Skin lesions in chronic renal dialysis

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ABSTRACT

Objective: Cutaneous and mucosal disorders are the most common problems in patients on long-term hemodialysis. The dialysis prolongs the life expectancy, giving time of these changes to manifest. The aim of this study was to evaluate the prevalence of dermatologic problems among patients with chronic renal disease (CRD) undergoing hemodialysis. **Methods:** One hundred forty-five patients with chronic renal disease undergoing hemodialysis were studied. All patients were thoroughly examined for skin changes, hair, nails and mucous membranes by a single examiner and laboratory tests were assessed. The data were stored in a database Microsoft Excel and analyzed using descriptive statistics. The continuous variables were compared using *Student's t*-test and categorical variables the chi-square test or Fisher's Exact test. **Results:** The study included 145 patients, mean age of 53.6 ± 14.7 years, predominantly male (64.1%) and caucasian (90.0%). The average time of dialysis was 43.3 ± 42.3 months. The main underlying diseases were: hypertension in 33.8%, *diabetes mellitus* in 29.6% and chronic glomerulonephritis in 13.1% of the patients. The main dermatologic manifestations observed were: xerosis in 109 (75.2%), ecchymosis in 87 (60.0%), pruritus in 78 (53.8%) and lentigo in 33 (22.8%) patients. **Conclusion:** Our study showed the presence of more than one alteration per patient. Cutaneous alterations are frequent in patients on dialysis. Further studies are needed to better characterization and management of these dermatosis.

Keywords: dialysis, kidney failure, chronic, skin diseases.

INTRODUCTION

Patients with chronic kidney disease (CKD) are often burdened by skin lesions. These lesions affect both the structure and the color of the skin.[1] Many systemic diseases produce cutaneous manifestations before or after the onset of systemic events. Findings of this nature are extremely important in elucidating patient diagnosis.[2]

CKD refers to a syndromic diagnosis of progressive irreversible loss of kidney function. It is characterized by the degradation of biochemical and physiological functions of all bodily systems, causing neurological, gastrointestinal, cardiovascular, pulmonary, hematologic, endocrine-metabolic, and dermatological disorders secondary to the accumulation of catabolites (uremic toxins) and the onset of other organic alterations.[3]

Recent studies have reported increases in the number of patients with CKD in many countries, with *diabetes mellitus* (DM) as the main cause, a condition that, when left untreated, causes individuals to need dialysis. The number of diabetic patients included in renal replacement therapy has increased in recent years in most dialysis centers, with ranks coming mostly from DM type 2, as also seen in our country.[4]

Advancements in nephrology care technology have increased the survival of patients with kidney disease. Improvements were seen in quality of

life, renal replacement therapies such as peritoneal dialysis and hemodialysis, and kidney transplantation procedures. However, a few complications connected to CKD arose from long term dialysis, such as skin and mucosal injuries.[4-7]

Uremic pruritus affects more than half of the individuals on dialysis. Intense manifestations compromise patient quality of life.[8] The causes of uremic pruritus have not been fully established. Involved factors include xerosis, secondary hyperparathyroidism, increased serum phosphate and magnesium, intradermal proliferation of mast cells, contact with materials of the dialysis membranes, high histamine plasma levels, and iron-deficiency anemia.[9,10]

Increased pigmentation of the skin may be due to high concentrations of melanin in the basal and superficial layers of the dermis. The accumulation of beta-melanocyte-stimulating hormone (B-MSH) consequent to decreased renal function has been correlated with skin hyperpigmentation. Among other factors, the hepatitis C virus has been correlated with porphyrin metabolism disorders that may promote skin hyperpigmentation.[11,12]

It is estimated that more than 70% of the patients on dialysis have nail alterations such as half-and-half nails, characterized by pallor in the proximal portion of the nails and reddish to brownish coloration in the distal portion of the nails; absence of a lunula, characterized by the impossibility of seeing the visible portion of the nail matrix; splinter hemorrhage growing in dark reddish filiform longitudinal lines in the distal portion of the nail plate, among others.[13,14]

This study aimed to assess the prevalence of the main types of dermatosis in patients undergoing hemodialysis in one center.

Methods

The study design was approved by the Ethics Committee in Human Research of the Assisi Gurgacz School of Medicine (Permit Nº. 227/2011-CEP/FAG). The study was carried out at the Renalclin Clinic, an institution that serves 25 municipalities in western Paraná, offering dialysis, hemodialysis, and peritoneal dialysis services. At the time of the study, 162 patients were on dialysis at the institution. Patients on hemodialysis (n = 145) were invited to join the study. The protocol included an interview, physical examination, and lab tests for urea, creatinine, potassium, calcium, phosphorus, KT/V, AST, parathyroid hormone, hemoglobin, albumin, serum iron, ferritin, transferrin saturation, and transferrin. Clinical examination was performed before or after hemodialysis sessions in individual meetings held in a separate office. Physical examination was performed systematically and included the assessment of the patients' hair, skin, mucosas, and nails.

Data collection took place between December of 2011 and January of 2012. Patients on hemodialysis at Renalclin who signed the informed consent term were enrolled in the study. Patients in need of dermatological treatment were given specialized care by co-advisors to the study. Data sets were stored in Microsoft Excel and analyzed through descriptive statistics parameters such as mean values, standard deviation, minimum and maximum values, and gross and percent frequencies. Continuous variables were compared using *Student's t*-test; categorical variables were compared using the chi-square test or Fisher's exact test depending on the size of the sample.

Results

A total of 145 patients with a mean age of 53.7 ± 14.7 years (range 19-83 years) were enrolled in the study. Subjects were predominantly males (64.1%) and Caucasian (90.0%). Thirteen patients preferred not to join the study and four died. The mean duration of dialysis was 43.3 ± 42.3 months (range 2-192 months). The duration of hemodialysis session ranged from three to four hours, with a mean duration of three hours and 30 minutes. At Renalclin, hemodialysis is performed on Fresenius 4008 B (Fresenius Medical Care, Berlin, Germany) devices at blood flow rates ranging between 300-400 mL/min, using polysulphone or cellulose

acetate dialyzers. Arteriovenous fistula was the main access type used by hemodialysis patients. Prescriptions were individualized based on the needs of each patient. The mean dosage of erythropoietin was 36,428 U/month; the mean dosage of calcitriol was 1.43 mcg/week; and the mean dosage of parenteral iron was 300 mg/week. The main underlying conditions were hypertension (33.8%), *diabetes mellitus* (29.6%), and chronic glomerulonephritis (13.1%).

Table 1 describes the main patient characteristics. Four of the 145 enrolled patients had positive serology for hepatitis B, three for hepatitis C, and one for both types of hepatitis. None of the patients included in the study was positive for HIV. The main dermatoses observed were xerosis, in 109 patients (75.2%); ecchymosis in 87 (60.0%); pruritus in 78 (53.8%); and lentigo in 33 (22.8%). Table 2 shows all found dermatoses and Table 3 describes the skin and mucosal manifestations observed in the hemodialysis patients. The comparison of patients with and without pruritus revealed that individuals with pruritus had statistically higher potassium levels. Phosphorus plasma levels were higher in the group with pruritus, but the difference was not statistically significant (Table 4).

Table 1 Main characteristics of the 145 patients on hemodialysis

Variable	Frequency	Percent (%)
Gender		
Male	93	64.1
Female	52	35.8
Ethnicity		
Caucasian	128	90.0
Black	17	11.7
Cause of CKD		
Hypertensioin	49	33.8
Diabetes mellitus	43	29.6
Glomerulonephritis	19	13.1
Undetermined	23	15.9
Others	11	7.6

Discussion

Advancements in nephrology care technology have increased the survival of patients with chronic kidney disease. Improvements were seen in quality of life, renal replacement therapies such as peritoneal dialysis and hemodialysis, and kidney transplantation procedures. However, a few complications connected to CKD arose from different dialysis modes and baseline conditions, such as skin lesions.[2,4,6]

Cutaneous involvement in CKD is characterized by a wide range of manifestations, and many

Table 2 Manifestations in attachments seen in 145 patients on hemodialysis

Dermatoses	Total	Percent (%)
Hair		
Hair loss	48	33.1
Dry hair	39	26.9
Body hair loss	9	6.2
Hirsutism	1	0.7
Nails		
Onycholysis	33	22.7
Half-and-half nails	32	22.0
Absence of lunula	29	20.0
Splinter hemorrhage	28	19.3
Subungual hyperkeratosis	20	13.8
Onychomycosis	16	11.0
Beau's lines	4	2.7
Paronychia	2	1.4
Koilonychia	2	1.4
Leukonychia	1	0.6

Table 3 Cutaneous and mucosal manifestations seen in 145 patients on hemodialysis

Dermatoses	Total	Percent (%)
Skin		
Xerosis	109	75.2
Ecchymosis	87	60.0
Pruritus	78	53.8
Lentigo	33	22.8
Keratosis	33	22.8
Senile purpura	23	15.9
Skin cancer	5	3.4
Neurotic excoriation	5	3.4
Mucosal membranes		
Aphtae	25	17.2
Saburral tongue	21	14.5
Conjunctival hyperpigmentation	8	5.5
Queilite angular	4	2.7
Herpes simplex	3	2.0

Table 4 Characteristics of patients on hemodialysis - comparison between individuals with and without pruritus

Variable	With pruritus (n = 78)	Without pruritus (n = 67)	*p*-value
Gender			
Male	52 (66.6%)	41 (61.1%)	0.493*
Female	26 (33.3%)	26 (38.8%)	
Age	54.3 + 15.3	52.9 + 14.0	0.569†
Caucasian	69 (88.5%)	59 (88.1%)	0.940*
Causes of CKD			
Hypertension	25 (32.0%)	24 (35.8%)	0.691*
Diabetes mellitus	24 (30.7%)	19 (28.4%)	0.765*
Glomerulonephritis	10 (12.8%)	9 (13.4%)	0.914*
Lab workup			
Urea before	136 + 40.8	137 + 37.9	0.879†
Urea after	44 + 18.1	45 + 17.6	0.737†
Creatinine	10.3 + 3.1	10.9 + 4.0	0.321§
Potassium	5.8 + 1.2	5.1 + 1.4	0.001†
PRU	0.66 + 0.0	0.66 + 0.0	‡1.000†
Calcium	9.2 + 0.9	9.0 + 1.2	0.265§
Phosphorus	6.3 + 6.0	5.9 + 1.8	0.577§
Parathyroid hormone	317.6 + 435.8	335.4 + 238.0	0.757§
Hemoglobin	10.8 + 2.0	10.6 + 1.9	0.540†

* Chi-auare test; † *t*-test for homogeneous variance; ‡ Fisher's exact test; § *t*-test for non-homogeneous variance.

patients have multiple associated lesions, as seen in our study. The main observed dermatoses were xerosis, ecchymosis, pruritus and the consequent chafing, and lentigo, among other manifestations seen on skin, attachments, and mucosas.[4,15,16]

Xeroderma is a frequently reported complication among chronic terminal renal patients. Prevalence in dialysis populations is estimated at about 70%, as also seen in our study. The pathophysiological mechanism of xerosis is unknown, and may be related to structural or functional anomalies of the eccrine glands of individuals with advanced CKD.[14-16]

Ecchymosis is a common skin alteration in hemodialysis patients which occurs subsequently to platelet disorders. High concentrations of urea alter platelet aggregation and increase the accumulation of guanidinosuccinic acid (GSA). GSA inhibits platelet activity induced by adenosine diphosphate, thus becoming one of the factors responsible for uremic bleeding.[15,16]

The cause of uremic pruritus is not entirely understood. Triggering factors include xerosis, secondary hyperparathyroidism, high levels of serum phosphate and magnesium, intradermal proliferation of mast cells, materials of the dialysis membranes, increased plasma histamine levels, and iron deficiency anemia. Uremic pruritus may occur in a localized or generalized manner, and has been a frequent symptom in CKD, and especially of patients on dialysis.[17,18] In our study, 53.8% of the patients had pruritus, similarly to what had been reported by Lupi *et al.* in a recent study.[15,16,19]

The comparison of patients with and without pruritus revealed that individuals with pruritus had higher potassium and phosphorus levels, possibly as an outcome of poor compliance with dieting requirements or lower dialysis dosages. KT/V was low and the time of dialysis was below recommended levels. Improved patient management and more adequate dialysis dosing may reduce the incidence of pruritus.

Chronic aphthous stomatitis is a common disease characterized by the appearance of ulcerative lesions in the oral mucosa. Lesions may vary in size, number, and involved site. They usually resolve spontaneously and may relapse. The etiology is multifactorial, and has been correlated with trauma and systemic diseases such as infection and immune hematologic disorders. Prevalence in our study was 17.2%.[20,21]

Tongue alterations were seen in 14.5% of the patients, with saburral (white coated) tongues being the most frequent manifestation. In a study carried out in 2001, Junior *et al.* reported higher incidences, as over 50% of their patients had tongue alterations, with saburral tongues ranking first.[4,21]

Hair disorders such as hair loss and dry hair were observed in 33.1% and 26.9% of the patients, respectively. The occurrence of hair disorders in chronic hemodialysis patients has been attributed to heparin, endocrine disorders, hypervitaminosis A, accumulation of toxins,

drug therapies used in the management of CKD, drugs such as beta blockers, indomethacin, methyldopa, cimetidine, allopurinol, and iron deficiency anemia.[4,8,11]

Nail manifestations observed in our study included onycholysis (22.7%), half-and-half nails (22%), and absence of a lunula (20%). In a recent study with Brazilian individuals, Martinez *et al.* reported absence of lunula in 62.9% and half-and-half nails in 14.4% of their patients. Changes were more frequent in the dialysis population when compared to control subjects.[14,15,21,22]

Absence of the lunula is characterized by the impossibility of seeing the visible portion of the nail matrix. It may occur as a consequence of a number of metabolic manifestations, including anemia. Splinter hemorrhage is a frequent finding in dialysis patients, described as dark reddish filiform longitudinal lines growing in the distal portion of the nail plate.[14,15,21,22]

Lentigo, senile purpura, and altered skin coloration were also seen in our study. Pallor is believed to be correlated with chronic anemia, and a yellow-grayish skin tone to the accumulation of carotenoids and nitrogen pigments in the dermis. Hyperpigmentation may be due to excess melanin in the basal and superficial layers of the skin. Multiple analyses suggest that lentigo, purpura and other dermatoses occur due to accelerated skin aging caused by dialysis.[4,13,16]

Conclusion

Cutaneous manifestations are very common in CKD patients and impact their quality of life. Advancements in medicine have helped improve patient management and reduce the occurrence of some dermatoses such as uremic frost. However, some dermatoses such as xeroderma and uremic pruritus still prove quite challenging. The patients in our study had more than one type of dermatosis. Further studies are needed to better characterize and improve the management of dermatoses.

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