Cutaneous Manifestations in Patients of Chronic Renal Failure On Hemodialysis.



Medical Science

KEYWORDS : Chronic renal failure, Mucocutaneous manifestations, Hemodialysis

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ABSTRACT

The skin is the mirror for many systemic diseases including the renal system. 54 patients of chronic renal failure admitted for hemodialysis under day care unit of Medicine department in AVBRH, Sawangi, Wardha

were enrolled in the study.

Pallor was seen in 49 patients (90.74%). Pruritus was one of the major symptoms observed in 43 patients (79.63%). Xerosis was one of the major signs observed in 41 patients (75.93%). Majority of patients i.e. 20 (37.04%) had beau's lines as one of the major nail finding followed by koilonychia in 17 patients (31.48%), half and half nails in 5 patients (9.26%). Macroglossia was observed as the most prominent oral finding observed in 19 patients (35.19%). Cutaneous complications at the site of AV shunt of hemodialysis were not observed in our study.

Pallor, pruritus, xerosis, beau's lines and macroglossia were the prominent markers of patients with chronic renal failure.

Introduction

The skin is the mirror for many systemic diseases. It is the most visible and accessible organ of the body, may function as an important diagnostic window to the diseases affecting the internal organs including the renal system [1]. Cutaneous examination of patients with end stage renal disease (ESRD) have shown that 50-100% of patients have at least one dermatological disorder; this may be the result of uremia, hemodialysis or renal transplantation [2]. Some propose that the skin manifestations are due to the underlying pathogenic process that induced the renal disease, while others believe that skin changes are due to metabolic milieu resulting from the malfunctioning kidney.

Chronic renal failure (CRF) is relatively common and skin problems can affect the patient's quality of life. Physicians must be aware of cutaneous manifestations of kidney disease to offer appropriate therapies. With this background the present study was undertaken with the aims and objectives to study prevalence of various cutaneous manifestations among patients undergoing hemodialysis for chronic renal failure.

Methods and Materials

This cross sectional study was conducted in department of Dermatology in collaboration with department of Medicine, during 2011-2012 J.N. Medical College, Sawangi, Wardha. Ethical clearance was obtained from Institutional Ethics Committee.

54 patients of chronic renal failure admitted for hemodialysis under day care unit of Medicine department in AVBRH, Sawangi, Wardha were enrolled in the study after due consideration of inclusion and exclusion criteria. Inclusion criteria were patients of all age groups with renal failure, Patients of CRF undergoing hemodialysis. All patients of chronic renal failure irrespective of cause. Exclusion criteria were patients of acute renal failure, renal transplant recipients due to chronic renal failure. Patients undergoing hemodialysis following a renal transplant failure. Patients who had undergone peritoneal dialysis were not included.

Patients of chronic renal failure with cutaneous signs and symptoms, yet to undergo hemodialysis which might require it in future were also instructed to attend Dermatology OPD of AVBR Hospital, Sawangi. A detailed history with complete clinical examination was carried out in all cases. Improvement

in signs and symptoms of cutaneous findings, following dialysis were also recorded. Diagnosis of cutaneous conditions was made mainly on clinical grounds. Routine investigations findings of CBC, Urine examination, Blood urea, Serum creatinine and blood sugar levels were noted. Underlying cause for CRF was noted. Specific investigations like Skin biopsy, Gram stain for bacterial infections, Tzanck smear for viral infections, Potassium hydroxide mount for fungal infections were done wherever indicated, after informed consent.

Statistical analysis was done by using chi-square test from the data obtained and conclusions were drawn.

Observations and results-

In our study, patients of CRF with cutaneous findings were distributed between 20 to 70 yrs of age group range. Maximum number of patients i.e 32 (59.26%) belongs to age group 30-50 yrs with mean age being 43.33 years.

Out of 54 patient's maximum number of patients i.e. 43 (79.63%) were males and 11 (20.37%) were females.

Pallor was seen in 49 patients (90.74%) followed by pedal odema in 26 (48.15%), icterus in 14 (25.93%) and clubbing in 8 (14.81%).

Pruritus was one of the major symptoms observed in 43 patients (79.63%) followed by facial odema in 3 patients (5.56%) and anuria in 2 patients (3.70%). Xerosis was one of the major signs observed in 41 patients (75.93%) followed by hyperpigmentation of face in 8 patients (14.81%), diffuse muddy brown discoloration in 7 patients (12.96%), eczematisation and folliculitis in 3 patients each (5.55%), reactive perforating disorder (kyrle's disease) and purpura in 2 patients each (3.70%), follicular keratosis, herpes zoster, senile comedone, prurigo nodularis in 1 patient each (1.85%). [Table 1].

Majority of patients i.e. 20 (37.04%) had beau's lines as one of the major nail finding followed by koilonychia in 17 patients (31.48%). Other nail changes like longitudinal ridges and furrows was seen in 9 patients (16.67%) followed by half and half nails in 5 patients (9.26%), onycholysis and subungal hyperkeratosis in 2 patients each (3.70%) and onychomycosis, fragile nails, pitting in 1 patient each (1.85%). [Table 2].

In 54 patients of CRF, macroglossia was observed as the most prominent oral finding observed in 19 patients (35.19%) out of which 9 patients (16.67%) had prominent teeth indentations followed by angular chelitis in 3 patients (5.56%), hyperpigmentation of tongue in 2 patients (3.70%), uremic breath, bluish discoloration on hard palate, impaired taste, xerostomia and coated tongue in 1 patient each (1.85%). [Table3].

3 patients (5.56%) were found to have brittle and lusterless hair followed by sparse hair and diffuse hair loss in 1 patient each (1.85%).

In present study, no cause for CRF was detected i.e idiopathic was observed in 22 patients (40.74%) followed by hypertension in 14 patients (25.93%), renal parenchymal disease in 10 patients (18.52%), diabetes mellitus in 3 patients (5.56%), alcoholism in 2 patients (3.70%) and polycystic kidney disease, liver cirrhosis, koch's disease in 1 patient each (1.85%).

Out of 54 patients of CRF enrolled for the study, pruritus was present in 43 patients. Out of which hemodialysis was done in 32 patients. There was decrease in severity of pruritus after hemodialysis in 31 patients (57.41%) and no change in pruritus was observed in 1 patient (1.85%).

In 11 patients with pruritus hemodialysis was not done.

The Occurrence of various cutaneous manifestations in CRF patients including nail changes showed more or less same prevalence as compared to patients of CRF undergoing hemodialysis except for the findings of pruritus. Out of 54 patients, 16 patients were not affordable for treatment of hemodiaysis. In remaining 38 patients there was decrease in severity of pruritus after dialysis in 31 patients (57.41%) and no change was seen in 1 patient (1.85%). [Table no 4].

In our study of 54 patients of CRF, mean value for Hb% was 6.45 g%, urea 118.53 mg/dl and creatinine 7.36mg/dl.

Discussion:-

Most of the findings in our study were in accordance with other reports.

In present study maximum number of patients belongs to age group of 30-50 yrs with mean age being 43.33.

In present study, maximum patients were male's i.e 43 (79.63%) as compared to females 11 (20.37%). In majority of studies reviewed also showed male preponderance [3,4,5,6,7].

Pallor was one of the second commonest GPE findings seen in 49 patients (90.74 %). Percentage of pallor is high as compared to others, reason being loss of appetite due to CRF and unaffordability for the treatment of erythropoietin and blood transfusion especially in our rural setup. The range for pallor was reported between 50-90% [7]. It was also reported on higher side (85%) in Luqman et al [6]. The mean Hb% in 54 CRF patients was 6.45 g%.

In our study, pruritus was one of the major findings noted in 43 patients (79.63%). In previous study it varied between 19-90% [7, 8]. The possible reason for this variation may be difference in individual tolerance and threshold for itch due to racial and ethic background. Moreover the assessment of itch is also subjective based on perception [9,10,11,12]. Pruritus was the most common cutaneous abnormality in 55% of Egyptician CRF patients on hemodialysis. Udaykumar et al [7] reported pruritus in 53% of Indian patients. It is present in 64.6% patients in study conducted by Reema Mirza et al [4]. Its prevalence was 65.71% reported by Deshmukh S et al [3]. There was decrease in severity of pruritus after dialysis in 31 patients (57.41%) and no change was seen in 1 patient (1.85%). In other studies [3, 7] pruritus was reduced in 8.7% and 9.4% patients with hemodialysis. In our study although severity of pruritus was reduced after hemodialysis, it was not completely subsided.

In most of the studies it has been reported that after hemodialysis patient have experienced increase pruritus. This non amelioration of pruritus has been postulated to be due to inability of hemodialysis to clear blood off the pruritogenic middle molecular weight substances (range 300-1200) like beta 2 microglobulin, advanced glycosylation, end products and parathyroid hormone [13].

Improvement of pruritus depends upon type of membrane used during hemodialysis. Recent work suggests that patients dialysed using less permeable cuprophane membranes suffer pruritus more frequently than those using more permeable polysulphone membranes [14]. In our setup polysulphone membrane was used to dialysed the CRF patients, which could be the cause of decrease in severity of pruritus after hemodialysis in majority of our patients.

Other causes of pruritus are increased serum histamine level, metabolic derangements, xerosis, anemia, hypervitaminosis A, Sec. hyperthyroidism, mast cell proliferation and degranulation, pruritogenic cytokines and abnormal cutaneous innervations [15].

The prevalence of xerosis has been postulated between 46-90% in patients suffering from CRF [7]. In our study, xerosis was noted in 41 patients (75.93%). It is predominately seen over abdomen and lower limb. In our study there is no significant difference in prevalence of xerosis in patients of CRF with or without HD. A reduction in size of eccrine sweat gland may be a contributory, although dose of diuretic regimen are also implicated [16]. Other factors may be elevated plasma vitamine A, increase retinol binding protein & alkalinity of skin [17].

Udaykumar P, Deshmukh S, Mirza R, and Thomas E A et al reported the prevalence of xerosis to be 79%, 72%, 80%, 90.6 % and 66.7% respectively in their studies [7,3,4,5].

Deshmukh S et al [3] reported diffuse pigmentation of face in 7 patients (20%) and 4 patients (11.42%) had yellow tinge on their face. Thus overall prevalence of pigmentation was 31.42%. In our study of 54 patients, 8 patients (14.81%) had brown pigmentation of face and diffuse muddy pigmentation in 7 patients (12.96%). Thus overall prevalence in our study was 27.77%.

Udaykumar et al [7] reported prevalence of this pigmentation as 43% in their study.

Cause of diffuse hyperpigmentation may occur due to increase level of beta MSH as result of its inadequate excretion through kidney and dialysis [18].

The prevalence of acquired perforating disorder was 17.14% in study reported by Deshmukh S et al [3]. Udaykumar et al and Sultan et al reported prevalence of APD in 21% and 10% respectively.

In present study follicular keratosis was seen in 1 patient (1.85%) and kyrle's disease in 2 patients (3.70 %). So prevalence of APD was 5.55%. Khanna et al also reported APD in 3%. APD was seen in 3% in study of Sultan M M et al [19], while other studies showed APD 4.5-17% in patients of hemodialysis [7, 8].

Udaykumar et al[7] reported skin infections like bacterial (5%) and viral (2%) in their study which may be due to associated dibetes mellitus, low albumin, elevated intracellular calcium, acidosis, iron overload, inhibition of chemotactic factors and repititive vascular procedures.

In present study purpura was seen in 2 patients (3.70%), folliculitis in 3 patients (5.55%) & herpes zoster in (1.85%). Ecchymosis on legs and angular chelitis was seen in 3% patients each in study conducted by Luqman N et al [6]. Bacterial infections' including furuncle and carbuncle was seen in 4% and viral infections (herpes zoster) were seen in 2% patients of Luqman N et al study [6].

In our study, majority of patients i.e. 20 (37.04%) had beau's lines as one of the major nail finding followed by koilonychia in 17 patients (31.48%).

Other nail changes like longitudinal ridges and furrows was seen in 9 patients (16.67%) followed by half and half nails in 5 patients (9.26%), onycholysis and subungal hyperkeratosis in 2 patients each (3.70%) and onychomycosis, fragile nails, pitting in 1 patient each (1.85%).

Deshmukh S et al [3] in their study reported beau's line in 28.57%, half and half nails in 19.4% patients and subungal hyperkeratosis in 23.8% patients.

Udaykumar et al [7] in their study reported half and half nails in 21%, koilonychias in 18%, subungal hyperkeratosis in 12%, onycholysis in 10% and onychomycosis in 19%.

Prevalence of half and half nails, characteristic finding of CRF ranges from 16-50% [19,,20].

Sultan M M et al [19] reported prevalence of koilonychia in 39%, half and half nails in 28%.

Thomas E A et al [5] reported half and half nails in 36.36/%, onycholysis in 13.13%, onychomycosis in 7.07%, beau's line and koilonychia in 5.05 % each, subungal hyperkeratosis in 6.06%.

Shakya N B et al [21] in their study reported prevalence of half and half nails to be 12%.

Cause of half and half nails in patients of CRF is oedma of nail bed associated with a dilated capillary while the other half of nail appears normal [22].

In 54 patients of CRF, macroglossia was the most prominent oral finding observed in 19 patients (35.19%) out of which 9 patients (16.67%) had prominent teeth indentations followed by angular chelitis in 3 patients (5.56%), hyperpigmentation of tongue in 2 patients (3.70%), uremic breath, bluish macular discoloration, impaired taste, xerostomia and coated tongue in 1 patient each (1.85%).

Sultan M M, Udaykumar et al & Mathew et al [19, 7, 23] in their study reported the prevalence of macroglossia with teeth indentations to be 42%, 35% and 92% respectively.

Xerostomia was reported to be 1.85% in present study and reported to be 35% and 31% in Sultan M M and Udaykuamr et al [19, 9]. It was attributed to mouth breathing and dehydration. Angular chelitis was reported in present study to be 5.56%. It was reported to be 15% and 12% in Sultan M M and Udaykumar [19, 9].

Thomas E A [5] reported macroglossia with teeth markings in 9.09% pts, angular chelitis in 5.5%, ulcerative stomatitis 2.02% and xerostomia in 5.05%

For Angular chelitis, Luqman [6] reported prevalence to be 3%. Udaykumar P [9] reported macroglossia with teeth markings to be 35%, xerostomia 31%, ulcerative stomatits to be 29%, angular chelitis 12% and uremic breath 8%.

In our study brittle and lusterless hair was seen in 5.56% followed by sparse and hair loss in 1.85%. Other studies showed lusterless hair 20%, 7.07% and sparse hair 5.71%, 16.16% respectively[4,7] which could be due to decreased secretion of sebum.

In majority of studies like Luqman and Sultan MM [6, 19], diabetes mellitus and hypertension was found to be major cause for CRF but in our study 40.74% patients had idiopathic cause for CRF followed by hypertension in 25.93% and DM in 5.56%.

Dehmukh S et al [3] in their study of skin manifestations in patients of CRF on hemodialysis reported the mean of Hb%,

urea and creatinine to be 8.46~g% (SD=1.77g %), 118.77~mg (SD=46.86 mg/dl) and 6.47~mg/dl (SD=3.78 mg/dl) respectively.

Sultan MM et al [19] in their study reported mean Hb%, urea & creatinine to be 10.45 g% (SD= 1.64 g %), 109.75 mg/dl (SD= 28.88 mg/dl) and 13.20 mg/dl (SD=5.41 mg/dl) respectively.

Findings of our study pertaining to Hb%, urea & creatinine were more or less similar to the reports by Deshmukh and Sultan et al [3, 19].

In our study of CRF, pruritus was observed in significant number of 43 patients (79.62%). But there is no significant relation of pruritus with blood urea and serum creatinine value. This could be explained by the fact that others factors might play role in its etiopathogenesis.

Clinical conditions like calciphylaxis, nephrogenic fibrosing dermopathy, uremic frost, erythema papulatum uremicum, uremic roseola and uremic erysipeloid were mostly seen in fairly advanced cases and were also not observed in our study. Cutaneous complications at the site of AV shunt of hemodialysis like infection, phelitis, and hematoma were not observed in our study. In present era where hemodialysis is available at most of centres such advanced cutaneous manifetations of renal failure are rarely seen.

Table 1: Cutaneous findings in patients with CRF (Signs and Symptoms)

(Signs and		Symptoms)
Signs and Symptoms	No of patients	Percentage (%)
Pruritus	43	79.63
Hyperpigmentation of face	8	14.81
Facial Odema	3	5.56
Xerosis	41	75.93
Eczema	3	5.55
Follicular Keratosis	1	1.85
Purpura	2	3.70
Senile Comedone	1	1.85
Herpes Zoster	1	1.85
Folliculitis	3	5.56
Reactive perforating disorder (kyrle's disease)	2	3.70
Diffuse Muddy Brown discoloration	7	12.96
Varicose Veins	1	1.85
Anuria	2	3.70
Prurigo Nodularis	1	1.85

Table 2: Nails findings in patients with CRF

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Nails Findings	No of patients	Percentage (%)			
Half and Half Nails	5	9.26			
Koilonychia	17	31.48			
Beau's Lines	20	37.04			
Subungal Hyperkeratosis	2	3.70			
Longitudinal Ridges and furrows	9	16.67			
Pitting	1	1.85			
Onycholysis	2	3.70			
Fragile Nails	1	1.85			
Onychomycosis	1	1.85			

Table 3: Oral findings in patients with CRF

Oral Findings	No of patients	Percentage (%)
Macroglossia with prominent teeth markings	9	16.67
Macorglossia	10	18.52
Ureamic Breath	1	1.85
Hyperpigmentation of tongue	2	3.70
Bluish discoloration on hard palate	1	1.85
Impaired Taste	1	1.85
Angular Chelitis	3	5.56
Xerostomia	1	1.85
Coated Tongue	1	1.85

Table 4: Cutaneous manifestations in patients with & without hemodialysis

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Signs and symptoms Total no. of patients	No. and % of patients With dialysis out of 38	No. and % of patients Non dialysis out of 16		
Xerosis (41)	30/38 (78.94%)	11/16 (68.75%)		
Pruritus (43)	32/38 (84.21%)	11/16 (68.75%)		
Hyperpigmentation of face (8)	4/38 (10.52%)	4/16 (25%)		
Diffuse muddy discoloration (7)	6/38 (15.78%)	1/16 (6.25%)		
Macroglossia (19)	15 (39.47%)	4 (25%)		
Angular cheilitis (3)	12 (31.57%)	1 (6.25%)		
Hyperpigmentation (2)	1 (2.63%)	1 (6.25%)		
Beau's lines (20)	11 (28.94%)	9 (56.25%)		
Koilonychia (17)	12 (31.57%)	5 (31.25%)		
Longitudinal ridges (9)	5 (13.15%)	4 (25%)		
Half and half nails (5)	4 (10.52%)	1 (6.25%)		

REFERENCE

1. Mazyryk HA, Brodkin RH. Cutaneous clues to renal disease. Cutis 1991;47:241-8.| 2.Nunley, J.Dermatologic manifestations of renal disease. E Med J 2007; topic 550 (online). 3.Deshmukh S P, Sharma Y K, Dash K, Chaudhari N C, Deo K S. Clinicoepidemiological study of skin manisfestations in patients of chronic renal on hemodialysis. 2013; 4;18-21. 4.Mirza R, Wahid Z, Talat H. Dermatological manisfestations in chronic renal failure patients on hemodialysis. JLUMHS 2012; 11: 24-28. | 5.Thomas E A, Pawar B, Thomas A. A prospective study of cutaneous abnormalities in patients with chronic kidney disease. Indian J Nephrol 2012;22:116-20.| 6. Luqman N, Khalid M, Shaheen J A. Cutaneous manisfestations of chronic renal failure in Bahawalpur.JPAD 2012; 22:219-223.| 7. Udaykumar P, Balasubramanian S, Ramalingam KS, Lakshmi C, Srinivas CR, Mathew AC. Cutaneous manisfestations in patients with chronic renal failure on hemodiaysis. IJDVL2006;72;119-125.| 8.Pico MR, Lugo-Somolinos, Sanchez JL, Burgos-Calderon R. Cutaneous alterations in patients with chronic renal failure. Int J Dermatol 1992;31:860-3.| 9.Wikstrom B, Itchy skin- a clinical problem for hemodialysis patients. Nephrol Dial Transplant 2007;22:3-7. | 10. Jamal A, Subramanian PT, Pruritus among end stage renal failure patients on hemodialysis. Saudi J Kidney Dis Transpl 2000;11:181-5.| 11.Diouf B, Niang A, Ka EH, Badiane M, Mo-reira Diop T. chronic renal failure in one Dakar Hospital department. Dakar Med 2003; 48: 185-8.| 12. Sathle- Backdahl M. Ureamic pruritus. Semin Dermatol 1995;14:297-301. 3. Kato A, Hamada M, Maruyama Y, Hishida A. Pruritus and hydration state of stratum corneum in hemodialysis patients. Am J Nephrol 200;20:437-42. | 14. Stachle- Backdah M. Uremic pruritus. Clinical and experimental studies. Acta Derm Venereol 1989;145:1-4. | 15. Szepietowski JC, Schwartz RA, Uremic pruritus:Review. Int J Dermatol 1998;37:247-53.| 16. Cawley EP,Hoch -Bigeti C, Bondy GM. The eccrine sweat gland of patients in uremia. Arch Dermatol 1961;884:9.| 17. Szepirtowski JC, Riech A, Schwartz RA, Uremic xerosis. Nephrol Dial Transplant 2004;19:2709-12.| 18.Smith AG, Shuster S, Comaish JS, Plummer NA, Thody AJ, Alvarez-ude F, plasma immunoreactive beta melanocyte stimulating hormone and skin pigmentation in chronic renal failure. Br Med J 1975;1:658-9, J 19. Sultan M M, Mansour H H, Wahby I M, Houdery A S. Cutaneous manisfestations in Egyptian patients with chronic renal failure on regular hemodialysis. J Egypt Women Dermatol 2010; 7:49-55. 20 Dyachenko P, Monselise A, Shustak A, Ziv M, Rozenman D, nail disorders in patients with chronic renal failure and undergoing hemodialysis treatment: A case control study. J Eur Acad Dermatol Venereol 2007;21:340-4.| 21. Shakya N B, Rajbhandari S L, Sharma A, Deo R K, Jha S M. Cutaneous manisfestations in chronic renal failure patients. MJSBH 2010;9: 13-16.| 22. Headly CM, Wall B. ESRD- associated cutaneous manifestations in a hemodialysis population. Nephrol Nurs J 2002;29:525-39.| 23.Mathew MT, Rajarathnam K, Rajalaxmi PC, Jose L. the tongue sign of CRF; Further clinical and histopathological features of this new clinical sign of CRF. J Assoc Phy Ind 1986;34:52.