Original Article

Dermatological Manifestations in Pediatric Patients with Chronic Kidney Disease.

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ABSTRACT

Introduction: Skin changes are common in chronic kidney disease (CKD) yet data on different skin lesions in children are limited.

Aim of the study: We aimed to screen dermatological manifestations in our pediatric CKD patients, and their relationships with CKD stage, dialysis modality, clinical and metabolic parameters.

Methods: A descriptive cross-sectional study on pediatric CKD patients, who were divided equally into group 1; CKD stage 5 on regular hemodialysis [online-hemodiafiltration (OL-HDF), high flux conventional hemodialysis (HF-HD), or a hybrid of both], and group 2; CKD stage 2-4 on conservative management.

Results: We included 70 pediatric CKD patients, with mean (±SD) age, CKD, and HD durations of 9.23 (±3.9), 3.92 (±2.73), and 2.67 (±1.94) years respectively. Eight (22.9%) patients were on OL-HDF, 7 (20%) on HF-HD, and 20 (57.1%) on a hybrid of both. Xerosis was considered the most frequent skin manifestations (78.6%), followed by pruritus (62.9%), and pallor 35.7%, meanwhile 6 (8.57%) patients had hair and nail abnormalities, where 4 (5.33%) had hair loss, one (1.4%) had albinisms, and one patient (1.4%) had onychomycosis. Skin, hair, and nail abnormalities didn't differ significantly with CKD stages, HD modalities. Xerosis was associated with lower HD efficacy (Kt/V) and higher white blood cell count, while pruritis was associated with higher hemoglobin level.

Conclusion: Skin, nail, and hair abnormalities were not uncommon among our pediatric CKD patients, where xerosis and pruritis were the most common skin manifestations. Kt/V and total white blood cell count had related to xerosis, meanwhile hemoglobin level influenced pruritis.

Keywords

Chronic kidney disease, xerosis, pruritis, hemodialysis

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INTRODUCTION

Chronic kidney disease (CKD) is a major health problem worldwide with increasing incidence and prevalence. The kidney disease Improving Global Outcomes (KDIGO) guidelines have defined CKD as abnormalities of kidney structure or function, present for more than 3 months, with implications to health **[1].**

CKD, regardless of its cause, may be accompanied by various skin conditions. The most common symptom in children suffering from CKD is pruritus. Other signs include xerosis, skin hyperpigmentation, ecchymoses, acquired perforating dermatoses, nail lesions, calcinosis cutis, porphyria cutanea tarda, as well as eczematous lesions at the site of an arteriovenous fistula and skin infections **[2], [3].**

We aimed to study primarily the different dermatological, hair and nail manifestations in pediatric patients with CKD, in addition to studying the relationship with the CKD stage, dialysis modalities, and various clinical and metabolic parameters.

METHODS

This was a descriptive cross-sectional study, that was conducted at Pediatric Dialysis and Nephrology unit, Children's Hospital, Faculty of Medicine, Ain Shams University, Egypt, during the period from February 2023 to August 2023. An informed consent was obtained from legal guardians before enrollment in the study, with approval of Research Ethics Committee of Faculty of Medicine, Ain Shams university with number of (*FMASU MS 63/2023)*, after fulfillment of all the ethical aspects required for human research.

Study population

We included 70 pediatric patients with CKD aged from 1 to 16 years who met the inclusion and exclusion criteria. Estimated glomerular filteration rate (eGFR) was determined by Schwartz formula: eGFR = (0.41 x height in cm) ÷ serum cr (mg/dl). CKD staging was as follows:

- Stage 1 with normal or high GFR (GFR > 90 mL/min)
- Stage 2 Mild CKD (GFR = 60-89 mL/min)
- Stage 3A Moderate CKD (GFR = 45-59 mL/min)
- Stage 3B Moderate CKD (GFR = 30-44 mL/min)
- Stage 4 Severe CKD (GFR = 15-29 mL/min)
- Stage 5 End Stage CKD (GFR <15 mL/min)

Patients were divided equally into two groups according to the stage of CKD: group 1 (stage 5 on regular hemodialysis, CKD5d) and group 2 (stage 2-4 on conservative management). We included patients with CKD stage 2-5 on either conservative management (CKD 2-4), or regular hemodialysis (CKD5d) in the form of high flux conventional hemodialysis (HF-HD), online-hemodiafiltration (OL-HDF) or a hybrid of both thrice per week, four hourly sessions for at least one year. Meanwhile, our exclusion criteria were patients on iron chelation therapy, and those with known skin disease e.g., eczema, psoriasis.

Study Tools

Patients were divided into two groups according to the stage of CKD according to the Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines **[4]** into group 1 (stage 5 on regular hemodialysis, CKD5d) and group

2 (stage 2-4 on conservative management). Data were collected for all through:

Detailed history taking in the form of age, gender, cause and duration of CKD, blood transfusions and medication history. Hemodialysis (HD) details were collected in the form duration, modalities, dialysis adequacy calculated as (Kt/V): K = clearance—the amount of urea your dialyzer can remove (liters/minute), t = time—the duration of treatment (minutes), V = volume—the amount of body fluid (liters) **[5].**

Physical examination of weight, height, BMI, and blood pressure measurement, and examining the skin, nail, and hair, where xerosis and pruritis were graded as follow:

Xerosis severity in the study patients was assessed using a four-point xerosis assessment scale (0, normal skin, without any xerosis; 1, mild xerosis; 2, moderately dry skin with minimal flaking; 3, severe xerosis, heavy scaling visible) **[6].**

Pruritus was assessed using a visual analogue scale (VAS) on a scale of 0 (no itch) to 10 (worst possible itch). Subjects were asked to rate their pruritus perceived within the previous 24 h using the horizontal VAS, followed by the vertical VAS, numeric rating scale (NRS) and the 5-point verbal rating scale (VRS) (no pruritus (0 points), mild pruritus (1 point), moderate pruritus (2 points), severe pruritus (3 points), very severe pruritus (4 points)). The VAS is a 10-cm long line (oriented horizontally or vertically), on which patients indicated the intensity of pruritus by crossing the line at the point that corresponded to their pruritus severity, being informed that the beginning of the scale refers to no pruritus (0 points) and the end to the most severe pruritus they can imagine (10 points) **[7].** Numerical rating scale, verbal rating scale, and visual analogue scale for pruritis together with illustrated 22-point pruritis rating scale are shown in **Figures 1 and 2 [8], [9].**

Laboratory data: The most recent regular follow up investigations were collected from patients' medical records at the time of enrollment in the study including complete blood count, serum calcium, phosphorous, alkaline phosphatase, parathyroid hormone, uric acid, urea, and creatinine with estimation of GFR using modified Schwartz formula **[10].**

RESULTS

The clinico-demographic and dialysis data of the studied patients are seen in **Tables 1 and 2**, where the mean age (±SD) of our CKD patients was 9.23 (±3.9) years, and the mean (± SD) CKD and dialysis durations (for CKD5d group) were 3.92 (±2.73), and 2.67 (± 1.94) years respectively. We had a male predominance (61.4%). CAKUT was the most common CKD etiology in our studied patients (63.8%). Most of our CKD patients had received a hybrid of conventional high flux HD (HF-HD) and online-Hemodiafiltration (OL-HDF) (20, 57.1%), where 8 (22.9%) were purely on OL-HDF, and 7 (20%) on conventional HF HD with mean (± SD) dialysis adequacy and efficacy of (Kt/V) of 1.27 (± 0.24). Thirty percent of patients had hypertension that was controlled by different classes of anti-hypertensive medications in the form of mono or combined therapy of CCB (27.1%), ACEi (24.3%), alfa blockers (11.4%), BB (4.3%) and ARBs (2.9%). On reviewing the medication history of our patients, most of them received calcium supplement (81.42%), in addition to

phosphate binder (45.7%), iron supplementation (64.2%) and ESA (60%).

Skin abnormalities were reported in 64 patients (91.42%) from both study groups while hair abnormalities in the form of hair loss and sparse lusterless hair were reported in 8 (11.4%) patients and nail abnormalities in the form of onychomycosis were reported in only one patient (1.4%). The most common skin abnormalities were xerosis (55, 78.6%), followed by pruritus (44, 62.9%), pallor (25, 35.7%), and hyperpigmentation (14, 20%), where post inflammatory hyperpigmentation was reported in 3 cases (4.3%) **(Table 3 and Figures 3, 4 and 5).**

The CKD stage had no direct effect on skin, hair, and nail abnormalities, where there weren't significant changes between group 1 and group 2 patients, on either conservative management or hemodialysis **Table 4.** Xerosis was frequent in CKD5d patients with low dialysis efficacy, where lower Kt/V was associated with xerosis (p= 0.003), meanwhile all CKD patients who had a higher total leukocytic count, had more xerosis than those with lower counts (p=0.046), meanwhile hemoglobin level influenced pruritis, where higher hemoglobin level was significantly associated with pruritis, other than these, we couldn't find significant results with other clinico-demographic, laboratory data or medication history **Tables 5, 6 and 7.**

Table 1: Clinical and demographic data for the studied patients

		Mean / N	SD / %	Median (IQR)	Range
Age (years)		**9.23**	**3.99**	**10 (6 - 12)**	**(0.58 - 15)**
Sex	**Male**	43	61.4%		
	Female	27	38.6%		
CKD stage	**Stage 2**	2	2.9%		
	Stage 3	15	21.4%		
	Stage 4	18	25.7%		
	Stage 5	35	50.0%		
Primary disease diagnosis	**CAKUT**	44	63.8%		
	Podocytopathy	12	17.4%		
	SLE	4	5.7%		
	TMA	4	5.7%		
	Ciliopathy	2	2.8%		
	Nephrolithiasis	1	1.4%		
	Metabolic	1	1.4%		
	Chronic TIN	1	1.4%		
Duration of CKD (Years)		3.92	2.73	3.75 (1.5 - 6)	(0.33 - 10)
Duration of HD (Years) (N=35)		2.67	1.94	2.5 (1 - 4)	(0.5 - 8)
Type of dialysis (N= 35)	**Pure HF-HD**	7	20.0%		
	Pure OL-HDF	8	22.9%		
	Hybrid of both	20	57.1%		
HD Efficacy (Kt/v) (N=35)		1.27	0.24	1.3 (1.1 - 1.4)	(0.8 - 1.7)

CAKUT: congenital anomalies kidney and urinary tract, CKD: chronic kidney disease, HF- HD: high flux hemodialysis, HTN: Hypertension, OL-HDF: online hemodiafiltration, TIN: tubule-interstitial nephritis, SLE: Systemic Lupus Erythromatosis, TMA: thrombotic microangiopathy.

Table 2: The used medication and blood transfusion for the studied patients

Medications		N	%
Anti-hypertensive medications	CCB	19	2.9%
	ACEIs	17	24.3%
	Alfa Blocker	8	27.1%
	BB	3	4.3%
	ARBs	2	11.4%
Calcium supplement	No	13	18.6%
	YES	57	81.42%
Phosphate binder	No	36	51.4%
	YES	34	45.7%
Iron supplement		45	64.28%
ESA supplement		42	60.0%
PRBCS transfusion over the whole CKD duration	No	14	20.0%
	Yes	56	80.0%
Frequency of PRBCS transfusion during the whole dialysis duration	< 5 times	41	73.2%
	5-10 times	11	19.6%
	> 10 times	4	7.1%

ACEIs: angiotensin converting enzyme inhibitor, ARBs: angiotensin receptor blocker, BB: beta blocker, CCB: calcium channel blocker, ESA: erythropoietin stimulating agents; IV: intravenous, PRBCs: Packed Red Blood Cells.

Table 3: Skin, hair, and nail abnormalities in our CKD patients

Skin abnormalities (Total cases 70)		Group 1 (CKD5d, n=35) n (%)	Group 2 (CKD2-4, n=35) n (%)	Test of significances	
				Value	p-Value
Xerosis Total n = 55 (78.57%)	No	7 (20%)	8 (22.86%)	X^2= 0.085	0.771
	Yes	28 (80%)	27 (77.14%)		
Xerosis Grade	1	14 (50%)	14 (51.85%)	FE	1.00
	2	12 (42.86%)	12 (44.44%)		
	3	2 (7.14%)	1 (3.7%)		
Pruritis Total n = 44 (62.85%)	No	14 (40%)	12 (34.29%)	X^2= 0.245	0.621
	Yes	21 (60%)	23 (65.71%)		
Pruritis Grade	1	12 (57.14%)	14 (60.87%)	FE	0.947
	2	6 (28.57%)	7 (30.43%)		
	3	2 (9.52%)	2 (8.7%)		
	4	1 (4.76%)	0 (0%)		
Pallor Total n = 25 (35.71%)	No	20 (57.14%)	25 (71.43%)	X^2= 1.556	0.212
	Yes	15 (42.86%)	10 (28.57%)		
Hyperpigmentation Total n = 14 (20%)	No	23 (65.71%)	33 (94.29%)	X^2= 8.929	0.003
	Yes	12 (34.29%)	2 (5.71%)		
Nail abnormalities	No	35 (100%)	34 (97.14%)	FE	1.00
	Yes	0 (0%)	1 (2.86%)		
Hair Abnormalities	No	32 (91.43%)	33 (94.29%)	FE	1.00
	Yes	5 (8.57%)	3 (5.71%)		

Significant p value <0.05

Table 4: Relation between sociodemographic, clinical data and medications with xerosis.

		Xerosis		Test of significance	
		No	Yes		
		Mean ± SD - N (%) Median (IQR)	Mean ± SD - N (%) Median (IQR)	Value	p-Value
Age (years)		10.5 ± 3.15	8.88 ± 4.15	***t*** = 1.401	0.166
Sex	**Male**	10 (66.67%)	33 (60%)	X^2 = 0.221	0.638
	Female	5 (33.33%)	22 (40%)		
CKD stage	**Stage 2**	1 (6.67%)	1 (1.82%)	**FE**	0.261
	Stage 3	5 (33.33%)	10 (18.18%)		
	Stage 4	2 (13.33%)	16 (29.09%)		
	Stage 5	7 (46.67%)	28 (50.91%)		
Duration of CKD (Years)		4.5 (1.5 - 7)	3 (1.5 - 6)	***z*** = -0.839	0.401
Duration of HD (Years)		2.5 (1 - 4)	2.5 (1 - 3)	***z*** = -0.415	0.678
Type of dialysis	**Pure HF- HD**	1 (14.29%)	6 (21.43%)	**FE**	0.509
	Pure OL-HDF	3 (42.86%)	5 (17.86%)		
	hybrid of both	3 (42.86%)	17 (60.71%)		
HD Efficacy (Kt/v)		*1.5 (1.4 - 1.5)*	*1.3 (1.05 - 1.4)*	***z = -2.947***	***0.003***
ARBs		1 (6.67%)	1 (1.82%)	**FE**	0.385
ACEIs		4 (26.67%)	13 (23.64%)	**FE**	1.00
CCB		6 (40%)	13 (23.64%)	**FE**	0.325
BB		0 (0%)	3 (5.45%)	**FE**	1.00
Alfa blocker		2 (13.33%)	6 (10.91%)	**FE**	1.00
Calcium supplementations	**4 (26.67%)**	9 (16.36%)	**FE**	0.491	0.961
	15 (8667%)	46 (83.64%)	35 (79.52%)		
Phosphate binder	**9 (60%)**	27 (49.09%)	**FE**	0.262	0.907
	6(40%)	28 (50.91%)	22 (50%)		
Iron (oral)		1 (6.67%)	11 (20%)	**FE**	0.439
Iron (IV)		6 (40%)	27 (49.09%)	X^2 = 0.391	0.532
ESA		7 (46.67%)	35 (63.64%)	X^2 = 1.414	0.234
Calcimimetic		4 (26.67%)	12 (21.82%)	**FE**	0.734
Frequency of PRBCS transfusion during the whole dialysis duration	**< 5 times**	7 (77.78%)	34 (72.34%)	**FE**	1
	5-10 times	2 (22.22%)	9 (19.15%)		
	> 10 times	0 (0%)	4 (8.51%)		

*Student t-test of significance (t), *Chi-Square test of significance (X2), *Mann-Whitney test of significance (z), *Fisher's Exact test of significance (FE), ACEIs: angiotensin converting enzyme inhibitor, ARBs: angiotensin receptor blocker, BB: beta blocker, CCB: calcium channel blocker, CKD: chronic kidney disease, ESA: erythropoietin stimulating agents, HF-HD High Flux hemodialysis, IV: intravenous, OL-HDF: online-hemodiafiltration, PRBCs: Packed Red Blood Cells. Significant p value <0.05.

Table 5: Relation between lab investigations and xerosis.

	Xerosis		Test of significance	
	No	Yes		
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	Value	p-Value
Hemoglobin (g/dl)	10.32 ± 1.27	9.47 ± 1.55	***t*= 1.950**	0.055
TLC (10^3/µL)	***7 (4.7 - 8.3)***	***8 (6.5 - 11)***	***z= -1.992***	***0.046***
Serum iron (µg/dl)	85 (54 - 100)	75 (60 - 109)	***z*= -0.150**	0.880
Ferritin (ng/ml)	210 (155 - 618)	210 (171 - 556)	***z*= -0.172**	0.864
TSAT	245 (205 - 280)	231 (195 - 270)	***z*= -0.616**	0.538
PTH (pg/ml)	32 (25 - 49)	35.2 (26.4 - 45.7)	***z*= -0.272**	0.786
Serum calcium (mg/dl)	208 (95 - 773)	215 (95 - 811)	***z*= -0.007**	0.994
Uric acid (mg/dl)	9.24 ± 0.57	8.76 ± 0.98	***t*= 1.823**	0.073
PO4 (mg/dl)	3.33 ± 0.99	4.05 ± 1.37	***t*= -1.901**	0.062
ALP (U/L)	5.32 ± 1.27	5.66 ± 1.7	***t*= -0.730**	0.468
Blood Urea (mg/dl)	155 (125 - 420)	175 (120 - 289)	***z*= -0.430**	0.668
eGFR (ml/min/m^2)	4.01 ± 0.4	3.79 ± 0.55	***t*= 1.439**	0.155
Hemoglobin (g/dl)	39 (29 - 75)	60 (34 - 85)	***z*= -1.009**	0.313
TLC (10^3/µL)	18 (5 - 32)	7 (6 - 26)	***z*= -0.606**	0.545

*Student t-test of significance (t), *Mann-Whitney test of significance (z), ALB: albumin, ALP: alkaline phosphatase, eGFR: estimated glomerular filtration rate, PO4: phosphorus, PTH: parathyroid hormone, TIBC: total iron binding capacity, TLC: total leucocytic count, TSAT: transferrin saturation. Significant p value <0.05.

Table 6: Relation between sociodemographic, clinical data and medications with pruritis

		PRURITIS		Test of significance	
		No	Yes		
		Mean ± SD -- N (%) Median (IQR)	Mean ± SD -- N (%) Median (IQR)	Value	p-Value
Age (years)		9.34 ± 4.57	9.16 ± 3.66	**t**= 0.178	0.859
Gender	**Male**	15 (57.69%)	28 (63.64%)	X^2= 2.44	0.622
	Female	11 (42.31%)	16 (36.36%)		
CKD stage	**Stage 2**	1 (3.85%)	1 (2.27%)	**FE**	0.417
	Stage 3	3 (11.54%)	12 (27.27%)		
	Stage 4	8 (30.77%)	10 (22.73%)		
	Stage 5	14 (53.85%)	21 (47.73%)		
Duration of CKD (Years)		3 (1.5 - 5)	4 (1.5 - 6)	**z**= -0.761	0.446
Duration of HD (Years)		2.25 (1 - 3)	2.5 (1 - 4)	**z**= -0.610	0.542
Type of dialysis	**Pure HF HD**	3 (21.43%)	4 (19.05%)	**FE**	0.808
	Pure OL-HDF	4 (28.57%)	4 (19.05%)		
	hybrid of both	7 (50%)	13 (61.9%)		
HD Efficacy (Kt/v)		1.35 (1.1 - 1.4)	1.3 (1.1 - 1.4)	**z**= -0.017	0.986
ARBs		0 (0%)	2 (4.55%)	**FE**	0.526
ACEIs		6 (23.08%)	11 (25%)	X^2= 0.033	0.856
CCB		7 (26.92%)	12 (27.27%)	X^2= 0.001	0.975
BB		1 (3.85%)	2 (4.55%)	**FE**	1.00
Alfa blocker		3 (11.54%)	5 (11.36%)	**FE**	1.00
Calcium supplementations	**No**	4 (15.38%)	9 (20.45%)	**FE**	0.961
	YES	22 (84.61%)	35 (79.52%)		
Phosphate binder	**No**	14 (53.85%)	22 (50%)	**FE**	0.907
	YES	12 (46.16%)	22 (50%)		
Iron (oral)		5 (19.23%)	7 (15.91%)	**FE**	0.751
Iron (IV)		13 (50%)	20 (45.45%)	X^2= 0.136	0.713
ESA		17 (65.38%)	25 (56.82%)	X^2= 0.5	0.48
Calcimimetic		7 (26.92%)	9 (20.45%)	X^2= 0.388	0.533
Frequency of PRBCS transfusion during the whole dialysis duration	**< 5 times**	15 (78.95%)	26 (70.27%)	**FE**	0.89
	5-10 times	3 (15.79%)	8 (21.62%)		
	> 10 times	1 (5.26%)	3 (8.11%)		

*Student t-test of significance (t), *Chi-Square test of significance (X^2), *Mann-Whitney test of significance (z), *Fisher's Exact test of significance (FE), ACEIs: angiotensin converting enzyme inhibitor, ARBs: angiotensin receptor blocker, BB: beta blocker, CCB: calcium channel blocker, CKD: chronic kidney disease, ESA: erythropoietin stimulating agents, HF HD: high flux hemodialysis, IV: intravenous, OL-HDF: online-hemodiafiltration, PRBCs: Packed Red Blood Cells. Significant p value <0.05.

Table 7: Relation between lab investigations and pruritus.

	Pruritus		Test of significance	
	No	Yes		
	Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	Value	p-Value
Hemoglobin (g/dl)	***9.11 ± 1.33***	***9.97 ± 1.56***	***t= -2.363***	***0.021***
TLC (10^3/µL)	7.75 (5.6 - 12)	7.5 (6.1 - 9)	***z***= -0.621	0.535
Serum iron (µg/dl)	70 (45 - 109)	83 (71 - 103.5)	***z***= -1.508	0.132
Ferritin (ng/ml)	207.5 (136 - 575)	215 (175.5 - 522.5)	***z***= -0.419	0.675
TSAT	32.5 (23 - 40)	37.5 (27 - 51)	***z***= -1.757	0.079
PTH (pg/ml)	184 (110 - 877)	220 (95 - 692.5)	***z***= -0.462	0.644
Serum calcium (mg/dl)	8.6 ± 1	9.02 ± 0.85	***t***= -1.854	0.068
Uric acid (mg/dl)	3.91 ± 1.27	3.88 ± 1.37	***t***= 0.071	0.943
PO4 (mg/dl)	5.79 ± 1.89	5.47 ± 1.43	***t***= 0.790	0.432
ALP (U/L)	197 (120 - 322)	165 (122.5 - 261)	***z***= -0.401	0.688
Blood Urea (mg/dl)	62.5 (35 - 86)	50 (28.5 - 80)	***z***= -1.228	0.219
eGFR (ml/min/m^2)	7 (5 - 19)	15 (6 - 32)	***z***= -1.341	0.180

*Student t-test of significance (t), *Mann-Whitney test of significance (z), ALB: albumin, ALP: alkaline phosphatase, eGFR: estimated glomerular filtration rate, PO4: phosphorus, PTH: parathyroid, TIBC: total iron binding capacity, TLC: total leucocytic count, TSAT: transferrin saturation. Significant p value <0.05

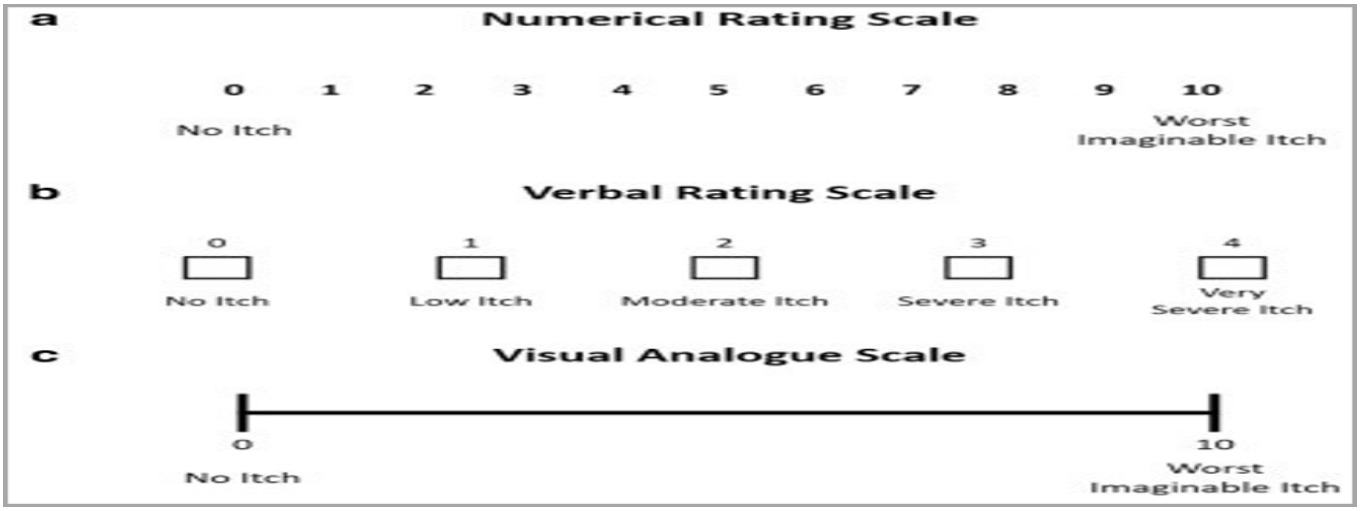

Figure 1: Numerical rating scale, verbal rating scale, and visual analogue scale for pruritic. **[8]**

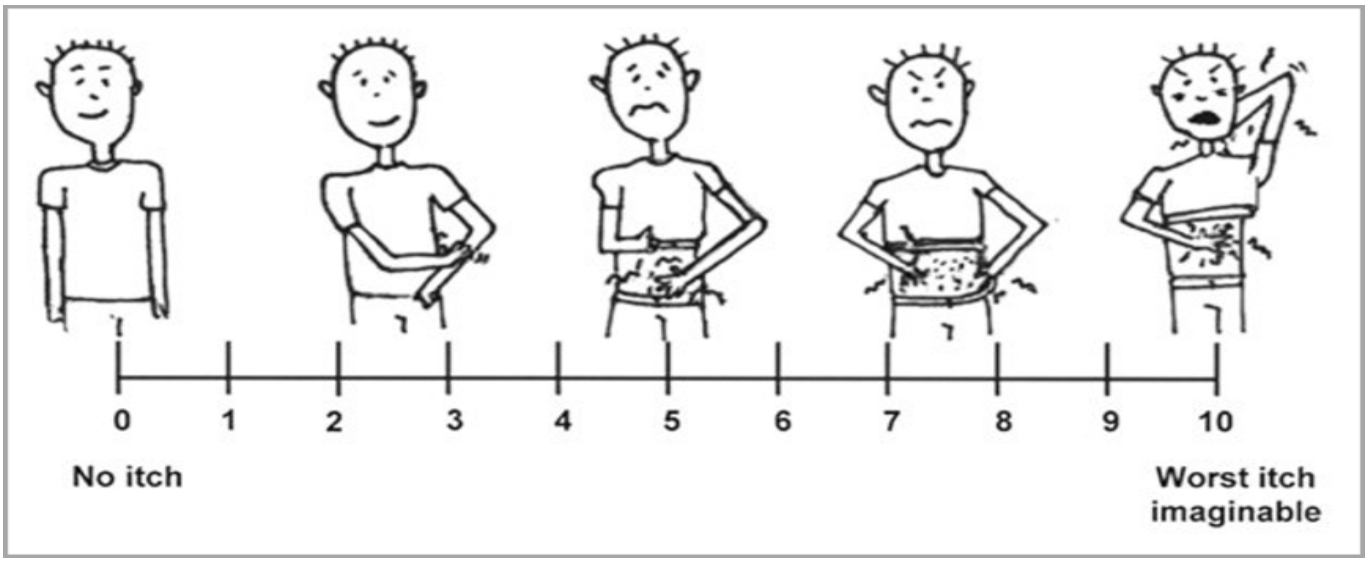

Figure 2: Illustrated 11-point pruritus rating scale, with 0 representing no itch and 10 representing the worst itch imaginable. **[9].**

Figure 3: Onychomycosis

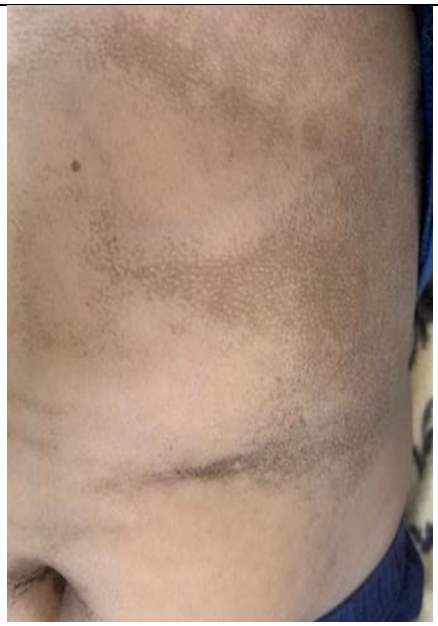

Figure 4: Hyperpigmentation

Figure 5: Xerosis

DISCUSSION

Our cohort showed a male predominance, and the most common cause of CKD was CAKUT, like other studies, where the most common etiology for CKD is CAKUT, more commonly occurring in boys **[11, 12].** Most of our cohort reported skin abnormalities (91.42%), on the other hand, hair and nail abnormalities were not uncommon (11.4%, 1.4% respectively). Similarly, higher prevalence of dermatoses in previous CKD pediatric and adult studies was reported. Skin changes were detected in 86% of pediatric Sudanese children with CKD, where most patients presented with more than one change, associated with anemia and uremia **[13].** Meanwhile in the adult studies, the prevalence was variables reported 94.3% **[14],** 95% **[15]** and 96% **[16]** respectively.

Dermatosis prevalence rates within the CKD population might differ due to variations in the features of the study participants, including age, the underlying cause of CKD, the stage, and the form of renal replacement therapy (RRT).

The most common skin abnormalities in our cohort were xerosis (78.6%), followed by pruritus (62.9%), pallor (35.7%), and hyperpigmentation (20%). The cause of uremic xerosis could be attributed to multiple mechanisms, including underlying abnormality in the epidermis in CKD patients, such as atrophy and poor sweat gland output, that might cause decreased epidermis moisturizing **[17].** Abnormalities in pH levels of the stratum corneum, which control the ichthyosis patients' natural skin exfoliation process, might be one of the potential reasons of dry skin in dialysis patients **[18]**. Proteases are involved in the exfoliation of the stratum corneum and can be activated by a decrease in pH on the skin's surface **[17].** Proinflammatory mediators may have a role in mediating uremic pruritus, additionally, uremic xerosis is an important determinant of uremic pruritus **[19].**

These prevalence rates somehow agreed with the pediatric Sudanese study by Kheir Elseed L. et al**. [13],** where they found that skin changes were mainly xerosis (68%), followed by pruritus (64%), and hyperpigmentation (28%), meanwhile the hair changes were higher than ours and accounted for 30%. The prevalence has been changed from the previous Egyptian case-controlled study **[20]**, where xerosis was 53.5%, and pruritus was 18.6% in their pediatric hemodialysis patients. On the contrary, a pediatric prospective, case-control study of Pratyusha K, et al. **[21]** found that the most common skin manifestation was pallor (75.5%), followed by xerosis (48.5%), atopic diathesis (41.5%) and the least one was pruritus (13%). Another study mentioned xerosis as the most common finding in their patients (58%) and was even more common in the dialytic (66%) group, both in number of patients and severity. The second most common finding was pallor (55%), which was also seen more in the dialytic group (60%). Other major findings were pruritus (49%) and hyperpigmentation (37%). The intensity of pruritus was higher in non-dialytic patients **[22].**

In our study, the CKD stage had no direct effect on skin, hair, and nail abnormalities. We found no significant differences between patients on either conservative management (CKD 2-4) or hemodialysis (CKD5d). Similarly, the pediatric prospective, case-control study of

Pratyusha K, et al. [21] found no significant association between the CKD stage and the occurrence of pruritus. On the contrary, a Polish pediatric study [7] noticed that xerosis was more common in hemodialysis (67.6%) patients compared to those on conservative treatment (42.1%), as excessive ultrafiltration is a common dialysis complication leading to xerosis in many cases.

On studying factors affecting the development of xerosis, we found that lower dialysis efficacy (Kt/V) was associated with higher incidence of xerosis, which may be due to less toxins removal contributing to xerosis. Additionally, we found that higher total leukocytic count (TLC) was significantly associated with xerosis. This might be a result rather than a cause as disturbed skin barrier observed in uremic xerosis in children with CKD may increase the risk for cutaneous infections and inflammation, elevating neutrophil count and subsequently TLC [7]. However, we couldn't find significant associations with other clinico-demographic, dialysis, and laboratory data.

This agrees with AI-Rubaia et al. et al. [23] who made a descriptive study on 174 CKD adult patients and found that high dialysis efficacy rates were associated with low incidence of xerosis. On the contrary, the pediatric study by Wojtowicz-Prus et al. [7] found that xerosis was more common in hemodialysis patients than those receiving conservative treatment, as excessive ultrafiltration is a common dialysis complication leading to xerosis in many cases, additionally patients with hypocalcemia had more xerosis. The difference from our results might be because a significant percentage of our patients received OL-HDF sessions where excessive ultrafiltration is less common.

On studying factors affecting the development of pruritus, we found that pruritic patients had higher hemoglobin levels than non-pruritic ones, otherwise no significant associations were found between pruritis and other clinico-demographic, dialysis, and laboratory data. A cohort adult study [24] on 70 CKD patients reported nearly the same results, where there was no correlation between occurrence of pruritus and demographic or clinical data, however, they noticed that higher dialysis efficacy (Kt/V), and dialysis duration may reduce the prevalence of pruritus. On the other hand, a study by Pisoni et al. **[25]** that was conducted on 300 dialysis units in 12 countries, stated that increasing dialysis dose leads to an improvement in uremic pruritus in hemodialysis patients owing to better removal of uremic toxins, additionally, iron deficiency anemia, hypercalcemia, and hyperphosphatemia were associated with pruritus.

Also, a CKD pediatric study [7] reported that pruritus was slightly higher in patients receiving hemodialysis than those receiving conservative treatment (23.5% vs. 18.4%), where they explained this by assuming that itching in CKD pediatric patients might be a symptom secondary to systemic disease, and that it progresses with the CKD stage thus patients on dialysis were more affected. Pallor (35.7%), and hyperpigmentation (20%), were commonly seen at the sun exposed areas; meanwhile post inflammatory hyperpigmentation was reported in 4.28%.

The low incidence of these dermatological manifestations in our CKD patients, might be attributed to proper management of anemia with appropriate

supplementation of ESA and hematinic, additionally due to the used dialysis modalities; OL-HDF, HF HD and hybrid of both, which probably have positive impact on anemia and hyperpigmentation, as the pathophysiology of hyperpigmentation is thought to involve the accumulation of middle-molecular-weight molecules like urochrome pigments, carotenoids, and α- and β-melanocyte-stimulating hormone [26]. These molecules are easily cleared by high-flux haemodialysis (HF-HD) and OL-HDF hemodiafiltration (HDF) [27], [28]. On the contrary, Attia EA et al., [20] had previously included some CKD5d pediatric patients from our center, where pallor accounted for 18.6% and hyper-pigmentation was seen in 39.5%, nevertheless, these results were obtained from our center before the era of the implementation of HDF and HF-HD at our dialysis unit.

Previous pediatric [21] and adult [14] studies found that the most common manifestation in their patients was pallor due to the high prevalence of iron deficiency anemia in their CKD patients. The difference in prevalence of hyperpigmentation and pallor might be attributed to the criteria used in diagnosis of pallor, where we depended on skin examination for diagnosis of pallor, while others [29] reported pallor in all their study participants when mucosal pallor was considered.

Hair abnormalities in the form of hair loss, sparse and lusterless hair accounted for 11.4% of cases, where hair loss was related to the primary disease diagnosis, which was SLE, meanwhile sparse and lusterless hair was due to low sebum secretion. Another pediatric study [20] reported hair changes in 34.9% patients, including hair loss and dry brittle hair, meanwhile an adult study [21] found hair changes in 30% of their CKD patients, where the flag hair was the commonest finding (19.5%), followed by tractional alopecia (5.5%) due to the turbans custom wearing in male patients, and hair braiding and tying in female patients, additionally, diffuse hypertrichosis (5%) that was attributed to prednisolone therapy owing to the primary renal disease. Obviously, the difference in prevalence of hair changed can be attributed to the original disease as well as traditional and nutritional factors.

Nail abnormalities in the form of onychomycosis were reported in only one of our patients (1.4%), owing to chronic steroid use due to his primary diagnosis of podocytopathy, meanwhile 34.9% of patients had nail changes as reported in another study **[20]** that reflected different systemic diseases and age groups. Also, nail changes were reported in 44.5% [21], however it was nonspecific.

LIMITATIONS OF THE STUDY

Limitations of our study include small number of patients and limited geographic distribution of patients, being from urban areas mostly.

CONCLUSION

Dermatological changes are not uncommon in pediatric CKD patients, where xerosis and pruritis were the most reported skin changes while hair and nail changes were less frequently reported. The higher dialysis efficacy was associated with less development of xerosis and probably less prevalence of pallor, while higher TLC was associated with xerosis. The stage of CKD had no direct effect on

the development of skin, nail, and hair changes. Prompt diagnosis of these symptoms, and appropriate treatment can enhance quality of life in pediatric CKD patients.

RECOMMENDATIONS

Periodic dermatological assessment of pediatric CKD patients is essential and will ensure a better quality of life for these patients.

ABBREVIATIONS

ACEi	Angiotensin-converting-enzyme inhibitors
ARBs	Angiotensin receptor blockers,
BB	Beta blockers
CAKUT	Congenital anomalies of the kidney and urinary tract
CCB	Calcium channel blocker
CKD	chronic kidney disease
CKD5d	CKD stage 5 on regular hemodialysis
ESA	Erythropoiesis-Stimulating Agents
GFR	Glomerular filtration rate
HD	hemodialysis
HF-HD	high flux conventional hemodialysis
K/DOQI	the Kidney Disease Outcomes Quality Initiative
KDIGO	kidney disease Improving Global Outcomes
Kt/V	hemodialysis efficacy
NRS	Numeric rating scale
OL-HDF	online-hemodiafiltration
RRT	renal replacement therapy
SD	standard deviation
TLC	total leukocytic count
VAS	VAS: Visual analogue scale

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STATEMENTS

Ethics approval and consent to participate.

This study was approved by the Ethics Committee of Faculty of Medicine, Ain Shams University, with the ethics code. Ethical approval was obtained from the Research Ethics Committee of Faculty of Medicine, Ain Shams university (*FMASU MS 63/2023)*. Also, written informed consent was obtained from the parent of the participating children.

Consent for publication

"Not applicable"

Availability of data and material

"Available for your request, anytime"

Conflict of interest

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