Cutaneous Manifestations in Patients with Chronic Kidney Disease on Hemodialysis at Prince Hashem Bin Al-Hussein Hospital in Al-Zarqa

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ABSTRACT

Objective: The aim of the study was to assess the frequency of cutaneous manifestations in patients with chronic kidney disease on hemodialysis.

Methods: A retrospective study, including 75 patients with chronic kidney disease at Prince Hashem Hospital in Al-Zarqa-Jordan, were seen and properly evaluated for their current skin problems. Their files were reviewed. Patients' age, sex, associated medical illnesses, underlying causes of renal failure, the duration of renal failure and the duration of hemodialysis were included. Descriptive statistical analysis was used.

Results: There were 31 female (41.3%) and 44 male (58.7%) patients, the mean age of the study group was 53.9 years, 66 patients (88%) complained of skin problems. The most common problem was xerosis in 61 patients (82.3%), pallor in 60 patients (80%), pruritus in 45 patients (60%), pigmentary changes in 45 patients (60%), oral mucosal changes were seen in 48 patients (64%), hair changes in 34 patients (45%), nail changes in 29 patients (39%) and other cutaneous changes such as purpura in 14 patients (18.6%), acquired perforating folliculitis in six patients (8%) and nephrogenic fibrosing dermopathy in two patients (2.7%).

Conclusion: Cutaneous manifestations are very common in patients with chronic kidney disease undergoing hemodialysis. Pruritus was the most troublesome symptom and xerosis was the commonest finding. More attention to cutaneous changes may help to relieve some of patient's co-morbid symptoms and improve their quality of life.

Key word: Chronic kidney disease, Cutaneous manifestations, Hemodialysis, Pruritus, Renal failure (RF), Xerosis.

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Introduction

Chronic kidney disease (CKD) may cause dysfunction of multiple organs; one of them is the skin, which may show different cutaneous manifestations related to renal failure. It has been noted that newer changes are being described since the introduction of hemodialysis,[1] which prolongs the life expectancy of CKD patients, allowing more and newer changes to appear and evolve.[2] Pico *et al.*

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showed that all patients with CKD had one or more skin changes.[1] Our study was done to evaluate the prevalence of dermatological problems in patients with CKD undergoing hemodialysis (HD).

Methods

Seventy five patients with CKD on HD at the dialysis unit of Prince Hashem Hospital in Al Zarqa were evaluated by three dermatologists from October 2007 to September 2008. This retrospective study was done by taking a detailed history and complete skin examination. Patients' files were reviewed. The patient's sex, age, causes of renal failure, presence of other associated medical illnesses, drug history, duration of renal failure and hemodialysis, the presence of skin changes and the duration of each were included.

Specific investigations like skin biopsy, potassium hydroxide mount preparation and culture for fungi and culture and sensitivity for bacterial infections were done when needed. Routine investigations such as complete blood count (CBC) and renal function were recorded. Informed consents were taken from patients whose photos were taken. Descriptive statistical analysis was used.

Results

Seventy five patients (31 females and 44 males) were examined. Most of them were between (4^{th} to 7^{th}) decades of life; 2 patients were less than 20 years of age and 2 patients were more than 80 years old. 32 patients (42.7%) were within 5th and 6th decades. The age and number of patients are shown in Table I. The most common cause of RF was hypertension which was the cause in 34 patients (45%), then diabetes in 26 patients (35%), then SLE in 15 patients (20%). Other causes leading to RF are shown in Fig.1.

The duration of renal failure and hemodialysis varied from a few months to more than 20 years. 45 patients (60%) were known to have renal failure within less than five years.18 patients (24%) were known to have renal failure within 5 to 15 years. And 11 patients (15%) were known to have renal failure for more than 15 years. Regarding hemodialysis, 50 patients (66.7%) were on HD within less than five years, 17 patients (22.7%) were on HD within five to 15 years. And 8 patients (10%) were on HD for more than 15 years, as are shown in Fig. 2.

All patients showed at least one cutaneous manifestation, although only 66 patients (88%) complained of skin problems. The most common problem was xerosis as it was seen in 61 patients (82.3%), followed by pallor in 60 patients (80%), pruritus in 45 patients (60%) and pigmentary changes in 45 patients (60%). Other cutaneous changes such as purpura was seen in 14 patients (18.6%), acquired perforating folliculitis in six patients (8%) and nephrogenic fibrosing dermopathy in two patients (2.7%), as shown in Table II. Sparse body hair in 18 patients (24%), diffuse scalp hair loss in 16 patients (21.3%), half and half nail in 11 patients(15%), Terry's nail was seen in eight patients (10%), koilonychia in four patients (5.3%), brittle nail in three patients (4%). Hair and nail changes are shown in Table III. Oral mucosal changes as coated tongue was seen in 48 patients (64%), ulcerative stomatitis and angular cheilitis were seen in 40 patients (53.3%), xerostomia was seen in 23 patients (30.6%), macroglossia and teeth marking were seen in eight patients (10%), as shown in Table IV.

Discussion

Xerosis was the most common finding in our study; which was found in 82.3% of our patients. Data from different studies recorded the prevalence of xerosis ranging from 46%-90%.[2,34] This high prevalence in our patients may be due to the fact that most of our patients did not use emollients regularly, did not drink enough amount of fluid and due to the dry non-humid climate of our country.

Different causes have been implicated which may precipitate and aggravate xerosis including a reduction in the size of eccrine sweat glands,[5] high dose diuretic regimen used to treat CKD,[6] elevated plasma vitamin A,[5] elevated retinol binding protein,[7] dietary restrictions and protein malnutrition.[5] Prophylactic use of emollients is mandatory to decrease severity of xerosis and itching,[8] other than that; until now no specific treatment for xerosis has been found. Our patients were encouraged to apply emollients regularly all over their bodies and to increase oral fluid intake.

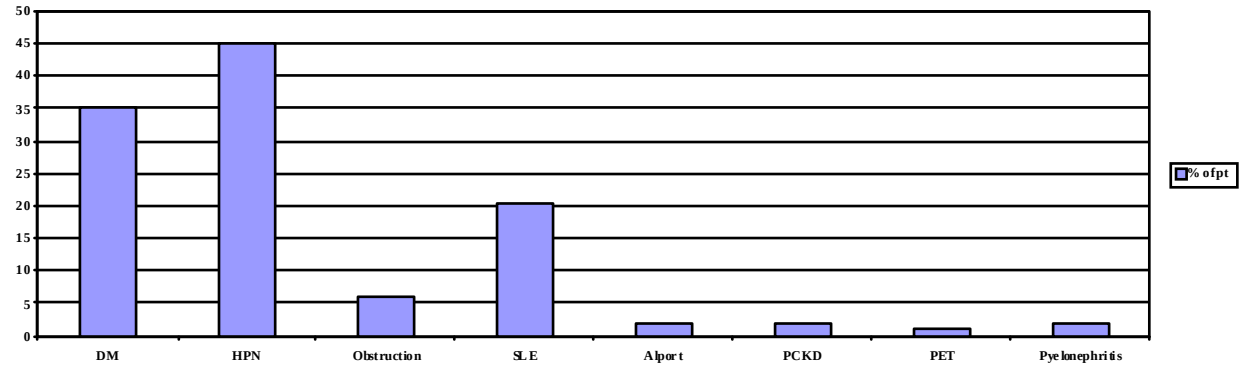

Fig. 1: Causes of CKD and percentage of affected patients

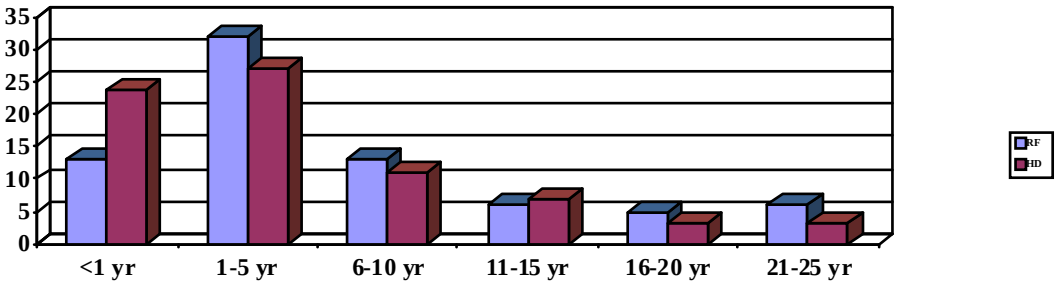

Fig. 2: Duration of renal failure, hemodialysis and number of patients

Table I: Age group and number of patients

Age group	Number of patients
10 – 20 year	2
21 - 30 Yr	4
31 – 40 Yr	11
41 – 50 Yr	12
51 – 60 Yr	16
61 – 70 Yr	16
71 - 80 Yr	12
> 80 Yr	2

Table II: Cutaneous manifestations, number of affected patients and their percentage

Cutaneous manifestations	No. of patients	%
Xerosis	61	82.3
Pruritus	45	60
Pallor	60	80
Pigmentary changes	45	60
Purpura	14	8.6
Acquired perforating folliculitis	6	8
Nephrogenic fibrosing dermopathy	2	2.7
Scleredema	1	1.3
Diabetic bullae	3	4
Multiple milia	2	2.7
Actinic keratosis	2	2.7
Seborrheic dermatitis	3	4
Chondrodermatitis nodularis helicis	1	1.3
AV shunt related: Hematoma	4	5.3
Phlebitis	2	2.7
Contact dermatitis	7	9.3

Table III: Hair and nail changes, number of affected patients and their percentage

Hair changes	No. of patients	%
Sparse body hair	18	24
Diffuse scalp hair loss	16	21.3
Nail changes	**No. of patients**	**%**
Half and half nail	11	15
Terry's nail	8	10
Brittle nail	3	4
Koilonychias	4	5.3
Clubbing	2	2.7
Thickened nail	1	1.3

Table IV: Oral mucosal changes, number of affected patients and their percentage

Oral mucosal changes	No. of patients	%
Macroglossia and teeth marking	8	10
Xerostomia	23	30.6
Ulcerative stomatitis, angular cheilitis	40	53.3
Coated tongue	48	64

Pruritus is the most characteristic and bothersome cutaneous symptoms of CKD,[9] it is not usually present in acute renal failure and does not necessarily subside with dialysis.[10,11]

Pruritus mostly improves with kidney transplant.[12] Its prevalence among hemodialysis patients ranges from 19%-90%,[1,2] and in our study it was 60%. 15 patients (20%) showed significant improvement of pruritus after being started on HD. The prevalence of pruritus is high in our patients because most of them had urine output less than 500ml per 24 hours, had severe xerosis of the skin, had anemia and impaired serum electrolyte level, all of these factors will precipitate and aggravate pruritus.

The exact etiology of pruritus is still unknown, but it has been associated with the degree of renal insufficiency; once the urine output is < 500ml the pruritus will be more,[1,6] secondary hyperparathyroidism,[13,14] xerosis,[14] increased serum level of histamine; due to allergic sensitization to various dialyzer membrane component and impaired renal excretion of histamine, Iron deficiency anemia,[15] increased serum level of electrolyte as Magnesium, Calcium and Phosphorous, proliferation of non specific enolase positive sensory nerve in the skin and hypervitaminosis A.[2] Thus slowly accumulated or deposited pruritogens the nature of which is uncertain is the likely cause for pruritus.[16]

Treatment options for pruritus include: UVB radiation; which suppress histamine releasing factors in patient's serum; and it decreases vitamin A level in the epidermis, topical Capsaicin cream,[17] oral Cholestyramine,[15] activated Charcoal, Naltrexone as an opioid antagonist, Erythropoietin, Ondansetron which is a serotonin receptor antagonist,[14] and low dose Gabapentin.[18] Most of our patients showed excellent improvement of pruritus just after start using emollients regularly. Two patients were referred for narrow band UVB treatment in another hospital but they did not continue treatment because of the long distance they had to travel to have the session.

Pallor was reported as the hallmark of chronic renal failure.[19] It was observed in 80% of our patients. Udayakumar *et al.* detected pallor in 60% of their patients.[2] The incidence is higher in our patients because most of them were anemic and the patients in that group were of darker skin type, so may be pallor was not evident clinically. Pallor is due to reduced erythropoiesis,[20] increased hemolysis and dietary deficiency of vitamin B and iron which lead to anemia.[16]

Pigmentary changes in the form of hyperpigmentations were prominent over sun exposed areas and at sites of previous itching as post inflammatory hyperpigmentation,[21] as shown in Fig. 3. It was seen in 60% of our patients. Nunley *et al*. reported this prevalence as 45%.[22] The incidence was higher in our patients as most of them were skin type 3, so they are more liable for post inflammatory hyperpigmentations and they are exposed to sun

Fig. 3: Excoriation marks and post inflammatory hyperpigmentations

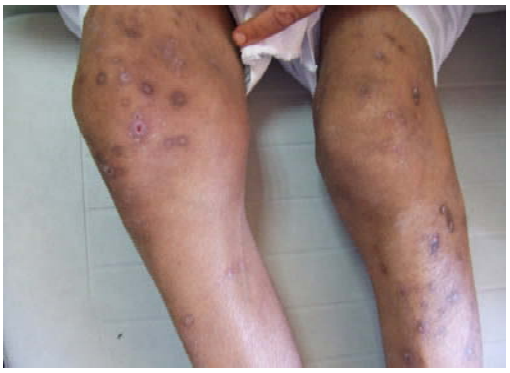

Fig. 4: Acquired perforating disorder

Fig. 5: Half and half nail changes and severe dryness of skin

Fig. 6: Diffuse scalp hair loss

frequently without using sunscreens. Pigmentary changes are due to increased melanin in the basal epidermis and superficial dermis, as the kidney cannot excrete B-MSH.[6,23]

Acquired perforating disorder is hyperkeratotic follicular papules, severely itchy, mainly over extremities, as shown in Fig. 4. It was seen in six patients (8%), and three of them had documented histopathological report. Sultan *et al*. and Udayakumar *et al.* reported this prevalence as 10%-21% respectively.[2,24] It is due to transepidermal elimination of altered dermal substance.[25,26]

Purpura is due to heparin, which is used during dialysis, and also due to a defect in primary hemostasis, as abnormal platelet function.[27,28] It was seen in 18.6% of our patients. Singh reported purpura to be seen in 19% of CRD not on dialysis.[29] So our prevalence goes with what was reported in the literature.

Most common nail change is half and half nail (proximal white and distal brown or normal pink color), as shown in Fig. 5, it was seen in 15% of our patients. Previous studies reported its prevalence as 16%-60%.[30] Then Terry's nail (proximal white and distal 1-2 mm of nail is pink) was seen in 10% of our patients. Other nail changes include brittle nail, koilonychias, clubbing and thickened nail.

Hair abnormalities in the form of diffuse scalp and body hair loss, as shown in Fig. 6, which were seen in 21% of our patients. Singh *et al.* have reported its prevalence by 30%.[29]

Oral mucosal changes are common and were reported to occur in 90% of patients.[31] In our patients xerostomia was seen in 30%, ulcerative stomatitis in 20% and angular chelitis in 22%. All these changes are related to dehydration and poor oral hygiene.[32,33] Our patients were encouraged to increase oral fluid intake and to have better oral hygiene.

Patients with CKD have impaired cellular immunity.[6] This could explain the increased incidence of cutaneous infections,[6] including viral bacterial and fungal infections, such as tinea pedis in (80%) of patients, candidal vaginitis in (60%) of female patients, erosio interdigitalis blastomycetica in (12%), warts in (9%), herpes simplex in (2%) and impetigo in (2%). Bencini *et al*. reported the incidence of fungal infection in

HD patients to be 67%.[6] Other studies reported the incidence of bacterial infections to be 27% and the viral infections to be 12%.[2] Prompt recognition and treatment of cutaneous infections, can terminate the infections quickly and relief some of patients co-morbid illnesses.

Nephrogenic fibrosing dermopathy or scleromyxedema like illness of renal disease,[26] a recently described disorder of unknown cause.[2] It presents as indurated erythematous, yellowish or skin colored plaques. Nodules and contractures occur in more advanced disease. The face is usually spared. It was seen in two of our patients.

Other cutaneous manifestations which were seen in our patients were scleredema which was seen in one patient, diabetic bullae in three patients, multiple milia in two patients, actinic keratosis in two patients, seborrheic dermatitis in three patients, chondrodermatitis nodularis helicis chronica in one patient. Nine patients did not complain of any skin problems, but upon examination found to have xerosis of the skin. Some patients had complications related to AV shunt, such as contact dermatitis which was seen in seven patients, hematoma in four patients and phlebitis in two patients.

Conclusions

All of our 75 patients with CKD undergoing HD had at least one cutaneous manifestation. Xerosis was the commonest finding; pruritus was the most troublesome symptom. Some prophylactic measures can prevent or decrease the severity of these cutaneous symptoms such as the use of emollients and sunscreens, sun avoidance, good oral hygiene, nutritional supplementations and prompt recognition and treatment of cutaneous infections.

Periodic evaluation by a dermatologist is mandatory for the earlier diagnosis and management of cutaneous lesions, which may alleviate most of these findings and relieve some of patient's co-morbid symptoms.

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