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Half and Half Nail (Lindsay's Nail) for Prediction of Biochemical Disorders and Unveiling its Etiopathogenesis in Chronic Kidney Disease Stage 5

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ABSTRACT

Background: Specific nail abnormalities, such as half-and-half nails (sometimes called Lindsay's nails), are frequently associated with chronic kidney disease (CKD). In 1963, William B. Bean first noted it in two of his renal illness patients. Half-nail deformities have a mysterious origin that has yet to be identified. It doesn't improve with dialysis, but it goes away completely following a kidney transplant.

Objective: This study was aimed to shed light on study the predictive value of half-and-half nail for biochemical disorders in patients with CKD stage 5 and try to unveil its etiopathogenesis.

Patients and methods: This case-control study included a total of 100 patients with chronic kidney disease, stage 5, classified into four equal groups, the first two groups were without hemodialysis, and One has regular nails, while the other has half-and-half nails, the second two groups were on hemodialysis and one without half and half nails and the other group with half-and-half nails.

Results: According to kidney function tests and other laboratory results, this study found no statistically significant difference (p value >.05) between the study groups. Patients with half-and-half nails had a higher mean age and duration of hemodialysis, both of which were statistically significant ($p<0.05$), and additionally, the research groups varied greatly in terms of the prevalence of DM as a root cause of CKD.

Conclusion: It could be concluded that there are significant positive correlations between age, duration on hemodialysis, diabetes as causes of chronic kidney disease (CKD), and presence of half -and- half nails.

Keywords: Half-and-half nails, chronic kidney disease, Diabetes mellitus, hemodialysis

INTRODUCTION

To have CKD, also known as chronic renal disease, is that you have kidney damage or an eGFR of less than 60 ml/min/1.73 m^2 that has persisted for at least three months. It is a condition characterized by a progressive decrease in kidney function that eventually necessitates renal replacement therapy (dialysis or transplantation) [(1)].

One of the main causes of chronic renal failure (CRF) and the subsequent need for dialysis in patients is the development of diabetes mellitus and hypertension. Other diseases as chronic glomerulonephritis, amyloidosis, systemic erythematous lupus, and some genetic diseases (polycystic kidneys) may impair kidney function [(2)].

Almost all the body's systems are impacted by CRF, which can lead to neurological, gastrointestinal, cardiovascular, pulmonary, hematological, endocrine, metabolic, illness of the skin or the nails. Patients with CRF have been seen to experience alterations in skin pigmentation, bullous dermatosis, metastatic calcinosis, perforating diseases, xerosis, and pruritis [(3)].

Half-and-half nails, absent lunula, and splinter hemorrhages are the nail conditions most frequently observed in CRF patients [(4)].

It was in 1963 when William B. Bean first described half-and-half nails in two of his renal illness patients [(5)]. One of its other names is " Lindsay's nails" which was established by Lindsay in 1967. About 40% of individuals with chronic renal illness have this finding, although it is not pathognomonic [(6)].

In this case, the nail bed is dominated by a brownish-red distal band, which occupies 20-60% of the nail bed, and is clearly separated from the white proximal band. Nails, particularly fingernails, are susceptible, but toenails can get it too. Band width has no effect on serum creatinine concentrations [(6)]. According to the 1968 description by Baran, Gioanni, it has a tight relationship with chronic renal illness [(7)].

Little is known about what may have led to its creation. There's a suggestion that urea's toxicants activate melanocytes, leading to an increase in distal nail melanin deposition. Other possible explanations include thickening of the capillary walls and increased nail bed capillary density. Proximal white band may be caused by chronic anemia [(8)].

Nail changes of a similar nature have been associated to a wide variety of diseases and disorders, such as Crohn's, Kawasaki, Behcet's, cirrhosis, zinc deficiency, pellagra, and HIV infection. On the other hand, it is a very reliable clinical indicator of end stage renal disease [(9)].

Because this illness is benign and simply needs counselling and assurance, treatment is only cosmetic. The transition band often doesn't alter following dialysis, but it does after a successful kidney transplant. Typically, disappearance takes two to three weeks [(10)].

The study's primary objective was to study the predictive value of half-and-half nail for biochemical disorders in patients with CKD stage5 and try to unveil its etiopathogenesis.

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PATIENTS AND METHODS

This case-control study included a total of 100 patients with chronic kidney disease, stage 5, attending at Kobry El-Kobba Military Hospital's Hemodialysis Unit and Outpatient Clinic, Department of Internal Medicine, Benha University Hospital. This study was conducted between September 2020 to September 2021.

The included 100 CKD patients, stage 5 were divided into four equal groups; **Group 1** consisted of 25 patients **not** on hemodialysis without half-and-half nails, **Group 2** consisted of 25 patients **not** on hemodialysis with half-and-half nails, **Group 3** consisted of 25 patients on hemodialysis without half-and-half nails, and **Group 4** consisted of 25 patients on hemodialysis with half-and-half nails,

Inclusion criteria included patients with chronic kidney disease, stage 5.

Exclusion criteria included patients with acute renal failure, CKD stages 1, 2, 3, 4, Crohn's disease, Kawasaki disease, Behcet's disease, cirrhosis, zinc insufficiency, pellagra, HIV infection, and those receiving renal transplantation.

All patients were subjected to medical history taking, nails examination, photographing of any lesions they had, echocardiography, and electrocardiography (ECG). Laboratory investigations included complete blood count (CBC), serum creatinine, serum urea, and serum uric acid were done. Various other blood and urine tests, including the sedimentation rate (ESR), C-reactive protein (CRP), albumin, calcium, phosphorus, sodium, potassium, bicarbonate, alkaline phosphatase, parathyroid hormone, fasting blood sugar, glycosylated hemoglobin (HbA1c), lipid profile, ferritin, and albumin creatinine ratio (ACR) were collected from the most recent data in the patients' files.

Ethical consent:

An approval of the study was obtained from Benha University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical methods

SPSS version 26 was used for the coding and analysis of the gathered data (IBM Corp., Armonk, NY, USA). Mean and standard deviation were used to describe the quantitative data, while frequencies (the number of occurrences) and relative frequencies (the proportion of occurrences) were used to summaries the categorical data. Comparisons between groups were made using unpaired t tests. The Chi-square (X^2) test was utilized in order to examine differences in category information. The exact test was used instead when the expected frequency was less than 5. Elements deemed to be useful predictors of the occurrence were isolated using a logistic regression model. If the probability value was less than 0.05, then the result was significant.

RESULTS

Of the included 100 patients the overall percentage of male gender was 92% (92) and female gender 8% (8), with mean age 62.410±13.623 years and overall average duration of hemodialysis (only 50 patients) 36.660±31.589 months. The kidney function tests and the other laboratory results in this study did not differ significantly (p value > 0.05) between the study groups. Patients with half-and-half nails had significantly higher averages age and duration of hemodialysis (p <0.05). (Tables 1–2). Also, Diabetes mellitus as a risk factor for chronic kidney disease (CKD) led to a statistically significant difference in the study populations (Tables 3).

Table (1): Association between age distribution and half-and-half nail in the study groups

Group	Age (Years)	Groups						T-Test	
		No Half and half nail			Half and half nail			t	P-value
Non-Hemodialysis	Range (Years)	18	-	81	43	-	84	-2.046	**0.046***
	Mean ±SD (Years)	60.120	±	17.829	68.320	±	9.141		
Hemodialysis	Range (Years)	35	-	76	26	-	80	-2.381	**0.021***
	Mean ±SD (Years)	56.600	±	11.405	64.600	±	12.332		

Table (2): Association between duration of hemodialysis and half-and-half nail in the study groups

Group	Duration of hemodialysis (Months)	Groups						T-Test	
		No Half and half nail			Half and half nail			t	P-value
Hemodialysis	Range (Months)	4	-	96	12	-	132	-2.696	**0.010***
	Mean ±SD (Months)	25.320	±	22.302	48.000	±	35.665		

Table (3): Association between etiology of chronic kidney disease and half-and-half nail in the study groups

Group	Etiology of CKD	Groups				Chi-Square	
		No Half and half nail		Half and half nail			
		N	%	N	%	X^2	P-value
Non-Hemodialysis	DM	6	24.00	14	56.00	4.083	**0.043***
	HTN	11	44.00	7	28.00	0.889	0.346
	Chronic interstitial nephritis	0	0.00	0	0.00	-	-
	Chronic glomerulonephritis	0	0.00	0	0.00	-	-
	Polycystic kidney disease	2	8.00	0	0.00	0.521	0.471
	Obstructive	3	12.00	2	8.00	0.200	0.655
	Unidentified	3	12.00	2	8.00	0.200	0.655
Hemodialysis	DM	4	16.00	15	60.00	6.368	**0.012***
	HTN	9	36.00	5	20.00	1.143	0.285
	Chronic interstitial nephritis	4	16.00	2	8.00	0.667	0.414
	Chronic glomerulonephritis	2	8.00	0	0.00	0.521	0.471
	Polycystic kidney disease	3	12.00	0	0.00	1.418	0.234
	Obstructive	1	4.00	1	4.00	0.000	1.000
	Unidentified	2	8.00	2	8.00	0.000	1.000

By logistic regression analysis ,there was increasing risk of developing half-and-half nails with presence of DM of patients on non-hemodialysis by univariate logistic regression analysis and there was increasing risk of developing half and half nails with increasing of age, duration of hemodialysis and presence of DM of patients on hemodialysis by univariate logistic regression analysis, also there was increasing risk of developing half-and-half nails with increasing of duration of hemodialysis and presence of DM of patients on hemodialysis by Multivariate logistic regression analysis (Tables 4–5).

Table (4): Univariate logistic regression analysis of various variables for prediction of half-and-half nails in non-hemodialysis groups

	Univariate analysis			
	p-value	OR	95%CI	
Age (Years)	0.06	1.05	0.99	1.10
Gender	0.559	2.087	0.177	24.615
Uric acid (mg/dL)	0.384	1.151	0.838	1.581
PLT count (10^3/µl)	0.166	1.006	0.998	1.013
HB (g/dL)	0.910	1.020	0.726	1.433
WBCS count (10^3/µl)	0.901	0.989	0.826	1.184
ESR (mm/hr)	0.686	1.003	0.988	1.019
CRP (mg/L)	0.791	0.996	0.963	1.029
Albumin (g/dL)	0.415	1.699	0.475	6.072
Ca (mg/dL)	0.302	1.328	0.775	2.277
Phosphorus (mg/dL)	0.539	0.792	0.377	1.665
Na (mEq/L)	0.715	0.971	0.827	1.139
K (mEq/L)	0.265	1.700	0.669	4.322
Parathyroid hormone (pg/mL)	0.081	0.997	0.995	1.000
Ferritin (ng/L)	0.310	1.002	0.998	1.007
Serum cholesterol (mg/dL)	0.309	1.007	0.994	1.019
TG (mg/dL)	0.886	1.001	0.993	1.008
LDL (mg/dL)	0.920	0.999	0.981	1.018
HDL (mg/dL)	0.857	1.006	0.943	1.073
VLDL (mg/dL)	0.943	1.002	0.947	1.060
Serum creatinine (mg/dL) Pre	0.440	1.353	0.628	2.915
Blood urea (mg/dL) Pre	0.063	1.019	0.999	1.039
DM	**0.024***	**4.030**	**1.201**	**13.526**
HTN	0.242	0.495	0.153	1.606
Obstructive	0.639	0.638	0.097	4.188
Unidentified	0.639	0.638	0.097	4.188
HbA1c (%)	0.740	1.124	0.564	2.240
FBS (mg/dL)	0.856	1.003	0.966	1.042
2hpp (mg/dL)	0.942	1.000	0.989	1.012
ACR (mg/g)	.926	1.000	.996	1.004

Table (5): Univariate and Multivariate logistic regression analysis of various variables for prediction of half-and-half nails in hemodialysis groups

	Univariate analysis				Multivariate analysis			
	p-value	OR	95%CI		p-value	OR	95%CI	
Age (Years)	**0.028***	**1.060**	**1.006**	**1.117**	0.068	1.054	0.996	1.116
Gender	0.639	1.568	0.239	10.300				
Duration of hemodialysis (Months)	**0.023***	**1.031**	**1.004**	**1.058**	**0.028***	**1.030**	**1.003**	**1.057**
Uric acid (mg/dL)	0.581	0.902	0.625	1.301				
PLT count (10^3/µl)	0.109	1.009	0.998	1.021				
HB (g/dL)	0.560	0.882	0.579	1.345				
WBCS count (10^3/µl)	0.174	1.266	0.901	1.780				
ESR (mm/hr)	0.366	1.010	0.989	1.031				
CRP (mg/L)	0.088	1.054	0.992	1.119				
Albumin (g/dL)	0.842	0.819	0.116	5.807				
Ca (mg/dL)	0.506	1.210	0.690	2.120				
Phosphorus (mg/dL)	0.474	.860	0.568	1.300				
Na (mEq/L)	0.298	1.078	0.936	1.243				
K (mEq/L)	0.221	1.550	0.768	3.128				
Parathyroid hormone (pg/mL)	0.230	0.999	0.997	1.001				
Ferritin (ng/L)	0.070	1.002	1.000	1.005				
Serum cholesterol (mg/dL)	0.088	0.987	0.973	1.002				
TG (mg/dL)	0.655	0.999	0.992	1.005				
LDL (mg/dL)	0.876	1.002	0.981	1.022				
HDL (mg/dL)	0.765	0.989	0.923	1.061				
VLDL (mg/dL)	0.945	1.002	0.937	1.073				
Serum creatinine (mg/dL) Pre	0.683	1.055	0.817	1.362				
Serum creatinine (mg/dL) Post	0.882	0.964	0.593	1.568				
Blood urea (mg/dL) Pre	0.100	1.017	0.997	1.037				
Blood urea (mg/dL) Post	0.987	1.000	0.966	1.035				
DM	**0.002***	**7.875**	**2.071**	**29.940**	**0.004***	**9.681**	**2.095**	**44.741**
HTN	0.213	0.444	0.124	1.592				
Chronic interstitial nephritis	0.393	0.457	0.076	2.755				
Obstructive	1.000	1.000	0.059	16.928				
Unidentified	1.000	1.000	0.130	7.717				
HbA1c (%)	0.680	1.226	0.465	3.235				
FBS (mg/dL)	0.759	1.006	0.966	1.048				
2hpp (mg/dL)	0.871	1.001	0.986	1.017				

DISCUSSION

Nail abnormalities are common in chronic renal disease, affecting more than 75% of patients on hemodialysis [(11)]. Half-and-half nails, or Lindsay's nails, were first hypothesized by Bean in 1964 and defined in patients with chronic renal sickness by Lindsay in 1967. This transformation is diagnostic of CKD regardless of whether dialysis is being used to treat the disease. Many different diseases and even healthy persons might display these symptoms.

Usually defined as having a white proximal section and a brown, pink, or red distal band that is readily separated by a transverse line, half-and-half nails can occur on both fingernails and, much less frequently, toenails [(12)]. It was also observed that the nail plate pressure did not cause these nail modifications to disappear [(13)].

The specific mechanism of half-and half nails is unknown. Tissue concentration of MSH may be higher than previously thought, according to one theory [(8)].

One such explanation is that they result from nail bed edema [14]. Half-and-half nails do not yet have a known cure; however, kidney transplantation may bring about remission [15].

In the current study, 50% of the patients had half-and-half nails including 25 patients on hemodialysis and 25 patients on non-hemodialysis, which was higher than in previous studies. **Thomas *et al.*** [16] found that 36.36% prevalence of half-and-half nails and more commonly seen in hemodialysis patients which was in agreement with the findings of the present study. Also, **Rashpa *et al.*** [17] **and Khanna *et al.*** [18] reported that half-and-half nails were found in 16.4%, and 28% respectively, of their patients. We found also 25% of the patient having half-and-half nails on hemodialysis which was consistent with the findings of other previous studies of **Raiesifar *et al.*** [19], **Baghestani *et al.*** [20] **and Udayakumar *et al.*** [21] which reported the prevalence of half-and-half nails as 50%,35%, and 21%, respectively. In the studies of **Yaghoubi *et al.*** [22] **and Tajbakhsh *et al.*** [23] the prevalence of half-and-half nail was reported to be 5.8% and 8%, respectively, which was in contrast with the results of the present study.

In our study we found a significant correlation between presence of half-and-half nail and old age with mean age of patients had half-and-half nail on non-hemodialysis was 68.320 ± 9.141 years and on hemodialysis was 64.600 ± 12.332, which agreed with the findings of study of **Rashpa *et al.*** [17] where the mean age of patients on non-hemodialysis was 61.5 ±12.3 years and on hemodialysis was 51.8 ±13.3 in despite the difference in sample size. Also, **Hajheydari and Makhlough** [24], found a significant association of the half-and-half nails with the age of the patients on hemodialysis which agreed with the findings of our study, but he reported that there were no significant changes with hemodialysis duration which was in contrast with the results of the present study. In addition, **Tajbakhsh *et al.*** [23] found a significant correlation between half-and-half nail and age of patients of hemodialysis and the mean age of the patients was 73.9 ± 11.3 which was in consistent with the results of the present study in despite the difference in sample size. On the other hand, **Thomas *et al.*** [16], **Aqil *et al.*** [25] **and Mourad *et al.*** [26] found no significant relationship between nail involvement and patient age which was in contrast with the results of the present study.

In our study we found a significant correlation between presence of half-and-half nail and duration of hemodialysis where the mean duration of patients had half-and-half nail on hemodialysis was 48.000 ± 35.665 months. These results were nearly agreed with **Rashpa *et al.*** [17] **and Khanna *et al.*** [18] who reported that the mean duration of hemodialysis was 15.6 ±10.6 and 10.8 ± 9.5 months respectively in despite the difference in sample size. Also, our study was in agreement with the findings of previous studies by **Tercedor *et al.*** [4] **and Pico *et al.*** [27]. On the other hand, **Saray *et al.*** [3], **Aqil *et al.*** [25], **Dyachenko *et al.*** [28], **and Salem *et al.*** [29] found no correlation between presence of half-and-half nail and duration of hemodialysis which was in contrast with the results of the present study.

In our study we found that The etiology of CKD showed that diabetic nephropathy was the most common cause of CKD in 15 (60%) patients with half-and-half nail on hemodialysis and 14 (56%) patients with half-and-half nails on non-hemodialysis which was in agreement with the findings of study of **Rashpa *et al.*** [17] which reported that diabetic nephropathy was the cause of CKD in 21 patients on hemodialysis and 48 patients on non-hemodialysis in despite the diffe

rence in sample size, also **Thomas *et al.*** [16] reported diabetic nephropathy in 42 patients in despite the difference in sample size, was consistent with the the findings of the current study. In addition, **Tajbakhsh *et al.*** [23] **and Tajalli *et al.*** [30] reported that diabetic nephropathy was the most common cause of CKD in 17, 45 patients on hemodialysis respectively, which despite the difference in sample size, was consistent with the findings of the present study. on the other hand, **Khanna *et al.*** [18] reported that Chronic glomerulonephritis was the cause of CKD in 90 patients while **Raiesifar *et al.*** [19] reported that Hypertensive nephropathy was the cause of CKD in 32 patients which was in contrast with the results of the present study in despite the difference in sample size. On the other hand, **Dyachenko *et al.*** [28] reported that no significant relationship between nail involvement and underlying diseases.

In our study, there was increasing risk of developing half-and-half nails with presence of DM of patients on non-hemodialysis by univariate logistic regression analysis.

In our study, there was increasing risk of developing half-and-half nails with increasing of age, duration of hemodialysis and presence of DM of patients on hemodialysis by univariate logistic regression analysis.

In our study, there was increasing risk of developing half-and-half nails with increasing of duration of hemodialysis and presence of DM of patients on hemodialysis by Multivariate logistic regression analysis.

CONCLUSION

It could be concluded that there are significant positive correlations between age, duration on hemodialysis, diabetes as causes of chronic kidney disease (CKD), and presence of half -and- half nails.

Based on the results of the current study, it is recommended to perform further studies with larger sample sizes and longer duration to do more

investigations for half and half nails and making the results be easily generalizable.

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REFERENCES

1. **Inker L, Astor B, Fox C *et al.* (2014):** KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis., 63(5):713-35.
2. **National Kidney Foundation (2012):** KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis., 60:850–886.
3. **Saray Y, Seçkin D, Güleç A *et al.* (2004):** Nail disorders in hemodialysis patients and renal transplant recipients: a case- control study. J Am Acad Dermatol., 50:197–202.
4. **Tercedor J, Hernandez B, Rodenas J (2001):** Nail diseases in hemodialysis patients: Case-control study. Br J Dermatol., 144: 415-448.
5. **Bean W (1963):** A discourse on nail growth and unusual fingernails. Trans Am Clin Climatol Assoc., 74:152–167.
6. **Lindsay P (1967):** The half-and-half nail. Arch Intern Med., 119(6): 583–7.
7. **Baran R, Gioanni T (1968):** Half and half nail (equisegmented azotemic fingernail). Bull Soc Fr Dermatol Syphiligr., 75:399–400.
8. **Galperin T, Cronin A, Leslie K (2014):** Cutaneous manifestations of ESRD. Clin J Am Soc Nephrol., 9:201–218.
9. **Markova A, Lester J, Wang J *et al.* (2012):** Diagnosis of common dermopathies in dialysis patients: A review and update. Semin Dial., 25(4): 408–18.
10. **Iorizzo M, Daniel C, Tosti A (2011):** Half and half nails: A past and present snapshot. Cutis, 88:138-9.
11. **James W, Berger T, Elston D (2011):** Andrew's Diseases of the Skin. E-Book. Elsevier Health Sciences. Pp. 773. https://www.elsevier.com/books/andrews-diseases-of-the-skin/james/978-0-323-54753-6
12. **Cabana M, Ensor A, Tunnessen W *et al.* (1998):** Picture of the month: Half-and-half fingernails. Arch Pediatr Adolesc Med., 152(9): 923-4.
13. **Gagnon A, Desai T (2013):** Dermatological diseases in patients with chronic kidney disease. J Nephropathol., 2(2): 104–9.
14. Brewster **U (2006):** Dermatologic manifestations of end-stagerenal disease. Hospital Physician, 42:31–35.
15. **Lupi O, Sessim M, Duarte D *et al.* (2011):** Cutaneous manifestations in end-stage renal disease. An Bras Dermatol., 86:319–326.
16. **Thomas E, Thomas A, Pawar B (2012):** A prospective study of cutaneous abnormalities in patients with chronic kidney disease. Indian Journal of Nephrology, 22(2): 116. doi:10.4103/0971-4065.97127.
17. **Rashpa R, Mahajan V, Kumar P *et al.* (2018):** Mucocutaneous Manifestations in Patients with Chronic Kidney Disease: A Cross-sectional Study. Indian Dermatol Online, 9 (1): 20-26.
18. **Khanna D, Singal A, Kalra O (2010):** Comparison of cutaneous manifestations in chronic kidney disease with or without dialysis. Postgraduate Medical Journal, 86(1021), 641–647.
19. **Raiesifar Z, Tahery N, Shirzadegan R *et al.* (2019):** Assessment of Skin Manifestations in End-Stage Renal Disease Patients Undergoing Hemodialysis in Shahid Beheshti Hospital of Abadan and Vali-e-Asr Hospital of Khorramshahr. Jundishapur J Chronic Dis Care, 8(1):e83381. doi: 10.5812/jjcdc.83381
20. **Baghestani S, Zare S, Mohammadi F *et al.* (2010):** Cutaneous manifestions in chronic renal failure patients under hemodialysis in Shahid Mohammadi Hospital Dialysis Center in Bandar Abbas. Journal of Dermatology and Cosmetic, 1(4): 187-194.
21. **Udayakumar P, Balasubramanian S, Ramalingam K *et al.* (2014):** Cutaneous manifestations in patients with chronic renal failure on hemodialysis. Indian J Dermatol Venereol Leprol., 72:119-125.
22. **Yaghubi R, Niloufar S, Latifee S (2002):** Cutaneous manifestations of end stage renal disease under hemodialysis. Iran J Dermatol., 5:29–34.
23. **Tajbakhsh R, Dehghan M, Azarhoosh R *et al.* (2014):** "Mucocutaneous manifestations and nail changes in patients with end-stage renal disease on hemodialysis." Saudi journal of kidney diseases and transplantation: an official publication of the Saudi Center for Organ Transplantation. Saudi Arabia, 24(1): 36-40.
24. **Hajheydari Z, Makhlough A (2008):** Cutaneous and mucosal manifestations in patients on maintenance hemodialysis: a study of 101 patients in Sari, Iran. Iranian Journal of Kidney Diseases, 2(2):86-90.
25. **Aqil N, Nassiri A, Gallouj S *et al.* (2019):** Nail Disorders in Patients with Chronic Renal Failure. J Dermatol Res Ther., 5: 065. doi.org/10.23937/2469-5750/1510065
26. **Mourad B, Hegab D, Okasha K *et al.* (2014):** Prospective study on prevalence of dermatological changes in patients under hemodialysis in hemodialysis units in Tanta University hospitals, Egypt. Clin Cosmet Investig Dermatol., 7:313-9.
27. **Pico M, Lugo-Somolinos A, Sánchez J *et al.* (1992):** Cutaneous alterations in patients with chronic renal failure. Int J Dermatol., 31: 860-63.
28. **Dyachenko P, Monelise A, Shustak A *et al.* (2007):** Nail Disorders in patients with chronic renal failure and undergoing haemodialysis treatment: A case control study. J Eur Acad Dermatol Venereol., 23: 340-344.
29. **Salem A, Al Mokadem S, Attwa E *et al.* (2008):** Nail changes in chronic renal failure patients under haemodialysis. J Eur Acad Dermatol Venereol., 22: 1326–31.
30. **Tajalli F, Mirahmadi S, Mozafarpoor S *et al.* (2021):** Mucocutaneous manifestations of patients with chronic kidney disease under hemodialysis: A cross-sectional study of 49 patients. Dermatologic Therapy, 34(4). doi:10.1111/dth.15015.