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Original Research Article

Mucocutaneus Manifestations in Patients of Chronic Kidney Disease

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Abstract: The incidence of chronic kidney disease and end stage renal disease are becoming significant medical problems. Cutaneous involvement can occur not only due to disease but also the predisposing factors and therapeutic dialysis. All diagnosed patients of CKD attending our institute over a one year period were included in the study. To study dermatologic manifestations in patients of chronic kidney disease including patients on renal replacement therapy. Patients with associated liver dysfunction, malignancy or pre-existing skin disorders were excluded from the study. All included patients who gave consent were examined for any dermatological involvement. The study included total of 203 patients. The most common cause of CKD in the study population was hypertension present in 71.4% of the patients followed by diabetes in 36.9%. In 93% of the patients at least one dermatological manifestation was seen with pallor being the most common (61.1%), followed by neurosis in 50.2% and hyperpigmentation in 29.5%. Sallow yellow discolouration was seen in 28.6% and pruritus in 28.1% of the patients. Purpura (14.8 %), perforating dermatosis (2%), bullous disorders 1(0.5%), follicular hyperkeratosis 10(5%), diabetic aeropathy 7(3.4%), pressure sore 3(1.5%), uremic frost 1(0.5%), delayed wound healing 2(1%) were the other dermatological involvement observed.. Pruritus was more common in patients on chronic dialysis (46.42%) than in the unanalysed subjects (24.8%). The most common nail finding was half and half nail seen in 53(26%) of patients. Nail, hair and oral mucosal changes were found in 68.47%, 19.7% and 53.2 % patients respectively. Cutaneous findings are quite common in chronic kidney disease. The understanding of the correlation between the two systems helps in managing the patient effectively.
Keywords: kidney disease, dermatologic manifestations, dermatosis

INTRODUCTION

Chronic kidney disease (CKD) and renal failure have been recognised as significant medical problems for the last two centuries [1]. It is estimated that 0.1 million new patients of end stage renal disease (ESRD) enter renal replacement programs annually in India [2]. The aetiology of ESRD is diverse and includes diabetes mellitus, hypertension, chronic glomerulonephritis, pyelonephritis and polycystic kidney disease [3]. The increase in number of CKD patients can be partially attributed to the epidemic of chronic diseases and the increased life expectancy. India has the largest number of diabetics in the world with a prevalence of 2.8% in rural and 6.0% in urban adults [4]. The prevalence of hypertension has been reported to be 24% in urban adults and 17% among rural adults [4]. It is estimated that 25-40% of these patients are likely to develop CKD [5]. Renal transplantation and dialysis are the treatment modalities. Dialytic therapy cannot replace the endocrine function lost with renal failure leading to development of multiple metabolic abnormalities like metabolic acidosis, anaemia, abnormalities in calcium-phosphate homeostasis, hyperparathyroidism, hyperlipidaemia, and glucose intolerance due to loss of kidney function. These metabolic changes predispose patients with ESRD to bone disease, vascular calcification, and an increase in cardiovascular morbidity and mortality and reflects in various body organs including the skin [6]. Cutaneous changes may occur due to predisposing cause or due to renal failure itself. Life expectancy in patients of renal failure is increasing so are the associated dermatological conditions. Changes in skin colour are universal and striking. Some have reported xerosis as the most common manifestation while others have observed pruritus to be the most frequent. The aim of this study was to observe the dermatological problems associated

with renal failure in medical college of Himachal Pradesh over one year period.

MATERIAL AND METHOD

All diagnosed patients of CKD attending our institute over a one year period were included in the study. The diagnosis of CKD was made by the physician depending upon the clinical, biochemical, radiological and histopathological findings as per the requirement. Patients with associated liver dysfunction, malignancy or pre existing skin disorders were excluded from the study. All included patients who gave consent were examined for any dermatological involvement.

RESULTS

Out of the total study population of 203 patients, 122(60.1%) were males and 81(39.9%) were females. The mean age of the study population was 53.21±16.5 years with a range of 20-89 years. The mean age for males was 53.61 years and for females was 52.59 years. Out of these 60.1 % were males and 39.9 % females. Disease was commonest in age group of >70 years in males and 40-49 years in females as shown in fig.1

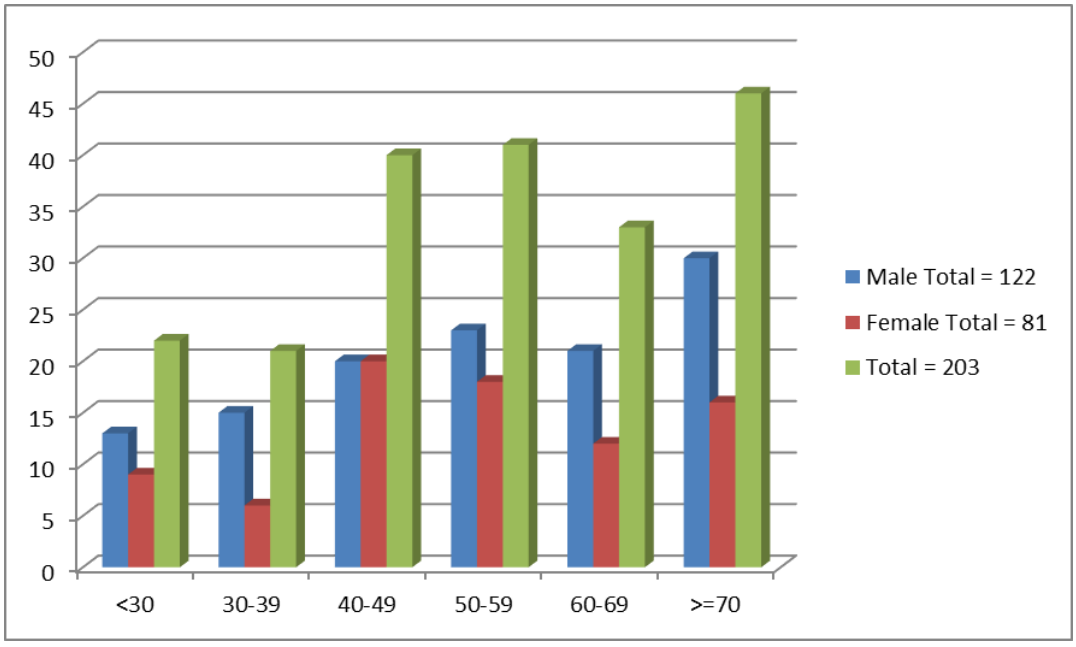

Fig-1: Age and sex distribution of patients

The most common cause of CKD in the study population was hypertension present in 145(71.4%) of the patients followed by diabetes in 75(36.9%). Further distribution is depicted in table 1. Forty two patients had both hypertension and diabetes.

Table-1:Distribution of predisposing causes of chronic kidney disease

Cause of CKD	n (%)*
Diabetes	75 (36.9)
Hypertension	145 (71.4)

CGN(Chronic Glomerulonephritis)	11 (5.4)
CIN(Chronic Interstitialnephritis)	18 (8.9)
PCKD(Polycystic kidney disease)	4 (2)
Obstructive uropathy	10 (4.9)
Misc(miscellaneous)	5 (2.5)

Out of 203 patients, 165(81.3%) were in stage 5 i.e. ESRD, 28(13.8%) were in stage 4, 10(4.9%) were in stage 3. Patients in stage 3 and 4 were categorized together as pre-ESRD and comprised a total of 18.7% of the study population. None of the patients were in stage 1 and stage 2 of CKD.

Among 203 patients in the study population 189(93%) showed some cutaneous manifestation. The most common cutaneous finding was pallor seen in 124(61.1%) patients followed by xerosis seen in 102 (50.2%) patients. Third most common cutaneous manifestation was hyperpigmentation seen in 60(29.5%) patients. Further distribution is depicted in table 2

Table-2: distribuion of cutaneous manifestations in patients of chronic kidney disease

Dermatological findings	**n (%) ***
Pallor	124 (61.1)
Xerosis	102 (50.2)
Hyperpigmentation	60 (29.5)
Sallow Yellow Discoloration	58 (28.6)
Pruritus	57 (28.1)
Purpura	30 (14.8)
Purpura On Venipuncture Site	24 (11.8)
Infection	18 (8.9)
Follicular Hyperkeratosis	10 (4.9)
Diabetic Dermopathy	7 (3.4)
Perforating Dermatosis	4 (2)
Pressure Sore	3 (1.5)
Delayed Wound Healing	2 (1)
Uremic Frost	1 (0.5)
Bullous Dermatosis	1 (0.5)

Among 57(28.1%) patients who had pruritus, it was mild (grade 1) in 70%, moderate (grade 2) in 28% and severe (grade 3) in 1.7%. Intermittent type of pruritus was the commonest seen in 40.3% of the patients. Continuous and nocturnal pruritus was equally distributed in 29.8% each. The commonest location of pruritus was localised seen in 31(54.4%) of the patients followed by patchy in 15(26.3%) and generalized in (19.3%) patients. Extremities were the most common site of involvement. Among patients having pruritus, 18 patients (31.6%) showed evidence of complication of pruritus in the form of excoriations [n=12(66.6%)], lichen simplex chronicus [n=2(11%)) and prurigo nodularis [n=4(22.2%)]. Amongst a total 102(50.2%) patients had xerosis.Details of xerosis are as seen in table 3.

Table-3: Details of clinical pattern of xerosis in patients of chronic kidney disease

XEROSIS GRADING	**n (%)**
Grade 1	88 (86)
Grade 2	14 (14)
Xerosis Distribution	
Localised	52 (50.98)
Generalised	23 (22.5)
Patchy	27 (26.47)
Location Of Xerosis	
Face Only	2 (1.9)
Face And Trunk	2 (1.9)
Generalised	23 (22.5)
Trunk Only	13 (12.7)
Trunk And Extremities	25 (24.5)
Extremities Only	37(36.2)

There were 60 patients who had hyperpigmentation of which localized type was seen in 70 %, patchy in 25 % and gneralized in 5%. Location of hyperpigmentation was as shown in Fig 2.

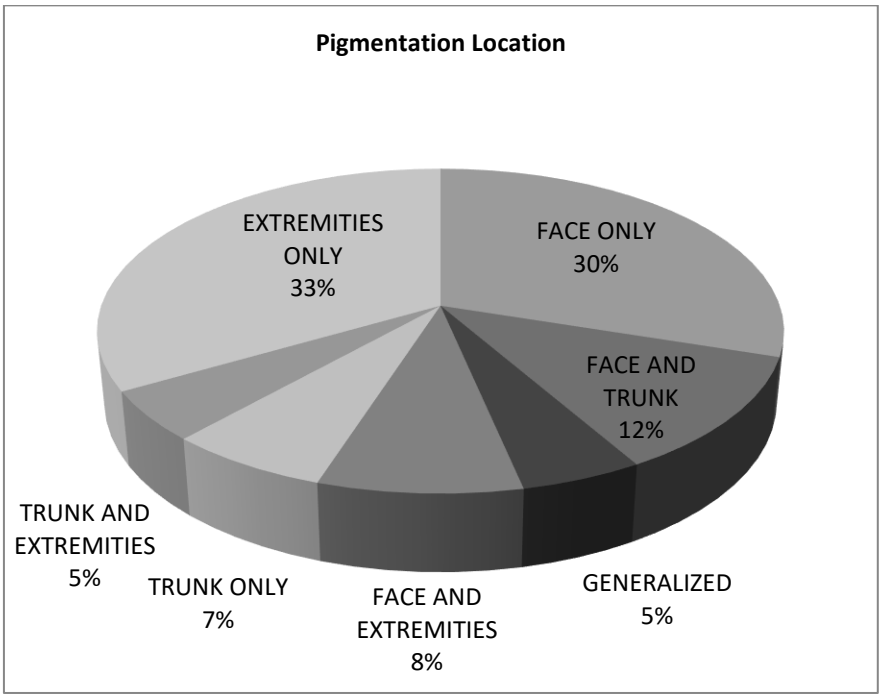

Fig-2 Pigment location in patients of chronic kidney disease

A total of 139(68.47%) of the patients showed some nail abnormality. The most common nail finding was half and half nail seen in 53(26%) of the patients. Next in frequency was subungual hyperkeratosis seen in 36(17.7%) followed by brown nail in 20(9.9%). Various other nail changes found are as depicted in table 4

Table-4: Nail findings in chronic kidney disease

Nail findings	n (%)*
Half And Half Nails	53 (26.1)
Subungual Hyperkeratosis	36 (17.7)
Brown Nails	20 (9.9)
Koilonychia	17 (8.4)
Longitudinal Striations	15 (7.4)
Leukonychia	10 (4.9)
Beau's Line	10 (4.9)
Clubbing	9 (4.4)
Onychogryphosis	9 (4.4)
Splinter Haemorrhages	7 (3.4)
Shiny Nails	6 (3.0)
Melanonychia	6 (3.0)
Onychomycosis	4 (1.9)
Absent Lunula	1 (0.5)
Mee's Lines	1 (0.5)

Among 203 patients, hair changes were found in 40(19.7%) patients. The most common abnormality found was decreased body hair in 29(14.3%), followed by decreased scalp hair and discolouration in 3.4 % each and dry hair in 1.4 % Oral mucosal changes were found in 108(53.2%) of the patients, the most common of which was xerostomia(27%). Next in frequency was coated tongue seen in (24.6%) followed by furred tongue (12.3%). Further details are depicted in Fig.3

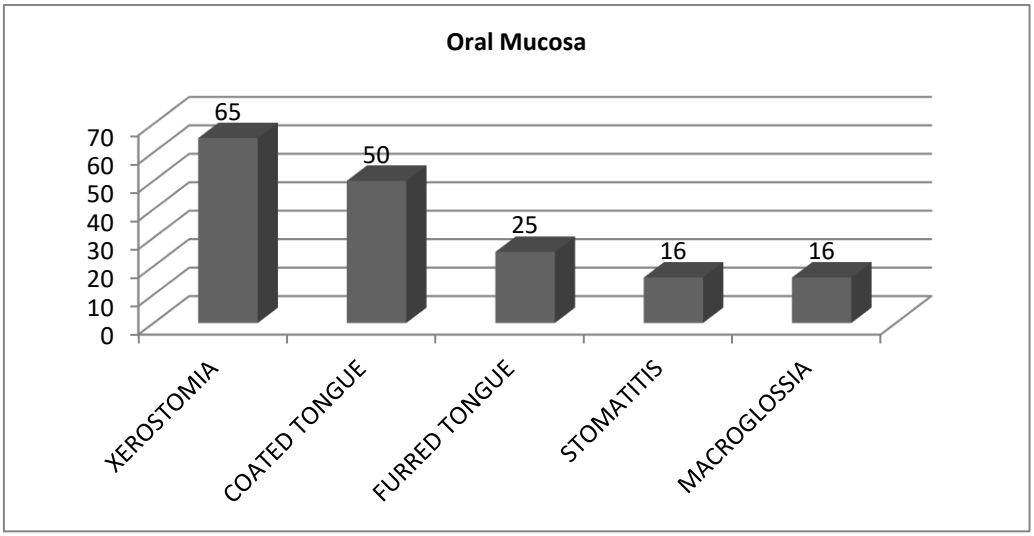

Fig-3: oral involvement seen in patients of chronic kidney disease.

A total of 18(8.8%) of the patients had infection.The commonest infections were bacterial and fungal (38.9%) each followed by viral in 16.7% of the patients The different category of infections seen are depicted in table 5.

Table-5: Infections associated with patients of chronic kidney disease

Infections	n (%)
Fungal	7 (38.9)
Bacterial	7 (38.9)
Viral	3 (16.7)
Scabies	1 (5.5)

DISCUSSION

Chronic kidney disease (CKD) is a pathophysiologic process with multiple etiologies, resulting in attrition of the nephron number and function, and frequently leading to end stage renal disease (ESRD). In turn ESRD represents a clinical state or condition in which there has been an irreversible loss of endogenous renal function of a sufficient degree to render the patient permanently dependent upon renal replacement therapy.

In our country due to delay in seeking medical care, combined with the inadequate availability and unaffordability of facilities for dialysis and renal transplant, most patients remain untreated or under treated. The presence of tropical climate associated high incidence of infection, poor socio-economic status, higher prevalence of malnutrition and relatively darker skin tones of the Indian population significantly alter the presence as well as assessment of the clinical spectrum of dermatologic manifestations as compared to the more developed nations.

Skin is the most visible and easily accessible organ of the body. It reacts sensitively to internal and extraneous stimuli and may function as an important diagnostic window to disease affecting internal organs including the renal system. A thorough dermatological examination can bring forth the subtle manifestations of the disease and guide the clinician to further patient management.

Out of the total study population of 203 patients, 122(60.1%) were males and 81(39.9%) were females. This is similar to study by Khan *et al*. where there were 39.1% females and 61.9 % males [7]. The age of patients ranged from 20 to 89 years with the largest group of patients (22.6%) aged 70 years and above. The mean age of the population was 53.21 years. The mean duration of disease was 17.5 months. In the study by Deepshikha *et al*. the patients ages ranged from 18-85 years (40.2±15.2) with largest group of patients (29%) aged 18-30 years. Mean duration of disease was 17.1 months [8].

The most common cause of CKD in the study population was hypertension present in 145(71.4%) of the patients followed by diabetes in 75(36.9%). Forty two patients (20.6%) had both diabetes and hypertension. This was similar to the study of Maha M Sultan where hypertension was the commonest cause (60%) followed by diabetes (14%) [9]. P Udaykumar *et al.* [10] reported diabetes to be the most common cause(38%) while Deepshikha *et al.* reported chronic glomerulonephritis(45%) to be the commonest cause followed by diabetes(22%) followed by hypertension(12%) [8].

Dermatological manifestations at the time of examination were present in 93% of the patients. This was consistent with the finding of Hajheydari *et al.* (94%) [11]. Deepshikha *et al*. observed cutaneous lesions in 96% of patients in their study [8]. The most common cutaneous finding was pallor affecting 124(61.1%) patients followed by xerosis in 102 (50.2%) and hyperpigmentation in 60(29.5%). We found pallor affecting 61.1% patients consistent with another Indian study by Udaykumar (60%). Pico *et al*. observed pallor in 8% of the patients on hemodialysis [12]. The higher incidence of pallor in our study could be due to malnutrition and iron deficiency anaemia which is more prevalent in the Indian scenario as compared to the west.

We found xerosis affecting 102(50.2%) of the patients in our study. Gilchrest *et al*. observed xerosis in 69% of undialysed uraemics and 70% of patients on hemodialysis [13]. These figures were reported as 62% and 91% by Yosipowitch *et al.* [14]. The lower incidence of xerosis in our area could be because of liberal use of locally available apricot seed oil in our area. A few studies have reported lower prevalence rates of xerosis in the range of 10-20% [11, 16]. High humidity in their area led to decreased incidence of xerosis.

Xerosis was also more prevalent in patients of ESRD who were on chronic dialysis (78.57%) than in the undialysed subjects (48.9%) which was also statistically significant (p- value=.006). No difference

was found in the grading of xerosis between the groups. This is similar to other studies where the incidence of xerosis has been reported to be more in patients of dialysis compared to those on conservative management [16] Water depletion in the dermis, caused by a fluid shift during a single dialysis session, has been proposed as an explanation for uremic xerosis. Skin perfusion has also been demonstrated to be impaired which may contribute to skin dehydration [16].

Diabetics had a slightly higher percentage (56%) of xerosis than non-diabetics (46.87%) but the difference was not statistically significant. This is similar to the finding of Udaykumar [10]. Xerosis is a known complication of diabetes. This is due to reduced hydration state of the stratum corneum and decreased sebaceous gland activity in patients with diabetes, without any impairment of the stratum corneum barrier function [17]. Even in the absence of clinically apparent xerosis, patients with diabetes have an impaired desquamation process [18].

The incidence of pruritus in various studies has been reported as 25-53% [7, 10, 11]. This is similar to our finding of pruritus which was present in (28.1%) patients. Pruritus was mild (grade 1) in 70%, moderate (grade 2) in 28% and severe (grade 3) in 1.7%. Intermittent type and localized involvement was commonest. Extremities were the most common site of involvement. Pruritus was more common in patients on chronic dialysis (46.42%) than in the unanalysed subjects (24.8%) and it was statistically significant (p-value = 0.0365). Other studies have also found higher prevalence of pruritus in patients receiving dialysis than those on conservative treatment, confirming that dialysis may actually precipitate pruritus in this group of patients [16]. This increased incidence in dialysis patients may be explained on the basis of increased serum histamine levels due to allergic sensitisation to various dialyser membrane components and impaired renal excretion of histamine [10].

Sallow yellow discoloration was found in 28.6% patients. Studies that have shown lesser prevalence of sallow yellow discoloration have been done in populations with relatively darker skin colour [8, 10]. As compared to the population in our study group and those showing higher prevalence have been done in populations with a fairer skin colour. The characteristic colour is due to deposition of retained lip soluble pigments such as lip chromes and carotenoids in the epidermis and subcutaneous tissue.

The incidence of hyperpigmentation has been variably reported between 7.5- 54% [9,12,16] This is similar to our finding of hyperpigmentation seen in 29.5% of the patients Skin pigmentation is a common problem for dialysis patients, but little is known about the factor responsible for the colour intensity. Middle-molecular-weight (MMW) substances have been suggested to be responsible for the skin colour. Several papers have reported that β2-microglobulin (β2-MG) correlates with the skin colour [19]. Deepshikha *et al.* found that the mean duration of disease was higher for patients with pigmentation which was statistically significant [8].

Purpura has been reported in 9%-30% patients in various studies [7-10]. We found purpura in 14.8% of the patients while it was found in 11.8% of the patients at venepuncture sites. Presence of both coagulation abnormality and platelet dysfunction predispose the patients to development of petechial and abnormal bruising. We found perforating disorder in 4(2%) of the patients. The reported prevalence varies between 4.5 – 17% [10, 12, 20]. These changes were significantly more prevalent in diabetic patients and patients on chronic dialysis.

Infections have been reported in 29-70% of CKD patients [8-10]. The high prevalence of skin infection is an expected finding as opportunistic infections are a common occurrence in these patients due to lymphopenia, decreased B cell activity, and alteration of the T cell subsets and activities.39 A few studies have reported a lower prevalence of infections [7-11]. In our study a total of 18(8.8%) of the patients had infection. The commonest infections were bacterial and fungal (38.9%) each followed by viral in (16.7%) of the patients. The lower incidence of infections in our study could be due to cold weather conditions prevailing in the region as infections are more common in hot and humid weather.

We found nail changes in 139(68.47%) of the patients a figure similar to that reported from various other studies of 66% to 79% [12,21,22]. The prevalence of nail changes in patients on dialysis has been variable in different studies (52-70%). In undialysed ESRD patients the reported prevalence is 60% [22]. The most common nail finding was half and half nail seen in 53(26%) of the patients, similar to P Udaykumar *et al.* (21%) and Deepshikha *et al.* (28.5%) [8,10]. Previous studies have found a prevalence of 16-50.6% [12]. Next in frequency was subungual hyperkeratosis seen in 36(17.7%) patients. This was similar to the finding of

Khan *et al.* (16.9%) [7]. P Udaykumar reported subungual hyperkeratosis in (12%) and Hajheydari *et al.* in (4%) [10,11]. Third most common nail abnormality was brown nail in 20(9.9%) similar to the finding of Maha M. Sultan *et al.* 37(6%) [9]. The most common finding was apparent leukonychia (17%) in the study by Hajheydari *et al.* and Khan *et al.* (28.3%) [7,11]. Sultan *et al.* 37found that koilonychia was the most common nail abnormality seen in 39% of the patients [9].

Among 203 patients, hair changes were found in 40(19.7%) patients. The reported prevalence of hair changes in CKD has been in the range 15-57% [7,10]. Hair changes reported by P Udaykumar *et al*. included sparse body hair (30%), sparse scalp hair (11%) and brittle and lusterless hair (16%) [10]. Khan *et al.* reported that hair loss was the most common seen in (45.7%) patients and drying and hair fragility (31.4%) and hair discolouration (22.8%) [7]. It has been shown that long-term chronic diseases result in hair loss. Xerosis and pruritus are the reasons of hair loss.

Oral mucosal changes were found in 108(53.2%) of the patients, the most common was xerostomia (32%). Next in frequency was coated tongue seen in (24.6%) followed by furred tongue in (12.3%). Oral mucosal changes have been reported in up to 90% of patients with CRF [23]. Hajheydari *et al.* reported mucosal involvement in 24% of the patients [11]. Furred/scrotal tongue and deficiency glossitis was seen in 14% and 3% of the patients respectively. Frequency of herpes simplex and gingivitis were 3% and 2% respectively [11]. Various oral changes were xerostomia (35%), coated tongue (27%), angular cheilitis (15%) and ulcerative stomatitis (9%) in the study by Maha M Sultan *et al.* [9].

Various other changes found in our study were diabetic dermopathy 7 (3.4%), follicular hyperkeratosis 10(5%), bullous disorder 1(0.5%), uremic frost 1(0.5%), pressure sores 3(1.5%) and delayed wound healing 2(1%). The patient with uremic frost had a pre-dialysis blood urea level of more than 200 mg / 100 ml. No case of nephrogenic systemic fibrosis, benign nodular calcification or calciphylaxis was found in the study.

CONCLUSION

Chronic kidney disease (CKD) and renal failure have been recognised as significant medical problems. Skin is the most visible and easily accessible organ of the body. It may function as an important diagnostic window to disease affecting internal organs. Although many of the manifestations are nonspecific, these are present in higher percentage of chronic kidney disease patient as compared to the general population. Awereness about these manifestations and their association with chronic kidney disease may be helpful in early recognition and treatment of these cutaneous problems. Furthermore as these skin changes are sometimes present long before chronic kidney disease is diagnosed, their recognition may help on earlier diagnosis of chronic kidney disease and early institution of treatment, resulting in prolonged survival and reduced morbidity of chronic kidney disease patients.

REFERENCES

1. National Institutes of Health. US Renal Data System, USRDS 2010 Annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. National Institute of Diabetes and Digestive and Kidney Diseases. 2010.
2. Kher V. End stage renal disease in developing countries. Kidney Int 2002; 62: 350-62.
3. Goldsmith DJA, Black MM. Skin disorders in the setting of renal failure: Invited Editorial. J Eur Acad Dermatol Venereol 2001;15:392-8
4. Singh RB, Bajaj S, Niaz MA, Rastogi SS, Moshiri M. Prevalence of type 2 diabetes mellitus and risk of hypertension and coronary artery disease in rural and urban population with low rates of obesity. Int J Cardiol 1998; 66(1):65-72.
5. Reddy KS, Shah B, Varghese C, Ramadoss A. Chronic diseases. Lancet 2005; 366: 1746-51.
6. Knable AL. Cutaneous Nephrology. Dermatol Clin 2002;20:513-21
7. Khan R , Quaiser S , Haque SF , Sachdeva S. Cutaneous Manifestations in Patients of Chronic Kidney Disease. Int J Cur Bio Med Sci. 2011; 1(3): 113-5.
8. Khanna D, Singal A, Kalra OP. Comparison of cutaneous manifestations in chronic kidney disease with or without dialysis. Postgrad Med J 2010;86: 641-7.
9. Sultan MM, Mansour HH, Wahby IM, Houdery AS. Cutaneous Manifestations in Egyptian Patients with Chronic Renal Failure on Regular Hemodialysis. J Egypt Women Dermatol Soc 2010; 7: 49 – 55.
10. Udayakumar P, Balasubramanian S, Ramalingam KS, Lakshmi C, Srinivas CR, Mathew AC. Cutaneous manifestations in patients with chronic renal failure on hemodialysis. Ind J Dermatol Venereol Leprol 2006; 72: 119-25.

11. Hajheydari Z, Makhlough A. Cutaneous and Mucosal Manifestations in Patients on Maintenance Hemodialysis: A Study of 101 Patients in Sari, Iran. Iran J Kidney Dis 2008;2:86-90.
12. Pico MR, Lugo-Somolinos A, Sanchez JL, Burgos-Calderon R. Cutaneous alterations in patients with chronic renal failure. Int J Dermatol 1992;31:860
13. Gilchrest BA, Rowe JW, Mihm MC Jr. Clinical and histological skin changes in chronic renal failure: evidence for a dialysis-resistant, transplant-responsive microangiopathy. Lancet 1980; 13: 1271-5.
14. Yosipovitch G, Reis J, Tur E, Sprecher E, Yarnitsky D, Boner G. Sweat secretion, stratum corneum hydration, small nerve function and pruritus in patients with advanced chronic renal failure. Br J Dermatol 1995; 133: 561-4.
15. Mazuryk HA, Brodkin RH. Cutaneous clues to renal disease. Cutis 1991; 47: 241-8
16. Nigeria Falodun O, Ogunbiyi A, Salako B, George AK. Skin changes in patients with chronic renal failure. Saudi J Kidney Dis Transpl 2011;22:268-72
17. Sakai S, Kikuchi K, Satoh J, Tagami H, Inoue S. Functional properties of the stratum corneum in patients with diabetes mellitus: similarities to senile xerosis. Br J Dermatol 2005;153:319–23
18. Yoon HS, Baik SH, Oh CH: Quantitative measurement of desquamation and skin elasticity in diabetic patients. Skin Res Technol 2002 8:250–4
19. Shibata M, Nagai K, Usami K, Tawada H, Taniguchi S. The quantitative evaluation of online haemodiafiltration effect on skin hyperpigmentation. Nephro. Dia. Transplant 2011; 26 : 988-92
20. Tawade Y V, Gokhale B B. Dermatologic manifestations of chronic renal failure. Ind J Dermatol Venereol Leprol 1996; 62:155-6.
21. Naderi N, Mahdavi-Mazdeh M, Firouz A, Heydari Seraj M. Cutaneous manifestations of end stage renal disease under hemodialysis in hemodialysis ward at Imam Khomeini hospital in Tehran in 2003. Iran J Dermatol.2005; 6:489-95.
22. Saray Y, Seckin D, Gulec AT, Akgun S, Haberal M. Nail disorders in haemodialysis patients and renal transplant recipients: a case-control study. J Am Acad Dermatol 2004; 50: 197-202.
23. Cohen GS. Renal disease. In: Lynch MA, editor. Burket's Oral medicine: Diagnosis and treatment. 9th ed. Philadelphia: Lippincott-Raven; 1997. p. 487-509.