CUTANEOUS MANIFESTATIONS IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON HEMODIALYSIS AND IT'S CORRELATION WITH RENAL FUNCTION, DIALYSIS CYCLE AND HAEMOGLOBIN

Pradhan M[1], Chhetri G[2], Rai D[3], Paudel S[4]*

Affiliation

1. *Lecturer, Department of Dermatology, Nobel Medical College, Biratnagar Nepal*
2. *Lecturer, Department of Medicine, Nobel Medical College, Biratnagar Nepal*
3. *Resident, Department of Dermatology, Nobel Medical College, Biratnagar Nepal*
4. *Intern, Nobel Medical College, Biratnagar Nepal*

ARTICLE INFO

Article History

Received : 18 June, 2018

Accepted : 12 August, 2018

Published : 31 August, 2018

ORA 77

DOI : http://dx.doi.org/10.3126/bjhs.v3i2.20963

**** Corresponding Author***

Dr. Manish Pradhan
Lecturer
Department of Dermatology and Venerology
Nobel Medical College Teaching Hospital, Biratnagar
Email: drmanishpradhan1@gmail.com
ORCID: https://orcid.org/0000-0001-6817-4160

Citation

Pradhan M, Chhetri G, Rai D, Paudel S. Cutaneous Manifestations In Patients With Chronic Kidney Disease On Hemodialysis And It's Correlation With Renal Function, Dialysis Cycle And Haemoglobin. BJHS 2018;3(2)6:468-474.

ABSTRACT

Introduction

Skin is the mirror of an internal disease, including the renal system. Chronic kidney disease presents with variety of skin diseases, which is caused either by kidney disease or by treatment modalities.

Objective

To evaluate the prevalence of various skin disease in patients with chronic renal disease and relation of various skin diseases with serum creatinine, blood urea, hemoglobin and number of hemodialysis cycle.

Methodology

A cross-sectional analytical study was conducted in hundred patients of either sex, aged 18 years and above; with chronic kidney disease (stage V) admitted for dialysis in Nephrology department of Nobel Medical College and teaching hospital, Biratnagar, Nepal. The study groups were evaluated for various skin manifestation and parameters of renal function like blood urea and serum creatinine.

Results

Among the total patients (n=100), 84 patients presented with complain of skin manifestation but on detail examination 97 patients had at least one skin disease. The causes leading to chronic kidney disease were found to be hypertension 58%, diabetes mellitus 49%, IgA nephropathy 7%, systemic lupus erythematosus 7% and glomerulonephritis 4%. Xerosis was the commonest skin disease encountered in these patients amounting to 71% among which 43 were hypertensive and 34 were diabetic. Xerosis was followed by pruritus (62%), pallor (54%), mucosal changes (39%), skin infection (36%), hair changes (34%), pigmentation (33%) and nail changes (29%). Serum creatinine showed statistically significant association with pruritus (p=0.030) and pigmentation (p=0.010), similarly blood urea showed significant association with pruritus (p=0.001). Similarly, number of dialysis cycle showed significant association with pigmentation of skin (p=<0.001).

Conclusion

Chronic kidney disease is associated with variety of skin diseases. The commonest were xerosis and pruritus. Early detection and appropriate intervention can relieve and decrease suffering.

KEY WORDS

hemodialysis, kidney disease, skin disease

INTRODUCTION

Chronic kidney disease (CKD) is a progressive loss of kidney function over a period of months or years through five stages. It is defined as kidney damage or glomerular filtration rate <60 ml/min/1.73m^2 for months or more irrespective of the cause.[1]

Skin is the mirror of an internal disease, and it has always helped the clinician to diagnose systemic diseases. As we know, CKD presents with an array of skin diseases; from benign and asymptomatic to the physically disabling and life threatening.[2]Many of them, have a debilitating effect on quality of life. These skin disease can occur before dialysis or following the initiation of hemodialysis treatment.[3]It has been found that 82% patients with end stage renal disease have at least one associated cutaneous change.[4]

As the incidence and prevalence of chronic kidney disease is increasing day by day in this modern world; the incidence and prevalence of associated skin diseases are also increasing. So, their early recognition and treatment is quite essential to reduce morbidity and mortality.[3] The prevalence of cutaneous manifestation is high among dialysis patients. This occurs because of numerous factors such as uremia, metabolic disorders, dialysis and side effects of immunosuppressive drugs.[5]

Some of these skin diseases disappear following kidney transplantation, confirming that the metabolic milieu resulting from the malfunctioning kidney is responsible for some of these changes.[6]

Patients on hemodialysis (HD) are known to develop skin diseases ranging from infections to malignancies. In addition, new cutaneous lesions may develop with increasing age. Sometimes, cutaneous changes maybe the first important sign in patients with chronic renal failure.[5] Moreover, skin diseases are generally seen in patients with moderate renal impairment (CKD stage 3 and 4) before progressing to End Stage Renal Disease; so persistent xerosis or intractable pruritus commends for further search for underlying renal impairment.[7]

Though important for maintenance of homeostasis in patients with End stage renal disease (ESRD), neither dialysis is efficient in removing substances compared to healthy kidneys nor can it replace other endocrine functions lost with renal failure leading to various metabolic disorders and associated skin complications.[7] With advancement of technology and improved dialysis therapy in the west, cutaneous complications in patients with renal disease are in decreasing trend; unlike the case in developing countries like Nepal. Moreover, the ignorant Nepalese population is subjected to harmful effects of tropical climate, with the associated higher incidence of infections and malnutrition; all contributing to the skin diseases in CKD patients.

Because skin diseases may have a cosmetically destructive effect, in addition to complications such as pruritus that disturbs the patient's comfort, this study was done to determine the prevalence of mucocutaneous manifestations in patients on hemodialysis along with relation of various skin disorders with the parameters of renal function like serum creatinine, blood urea, hemoglobin and number of dialysis cycles.

METHODOLOGY

In this cross sectional, analytic study; 100 patients of either sex, aged 18 years and above; admitted with the diagnosis of CKD for dialysis in Nephrology department of Nobel Medical College and teaching hospital, Biratnagar, Nepal, recruited during the period of January 2017 to December 2017, were chosen randomly as candidates for the study after taking ethical clearance from the institutional review board. Written consent was obtained from all candidates. All the patients were examined in detail by dermatologist in a location with adequate light. Diagnosis of the disease was made clinically. Demographic details like age, sex, cause of renal failure, duration on dialysis was taken from patient's files. Information about patients' laboratory tests was obtained from mean of three recent tests.

Inclusion criteria

Patients with chronic kidney disease (stage V) of age above 18 years undergoing hemodialysis.

Exclusion criteria for cases

Patients with acute renal failure, patients who had undergone renal transplantation and who had undergone peritoneal dialysis

The normal value for serum creatinine, blood urea and hemoglobin was taken to be 0.6-1.2 mg/dl, 7-20 mg/dl and 12-16 gm/dl respectively.

Statistical Analysis

Data were analyzed using SPSS software (Version 22). The Independent t-Test was used to evaluate the association of skin disease with serum creatinine, blood urea, hemoglobin and number of dialysis cycle and chi-square test was used with for qualitative data. P value was calculated and less than 0.05 was considered to be statistically significant.

RESULT

Out of total 100 patients enrolled in the study, 59% (n=59) were male and 41% (n=41) were female. The mean age (years) of the patients was 55.81±17.94, youngest being 18 and oldest being 88. The duration of chronic kidney disease varied from 1 month and several years and the mean of dialysis cycles done was 11.43 ± 16.11; with the minimum cycle being 2 and maximum cycle being 106. The causes leading to chronic kidney disease were found to be hypertension in 58%; among them 38% were male and 20% were female; diabetes mellitus 49%; among them, male were 30% and female were 19%; IgA nephropathy 7%, systemic lupus erythematosus 7%; among them females were 6 and male, and glomerulonephritis in 4%, as shown in Table 1. Among the patients having chronic kidney disease, 27 were suffering from both hypertension and diabetic mellitus.

Among the total patients (n=100), 84 patients presented with complain of skin manifestation but on detail examination 97 patients had at least one skin disease. Xerosis was the most common skin disease seen in these patients, and this was seen in 71% of the patients among which 43 were hypertensive and 34 were diabetic. Xerosis was followed by pruritus seen in 62%, pallor seen in 54%, mucosal changes seen in 39%, skin infection seen in 36% (fungal=21%, bacterial 9% and viral=6%), pigmentation seen in 33% (29 % hyperpigmentation and 6 % yellow tinge), nail changes seen in 29% and hair changes in 34%as shown in Table 1.

Other skin disease observed in our study were alopecia areata in 2 patients, followed by ecchymoses in 1, acneform eruptions in 1, seborrhoeic keratosis in 1, eczema in 1 and lichen planus in 1.

The mean serum creatinine was 11.44 ± 5.81mg/dl with minimum of 1.4mg/dl and maximum 28mg/dl. Similarly blood urea was 159.18 ± 51.17mg/dl with minimum of 22mg/dl and maximum of 288mg/dl in our study group. The independent-samples T test was carried out between different dermatological manifestation and serum creatinine, blood urea, hemoglobin and number of dialysis. There was statistically significant association of serum creatinine with pruritus (p=0.030) and pigmentation (p=0.010). Similarly, blood urea shows significant association with pruritus (p=0.001). However all other skin, mucosal and nail changes did not show any association with serum creatinine and blood urea as shown in Table 2.

In the same way, mean hemoglobin in our study was 6.65 ± 2.03g/dl with minimum of 2g/dl and maximum 10g/dl. On further evaluation, hemoglobin was found to be statistically significant with pallor (p=<0.001) and clubbing (p=<0.001)) in patient having chronic kidney disease undergoing hemodialysis. In our study, 14% had hemoglobin level less than 5 g/dl; 52% had hemoglobin levels between 5-8 g/dl and 34 % had hemoglobin level more than 8 g/dl. Similarly, number of dialysis cycle shows significant association with pigmentation of skin (p=<0.001) and angular cheilitis (p=<0.001). However, in our study there was no significant association of hemoglobin and number of dialysis cycle with other skin manifestation in patient of chronic kidney disease as shown in Table 3.

Chi square test illustrated the association between pruritus and patient with chronic kidney disease with diabetic mellitus (p=0.044). However, there is no association of pruritus with chronic kidney disease with hypertension (p=0.145). Similarly xerosis shows no significant association with chronic kidney disease with diabetic mellitus and hypertension (p=0.449 and p=0.277 respectively).

TABLE 1: The causes of chronic kidney disease (stage V) and prevalence of dermatological manifestation in patients undergoing dialysis.

Dermatological manifestation	Total 100 (100%)	Hypertension 58 (58%)	Diabetic Mellitus 49 (49%)	SLE 7 (7%)	Glomerulo-nephritis 4(4%)	IgA nephropathy 7(7%)
Skin changes						
Xerosis	71 (71%)	43	34	4	3	6
Pruritus	62 (62%)	39	35	5	2	4
Pallor	54 (54%)	34	25	3	1	3
Acquired perforating dermatoses	2 (2%)	-	2	-	-	-
Pigmentation	33 (33%)	24	19	-	-	1
Skin infection						
Fungal	21 (21%)	11	10	2	1	1
Bacterial	9 (9%)	5	4	1	-	2
Viral	6 (6%)	3	4	-	-	
Nail changes						
Half and half nails	8 (8%)	5	5	-	-	-
Leuconychia	7 (7%)	2	3	1	-	1
Longitudinal ridges	7 (7%)	4	4	-	1	-
Onychomycosis	13 (13%)	8	8	-	-	1
Clubbing	3 (3%)	3	1	-	-	
Mucosal changes						
Xerostomia	32 (32%)	22	16	-	1	2
Macroglossia	22 (22%)	13	10	1	2	-
Fissured tongue	11 (11%)	7	4	-	1	-
Ulcerative stomatitis	7 (7%)	5	3	-	2	-
Angular cheilitis	4 (4%)	3	1	-	-	-
Hair changes						
Sparse scalp hair	23 (23%)	16	14	-	-	-
Brittle lusterless hair	11 (11%)	6	6	-	-	-
Others	7 (7%)	3	4	-	-	-
None	3 (3%)	1	1	1	1	-

TABLE 2: Relation of various dermatological manifestation in chronic kidney disease with serum creatinine and blood urea using independent-samples t-Test.

Dermatological manifestation	Serum creatinine (mg/dl)		Blood urea (mg/dl)	
	Mean ± S.D.	P value	Mean ± S.D.	P value
Skin changes				
Xerosis	11.46 ± 5.75	0.943	159.06 ± 49.80	0.971
Pruritus	12.78 ± 5.97	0.030*	172.69 ± 41.94	0.001*
Pallor	11.33 ± 5.55	0.848	162.34 ± 54.56	0.505
Skin infection	10.38 ± 5.35	0.176	147.86 ± 47.94	0.097
Acquired perforating dermatoses	9.15 ± 1.34	0.577	124.00 ± 59.40	0.329
Pigmentation	13.56 ± 6.31	0.010*	170.36 ± 50.98	0.126
Nail changes				
Half and half nails	8.54 ± 3.69	0.142	126.95 ± 41.17	0.06
Leuconychia	12.74 ± 7.62	0.539	176.57 ± 49.55	0.354
Longitudinal ridges	13.23 ± 4.31	0.400	169.43 ± 33.75	0.585
Onychomycosis	11.24 ± 5.35	0.897	155.54 ± 54.90	0.785
Clubbing	6.50 ± 2.26	0.136	110.53 ± 69.21	0.095
Mucosal changes				
Xerostomia	11.95 ± 6.55	0.543	158.74 ± 56.81	0.953
Macroglossia	10.39 ± 5.91	0.340	152.86 ± 56.76	0.515
Fissured tongue	12.11 ± 6.85	0.685	168.15 ± 71.83	0.540
Ulcerative stomatitis	13.23 ± 7.62	0.400	162.86 ± 67.94	0.845
Angular cheilitis	11.35 ± 5.27	0.976	153.00 ± 86.11	0.807
Hair changes				
Sparse scalp hair	12.27 ± 6.85	0.435	172.00 ± 42.78	0.172
Brittle lusterless hair	13.16 ± 5.72	0.298	147.46 ± 62.79	0.423
Total	11.44 ± 5.81		159.18 ± 51.17	

*Statistically significant at p<0.05.

TABLE 3: Relation of various dermatological manifestations in chronic kidney disease with hemoglobin and number of hemodialysis using independent-samples t-Test.

Dermatological manifestation	Hemoglobin (g/dl)		No. of hemodialysis cycle	
	Mean ± S.D.	P value	Mean ± S.D.	P value
Skin changes				
Xerosis	6.59 ± 1.94	0.654	11.13 ± 15.95	0.770
Pruritus	6.84 ± 2.06	0.236	10.85 ± 13.09	0.651
Pallor	5.11 ± 1.21	<0.001*	9.78 ± 11.69	0.291
Infection	6.47 ± 1.70	0.513	12.75 ± 15.25	0.541
Acquired perforating dermatoses	9.00 ± 0.00	0.098	4.00 ± 1.41	0.513
Pigmentation	6.85 ± 2.02	0.495	24.30 ± 23.12	<0.001*
Nail changes				
Half and half nails	5.63 ± 1.69	0.137	6.63 ± 4.44	0.382
Leuconychia	6.71 ± 2.98	0.931	4.71 ± 2.63	0.255
Longitudinal ridges	6.14 ± 2.19	0.495	7.86 ± 6.64	0.545
Onychomycosis	5.92 ± 1.75	0.167	12.08 ± 14.35	0.878
Clubbing	2.67 ± 0.58	<0.001*	5.00 ± 1.73	0.485
Mucosal changes				
Xerostomia	6.75 ± 1.92	0.737	16.06 ± 23.65	0.048
Macroglossia	6.32 ± 1.84	0.387	13.95 ± 24.44	0.408
Fissured tongue	6.36 ± 2.66	0.622	11.82 ± 13.25	0.933
Ulcerative stomatitis	7.29 ± 2.36	0.392	12.14 ± 19.46	0.904
Angular cheilitis	8.00 ± 2.00	0.175	39.50 ± 48.18	<0.001*
Hair changes				
Sparse scalp hair	6.09 ± 1.90	0.130	10.26 ± 12.61	0.694
Brittle lusterless hair	6.18 ± 1.89	0.420	10.73 ± 6.80	0.879
Total	6.65 ± 2.03		11.43 ± 16.11	

*Statistically significant at p<0.05.

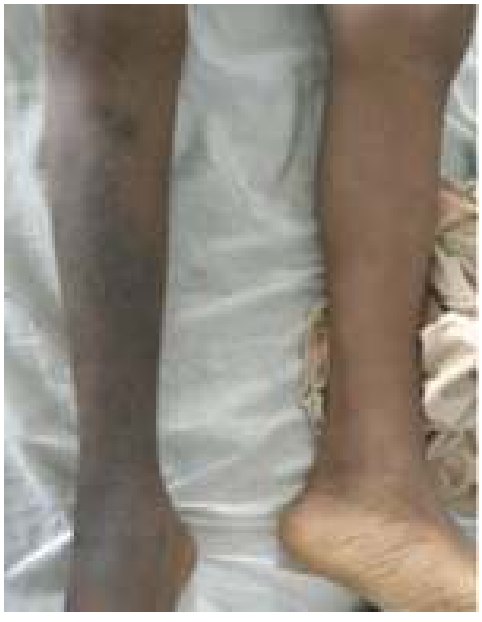

Figure 1: Pigmentary changes in patient with CKD on hemodialysis

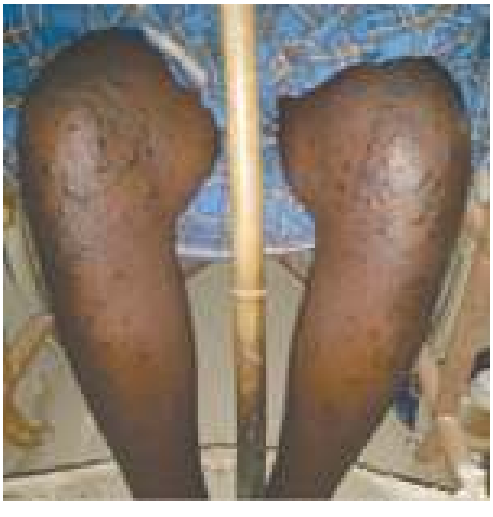

Figure 2: Acquired Perforating Dermatosis in patient with CKD on hemodialysis

Figure 3: Sparse hair in patient with CKD hemodialysis

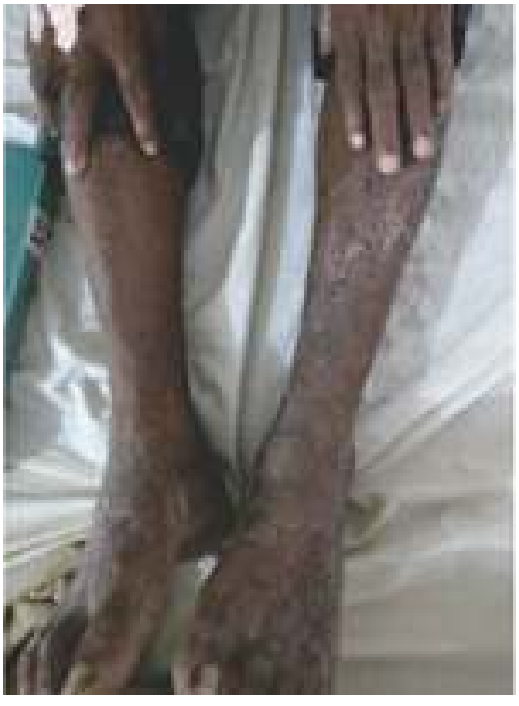

Figure 4: Eczema in patient with CKD on hemodialysis

DISCUSSSION

Patients with chronic kidney disease who were on hemodialysis presented with a wide spectrum of skin diseases, which is quite a fact as 97% of the patients in our study, showed at least one skin disease.

Xerosis was the most common finding in our study, which was seen in 71% of the patients in our study. Like our result Udaykumar et al. reported it in 79 % of the patients and Baghel et al. reported it to be seen in 66.2 %.[4,5] In contrast to our result, Gurucharan et al. reported high result with 90 % of the patients and Hajheydari et al. reported it to be seen in only 22.8 %. [8,9] In Nepal, Shrestha P et al. reported it to be seen in 54 % of the patients on hemodialyisis.[2]Amatya B et al. did study on CKD patients including patients on dialysis and medical treatment and found xerosis in 28 % of patietns.[10]The difference in result may be due to patient skin type, primary disease leading to CKD, drugs used in treatment and difference in climatic condition of patience residence. Xerosis may be due to reduced size and function of eccrine sweat gland or may due to use of high dose of diuretics.[4]

Pruritus was present in 62 % of our patients. The severity of pruritus varied and some patient gave history of improvement of pruritus after dialysis. There was significant relation of pruritus with blood urea and serum creatinine level. Dyanchenko P et al. reported pruritus in 74.3% of hemodialysis patients at some point.[11]Udaykumar et al. reported it in 53 % of the patients, Baghel et al. reported it to be seen in 51.25 %, Hajheydari et al. found in 38.6% patients and Pico et al. reported pruritus in 42%. [4,5,9,12] In Nepal, Shrestha P et al. reported pruritus in 40 % of the patients and Amatya B et al. in 15 % of the patients. [2,10] The exact

cause of increased itching in CKD patient in unknown. Hemodialysis can initiate the symptom as well as improve it. It may be due to increased serum histamine levels because of allergic sensitization to diverse dialyzer membrane components as well as impairing renal excretion of histamine. There is an abnormal pattern of cutaneous innervations in CKD, which occurs due to slowly accumulated pruritogen, the nature of which is uncertain.[4,5] It may be secondary to anemia, xerosis, hypervitaminosis A, secondary hyperparathyroidism or increase levels of magnesium, calcium and phosphates and serum histamine.[4]

Another manifestation commonly seen in our patient was pallor, which was seen in 54 % of patient. It was significantly associated with hemoglobin level. It is an early and common sign in renal failure resulting from reduced erythropoiesis and increased haemolysis.[5]Udaykumar et al. reported pallor in 60% patients, Baghel et al. reported in 57.5% patients and Dyanchenko et al. in 75.7% patients on haemodialysis.[4,5,11]

Pigmentary changes were seen in 33 % of patients and there was significant relationship between pigmentary changes with serum creatinine level and number of dialysis cycles. Hyperpigmentation was seen in 29 % of the patient and yellow tinge on the skin was seen in 5 % of the patients. Result of pigmentary changes in CKD are variable. Udaykumar et al. reported pigmentary changes in 43% of patients and Baghel et al. reported in 13.75 % of patients whereas Hajheydari et al. reported in 66.3% patients, Dyanchenko et al. in 75.7% patients, and Pico et al reported diffuse pigmentation in 70% patients.[9,11,12] In Nepal Shrestha P et al. and Amatya B et al. reported it in 35 % and 20 % of the patients respectively.[2, 10]Hyperpigmenatation of the skin in CKD patient is attributed to increasing level beta melanocyte stimulating hormone due to its decreased excretion in CKD patient. A yellowish tinge has been attributed to deposition of carotenoids and nitrogenous pigments in the dermis or the presence of lipochromes and carotenoids in the epidermis and subcutaneous tissue.[13]There are reports of hypopigmentary skin changes in CKD like vitiligo and postinflammatoryhypopigmentation, which was not found in our patients.[4,5]

Perforating disorders such as perforating folliculitis, Kyrels disease and reactive perforating collagenosis have been described in CKD.[14] In our study perforating dermatosis was seen in 2 % of the patients. Trauma to the skin secondary to xerosis and pruritus may be the cause for this. Ashokan et al. reported perforating disorder in 7.5% of patients, Uday kumar et al. in 21% patients and Baghel et al. in 2.5% of the patients.[3,4,5]

Infection was also seen in major group of study population in 36 %. The major type of infection was fungal infection (21%) followed by pyodermas (9%) and viral infection (6%).Udaykumar et al. reported fungal infection in (30%), bacterial in (13%) and viral in (12%).[4]Ashokan et al. reported infection in 17.5% of the patients and Amatya B et al. reported infection in only 5%.[3,10]

Nail changes was seen in 29 % of the patients. Half and half nail, leuconychia, longitudinal ridges, onychomycosis and clubbing were seen. Nail changes were reported by Ashokan et al. in 21.67 % and Udaykumar et al. reported in 21% patients, of the patients like our relsult.[3,4] Contradicting with our result Shrestha P et al. reported in 62 % and Amatya Bet al. in 82 % which was high compare to our result.[2,10]

Mucosal changes were seen in 39% of the patients. Xerostomia, macroglossia, fissured tongue, ulcerative stomatitis and angular cheilitis was seen. Shrestha P et al. reported mucosal changes in 22 % patients, Ashokan et al. 7.5% and Baghel et al. in 19 % and of the patients.[2,3,5]

Hair changes were seen in 34 % of the patients. Sparse scalp hair and brittle lusterless hair was the hair changes observed. Shrestha P et al. reported hair changes in 12 % patients, Ashokan et al. in 15% and Baghel et al. in 19 % of the patients.[2,3,5]

In CKD patient skin changes like metastatic calcification of the skin, skin cancer, gynaecomastia, uremic frost, Nephrogenicfibrosingdermopathy has also been reported.[3, 4]These findings were not observed in our patients. There has also a report of skin changes in AV fistula that was not observed in our study.[3,4,5]

Other miscellaneous skin findings were also observed in our patients, which may not be attributed to CKD and dialysis. Other findings observed were alopecia areata, ecchymoses, acneform eruptions, seborrhoeickeratosis, eczema and lichen planus.

CONCLUSION

Skin manifestations are common in patient with CKD. This increases morbidity in this patient with impairment in quality of life and they are resistant to treatment. In developing country like Nepal where dialysis facilities are available only in limited hospital proper evaluation and timely management of this condition can cause improvement in quality of life of these patients.

RECOMMENDATIONS

We recommend the patient with chronic kidney disease for early evaluation of skin disease and early intervention.

LIMITATION OF STUDY

The study could have been better if patient of CKD on medical treatment and patients with peritoneal dialysis were also included along with patient on hemodialysis.

ACKONWLEDGEMENT

We are very grateful to Dr Sailendra Shrestha for granting permission to evaluate and perform research on patient with chronic kidney disease.

CONFLICT OF INTREST

None

FINANCIAL DISCLOSURE

None

REFERENCES

1. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Ressert J. Definition and classification of chronic kidney desease: A position statement from kidney disease: Improving global outcomes (KDIGO). Kidney Int 2005 Jun; 67(6): 2089-100. PMID: 15882252.
2. Shrestha P, Mathur M. Dermatologic manifestations in chronic kidney disease patients on hemodialysis. NJDVL 2014; 12 (1): 34-40. DOI: 10.3126/njdvl201412105.
3. Asokan S, Narasimhan M, Rajagopalan V. Cutaneous manifestations in chronic renal failure patients on hemodialysis and medical management. Int J Res Dermatol 2017:3:24-32. DOI: 10.18203/ Int J Res Dermatol20170432.
4. Udayakumar P, Balasubramanian S, Ramalingam KS. Cutaneous manifestations in patients with chronic renal failure on haemodialysis. Indian J DermatolVenereolLeprol. 2006; 72:119-25. PMID: 16707817.
5. Baghel N, Awasthi S, Kumar SS. Cutaneous manifestations in patients with chronic kidney disease on hemodialysis. Int J Res Med Sci 2017; 5:1673-8. DOI: 10.18203/ijam20173217.
6. Falodun O, Ogunbiyi A, Salako B, George A. Skin changes in patients with chronic renal failure. Saudi J Kidney DisTranspl 2011; 22:268-272. PMID: 21422624.
7. Khanna D, Singal A, Kalra OP. Comparison of cutaneous mani festations in chronic kidney disease with or without dialysis. Postgrad Med J 2010; 86:641-647. PMID: 21037238.
8. Singh G, Verma AV, Singh G, Singh SJ. Cutaneous changes in chronic renal failure. Ind J DermatolVenerolLeprol. 1998; 58:320-2. PMID: 28128158.
9. Hajheydari Z, Makhlough A. Cutaneous and mucosal manifestations in patients on maintenance haemodialysis. Iran J Kidney Dis. 2008; 2:86-90. PMID: 19377214.
10. Amatya B, Agrawal S, Dhali T, Sharma S, Pandey SS. Pattern of skin and nail changes in chronic renal failure in Nepal: a hospital based study. J Dermatol 2008 Mar; 35(3): 140-5. PMID: 18346256.
11. Dyanchenko P, Shustak A, Rozenman D. Hemodialysis-related pruritus and associated cutaneous manifestations.Int J Dermatol. 2006 Jun; 45(6): 664-7. PMID: 16796623.
12. Pico MR, KLugo-somolinos A, Sanchez JL, Burgos-claderon R. Cutaneous alterations in patients with chronic renal failure. Int J Dermatol 1992; 31:860-30. PMID: 1478764
13. Smith AG, Shuster S, Comaish JS, Plummer NA, Thody AJ, Alvarez-Ude F, Kerr DN. Plasma immunoreactive beta-melanocyte-stimulating hormone andskin pigmentation in chronic renal failure. Br Med J. 1975 Mar 22; 1(5959): 658-9. PMID: 1125653.
14. Heilman ER, Friedman RJ. Degenerative diseases and perforating disorders. In: Elder D, Elenitsas R, Jaworsky C, Johnson Jr. B, editors. Lever's histopathology of the skin. 8th ed. Lippincott-Raven: Philadelphia; 1997. p. 341-51. Available from www. levershisto-pathology.com