BANTAO Journal 2017; 15(2): 52-57

BJ

BANTAO Journal

Original article

Prevalence of Dermatologic Manifestations Among Patients on Chronic Hemodialysis: Single Center Study

Amir Abdollah Zangivand[1], Mohsen Taherkhani[2], Kamran Soleimanitadi[1] and Fatemeh Samieerad[3]

[1]Takestan Social Security Organization hospital C.E.O., Takestan, Iran, [2]Department of Dermatology, Qazvin University of Medical Sciences, Qazvin, Iran, [3]Department of Pathology, Qazvin University of Medical Sciences, Qazvin, Iran

Abstract

Introduction. A large number of studies have revealed different cutaneous manifestations in patients with CKD, but few of them have compared the prevalence of these manifestations in CKD patients with general population. It was our aim to compare the prevalence of dermatologic manifestations among patients on maintenance HD in Tamin Ejtemaei Hospital in Takestan (located in Qazvin province) with the general population.
Methods. Forty-five patients undergoing regular hemodialysis and 45 individuals who were randomly selected from healthy hospital staff, were examined for dermatologic manifestations. The statistical analysis was performed with the statistical package SPSS Software (version 11.0, SPSS Inc., Chicago, Ill, USA). P value less than 0.05 was considered significant.
Results. Thirty-four (75.5%) hemodialysis patients and 11(24.4%) from the control group were found to have at least one dermatologic manifestation. Of all skin manifestations, most commonly observed in hemodialysis patients were pruritus and xerosis. Also, fungal, bacterial and viral infections were seen in hemodialysis patients. Seborrheic keratosis, skin Bowen's disease and skin basal cell carcinoma were seen in these patients.
Conclusion. These skin manifestations cause decreased patient function and poor quality of life. For better management of patients, awareness of involved medical team is necessary. These patients need periodical dermatologic evaluation.

Keywords: skin manifestations, hemodialysis

Introduction

Chronic kidney disease (CKD) is a progressive loss of renal function that is classified into 5 stages according to abnormally decreased and deteriorated glomerular filtration rate [1,2].

Patients with CKD on hemodialysis (HD) may experience a wide variety of dermatologic, mucosal membranes, hair and nail manifestations including hyperpigmentation, ichthyosis, pruritus, xerosis, onychomycosis, onycholysis, subungual hyperkeratosis, splinter hemorrhages, brittle hair, and sparse body scalp hair during treatment. Sometimes these symptoms are not seen during diagnosis of kidney failure and are only detected in advanced cases of the disease but are more often associated, directly or indirectly, with uremia in its broadest sense [3].
A large number of studies have revealed different cutaneous manifestations in patients with CKD, but few of them have compared the prevalence of these manifestations in CKD patients with healthy individuals in the general population [4-6]. It was our aim to compare the prevalence of dermatologic manifestations among patients on maintenance HD in Tamin Ejtemaei Hospital in Takestan (located in Qazvin province) with the general population.

Materials and methods

From June 2016 to March 2017, 45 patients undergoing regular hemodialysis (HD group), and 45 individuals who were randomly selected from hospital staff without any history of kidney function impairment confirmed by renal function tests (control group), were examined for dermatologic manifestations by a qualified dermatologist. The dialysis mode was high-flux membrane by using synthetic membranes including Polyethersulfone_membranes without hemodiafiltration line. Residual renal function (RRF) with average urea and creatinine clearance [(CCr+CU)/2] in 24-h urine (if >1 mL/min and diuresis >100 mL/day, RRF) was considered.
Data collection tool consisted of a check list including the following information: demographic data such as gender, age, smoking, cause of renal failure, primary and secondary diagnoses, medications, duration of renal failure and HD, and dermatologic manifestation.

Correspondence to: Kamran Soleimanitadi, General physician, Takestan Social Security Organization hospital C.E.O., Takestan, Iran. Phone and fax: +98 28 333 699 991 E-mail: tak.tamin.hsp@gmail.com

The study was approved by the Ethics Committee of the Takestan Tamin Ejtemaei Hospital before its initiation, and the protocols used conformed to the ethical guidelines of the 1975 Helsinki Declaration. All participants were informed about the study protocols and a written consent was obtained from each one.
The statistical evaluation was performed by computer analysis with SPSS Software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc, Chicago, Ill, USA). Descriptive statistics such as mean and standard deviation were applied. One way ANOVA, Student's t-test, chi-square, or Fisher's exact test were used, where appropriate, for comparing clinical data between groups. P value less than 0.05 was considered significant.

Results

Among 45 patients in the HD group, 24 (53.3%) were men and 21(46.7%) were women. The mean age of these patients was 48.6±26.4 years (range 17 years-89 years) and the mean dialysis duration was 33.0±16.1 months. The causes of ESRD in the patients were as follows: diabetes mellitus (DM) in 35.5 %, hypertension (HTN) in 35%, chronic glomerulonephritis (CGN) in 11%, chronic interstitial nephritis (CIN) in 9% and other in 9% of subjects (Figure 1).

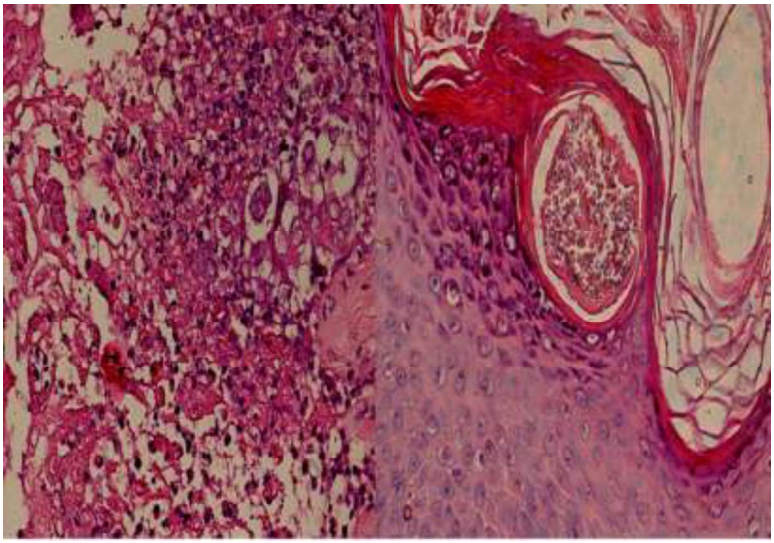

Fig. 1. The causes of ESRD in examined patients.
DM = diabetes mellitus, HTN= hypertension, CGN= chronic glomerulonephritis, CIN= chronic interstitial nephritis

Similar to the HD group, there were 24 males and 21 females in the control group. The mean age was 46.5± 16.5 years.
Overall, 34(75.5%) of HD patients and 11(24.4%) of control group were found to have at least one dermatological manifestation. Several patients had more than one dermatologic manifestation. Among skin manifestation, pruritus was found in 27 patients of the hemodialysis group, and in 8 individuals of the control group. Pruritus was found to be severe in diabetic patients. Xerosis was observed in 16 patients of hemodialysis group, and in 7 individuals of the control group. Skin infections such as fungal, bacterial and viral were seen in 13, 10, and 5 of HD patients, respectively (Figure 2, 3). Also seborrheic keratosis, skin Bowen's disease and skin basal cell carcinoma were seen in 6, 1 and 1 of HD patients, respectively (Figure 4, 5).

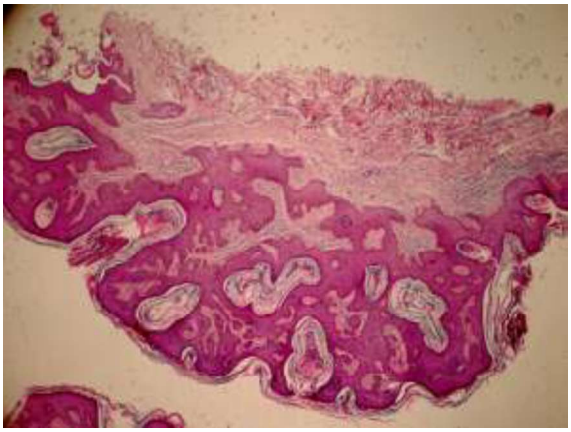

Fig. 2. a) Herpes simplex skin infections including epidermal necrosis, multinucleated keratinocytes with ground glass nuclei and moulding. **b)** Fungal skin infections, dermatophytes including pseudoepitheliomatous hyperplasia of epidermis, fungal spores and hyphae in horny cell layer (200, Hematoxylin & Eosin)

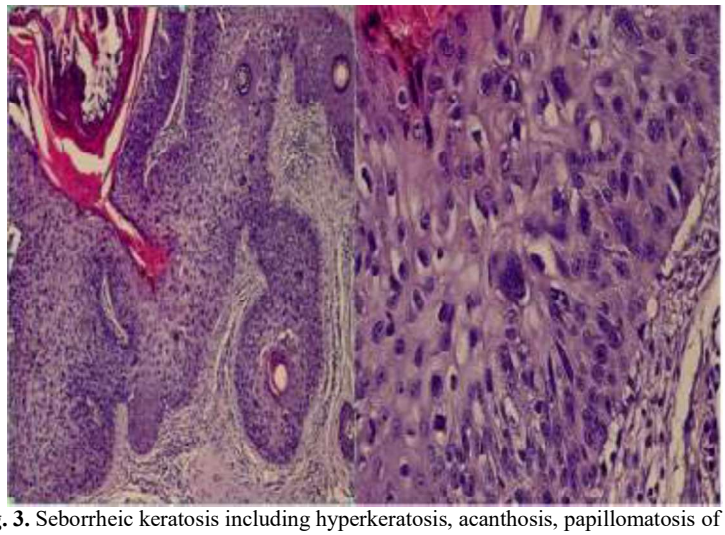

Fig. 3. Seborrheic keratosis including hyperkeratosis, acanthosis, papillomatosis of epidermis with true and pseudohorn cysts (40, Hematoxylin & Eosin)

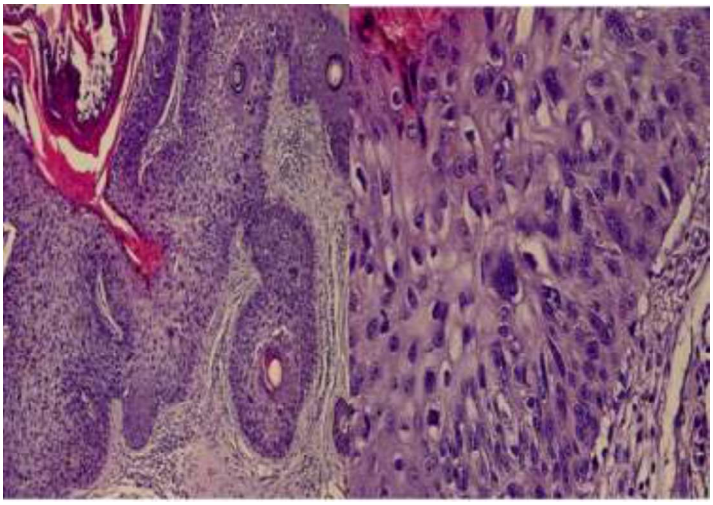

Fig. 4. a) Skin Bowen's disease including epidermal full thickness neoplastic proliferation with hyperkeratosis. B: necrosis, multinucleated keratinocytes with ground glass nuclei and molding (200, Hematoxylin & Eosin). **b)** Tumoral cells have hyperchromatic nuclei with multinucleation, and increased mitotic figures (400, Hematoxylin & Eosin).

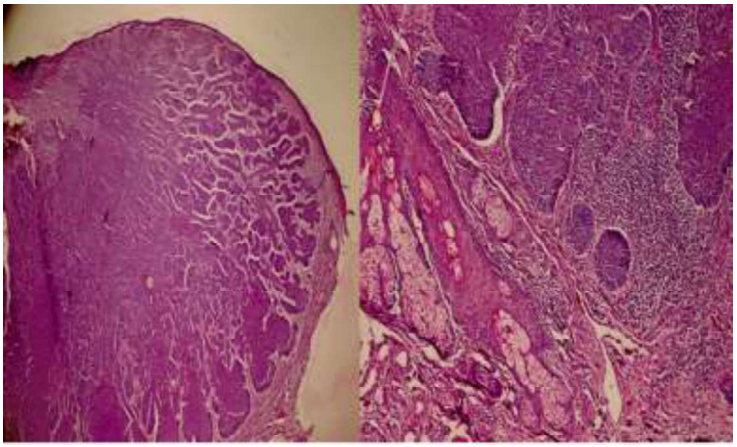

Fig. 5. a) Skin basal cell carcinoma including large tumor masses in the dermis. (100, Hematoxylin & Eosin). **b)** Basaloid tumor cells grow in syncytial pattern with peripheral palisading and cleft. (400, Hematoxylin & Eosin)

Onychomycosis was the most common fungal infections and herpes labialis and zoster were common viral infection in hemodialysis patients. Nail changes were observed in 33 patients of hemodialysis group and in 14 individuals of the control group. Hair changes were observed in 9 patients and mucosal changes were seen in 6 patients of hemodialysis group. The prevalence rates of the different types of manifestations detected in the patients on HD and in the controls are shown in Table 1.

Table 1. The prevalence rates of dermatologic manifestations in case and control groups

Dermatologic manifestations	HD group according to cause of ESRD						Control group	p-value
	HTN	DM	CGN	CIN	others	total		
Pruritus	7	10	3	3	4	27	8	< 0.05*
Xerosis	5	5	2	1	3	16	7	< 0.05*
Pigmentation	3	2	1	1	1	8	5	> 0.05
Fungal	4	6	1	1	1	13	4	< 0.05*
bacterial	3	4	1	1	1	10	3	< 0.05*
viral	1	2	1	0	1	5	3	> 0.05
Acne	1	1	0	1	1	4	4	> 0.05
Necrotic excoriation	1	3	1	0	0	5	3	> 0.05
Ichtus	1	1	0	1	1	4	3	> 0.05
Eczema	0	2	1	0	1	4	3	> 0.05
Aphthous stomatitis	2	0	1	0	1	4	4	> 0.05
Scrotal tongue	1	0	0	1	0	2	3	> 0.05
Furred tongue	0	1	1	0	0	2	2	> 0.05
Seborrheic dermatitis	1	1	2	1	1	6	5	> 0.05
Seborrheic keratoses	1	1	1	1	2	6	6	> 0.05
Skin Bowen's disease	0	1	0	0	0	1	0	> 0.05
Skin basal cell carcinoma	0	1	0	0	0	1	0	> 0.05
Drying and hair fragility	1	1	1	1	0	4	3	> 0.05
Scalp hair loss	1	1	1	0	0	3	2	> 0.05
Hair discoloration	0	0	1	1	0	2	1	> 0.05
Leukonychia	2	2	2	1	1	8	2	< 0.05*
Onychomycosis	1	3	0	0	1	5	2	< 0.05*
Half half nails(Lindsay's nails	2	2	1	1	1	7	2	< 0.05*
Onycholysis	2	2	1	0	1	6	4	> 0.05
Subungual hyperkeratosis	1	0	0	0	1	2	1	> 0.05
Pitting	0	1	0	0	0	1	1	> 0.05
Thin nail	0	0	1	0	0	1	1	> 0.05
Cyanosis	0	1	0	0	0	1	0	> 0.05
Clubbing	1	1	0	0	0	2	1	> 0.05

* *P* value < 0.05 as determined by *t* test

Of the 34 HD patients with at least 1 cutaneous or mucosal manifestation, 26(76.4%) patients were male, 16(47%) patients were ≥65 years of age, 23(67.6%) patients had diabetes mellitus, 23(67.6%) had hypertension, and 24 (70.5%) patients had long-term HD (> 8 years). These results were shown to be statistically related to gender, diabetes mellitus, hypertension and duration of HD (Table 2).

Table 2. Multivariate logistic regression analysis for overall dermatologic manifestation

Factor	HD patients with (n=57) & without (n=18) positive dermatologic manifestations OR(95% CI)	P-Value
Male gender	2.134 (1.056–5.487)	< 0.05*
Diabetes mellitus	1.184 (1.044–2.884)	< 0.05*
Hypertension	1.184 (1.044–2.884)	< 0.05*
Age ≥65	1.004 (0.658–1.586)	> 0.05
Long term hemodialysis	2.134 (1.056–5.487)	< 0.05*

* *P* value < 0.05 as determined by *t* test

Discussion

The occurrences of skin lesions in patients with CKD on hemodialysis are more common than in normal population. The pathogenesis of cutaneous lesions in patients on hemodialysis is multifactorial, including: main etiology of CKD, pro-inflammatory and inflammatory processes, biochemical and metabolic disturbances, uremia, electrolytes disorder, homeopathy and resulted multisystem dysfunction associated with therapeutic modulation effects [7]. Main of skin lesions are benign and their diagnosis is straightforward based on clinical pre-

sentation with good. Few of them including bullous lesions have unfavorable outcome with complication and their diagnosis is expensive since they are based on histopathology and immunofluorescence examinations [8]. The important causes of ESRD in our study subjects were compared with those in other studies [9]. Similar to other research results, in our study a significant number of subjects - 34(75.5%) complained on cutaneous presentations, which were more common in men [10,11]. In our patients, the most frequent dermatologic presentation was pruritus. These results are in agreement with those of De Marchi *et al.* [12] and Szepietowski *et al.* [13]. Among diabetic patients, pruritus was manifested in its severe form, which is similar to the findings of Kumar Kolla P *et al*. [14]. This might be due to multisystemic nature of DM and extensive inflammatory, immunologic interaction in disease course. The main underling etiology of pruritus in patients on hemodialysis is unclear but mutli factorial etiology and many predisposing effectors were described consists of cytokine associated pro inflammatory and inflammatory processes in hyperuremic status, hyper stimulation of inflammatory cellular elements including mast cells, basophils and platelets for degranulation of vasoactive amine including histamine, reactive proliferation and demargination of inflammatory cells including mast cells, hyperparathyroidism, hyperuremic induced polyneuropathy, xerosis, hypoalbominemia and raised of serum ferritin as an acute phase reactant in hyperuremic induced inflammatory status [15-19]. The second most common dermatologic presentation among our subjects was xerosis. This finding was supported by Kumar Kolla P *et al.* results [14]. In patients undergoing regular hemodialysis, sweat glands have diminished size and less than normal/impaired? function. Above changes present due to lower level of epidermal hydration and lipid content than normal epidermis. Also these patients received a large amount of diuretics and had high serum level of vitamin A [3]. Skin infections were seen in 28 of HD patients. This result is in agreement with the results obtained by Udaykumar *et al.*, but higher than those reported by Bakthavatchalu *et al*. [3,9]. Patients on hemodialysis are immunocompromised and immunodeficient subjects. They have decreased count and function of both B and T lymphocytes. Also, there is malfunction of reticuloendothelial system [20-22]. The poor hygiene status of patient also should be considered.

In our study, nail presentations in patients on HD were found in 33 subjects, which number is higher compared to the results of Bakthavatchalu P *et al*., but similar to those of Udayakumar *et al*. and Mookambika RV *et al*. [3,9,11]. The incidence of hair presentations in our HD patients was similar to that presented by Tawade YV *et al.* and Singh G *et al.*, but lower than that of Kumar Kolla P *et al*. findings [22,23,14]. Hair drying and fragility was associated with declined sebaceous discharge of sebaceous glands [3]. The mucosal manifestations were seen in 6 patients, which is similar to Kumar Kolla P *et al.* [14] findings compared to 90% incidence in Cohen GS study [25]. Few causes of oral mucosal changes in patients on HD were described and are as following: epithelial dehydration, breathing via mouth, high level of acid uric in saliva content, disturbances in metabolic pathway for converting acid uric to ammonia [14].

The non-melanocytic skin malignancies were seen in 2 of HD patients (basal cell carcinoma and Bowen's disease). This finding is consistent with the results published by Stewart JH *et al.* [26], results of Sułowicz J *et al.* [27] and Tercedor J *et al.* [28]. Patients undergoinge hemodialysis were at a higher risk of cancer including non-melanocytic skin malignancies. The few previously studies was performed for discovery of accurate underlying pathogenesis. For example, for a long period of time, these patients underwent multiple imaging interventions for optimal evaluation and management. Therefore, this notable cumulative exposure effect initiated and promoted oncogenic and carcinogenic effects. Therefore, these subjects identified as secondary immunodifficient group, due to underlying cause of ESRD, comorbid status, and use of many drugs. In these conditions, the patient is susceptible of developing malignancy [26,27].

One patient complained on indolent progressive painful pruritus skin papules over the trunk, which followed by vesicles formation. His medical history revealed diabetic nephropathy with hypertension, diabetic neuropathy; in addition he suffered from amputation of his left first and second toes due to diabetic foot. IgA-associated vesiculobullous disease of skin is unusual presentation in patients on HD. Today, accurate explanation of main underlying pathogenesis in these patients is impossible. However, genetic and environmental factors including many drugs and infectious causes /agents? were assumed for trigger etiology [29].

Conclusion

Many results of previous researches have revealed that patients on HD are susceptible to various benign or malignant or complex skin diseases. Skin manifestations can cause decreased patient function and poor quality of life. For better management of patients on HD, awareness of involved medical team about these presentations is necessary. These patients need periodical dermatologic evaluation.

Conflict of interest statement. None declared.

References

1. Goddard J, Turner AN, Cumming AD, Stewart LH. Kidney and urinary tract disease. In: Boon NA, Colledge NR, Walker BR, Hunter JA, eds. Davidson's Principles and Practice of

Medicine. *20th ed. Edinburgh: Churchill Livingstone, Elsevier* 2006; 455-518.
2. Watnick S, Morrison G. Kidney. In: Tierney LM, McPhee SJ, Papadakis MA, eds.Current Medical Diagnosis and Treatment. *43rd ed. New York: McGraw-Hill* 2004; 863-898.
3. Udayakumar P, Balasubramanian S, Ramalingam KS, *et al*. Cutaneous manifestations in patients with chronic renal failure on hemodialysis. *Indian J Dermatol Venereol Leprol* 2006; 72(2): 119-125.
4. Saray Y, Seckin D, Gulec AT, *et al*. Nail disorders in hemodialysis patients and renal transplant recipients: a case-control study. *J Am Acad Dermatol* 2004; 50(2): 197-202.
5. Charkhchian M, Beheshti A, Zangivand AA, Sedighi A. Nail disorder among patients on maintenance hemodialysis. *Dermatologica Sinica* 2013; 13: 7-10.
6. Beheshti A, Charkhchian M, Zangivand AA, *et al*. Dermatological manifestations among patients on maintenance hemodialysis. *WOUNDS* 2013; 25 (3): 61-67.
7. Morais C, Gerhardt B, Calvi Gussao B, *et al*. Skin diseases in hemodialysis and kidney transplant patients. *J Bras Nefrol* 2011; 33(2): 268-275.
8. Galperin TA, Cronin AJ, Leslie KS. Cutaneous manifestations of ESRD. *Clinical Journal of the American Society of Nephrology* 2014; 9(1): 201-218.
9. Bakthavatchalu P, Kombettu AP, Betkerur J, *et al*. Profile of skin changes and its association with biochemical parameters in hemodialysis patients. *J Evolution Med Dent Sci* 2016; 7(97): 7120-7124.
10. Shrestha P, Mathur M. Dermatologic Manifestations In: Chronic kidney disease patients on hemodialysis. *Nepal J Dermatol Venereol Leprol* 2016; 12(1): 34-40.
11. Mookambika RV, Murugan S. A study on dermatological manifestations among chronic kidney disease patients undergoing hemodialysis in a tertiary care centre. *Int J Res Med Sci* 2017; 5(5): 1814-1817.
12. De Marchi S, Cecchin E, Villalta D, *et al*. Relief of pruritus and decreases in plasma histamine concentrations during erythropoietin therapy in patiets with uremia. *N Engl J Med* 1992; 326: 969.
13. Szepietowski JC, Schwarts RA. Uremic pruritus. *Int J Dermatol* 1998; 37: 247.
14. Kumar Kolla P, Desai M, Pathapati RM, *et al*. *ISRN Dermatology* 2012, Article ID 679619, 4 pages.
15. De Marchi S, Cecchin E, Villalta D, *et al*. Relief of pruritus and decreases in plasma histamine concentrations during erythropoietin therapy in patiets with uremia. *N Engl J Med* 1992; 326: 969.
16. Schwarts IF, Iaina A. Management of uremic pruritus. *Semin Dial* 2000; 13: 177.
17. Stam F, van Guldener C, Schalkwijk CG, *et al*. Impaired renal function is associated with markers of endothelial dysfunction and increased inflammatory activity. *Nephrol Dial Transplant* 2003; 18: 892-898.
18. Stenvinkel P, Pecoits-Filho R, Lindholm B. Coronary artery disease in end-stage renal disease: No longer a simple plumbing problem. *J Am Soc Nephrol* 2003; 14: 1927-1939.
19. Zucker I, Yosipovitch G, David M, *et al*. Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis: Uremic pruritus is still a major problem for patients with end-stage renal disease. *J Am Acad Dermatol* 2003; 49: 842-846.
20. Farrel AM. Acquired perforating dermatosis in renal and diabetic patients. *Lancet* 1997; 349: 895-896.
21. McKerrow KJ, Hawthorn RJ, Thompson W. An investigation of circulating and in situ lymphocyte subsets and Langerhans cells in the skin and cervix of patients with chronic renal failure. *Br J Dermatol* 1989; 120: 745-755.
22. Vanholder R, Ringoir S. Infectious morbidity and defects of phagocytic function in end-stage renal disease: a review. *J Am Soc Nephrol* 1993; 3: 1541-1554.
23. Tawade YV, Gokhale BB. Dermatological manifestations of chronic renal failure. *Indian Journal of Dermatology, Venereology and Leprology* 1996; 62(3); 155-156.
24. Singh G, Singh SJ, Chakrabarty N, *et al*. Cutaneous manifestations of chronic renal failure. *Indian Journal of Dermatology, Venereology and Leprology* 1989; 55(3): 167-169.
25. Cohen GS. "Renal disease," in Burket's Oral Medicine; Diagnosis and Treatment, M. A. Lynch, Ed., pp. 487-509, Lipincott-Raven, Philadelphia, Pa, USA, 9th edition, 1997.
26. Stewart JH, Vajdic CM, van Leeuwen MT, *et al*. The pattern of excess cancer in dialysis and transplantation. *Nephrol Dial Transplant* 2009; 24: 3225-3231.
27. Sułowicz J, Wojas-Pelc A, Ignacak E, *et al*. Comparison of the incidence of skin cancers in patients on dialysis and after kidney transplantation. *Adv Dermatol Allergol* 2017; XXXIV(2): 138-142.
28. Tercedor J, Lopez-Hernandez B, Rodenas JM, *et al*. Multivariate analysis of cutaneous markers of aging in chronic hemodialyzed patients. *Int J Dermatol* 1995; 34: 546-550.
29. Yousuf Bhat Z, AbuMinshar M, Imran N, *et al*. Bullous Dermatosis in an End-Stage Renal Disease Patient:A Case Report and Literature Review. *Case Reports in Nephrology Volume* 2016, Article ID 6713807, 5 pages.