Dermatological Disorders in Chronic Kidney Disease with and without Maintenance Hemodialysis

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ABSTRACT

Introduction: Dermatological disorders are common complications of CKD affecting all most all patients. Present study aimed to evaluate these disorders in CKD with and without Maintenance Hemodialysis and their association with age, sex, severity and duration of CKD and dialysis.

Methods: It is a cross-sectional comparative study. Eighty-three patients with established CKD, without MHD (n=35) and with MHD (n= 48), were examined for dermatological disorders.

Results: The mean age of patients were 46±15.6 years with male to female ratio of 1.18:1. Among CKD without MHD, six patients were in stage 4 and 29 patients were in stage 5 with estimated GFR (24.4±3.9 and 5.6±2.9) ml/1.73m^2/min respectively by MDRD equation. CKD without and with MHD had similar age, sex, blood urea, hemoglobin. Dermatological disorders were found in 100% CKD patients with pallor 76 (91.5%), xerosis 63 (75.9%), pigmentary changes 54 (65%), pruritus 50 (60.2%), skin infection 40 (48.2%), vascular changes 14 (16.8%), mucosal changes 56 (67.5%), hair changes 49 (59%), non -specific nail changes 68 (81.9%) and specific nail changes 12 (14.4%). Specific 8 (22.8%) vs 4 (8.3%), p<0.03 and non- specific 32 (91.4%) vs 36 (75%), p<0.05 nail changes and hair abnormalities 26 (74.3%) vs. 23 (47.9%), p<0.01 were significantly lower in MHD patients.

Conclusions: Dermatological disorders were present in all CKD patients with significantly lower nail and hair changes in MHD. A further longitudinal study is necessary to find out pathophysiology and effect of treatment in these disorders.

Keywords: *chronic kidney disease; dermatological disorder; maintenance hemodialysis.*

INTRODUCTION

Dermatological disorders are common and diverse in patients with Chronic Kidney Disease (CKD) and xerosis, pruritus, pallor and hyperpigmentation are commonly encountered skin changes.[1-3] They can significantly affect patient's quality of life with negative impact in their mental and physical health and early detection and treatment of severe disorders can dramatically alter their course with improvement of quality of life.[4-6]

The prevalence of some of the disorders is associated with severity and duration of CKD and may precede or follow the onset of dialysis.[3,7] Maintenance hemodialysis (MHD) might improve some of the disorders by removing the risk factors related to uremia and predispose to develop newer disorders by prolonging the life.[8,9] Moreover, these disorders in CKD are also influenced

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by race, nutrition, geographic and socioeconomic conditions of patients.[10]

So, present study aimed to find out the dermatological disorders in Nepalese CKD with and without MHD and their association with age, sex, severity and duration of CKD and dialysis.

METHODS

It is a cross sectional and comparative study conducted in nephrology unit, Bir hospital and Shree Birendra Hospital from June 2008 to May 2009. The study was approved by Institutional Review Board of National Academy of Medical Sciences. Established CKD patients attending out-patient department with variable duration and severity on conservative management (CKD without MHD) and end stage renal disease on twice weekly MHD (CKD with MHD) for variable duration were included after informed written consent. CKD with previous history of intermittent peritoneal dialysis, acute renal failure and kidney transplantation were excluded.

A Per Forma was used for data collection. Patients demography including name, age, sex, occupation and address, duration of CKD and MHD, any dermatological complains at present or past and history of drug hypersensitivity were recorded. Hemoglobin, blood urea and serum creatinine was copied from patient's records. Then patients were thoroughly examined and skin, mucous membrane, hair and nail changes were noted. Scraping for fungus and pus for culture and sensitivity was done whenever necessary. The kidney function of CKD without MHD was determined by estimating the glomerular filtration rate (GFR) by MDRD (Modification of Diet in Renal Disease) equation and CKD staging done according to KDOQI (Kidney Disease Outcome Quality Initiative) clinical practice guideline.[11,12]

Statistical analysis was done using software SPSS 13. Chi-square test and Fisher exact test and Mann Whitney U test were used to find out statistical significance.

RESULTS

Total 83 patients with established CKD without MHD (n = 35) and with MHD (n = 48) were studied. Mean age of patients was 46 ± 15.6 years with age ranging from 16-78 years. Male patients were 45 and female patients were 38 with male to female ratio of 1.18:1.

Among CKD without MHD, 6 (17%) patients were in stage 4 and 29 (83%) patients were in stage 5 with estimated GFR (24.4 ± 3.9 and 5.6 ± 2.9) ml/1.73 m^2/min respectively by MDRD equation. CKD without and with MHD had similar age, sex, blood urea and hemoglobin and significant difference of duration of conservative treatment and dialysis respectively (Table 1).

Table 1. Demography, blood urea, haemoglobin and duration of treatment of study population.

Parameters	CKD without MHD (n = 35)	CKD with MHD (n = 48)	P value
Age (Years)*	45.2 ± 16.3	46.5 ± 15.3	0.70
Sex (Male vs Female)	16 vs 29	19 vs 29	0.18
Blood urea (mg/dl)*	176.8 ± 79.2	179.1 ± 51.3	0.88
Hemoglobin (gm/dl)*	6.8 ± 1.6	7.2 ± 2.1	0.32
Duration of treatment (months)†	8 (1- 168)	24 (2 – 216)	<0.01

(*mean + SD), Independent sample T test, †Median (Range), Mann Whitney U test

The specific skin manifestations observed in study population were pallor 76 (91.5%), xerosis 63 (75.9%), pigmentary changes 54 (65%), pruritus 50 (60.2%), vascular changes 14 (16.8%), gynecomastia four (4.8%) and panniculitis one (1.2%). These changes showed no statistical difference between CKD without and with MHD (Figure 1) and duration of treatment showed no influence in them.

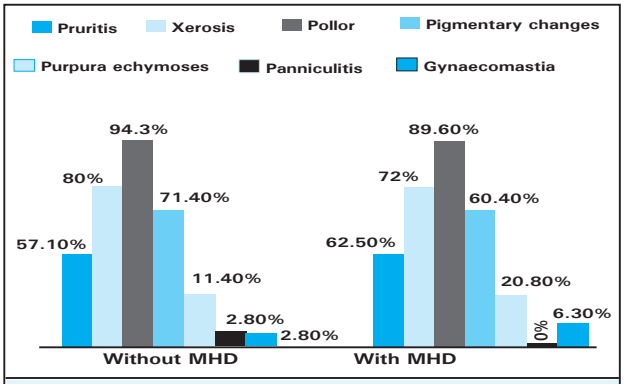

Figure 1. Specific cutaneous manifestation of CKD in study population.

On grouping the study subjects according to hemoglobin level, CKD without and with MHD had hemoglobin <8 gm/dl in 28 (80%) and 32 (66.7%), 8–10 gm/dl in three (8.6%) and 11 (22.9%) and >10 gm/dl in four (11.4%) and five (10.4%) patients respectively.

Pattern of pruritus, xerosis and skin pigmentation are shown in Table 2. Generalized and occasional pruritus affected majority of patients. In MHD patients with pruritus, onset of pruritus was present before dialysis in 28 (93.3%), after initiation of dialysis in two (6.7%) and dialysis improved pruritus in six (20%), worsened in three (10%) and no change in 21 (70%).

Table 2. Patterns of Pruritus, Xerosis and hyperpigmentation of study population.

Pattern of changes		CKD without MHD (n=35)	CKD with MHD (n=48)	Total (n=83)
Distribution of Pruritus n (%)	Generalized	17(48.6)	23(47.9)	40 (48.2)
	Localized	3 (8.5)	7 (14.6)	10 (12.0)
	Total	20 (57.1)	30 (62.5)	50 (60.2)
Duration of Pruritus n (%)	Occasional	15 (42.8)	27(56.2)	42 (50.6)
	Continuous	5 (14.2)	3 (6.2)	8 (9.6)
	Total	20 (57.1)	30 (62.5)	50 (60.2)
Xerosis n (%)	Without pruritus	16 (45.7)	27 (56.2)	43 (51.8)
	With pruritus	12 (34.3)	8 (16.7)	20 (24.1)
	Total	28 (80.0)	35 (72.9)	63 (75.9)
Ichythosis n (%)		2 (5.7)	5 (10.4)	7 (8.0)
Skin Pigmentation n (%)	Diffuse hyperpigmentation	17 (48.6)	23 (47.9)	40 (48.2)
	Sallow yellow Coloration	8 (22.8)	6 (12.5)	14 (16.8)
	Total	**25 (71.4)**	**29 (60.4)**	**54 (65.0)**

Xerosis (dryness of skin) was seen predominantly over the lower back and extremities and associated with pruritus in 20 (24.1%) and developed after the onset of illness. Ichythosis was seen in the lower limbs of seven (8.4%) patients and the scales were dark and thick.

Pigmentary changes were diffuse hyperpigmentation noted in sun-exposed parts of the body (face, dorsa of hands, extensor aspect of forearms and upper back) in 40 (48.2%) and sallow yellow color of the skin in 14 (16.8%). Vascular changes were purpura and petechiae present mainly on trunk and lower extremities. Panniculitis developed in a patient without MHD as subcutaneous firm, tender red nodules over the calf.

CKD without and with MHD also had oral mucosal changes 26 (74.3%) vs 30 (62.5%), P=0.25, hair changes (26 (74.3%) vs. 23 (47.9%), P<0.01) (Table 3) and specific (8 (22.8%) vs 4 (8.3%), P<0.03) and non- specific (32 (91.4%) vs 36 (75%), P<0.05) nail changes respectively (Table 4). Specific nail changes were half and half nails, brown nail bed arcs and Mee's lines. Muehrcke's bands were not observed.

Table 3. Oral mucosal and hair changes of study population.

Site of changes	Pattern of changes	CKD Without MHD (n = 35)	CKD with MHD (n = 48)	Total (n = 83)
Oral Mucosal Changes n (%)	Macroglossia with teeth indentation marks	2 (5.7)	4 (8.3)	6 (7.2)
	Angular stomatitis	-	1 (2.1)	1 (1.2)
	Xerostomia	5 (14.3)	8 (16.7)	13 (15.7)
	Uremic tongue	2 (5.7)	5 (10.4)	7 (8.4)
	Ulcerative stomatitis	6 (17.1)	4 (8.3)	10 (12.0)
	Teeth indentation marks	11 (31.4)	5 (10.4)	16 (19.3)
	Fissured tongue	-	3 (6.3)	3 (3.6)
	Total	26 (74.3)	30 (62.5)	56 (67.5)
Hair Changes n (%)	Dry lusterless hair	11(31.4)	18 (37.5)	29 (34.9)
	Sparse body hair	13 (37.1)	5 (10.4)	18 (21.7)
	Diffuse hair loss	2 (5.7)	-	2 (2.4)
	Total	26 (74.3)	23 (47.9)	49 (59.0)

Table 4. Nail changes of study population.

Type of changes	Pattern of changes	CKD without MHD (n = 35)	CKD with MHD (n = 48)
Specific Nail Changes n (%)	Half and half nails	4 (11.4)	3 (6.3)
	Brown nail bed arcs	3 (8.5)	1 (2.1)
	Mee's lines	1 (2.9)	-
	Total	8 (22.8)	4 (8.3)
Non Specific Nail Changes n (%)	Longitudinal ridging	11 (31.4)	19 (39.6)
	Koilonychia	5 (14.3)	3 (6.3)
	White nails	2 (5.7)	1 (2.1)
	Plathonychia	3 (8.6)	1 (2.1)
	Onychodystrophy	3 (8.6)	6 (12.5)
	Onycholysis	-	2 (4.2)
	Pitting	2 (5.7)	3 (6.3)
	Discolouration of nails	6 (17.1)	1 (2.1)
	Total	32 (91.4)	36 (75)

The study population also had fungal 15 (18.1%), bacterial 17 (20.5%), viral five (6.0%) and parasitic three (3.6%) skin infection (Figure 2). The fungal infections were Tinea versicolor, Tinea corporis, Tinea cruris and Candida intertrigo. Scraping for direct microscopic visualization of the fungus with 10% potassium hydroxide solution was positive in 12 patients. Wood's lamp examination was positive in two cases of Tinea versicolor. The bacterial infections were furunculosis, carbuncle, folliculitis, perianal infection, pitted keratolysis and ecthyma.

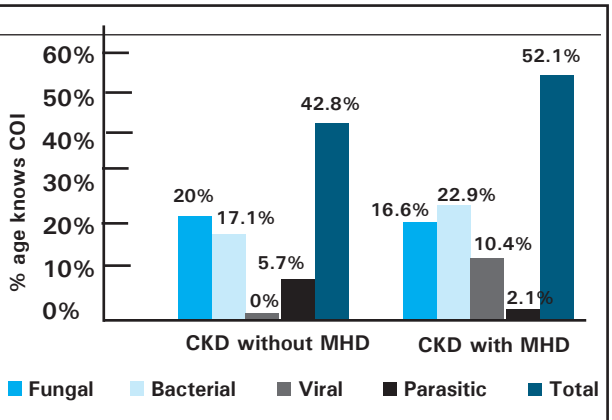

Figure 2. Cutaneous infections of study population.

Other nonspecific skin changes were fissure feet, cherry angoma, idiopathic guttate hypomelanosis, lichen simplex chronicus, acne on face, milia, seborrhoeic keratosis, freckle and Skin tag (Figure 3).

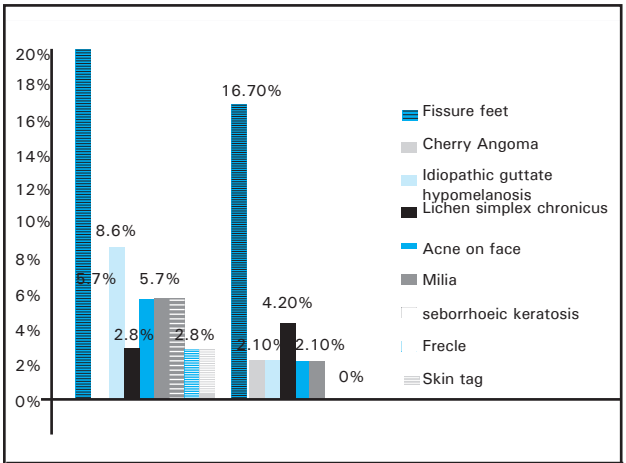

Figure 3. Non - specific cutaneous changes in study population.

DISCUSSION

Dermatological disorders in CKD are present in majority of patients with or without haemodialysis.[1-3] In present study all CKD patients without and with MHD showed one or more dermatological disorder and no association with age, sex and duration of conservative treatment and dialysis respectively contrary to previous report with increased skin manifestation related to longer duration of treatment.[3] Pallor, pruritus, hyperpigmentation and xerosis observed in present study were commonest skin changes with no difference between patients with and without MHD similar to reported before,[3] and the incidence was much higher than previously described in Nepalese CKD patients who showed higher incidence of pruritus in dialysis population.[13]

Pallor due to anemia was present 91.5% patients. Anemia in CKD results from decreased erythropoeisis, reduced red cell life span and blood loss during dialysis and it is treated either by erythropoietin therapy or repeated blood transfusion and degree of anemia governs the quality of life.[14] In present study 94.3% CKD without MHD and 89.6% with MHD were clinically pale with mean hemoglobin 6.8 gm/dl and 7.2 gm/dl respectively indicating poor quality of life of these patients.

Pruritus is a frequent symptom of CKD and could be severe and intractable with decreased quality of life.[4,5] It was found in 46.7% CKD without MHD,[15] and 41.9% to 67% with MHD.[16,17] In present study pruritus was present in 57.1% and 62.5% CKD without and with MHD respectively with majority having generalized and occasional pruritus. The cause of pruritus in CKD is multifactorial and may or may not improve with dialysis.[4,8,16] Pruritus was present before dialysis in 28% and dialysis showed improvement in 9%, aggravation in 19% and no improvement in 72%.[2] But in present study, majority (93.3%) patients on MHD had pruritus before dialysis with improvement in 20%, worsening in 10% and no change in 70%.

Xerosis (dryness of skin) was a leading disorder reported in 72-79% CKD,[2,3] and second common disorder (75.9%) in present study, predominantly over the lower back and extremities. Xerosis started in all after the onset of disease and associated with pruritus in 24.1%. Ichthyosis described in 90% of CKD patients,[15] was present in lower limbs as dark and thick scales in 5.7% and 10.4% CKD without and with MHD respectively.

Diffuse brown hyperpigmentation has been reported in 36.7% CKD without MHD[15] and 43% patients on MHD.[2] Such pigmentation is more marked in the sun exposed parts of the body. The incidence is higher with longer duration of dialysis and attributed to the deposition of melanin in the basal layer and superficial dermis due to failure of kidney to excrete β melanocytic hormone that is poorly dialyzable.[18] In present study, diffuse hyperpigmentation was present in 48.2% in sun-exposed parts of the body. Sallow yellow color of the skin related to retained urochromes and carotenoids in the epidermis and subcutaneous tissue observed in 16.8% patients was between previous reports of 10%,[2] and 40%.[1]

Purpura and ecchymosis are spontaneous cutaneous bleeding affecting 9-20% of CKD[2,19] patients and related to increased vascular fragility and platelet dysfunction due to high urea level that improves partly with dialysis.[20] In present study, purpura and petechial lesions were noted in 14 (16.8%) patients mainly in lower extremities. All of them had blood urea levels above 100mg/dl indicating that when azotemia is pronounced, hemorrhages are more frequent.

Oral mucosal changes in present study were seen in 74.3% and 62.5% CKD without and with MHD. The changes were xerostomia (15.7%) due to dehydration and mouth breathing, macroglossia with teeth indentation marks on tongue (7.2%), ulcerative stomatitis (12%) and uremic tongue (8.4%). These changes were much lesser than described in MHD patients with xerostomia (31-35%), macroglossia (35-42%), ulcerative stomatitis (9-29%), uremic tongue (8-27%).[2,9] As oral mucosal changes are predisposed by bad oral hygiene and superimposed bacterial infection, awareness of oral hygiene in CKD must be emphasized.

Several hair changes like diffuse hair loss, sparse hair loss and dry lusterless hair have been described in hemodialysis patients.[2,10] Dry lusterless hair due to decreased secretion of sebum has been described in 30% CKD not on dialysis,[19] and 16% on MHD.[2] It was observed in 31.4% and 37.5% CKD without and with MHD in present study respectively.

Nail changes are quite frequent in CKD. It was the leading dermatological disorder with significantly lower incidence in CKD with MHD than without MHD (70% vs 93%) showing the probable beneficial effect of hemodialysis in nail changes.[13] Similarly the specific and nonspecific nail changes in present study were significantly lower in CKD with MHD. But higher incidence of nail changes in MHD than stage 5 CKD without MHD (78% vs 62%) has also been reported.[3]

Half and half nail (the red pink or brown in their distal half and white in the proximal half) was observed in CKD with and without MHD in 21% and 13% in the past [2,15] and 6.3% and 11.4% in present study respectively.

CKD patients are susceptible to fungal, bacterial and viral cutaneous infections due to decreased immunity and it is observed in 40% patients with CKD with MHD.[2] In present study also CKD without and with MHD suffered from these infections.

CONCLUSIONS

The dermatological disorder was present in all CKD patients without and with dialysis and pallor, pruritus, xerosis and pigmentation were predominant changes with significant lower incidence of nail and hair changes in MHD patients. So, dermatological evaluation of CKD patients should be the regular practice and further prospective studies on pathophysiology and beneficial effect of dialysis, transplantation and other specific treatment on these disorders is recommended.

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