo nephritis (32%), and among systemic diseases with renal involvement, Diabetes mellitus was common. Non infectious skin and nail changes like Xerosis (70%), pruritus (52%), pigmentary changes (20%), anemia (65%), koilonychia (17%), half & half nail (12.5%),and infections (20%)like bacterial, viral,fungal were common. These changes were proportional to the severity of CKD. Most cutaneous manifestations in CKD are benign. Early diagnosis and medical intervention may alter the course of severe systemic diseases like nephrogenic systemic fibrosis and calcific uremic arteriopathy and even save a patient's life.

IMAGE 1:

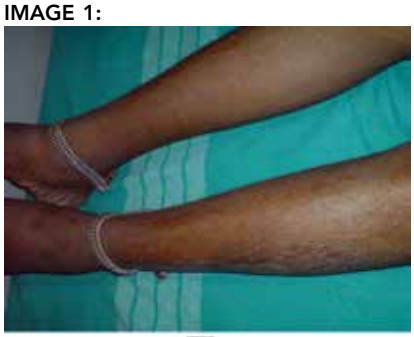


IMAGE 2:

IMAGE 3:

HYPERPIGMENTATION WITH ANEMIA

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