

Comparison of nail changes in chronic kidney disease under haemodialysis with patients on oral maintenance therapy

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Abstract

Objective To compare the frequency of nail changes in Chronic Kidney Disease patients undergoing haemodialysis with patients on maintenance therapy.

Methods This analytical cross-sectional study was carried out at Dermatology and Nephrology Department, Sahiwal Teaching Hospitals, Sahiwal, after approval from Institutional Ethical Review Committee. A total of 158 patients with chronic kidney disease of either sex and age were divided into two groups: Group A (patients under regular haemodialysis) Group B (patients on oral therapy). Patient's demographic, clinical and laboratory data were recorded in predesigned proforma. Data were analyzed by using SPSS version 28.

Results Out of total 158 patients, male female ratio was 1.1:1 and majority of patients (63.3%) were above age of 40 years. Most commonly reported nail changes in both groups were absence of lunula (65%, 57%), longitudinal ridging (54%, 58%) and onycholysis (45%, 35%) but variations were observed in their frequencies. There was no statistically significant difference in nail changes of both groups.

Conclusion Patients with CKD undergoing HD therapy have slight higher frequency of nail changes compared to patients on maintenance therapy. Further studies with large sample size may elaborate results.

Key words

Chronic kidney disease; Haemodialysis; Maintenance therapy.

Introduction

Chronic kidney disease (CKD) is defined as glomerular filtration rate (GFR) below 60ml/min per 1.73 m² for three months or more. In CKD,

renal functions progressively decline, in which patient needs replacement therapy in order to retain normal functions of kidney.¹ Multiple systems of human body including the neurological, gastrointestinal, cardiovascular, pulmonary, hematological, endocrine and dermatological systems are affected by CRF.² Skin changes may commence from early stage of renal impairment to end stage renal disease. These cutaneous manifestations also observed in patents with hemodialysis and after kidney transplantation.³ It has been observed that 50-100% patients with end stage kidney disease

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develop skin changes. Xerosis, pruritus, pallor, pigmentary changes, acquired perforating dermatoses and nail changes are frequently reported skin manifestations.⁴

Nail changes occurrence in chronic kidney diseases among various populations varies. It ranges from 60 to 75% in different studies. Etiopathogenesis of nail disorders in CKD has not yet been known exactly. Nail disorders usually persist even with the replacement therapies for the renal disease. Nail changes commonly reported are half-and-half nail, absent lunula, onychomycosis, leuconychia, onycholysis and splinter hemorrhage.^{5,6}

Multiple studies have been carried out previously to assess skin and nail changes in patients with CKD and those undergoing regular HD.^{6,7} The main rationale of carrying out this study is that internationally, there is limited data availability of such case control studies with the aim of comparison of nail changes in CKD undergoing HD and CKD patients on oral maintenance therapy. Thus, this will help in estimation of the extent of the disease and offer the patients timely diagnosis and treatment to decrease the morbidity.

This study was carried out with objective of comparing the frequency of nail changes in chronic kidney disease patients undergoing hemodialysis with CKD patients on oral maintenance therapy. Furthermore, we determine the associations of frequency of nail changes with demographic and laboratory parameters in both groups.

Methods

This analytical cross-sectional study was carried out in dermatology and nephrology department Sahiwal Teaching Hospital, Sahiwal after approval from Institutional Ethical Review

Committee (vide letter No. S.No-47-/IRB/SLMC/SWL, dated 06/06/2022). An informed written consent of study and nail pictures was taken. Sample size of 158 patients was calculated from Open Epi.

$$n = [DEFF * Np(1-p)] / [(d^2 / Z^2_{1-\alpha/2} * (N-1) + p * (1-p))]$$

Confidence level of 80% and margin of error 5%.

A total 158 patients with Chronic kidney disease of either sex and age greater than 14 years were enrolled in the study and divided equally into two groups through nonprobability consecutive sampling: Group A (patients under regular haemodialysis) Group B (patients on oral maintenance therapy). Patients with Genodermatoses with nail changes and history of nail trauma were excluded from study. History was taken and general physical and nail examination was performed. Nail changes were reviewed by two consultant dermatologists. Complete blood picture and kidney function tests and fasting blood glucose levels were conducted. All demographic, clinical data including nail changes and laboratory data of patients were recorded in predesigned proforma. Data was analyzed by using SPSS version 26

Data was analyzed using SPSS version 25. Qualitative variables such as sex and nail changes were presented as frequencies and percentages. Quantitative variables such as age were presented as mean and SD. To determine the change in frequency of nail changes in two groups chi-square test was used. P value <0.05 was considered significant.

Results

Out of total 158 CKD patients, male to female ratio was 1.1:1 with more male patients (58%) as compared to female (42%) in hemodialysis patients (group A) while female (52%) subjects were more than males (48%) in patients on

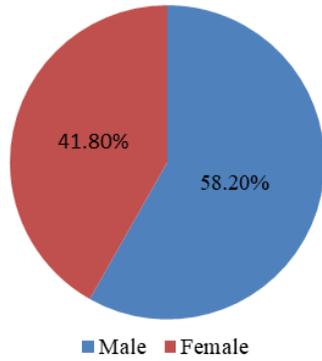


Figure 1 Gender distribution of patients in Haemodialysis group.

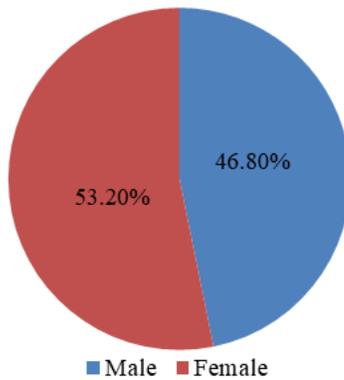


Figure 2 Gender Distribution of patients in maintenance group.

maintenance therapy (Group B) (**Figures 1, 2**). Majority of patients (63.3%) were above the age of 40 years as depicted in **Table 1**. Hypertension and diabetes mellitus were most frequently reported underlying disease in both group subjects. Among laboratory parameters mean hemoglobin level was less in group B and mean creatinine level was more in group A patients (**Table 2**).

Most commonly observed nail changes in both groups were absence of lunula (65%, 57%),

Table 1 Distribution of patients in each group according to age (n=158).

Age(years)	Group A n (%)	Group B N (%)
15-40	33 (20.88%)	25 (15.82%)
41-50	36 (22.78%)	33 (20.88%)
>50	10 (8.00%)	21 (13.29%)
Total	79 (51.66%)	79 (49.99%)
Mean±SD	44.22±14.50	48.92±19.51

longitudinal ridging (54%, 58%) and onycholysis (45%, 35%) but variation was seen in their frequencies. No statistically significant difference was observed in nail changes of both groups. Results showed slight higher frequency of nail changes among the hemodialysis group compared to patients on maintenance therapy. Frequency of different nail changes in both groups summarized in the **Table 3**.

Discussion

In chronic kidney disease, irremediable damage occurs affecting multiple organs leading to uremic syndrome if not treated timely. Variability and diversity in cutaneous and ungal manifestations of end stage renal disease have been observed in previous studies. Nail changes in CKD may result from uremia or treatment. We planned to measure frequency of nail changes with CKD patients on hemodialysis and on maintenance therapy. Nail abnormalities reported in the earlier studies ranged from 50% to 80% of end stage renal disease.^{2,5} Our study results showed no statistically significant difference in frequency of nail changes in both groups of CKD. This also has been reported in other studies.⁵

There was slight predominance of male patients in the study subjects which was concordance with other studies but in some studies higher

Table 2 Clinical and laboratory data of patients.

Underlying condition	Group A n (%)	Group B n (%)
Hypertension	37 (23.4%)	27(17.08%)
Diabetes mellitus	27(17%)	19(12.02%)
Obstructive	6(3.8%)	18(11.39%)
Drug-induced	6(3.8%)	7(4.4%)
Nephrotic	3(1.8%)	6(3.7%)
Polycystic	0(0%)	2(1.2%)
Laboratory parameters	Group A (Mean±SD)	Group B (Mean±SD)
Hb	10.18±11.74	9.72±2.43
Blood urea	107±57	122±59
Serum creatinine	7.5±3.6	5.6±3.5

Table 3 Frequency of nail changes in CKD.

Nail changes	Group A n (%)	Group B n (%)	P-value
Absent lunula	64 (40.50)	58 (36.7)	0.255
Longitudinal ridges	54 (34.17)	58 (36.7)	0.484
Onycholysis	45 (28.4)	52 (33)	0.253
Transverse ridges	37 (23.4)	28 (17.7)	0.146
Leukonychia	22 (13.9)	22 (13.9)	1.00
Half & half nails	18 (11.39)	20 (12.6)	0.710
Subungual hyperkeratosis	13 (8.2)	12 (7.6)	0.827
Melanonychia	10 (6.3)	7 (4.4)	0.441
Brittle nails	8 (5.06)	10 (6.3)	0.617
Ungual cyanosis	6 (3.7)	4 (2.5)	0.513
Beau lines	6 (3.7)	2 (1.2)	0.147
Splinter hemorrhages	5 (3.1)	6 (3.7)	0.755
Onychomycosis	3 (1.8)	2 (1.2)	0.649
Koilonychia	3 (1.9)	3 (1.8)	1.00
Paronychia	1 (0.6)	4 (2.5)	0.173
Muehrcke's lines	1 (0.6)	1 (0.6)	1.00
Anonychia	1 (0.6)	11 (6.7)	1.00

range of male proportion among CKD patients have also been reported.^{6,8}

In the current study, a majority of patients were above age of 40 years which was in concordance with studies carried out by Malkud *et al.* and Thomas *et al.*^{4,9} Underlying etiological factors of CKD varies worldwide. Diabetes Mellitus and hypertension are the commonest causes of end stage renal disease in the literature published.^{10,11} In this study, Hypertension (23.4% group A, 17% group B) was reported to be the most common cause followed by Diabetes Mellitus (17% group A, 12% group B) as a leading underlying causes of CKD which was in concordance with a study conducted by Pushpa *et al.* (hypertension 37.1%, diabetes 21.2%).⁸

Mechanisms leading to various nail changes in CKD patients are not exactly known. In this study, the most common nail changes observed in both groups (haemodialysis and maintenance therapy) of CKD were similar but difference existed in their frequencies (**Table 3**).

The absence of lunula is demonstrated by the nonvisual representation of the visible part of the nail matrix.² Absence of lunula (40.5%) was the

most reported nail findings in CKD on hemodialysis in this study. Higher frequency (60%, 48.8%) was observed by Pushpa *et al.* and Elahi *et al.*; respectively.^{8,12} In contrast, lower frequency (4%, 16%) was seen in studies carried out by Kabra *et al.* and Dyachenko *et al.* respectively.^{2,13} Frequency of absence of lunula findings (36.7%) in patients on maintenance treatment was similar (34.8%) to the study by Pushpa *et al.*⁸ Dyachenko *et al.* noticed lower frequency (13%) in CKD on maintenance treatment.¹³

Half and half nails manifest as proximal white portion and distal (20–60%) brownish portion with sharp demarcation. It is postulated as histologically an increase of vessel wall thickness and melanin deposition.¹⁴ In present study, half and half nail frequency was almost equal (11.8%, 12%) in both study groups of CKD. Variation existed in frequency of half and half in hemodialysis (38.8%) and maintenance treatment (21.7%) group of CKD in the study conducted by Pushpa *et al.*⁸ Higher frequency (76.6%) of half and half nails in CKD patients have been reported in a study by Sheikh *et al.*¹⁵

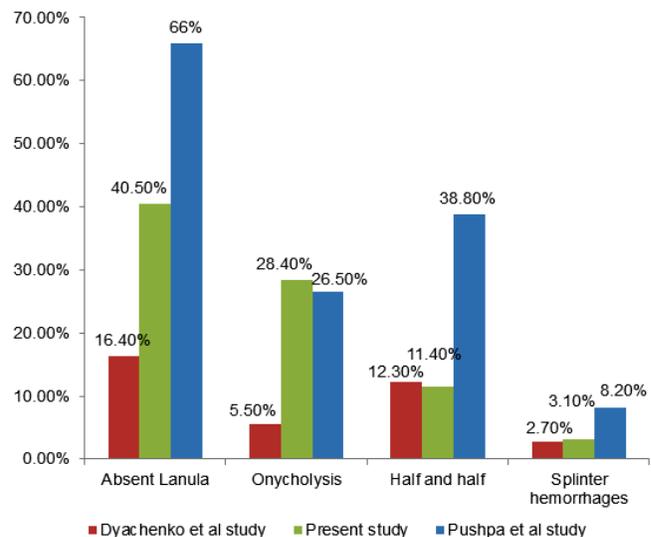


Figure 3 Comparison of frequency of nail changes in CKD on haemodialysis in various studies.

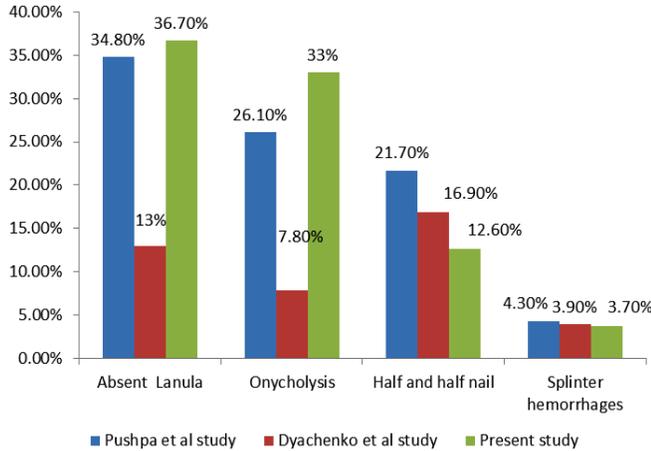


Figure 4 Comparison of frequency of nail changes in CKD on maintenance therapy in various studies.

Onycholysis was seen in a significant number of patients in both hemodialysis and maintenance treatment group of CKD in this study. Pushpa *et al.* noticed onycholysis close to the present study.⁸ Higher frequency (71.4%) of onycholysis was observed in a study done by Aqil *et al.*⁵ However in most studies, a lower frequency was noted. Other causes leading to onycholysis need to rule out such cases like trauma, fungal infection, eczema, drug reactions.

Splinter hemorrhages are non-blanchable longitudinal haemorrhages in the distal portion of the nail bed. It most mostly results from trauma. Other etiological factors of splinter haemorrhages are idiopathic, skin conditions as psoriasis, lichen planus, various systemic disorders, infections and vasculitis.¹⁶ Present study results showed 3.1% and 3.7% in both groups respectively of CKD. In contrast, Puspha *et al.* reported higher frequency of splinter haemorrhages in (8.2%, 4.3%) both groups of CKD.⁸

Frequency of longitudinal ridges in both study groups of CKD in our study were more than one third of total patients (34.2% and 36.7%). With advancing age longitudinal ridging increases in most cases. Vascular insufficiency, e.g. collagen vascular disease, rheumatoid arthritis, peripheral

vascular disease, frostbit. Although, no association of longitudinal ridges with specific disease has not been established.

Leuconychia may result from CKD, liver cirrhosis, chemotherapeutic agents or renal transplant. Current study results showed the same leuconychia frequency (13.9%) in both hemodialysis and maintenance groups of CKD. However, Adejumo *et al.* in his study reported higher frequency (28.3%) of leukonychia in CKD on hemodialysis as compared to CKD patients on maintenance therapy (10.7%).¹⁷ Likewise, higher frequency (25%) of leuconychia had been observed in the study carried out by Aqil *et al.*⁵

Melanonychia manifest as a brown to black discoloration of nail plate. It results from activation and hyperplasia of melanocyte. Common associations of melanonychia are lichen planus, psoriasis, drugs antimalarial, chemotherapeutic agents, congenital melanocytic naevus, melanoma and endocrine disorders like Addison disease.¹⁸ Present study reported melanonychia of 6.3% and 4.4% respectively in hemodialysis group and maintenance group of CKD patients. In contrast, Pushpa *et al.* observed higher frequency of melanonychia (27.2% and 30.4%) in hemodialysis and maintenance group of CKD.⁸ Lower frequency (4.6%) of melanonychia was noted in a study conducted by Adégbidi *et al.* which was in in concordance with the present study's results.¹⁹

The current study had a few limitations. Large sample size could further elaborate on variation in nail changes among study subjects in both groups.

To conclude our discussion, nail changes have been noticed in considerable number among both groups of chronic kidney disease patients. Multiple factors could be postulated in

occurrence of slight higher frequency of nail changes in hemodialysis group. Although variations existed in frequencies of these nail changes, there was no statistically significant difference in the two groups.

Conclusion

Patients with CKD undergoing HD therapy have slight higher frequency of nail changes compared to patients on maintenance therapy. Further studies with large sample size may elaborate on these results.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Conflict of interest Authors declared no conflict of interest.

Authors' contribution

ZR: Conception and design of study, acquisition, analysis & interpretation of data, final approval and proof reading, maintaining accuracy of the study.

SH, SUK: Design of study, acquisition and interpretation of data, final approval, maintaining accuracy of study.

AA, HK: Conception of study, acquisition and interpretation of data, final approval of the version, maintaining accuracy of whole work.

US: Conception and design of study, analysis and interpretation of data, final approval and proof reading of study, maintaining accuracy/ integrity of whole work.

References

1. Floege J, Bello A, Kowar B, Kossi ME, Nahas ME. Comprehensive clinical nephrology, 4th edition. United States of America: Elsevier Saunders; 2010:907- 10.
2. Kabra R, Acharya S, Shukla S, Kumar S. Nail Changes in the Chronic Kidney Failure– A Cross Sectional Study. *J Datta Meghe Inst Med Sci Uni.* 2022;**17**:2-6.
3. Goel V, Sil A, Das A. Cutaneous Manifestations of Chronic Kidney Disease, Dialysis and Post-Renal Transplant: A Review. *Indian J Dermatol.* 2021;**66(1)**:3-11.
4. Malkud S, Dyavannanavar V, Varala S. Cutaneous manifestations in patients with chronic kidney disease on hemodialysis. *J Pak Assoc of Dermatol.* 2020;**30(3)**:490-6.
5. Aqil N, Nassiri A, Gallouj S, Mernissi FZ. Nail Disorders in Patients with Chronic Renal Failure. *J Dermatol Res Ther.* 2019; **5**:065. doi.org/10.23937/2469-5750/1510065
6. Saray Y, Sec,kin D, Lin Gu Lec AT, Akgu Sn, Haberal M. Nail disorders in hemodialysis patients and renal transplant recipients: A case-control. *J Am Acad Dermatol.* 2004;**30(2)**:197-203.
7. Martinez MAR, Gregório CL, Santos VP, Bérqamo RR, Machado Filho CDS. Nail disorders in patients with chronic renal failure undergoing hemodialysis. *An Bras Dermatol.* 2010;**85(3)**:318-2.
8. Pushpa M, Murthy SC, Anvar MI. Mucocutaneous manifestations and nail changes in patients with end stage renal disease: A cross-sectional study. *J Pak Assoc of Dermatol.* 2021;**31(2)**:191-200.
9. Thomas EA, Pawar B, Thomas A. A prospective study of cutaneous abnormalities in patients with chronic kidney disease. *Indian J Nephrol.* 2012;**22(2)**:116-20.
10. Kohagura, K. The public health impact of hypertension and diabetes: a powerful tag team for the development of chronic kidney disease. *Hypertens Res.* 2023;**46**:339–40.
11. Wang M, Li J, Li Y, Yao S, Zhao M, Wang C, *et al.* The effects of hypertension and diabetes on new-onset chronic kidney disease: A prospective cohort study. *J Clin Hypertens.* 2020;**22**: 39– 46.
12. Elahi I, Nasir Z, Ahmed S, Raheel S. Chronic kidney disease; prevalence of nail changes. *Professional Med J.* 2018; **25(3)**:392-5.
13. Dyachenko P, Monselise A, Shustak A, Ziv M, Rozenman D. Nail disorders in patients with chronic renal failure and undergoing haemodialysis treatment: a case-control study. *J Eur Acad Dermatol Venereol.* 2007;**21(3)**:340-4.
14. De Berker D AR, Richert B, Baran R. Acquired Disorders of the Nails and Nail Unit. Griffiths C .EM, Barker J , Bleiker T, Chalmers R , Creamer D. Rook's Textbook of Dermatology. 9th Edition. UK. Wiley Blackwell: 2016; Pages.95.12
15. Sheikh M, Malik LM, Jahangir M. Cutaneous manifestations of chronic renal failure. *J Pak Assoc Dermatol.* 2014;**24 (2)**:150-5.

16. Harber R, Khoury R, Tomb R, Kechichian E. Splinter hemorrhages of the nails: A systematic review of clinical features and associated conditions. *Int J Dermatol*. 2016;**55(12)**:1304-10.
17. Adejumo OA, Madubuko RC, Olorok AB, Aina OT. Skin changes and dermatological life quality index in chronic kidney disease patients in a tertiary hospital in Southern Nigeria. *Niger J Clin Pract*. 2019;**22**:245-50.
18. Gradinaru TC, Mihai M, Beiu C, Tebeica T, Giurcaneanu C. Melanonychia - Clues for a Correct Diagnosis. *Cureus*. 2020; **12(1)**:e6621.
19. Adégbidi H, Akpadjan F, Houngbo O, Vigan J, Dégboé B, Agbessi N, *et al*. Epidemiological and clinical profile of dermatoses observed in chronic hemodialysis patients at the National Teaching Hospital (NTH-HKM) of Cotonou, Benin. *Dermatol Res Pract*. 2020; **2020**:9186309.