Frequency and Effect of Cutaneous Manifestations on Quality of Life in Patients with End-Stage Renal Disease Undergoing Hemodialysis

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ABSTRACT

Objective: To determine the frequency of skin manifestations found in end-stage renal disease (ESRD) patients undergoing dialysis, while assessing their effect on the quality of lives of the same patients.

Study Design: Descriptive cross-sectional study.

Place and Duration of the Study: Benazir Bhutto Hospital, Holy Family Hospital, and Hussain Lakhani Hospital, from 12th December 2021 to 13th October 2022.

Methodology: Seventy-three Patients undergoing hemodialysis were enrolled in the study. Skin manifestations were defined as "cutaneous signs and symptoms related to ESRD unrelated to the symptoms resulting from any primary dermatological disorder or other systemic diseases". Data on the skin manifestations of their disease and their effect on patients' quality of life were collected by using a 2-part questionnaire. The first part consisted of demographic details along with the type of skin disorders faced by the patient and the second part of the questionnaire comprised of the dermatology life quality index (DLQI). The data were entered and analysed using the statistical package for social sciences (SPSS) version 23.0.

Results: Xerosis and pruritus were most commonly reported (83.7%), followed by nail changes (18.6%) and skin discolouration (16.3%). The median duration of dialysis was 36 (1-180) months and there was no significant increase in skin symptoms with the increase in the duration of dialysis (p=0.082). The median DLQI score was 3 (range:0-10) A significantly higher number of females (n=14) reported associated mental discomfort with their skin symptoms of pruritis as compared to males (n=5, p=0.008).

Conclusion: Cutaneous manifestations have variable effects on the quality of life of ESRD patients. Adopting a multidisciplinary approach early in the management may help to minimise the mental discomfort of these patients and bring an improvement in their quality of life.

Key Words: *End-stage renal disease (ESRD), Hemodialysis, Skin manifestations, Pruritus, Quality of life.*

How to cite this article: Tameezuddin A, Malik IJ, Arshad D, Tameezuddin A, Chaudhary NA, Asad Z. Frequency and Effect of Cutaneous Manifestations on Quality of Life in Patients with End-Stage Renal Disease Undergoing Hemodialysis. *J Coll Physicians Surg Pak* 2023; **33(04)**:406-410.

INTRODUCTION

Chronic kidney disease (CKD) is defined as "a persistent abnormality in kidney structure or function (*eg*, glomerular filtration rate [GFR] <60 mL/min/1.73 m^2 or albuminuria ≥30 mg per 24 hours) for more than 3 months".[1]

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Received: December 10, 2022; Revised: January 16, 2023; Accepted: March 29, 2023
DOI: https://doi.org/10.29271/jcpsp.2023.04.406

It is commonly associated with diabetes and hypertension and is divided into five stages. Stage 5 (also known as ESRD) is clinically defined as renal failure with GFR of less than 15 mL/min/1.73 m^2. It represents an irreversible decline in kidney functions and the patients require long-term renal replacement therapy (dialysis, renal transplant).[2-4] Recent surveys show that the incidence of this disease is rising at an alarmingly high rate in Pakistan, with one study reporting it to be 100/million per year.[5,6]

Skin is very commonly involved during the disease course with pruritis and xerosis being the two most commonly reported findings and cutaneous involvement is more common in patients with ESRD.[7-10] The effect of skin symptoms and lesions on the mental health of CKD patients is of particular interest to clinicians

as addressing them brings about a quantifiable improvement in the patients' quality of life. Pruritis and xerosis cutis afflict many patients with ESRD and their adverse effects over the mental health of the patients is often underestimated.[11] The dermatology life quality index (DLQI) is one of the most commonly used validated questionnaires which has been used to assess the effect of skin diseases on the quality of life of patients.[12,13]

While there is a growing interest in the association of skin lesions with chronic kidney disease, their impact over the mental well-being of patients is often overlooked. There have been many published articles regarding the quality of life in patients with ESRD but the impact of specific dimensions of the disease such as the skin manifestations over the quality of these patients have not been explored frequently in the local as well as the international literature. This study intended to bridge the gap between the existing knowledge about the frequency of skin manifestations found in ESRD patients undergoing dialysis while assessing their effect on the quality of lives of the same patients. To find this association using specific quality of life index (DLQI) may help the clinicians to make informed decisions. This may ultimately help the healthcare professionals involved in the care of these patients to develop a better understanding of these cutaneous presentations and their early management which may help bring a positive change in their patients' lives. The objective of this study was to determine the frequency of skin manifestations found in ESRD patients undergoing dialysis while assessing their effect on the quality of lives of the same patients.

METHODOLOGY

This multicenter study was conducted at two government hospitals affiliated with Rawalpindi Medical University namely Benazir Bhutto Hospital and Holy Family Hospital Rawalpindi and one private hospital *i.e.*, Hussain Lakhani Hospital. All the hospitals had dedicated dialysis centers. It was carried out from 12th December 2021 to 13th October 2022. This is a descriptive cross--sectional study and the sample size was calculated to be 73 using WHO sample size calculator by the following formula:

$N = Z^2 * P*(1-P)/d^2$ where; Z = 1.96 at 95% confidence interval, d = margin of error which was fixed at 5%, and p = approximately 95%.[8]

Non-probability consecutive sampling technique was used for the collection of data. Diagnosed cases of ESRD who were on regular dialysis for at least one month were included. Patients who were acutely ill, or those with a diagnosed mental health disorder (anxiety, depression *etc.*) were excluded from the study along with the patients who had an established skin disorder unrelated to their kidney disease. Skin manifestations were defined as "cutaneous signs and symptoms related to end-stage-renal disease unrelated to the symptoms resulting from any primary dermatological disorder or other systemic diseases".

Data were collected after taking approval from the ethical review boards / head of departments of the concerned hospitals (ERB number for data collected at the allied hospitals of Rawalpindi Medical University was RSRS-2021-DER-22). Informed consent was taken from the patients before the start of the interview. License to use the DLQI was obtained through relevant authorities at Cardiff University UK (License ID CUQoL3651).

The data were collected by one-on-one interviews by using a 2-part questionnaire. The first part consisted of demographic details along with the type of skin disorders faced by the patient. The second part of the questionnaire comprised of the DLQI which consisted of 10 questions. Each question had a maximum score of 3 and total maximum score of the questionnaire was 30 with a minimum score of 0. Detailed dermatological examination was carried out (by the medical officer/ Internal medicine resident conducting the interview, according to a checklist approved by the consultant dermatologist) to corroborate the findings described by the patients.

The data were entered and analysed using the statistical package for social sciences (SPSS) version 23.0 (IBM Corp, Armonk, US). The results were reported as frequencies, percentages and figures. Chi-square tests were applied for qualitative variables. Normality of quantitative variables was evaluated by histograms, Shapiro-Wilk tests, and Kolmogorov-Smirnov tests. Non-parametric tests (Mann Whitney U test) were employed to compare the medians of quantitative variables across categories of qualitative ones. A p-value of less than 0.05 was considered significant.

RESULTS

Out of a total of 73 patients, 41 (56.2%) were males and 32 (43.8%) were females. The median age was 42 (20-100) years. The median duration of dialysis was 36 (1-180) months. Skin manifestations were reported by 43 patients (58.9%). There was no significant association of a specific gender with the development of dermatological signs and symptoms during the disease course (p=0.131). There was no significant increase in skin symptoms with the increase in the duration of dialysis (p=0.082). Table I shows the frequency of different skin manifestations reported by the study participants.

Out of the 43 patients with dermatological signs and symptoms, 29 (67.4%) reported that dialysis had an effect on their symptoms while no effect was reported by 14 (32.6%) patients. Out of these 29 patients, a majority (n=25, 86.2%) were of the opinion that the cutaneous features decreased in intensity and frequency after dialysis.

Five (11.6%) patients had consulted a dermatologist for the cutaneous features resulting from their kidney disease. There was a significant association between gender (5 females as opposed to no male) and seeking a dermatologist's opinion (p=0.020).

Of the 36 patients who had dry skin, 30 (83.3%) had used emollients for the relief of their symptoms and 24 patients (80%) out of them reported an improvement after application while the rest (6 patients; 20%) had no relief. A majority of patients (n=24, 66.7%) reported a generalised dryness of the whole body with no specific skin site predilection.

Table I: Frequency of different skin manifestations in ESRD patients.

Sign/symptom (N=43)	Present n (%)	Not present n (%)
Xerosis	36 (83.7%)	7 (16.3%)
Pruritis	36 (83.7%)	7 (16.3%)
Skin discoloration	7 (16.3%)	36 (83.7%)
Nail changes	8 (18.6%)	35 (81.4%)
Skin infection(s)	3 (7%)	40 (93%)
Rash secondary to drugs taking for kidney disease	3 (7%)	40 (93%)

Table II: Significant associations of gender.

Parameter		Gender		p-value*
		Male	Female	
DLQI median (Range)		3 (0-10)	4(1-10)	0.024
Mental discomfort	Yes	5 (29.4%)	14 (73.7%)	0.008
	No	12 (70.6%)	5 (26.3%)	
Dermatologist's consult for skin manifestations	Yes	0 (0%)	5 (22.7%)	0.020
	No	21 (100%)	17 (77.3%)	

**Mann Whitney U test was applied for testing the significant association of gender with DLQI score while the associations with mental discomfort and dermatologist's consult were sought by using Chi-Square test.*

More than half [n=19 (52.8%)] of the patients with pruritis reported that itching caused them mental discomfort. Generalised pruritis of the whole body was most commonly reported [n=17 (47.2%)] followed by pruritis on both upper and lower limbs (n=8, 22.2%). Isolated upper limbs pruritis was reported by 3 patients (8.3%).

Face and neck were the most common site of pigmentation with 3 (42.8%) out of the 7 patients with dyspigmentation reporting these sites as the areas of affliction. Two patients (28.6%) reported that they had alteration in skin color at the trunk.

The most common nail abnormality was reported to be rough/ragged nails [n=4 (50%)] followed by broken nails (n=1, 12.5%), nail pigmentation (n=1, 12.5%) and half and half nails (n=2, 25%).

Out of the 3 patients who reported having skin infections, one (33.3%) was found to have bacterial infection while one (33.3%) was found to have viral skin infection [*Herpes simplex*] in the past. Record could not be traced for one patient who reported to have infection.

Three (4.1%) patients reported that they had developed skin rash secondary to drug therapy of their kidney disease. Recombinant human erythropoietin injection was implicated in all the 3 patients

The median DLQI score was 3 (range: 0-10). The score was significantly higher in females (median 4, range=1-10) as compared to males [median 3 (range=0-10, p=0.024)].

A significantly higher number of females (n=14) reported associated mental discomfort with their skin symptoms of pruritis as compared to males (n=5, p=0.008).

DISCUSSION

CKD affects many organs of the body including skin, and the cutaneous manifestations include pruritis, xerosis, nail changes, dyschromias, purpura, mucosal changes along with certain specific dermatoses (such as acquired perforating dermatoses, calciphylaxis, calcinosis cutis, bullous diseases, eruptive xanthoma, and nephrogenic systemic fibrosis). There are many proposed mechanisms of these symptoms (proinflammatory T lymphocytes and cytokines, mu-receptor activation or the release of pruritogens in the causation of pruritis) but there has been no consensus regarding the exact pathogenesis of many of the cutaneous signs and symptoms.[8-10]

Out of the 73 patients enrolled in this study, a majority (58.9%) reported skin symptoms and signs. This was less than the frequency of skin lesions in a study conducted in Lahore, Pakistan, which reported that almost all the patients on hemodialysis had at least one skin manifestation.[13] In contrast, Masmaudi *et al*. reported a lower (38.4%) percentage of dermatological manifestations.[14] Despite these contrasting figures, there is a general consensus that the majority of patients with ESRD have established skin manifestations which has been attributed to a variety of factors such as delayed or suboptimal management of kidney disorder due to inadequate awareness of patients regarding early symptoms of their kidney diseases.[7,14] There was no significant increase in skin symptoms with the increase in the duration of dialysis in this study (p=0.082). Despite this finding, the causal relationship between the increase in risk of cutaneous complications with the duration of kidney disease cannot be ruled out and the early recognition of the disease with prompt management may help reduce the progression of advanced complications including dermatological disorders in patients with CKD.

Xerosis and pruritis were the most commonly reported symptoms (83.7%). This is in line with the findings of a multitude of other studies published internationally.[10,15] Most of the patients (80%) reported a decrease in skin dryness after using emollients which underlines the significance of this

simple yet highly effective treatment modality in the relief of these common dermatologic complaints in CKD patients.[16] Anees *et al*. reported skin pigmentation to be the predominant skin finding in their study (86%) as compared to this study in which pigmentary changes were revealed in less than one-quarter of patients. Pigmentation disorders are described with a variable frequency in different studies and the different findings may result from a wide spectrum of skin types globally as well as the accuracy of clinical examination.[14]

Nail changes were observed in 18.6% patients with skin manifestations and ragged/rough nails were the most common type of abnormality reported while skin infections were reported in less than 10 percent of patients. The frequency of these findings was lower than those reported in a study conducted in India, in which nail changes and skin infections afflicted 61% and 20% of patients, respectively.[17] Three patients reported that they had developed skin rash secondary to drug therapy of their kidney disease and interestingly, recombinant human erythropoietin injection was found to be the culprit in all the 3 patients. Erythropoietin has been implicated in a number of skin and systemic reactions secondary to its administration, but its benefits far outweigh the risks and since its introduction, this drug has been safely administered to millions of CKD patients worldwide.[18] There was no significant association of a specific gender with the development of dermatological signs and symptoms during the disease course (p=0.131).

The effect of skin lesions on the quality of life of ESRD patients has been often discussed but not frequently quantified, especially in this setup. DLQI is a validated questionnaire which has been used to assess the effect of skin diseases on the quality of life of patients. This ten-part questionnaire is used to quantify the impact of skin disorders on the mental health of these patients with total scores ranging from 0-30. The DLQI scores are interpreted as no impairment of quality of life (0–1), mild impairment (2–5), moderate (6–10), severe (11–20) or very severe impairment (21-30).[12,13] The median DLQI score was found to be 3 (range: 0-10) and there was a significant difference between the score reported by the two genders with higher scores being reported by females (p=0.024). Kurniawan *et al*. studied the impact of xerosis and pruritus on the quality of ESRD patients' lives and reported a median score of 2 (range:0-14).[11] Another study reported an adverse impact on the sleep quality of CKD patients due to skin symptoms (such as pruritus) but there may be a need to develop a specific scoring system to elaborate the effect of dermatological disorders in CKD patients in order to better quantify the mental health toll of these manifestations over the patients' well-being.[19]

A significantly higher proportion of female patients reported feeling mental discomfort due to pruritus (p=0.008). Similarly, all the CKD patients who had consulted a dermatologist for their skin symptoms were females (p=0.020). These significant findings reinforce the existing belief that the impact of skin lesions on the quality of life of females is much more than their male counterparts particularly in the developing countries.[20] The stigmatisation of the affected individuals and the entrenched gender roles in certain societies may exacerbate this problem. While the larger behavioural change of a society may require educational reforms and focused information campaigns, the role of physicians in helping their patients to navigate this treacherous path of coping and self-acceptance cannot be underestimated.[21,22] They are in a uniquely advantageous position to bring a positive change in their patients' lives and ensure the mental as well as the physical well-being of their patients. A multidisciplinary approach is often required in CKD patients due to a multitude of organ systems involved and the treating physicians should invite the input of a psychiatrist at an early stage to minimise the mental discomfort of their patients.

This study is one of the few studies in Pakistan which have tried to find the relationship between skin manifestations of ESRD and their impact on patient's quality of life. It was unique in its elaboration of the quantifiable mental impact of the cutaneous manifestations of ESRD using an internationally validated questionnaire *i.e*., DLQI. The relatively smaller sample size may affect the generalisability of the results but the study paves the path for further local research projects of larger scale in this setup in order to add to the existing databases and help the local clinicians in making evidence-based decisions regarding their patients' health.

CONCLUSION

Cutaneous manifestations of ESRD represent an often-overlooked aspect of this multi-system disorder. The skin lesions and symptoms have a mild to moderate impact on the quality of life of patients with chronic kidney disease as evident by the validated DLQI score, and their early management may help to improve the quality of their lives.

ETHICAL APPROVAL:

Ethical approval for conducting this study was obtained from the Ethical Review Board, Rawalpindi Medical University in September 2021 (Letter No. RSRS-2021-DER-22).

PATIENTS' CONSENT:

Informed consent was taken from the patients before the start of the interview and examination. The patients were informed about the intended use of their data in the research article.

COMPETING INTEREST:

There was no conflict of interest of any author associated

with the publication of this research and no funding was received for the publication of this manuscript.

AUTHORS' CONTRIBUTION:

AT, IJM: Involved in the conception of the design, collection and interpretation of data and drafting the manuscript including discussion and introduction.

DA, AT: Analysed the data and contributed towards the final draft of the manuscript mainly the results portion.

NAC, ZA: Involved in data collection, data analyses, proofreading, and literature review.

All the authors have approved the final version of the manuscript to be published.

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