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Mucocutaneous manifestations of patients with chronic kidney disease under hemodialysis: A cross-sectional study of 49 patients

Running title: Mucocutaneous signs & ESRD cases under hemodialysis

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Abstract

Background: Chronic Kidney Disease (CKD) is a common medical problem with well-known dermatologic manifestations, some of which highly disturb the patients' quality of life.

Objectives: This cross-sectional study was designed to identify the prevalence and type of cutaneous involvement in CKD patients.

Methods: The skin manifestations of 49 patients with CKD undergoing hemodialysis at Akhavan Hospital in Kashan, Iran, were recorded over two months.

Result: Diabetes (35%) was the most common cause of Chronic Renal Failure (CRF) in the patients, and the most common skin manifestations were xerosis (95.9%), uremic pigmentation (89.8%), scleral discoloration (87.8%), dental discoloration (85.2% among the patients with natural teeth), dry mouth (65.3%), varicosity (61.2%), pruritus (57.1%), skin atrophy (49%), lentigo (46.9%), subungual hyperkeratosis (42.9%), half and half nail dystrophy (34.7%) and purpura (26.5%).

Conclusion: Mucocutaneous involvement has a very high prevalence in CKD patients undergoing hemodialysis, and some of the cases are medically and cosmetically disturbing; therefore, with better knowledge about the type and prevalence of these involvements, the consequences can be better predicted and managed. Further studies are recommended to be conducted on the association between these signs and CKD grade, and clinical trials are also required for establishing the treatment options available for these signs and then assessing the patients' quality of life as a primary outcome measure.

Keywords: Chronic kidney disease, CKD, end stage renal disease, ESRD, skin, hemodialysis, cutaneous, mucocutaneous, dermatologic manifestation

Introduction

Chronic Kidney Disease (CKD) is a description of the structure and function of a person's kidneys. The underlying cause of CKD is not yet fully understood, but the disease is defined in association with other conditions, including cardiovascular diseases and diabetes.

The latest definition of CKD approved by international guidelines is a decrease in kidney function manifested by GFR <60 ml/min per 1.73 or markers of kidney damage with at least 90 days' duration regardless of the causes. CKD has five stages, classified by GFR, and the 3rd to 5th stages are known as End-Stage Renal Disease (ESRD), when the conditions are observed at least twice in 90 days (1)(2).

In the case of ESRD, some mucocutaneous presentations may be encountered secondary to CKD itself or due to the side-effects of routine hemodialysis, as CKD patients undergoing hemodialysis develop at least one skin manifestation (3).

The skin can guide clinicians as a tool for the evaluation of the patients' quality of life and demonstrate their body's general condition.

This study was designed and conducted to evaluate the prevalence of cutaneous and visible mucosal manifestations in patients with chronic renal failure undergoing hemodialysis at Akhavan Hospital in Kashan, Iran, over two months in a year in an attempt to find the mechanisms of controlling these manifestations.

Methods

This descriptive cross-sectional study was conducted on all the 49 patients undergoing hemodialysis at Akhavan Hospital in Kashan from August to October 2003. Data were collected through the patients' hospital records and history, dialysis sheets, medication records (kardexes) and physical examinations.

All the examinations were controlled by a dermatologist in a place with appropriate lighting and standard instruments for skin and mucosal examinations.

The patients' information about their pruritus severity was collected by one of the researchers, who filled out the questionnaire for the patients through face-to-face interviews. Pruritus was assessed in this study by the Visual Analog Scale (VAS).

All the data were entered into Microsoft Excel spreadsheets. The statistical analysis was carried out in SPSS version 11. The continuous data were described with an arithmetic mean and the categorical data with actual numbers and percentages.

“Ethical approval for this study was waived by Iran University of Medical Sciences for cross-sectional study in the year of performing the study. The authors collected the written informed consent from patients, without mentioning our patient's name, stating that the information and signs and symptoms of mucosal skin of the patients with kidney failure were collected as a part of their routine examinations. Only high-content informed consent was obtained from patients.”

Results

The 49 patients examined in this study had a mean age of 56.3 years, a 69.4% to 30.6% male to female gender ratio and a mean duration of dialysis of 34.5 months.

Diabetes was the most common cause of CRF in the patients (n=17), followed by HTN (n=11), glomerulonephritis (n=8), urological obstruction (n=4), pyelonephritis (n=1) and unknown causes (n=8). Table 1 presents the association between the cause of CRF and mucocutaneous manifestations.

The most common manifestations included xerosis (95.9%), uremic pigmentation (89.8%), scleral discoloration (87.8%), dental discoloration (85.2% among the patients with natural teeth), dry mouth (65.3%), varicosity (61.2%), pruritus (57.1%), skin atrophy (49%), lentigo (46.9%), subungual hyperkeratosis (42.9%), half and half nails (34.7%) and purpura (26.5%).

There were also two cases of squamous cell carcinoma and manifestations such as acne, bullous dermatosis, vitiligo, mucosal atrophy of the tongue, localized fungal infections, etc. (Table 2 presents more details).

Regarding pruritus, the patients reported their severity of pruritus as mild, irrespective of whether they had local or generalized pruritus.

In the case of pruritus, about 51% of those who reported this complication rated its severity as moderate, of which 70% cases were generalized. Table 3 presents other details on the distribution of the complications and whether they were widespread or localized.

There were no significant differences between men and women in terms of the studied variables, except with regard to two manifestations, including dry mouth and lentigo, in which there was a noticeable difference between the two genders (Table 4).

The patients who underwent dialysis three times per week had about twice as many skin manifestations as the patients who underwent hemodialysis twice a week.

The evaluation of blood calcium levels in the patients and its relationship with pruritus showed that the most prominent manifestation was mild regional pruritus in the group with blood calcium levels below 8 (i.e., low calcium) and scattered moderate pruritus in the group with Ca above 11 (Table 5).

In this study, the patients' accompanying symptoms had a curious association with their skin manifestations. This study assessed whether the patients had symptoms that are commonly observed in patients on long-term dialysis. These accompanying symptoms, which included headache, restless legs syndrome, nausea and vomiting, anorexia, etc. (listed in Table 4), were examined in association with the patients' skin manifestations. Some of the skin manifestations were fully linked to the patients' laboratory data (Table 6).

Discussion

CKD has become widespread in recent decades and caused many problems around the world. Diabetes is one of the major known causes of CKD (4).

In Iran, CKD patients undergoing hemodialysis develop several types of mucocutaneous manifestations (5), includingxerosis, skin pallor, pruritus, pigmentation, purpura, bullous lesions, perforating folliculitis, absent lunula, nail discoloration, half and half nails, lusterless hair, coated tongue xerostomia, macroglossia with teeth indentation (6), ecchymosis (5), leukonychia, and eczema(7).

In this study, 100% of the patients had at least one mucocutaneous manifestation, and xerosis was the most prevalent (95.92%) among them.

A study conducted in 2018 by Anees M. et al. reported the prevalence of xerosis as 83%, constituting the second most common manifestation in the examined patients after pigmentation (8).

Xerosis has been described as the most common skin manifestation in CKD patients in many studies (9, 10).

In a 2020 study by Adégbidi H. et al., however, xerosis had a very low prevalence of 48% (11).

The other skin manifestation with a high prevalence in the present study was uremic pigmentation (89.88%). In their 2018 study, Anees M. et al. reported the prevalence of pigmentation as 86% (8).

The third most common manifestation in the present study was sclera discoloration, with a prevalence of 87.86%, which has been reported in these patients in only a small number of articles, in which case their sclera has turned yellow. For example, in 2019, in an articlewritten by Dewi Sartika et al., the prevalence of icterus sclerosis in patients undergoing hemodialysis was 18.6%(12).

In general, hemodialysis patients experience more dental problems than the general population (13).

Another common mucocutaneous manifestation was dry mouth, which was noticed in 65.31% of the patients in the present study. Xerostomia is one of the most common manifestations in patients undergoing hemodialysis. A 2017 study by Honarmand M. et al.(14) also reported this manifestation.

Pruritus has been one of the most common cutaneous manifestations in many articles. Different studies have reported pruritus as one of the manifestations with a high rate of prevalence; meanwhile, in the present study, pruritus was not very common and had a rate of 57.14%.

In a 2019 study published by Rehman I. U. et al., the prevalence of pruritus was 61.4% (15).

In a 2010 study by Martinez M. A. et al., the prevalence of half and half nails was 14.4% (16). Also, in the study by Jamal A. in 2000, the prevalence of half and half nails in patients undergoing hemodialysis was 26% (17).

In this study, eight cases had vitiligo, and varicosity was detected in 30 cases. A 2001 study by Tanami Y. et al. used angiography and showed several varicose veins in patients undergoing hemodialysis (18).

Uremic pruritus is a multifactorial skin manifestation of ESRD and hemodialysis that affects the patients' living standards significantly (19).

About 50% of patients on dialysis and 25% of CKD patients who do not undergo dialysis develop this type of pruritus, which can lead to poor treatment and even mortality(20).

The severity of pruritus varies from patient to patient. In one study, 33% of those who had pruritus rated it as severe. Hyperphosphatemia and antihistamine intake were also more common in patients with severe pruritus(21).

The severity of pruritus is examined in patients using VAS(22). Intravenous dexamethasone and diphenhydramine are used to treat this condition (23).

A study examining the relationship between xerosis and pruritus found that itching increased dramatically with the severity of dry skin(24).

Another common skin manifestation in patients undergoing hemodialysis is subungual hyperkeratosis. In 2012, Onelmis H. et al. reported the prevalence of subungual hyperkeratosis as 34% (24).

The next common skin manifestation is atrophy of the skin, which was also observed in a 2017 study by Doi S. et al. in CKD patients (25).

The calcium level provides a useful tool for the management of treatment in patients undergoing hemodialysis. In addition, an increase or deficiency in calcium levels can cause some skin complications in hemodialysis patients, which have been examined in this study.A 2018 study on the calcium levels of hemodialysis patients showed that 20.6% of them had hypercalcemia and about 27.7% had calcium deficiency compared to hemodialysis patients with normal calcium levels, which may be considered an important complication in hemodialysis patients. Calcium deficiency or hypercalcemia can be detected by some skin manifestations (26).

In the present study, mucocutaneous fungal infection was detected in 6.12% of the patients. In another study, Naderi et al. reported this manifestation in 1.9% of their patients (27).

Patients undergoing hemodialysis experience different symptoms during their period of treatment. For example, in a 2017 study by Anita Joblonski et al.on the incidence of different symptoms in patients undergoing hemodialysis, 77% of the population reported tiredness, 63% sleep problems, 52% muscle cramps, 32% nausea and vomiting, 30% headaches, 22% restless legs, and 51% muscle weakness, but the association between these symptoms and skin manifestations was not investigated in their study (26). Skin and mucosa could be a site of many

presentations of various systemic involvements that should be kept in mind for better diagnosis, management and treatment (28-31).

Conclusion

To conclude, mucocutaneous manifestations were common in patients with CKD undergoing hemodialysis.

All the patients undergoing dialysis had at least one CKD-related skin manifestation.

CKD has many causes, but hypertension and diabetes were at the top of the list of causes among the patients in this research.

The most common skin manifestation was xerosis in the examined patients, followed by uremic pigmentation.

Further studies are recommended to be conducted on the skin manifestations of CKD patients undergoing hemodialysis in order to advance our control over them and raise the quality of life in these patients.

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Contributors

All the authors made extensive contributions to the final draft of this manuscript.

Declaration of Interest

We declare no competing interests.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical Approval

Ethical approval for this study was waived by Iran University of Medical Sciences for cross-sectional study in the year of performing the study. We only collected the written informed consent from patients-without mentioning our patient's name-stating that the information and signs and symptoms of mucosal skin of the patients with kidney failure were collected as a part of their routine examinations. Only high-content informed consent was obtained from patients.

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Table 1:

Cause of CRF Manifestation	Hypertension		Diabetes		Glomerulo-nephritis		Urologic obstructive complications		pyelonephritis		Unknown causes	
	percent	**number**	**percent**	**number**	**percent**	**number**	**percent**	**number**	**percent**	**number**	**Percent**	**number**
Pruritus	**54.55**	**6**	**70.59**	**12**	**50.00**	**4**	**25.00**	**1**	**0**	**0**	**62.50**	**5**
Xerosis	**90.91**	**10**	**100.00**	**17**	**100.00**	**8**	**100.00**	**4**	**0**	**0**	**100.00**	**8**
Uremic Pigmentation	**90.91**	**10**	**82.35**	**14**	**100.00**	**8**	**75.00**	**3**	**100**	**1**	**100.00**	**8**
Skin Atrophy	**63.64**	**7**	**58.82**	**10**	**25.00**	**2**	**75.00**	**3**	**0**	**0**	**25.00**	**2**
Dry Mouth	**90.91**	**10**	**64.71**	**11**	**25.00**	**2**	**50.00**	**2**	**0**	**0**	**87.50**	**7**
Varicosity	**72.73**	**8**	**64.71**	**11**	**75.00**	**6**	**50.00**	**2**	**0**	**0**	**37.50**	**3**
subungual hyperkeratosis	**45.45**	**5**	**47.06**	**8**	**37.50**	**3**	**50.00**	**2**	**0**	**0**	**37.50**	**3**
Lentigo	**63.64**	**7**	**58.82**	**10**	**12.50**	**1**	**50.00**	**2**	**100**	**1**	**25.00**	**2**
Half & Half Nail	**36.36**	**4**	**41.18**	**7**	**25.00**	**2**	**50.00**	**2**	**0**	**0**	**25.00**	**2**
Sclera discoloration	**100.00**	**11**	**82.35**	**14**	**87.50**	**7**	**100.00**	**4**	**0**	**0**	**87.50**	**7**
Dental discoloration	**36.36**	**4**	**23.53**	**4**	**75.00**	**6**	**75.00**	**3**	**0**	**0**	**75.00**	**6**
Purpura	**45.45**	**5**	**17.65**	**3**	**37.50**	**3**	**25.00**	**1**	**0**	**0**	**12.50**	**1**
Sebastian gland hyperplasia	**0.00**	**0**	**17.65**	**3**	**25.00**	**2**	**0.00**	**0**	**0**	**0**	**25.00**	**2**
Chronic disease anemia cutaneous manifestation	**9.09**	**1**	**17.65**	**3**	**12.50**	**1**	**25.00**	**1**	**0**	**0**	**0**	**0**
Vitiligo	**18.18**	**2**	**0.00**	**0**	**12.50**	**1**	**50.00**	**2**	**0**	**0**	**37.50**	**3**
Acnea	**0.00**	**0**	**5.88**	**1**	**0.00**	**0**	**0.00**	**0**	**100**	**1**	**25.00**	**2**
Shin spot	**0.00**	**0**	**29.41**	**5**	**0.00**	**0**	**0.00**	**0**	**0**	**0**	**0**	**0**
Hypertrichosis	**9.09**	**1**	**0.00**	**0**	**12.50**	**1**	**0.00**	**0**	**0**	**0**	**25.00**	**2**
Seborrheic wart	**9.09**	**1**	**5.88**	**1**	**12.50**	**1**	**25.00**	**1**	**0**	**0**	**12.50**	**1**
Bullous dermatitis	**0.00**	**0**	**5.88**	**1**	**12.50**	**1**	**0.00**	**0**	**0**	**0**	**0**	**0**
Prolonged wound healing	**0.00**	**0**	**17.65**	**3**	**0.00**	**0**	**0.00**	**0**	**0**	**0**	**12.50**	**1**
Pityriasis versicolor	**0.00**	**0**	**17.65**	**3**	**0.00**	**0**	**0.00**	**0**	**0**	**0**	**0**	**0**
Skin tag	**27.27**	**3**	**5.88**	**1**	**12.50**	**1**	**0.00**	**0**	**0**	**0**	**25.00**	**2**
Mocucutaneous fungal infection	**0.00**	**0**	**5.88**	**1**	**0.00**	**0**	**0.00**	**0**	**0**	**0**	**25.00**	**2**
Gingiva hyperplasia	**0.00**	**0**	**0.00**	**0**	**12.50**	**1**	**25.00**	**1**	**0**	**0**	**12.50**	**1**

Total patients with the special cause	**22.45**	**11**	**34.69**	**17**	**16.33**	**8**	**8.16**	**4**	**2.04**	**1**	**16.33**	**8**

Table 2: The prevalence of mucocutaneous manifestations in ESRD

Manifestation	Prevalence
Total	100
Xerosis	95.92
Uremic Pigmentation	89.80
Sclera discoloration	87.76
Dental discoloration	85.19
Dry Mouth (xerostomia)	65.31
Varicosity	61.22
Pruritus	57.17
Skin Atrophy	48.98
Lentigo	46.94
subungual hyperkeratosis	42.86
Half & Half Nail	34.69
Purpura	26.53
Vitiligo	16.33
Skin tag	14.29
Sebastian gland hyperplasia	14.29
Chronic disease anemia cutaneous manifestation	12.24
Shin spot	10.20
Seborrheic wart	10.20
Prolonged wound healing	8.16
Hypertrichosis	8.16
Acne	8.16

Pityriasis versicolor	6.12
Mucocutaneous fungal infection	6.12
Gingival hyperplasia	6.12
Bullous dermatitis	4.08

Table 3: Severity and distribution of mucocutaneous signs and symptoms in patients with CKD under hemodialysis

total		Severe								Moderate								Mild								SEVERITY / DISTRIBUTION / MANIFESTATION
		total		Generalized		Regional		Scattered		total		Generalized		Regional		Scattered		total		Generalized		Regional		Scattered		
percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	percent	number	
57/14	28	17/86	5	80/00	4	20/00	1	0/00	0	32/14	9	44/44	4	44/44	4	11/11	1	50/00	14	50/00	7	50/00	7	0/00	0	(Pruritus)
95/92	47	17/02	8	62/50	5	37/50	3	0/00	0	51/06	24	70/83	17	29/17	7	0/00	0	31/91	15	86/67	13	13/33	2	0/00	0	(Xerosis)
48/98	24	20/83	5	80/00	4	20/00	1	0/00	0	54/17	13	61/54	8	38/46	5	0/00	0	12/50	3	33/33	1	66/67	2	0/00	0	(Skin Atrophy)

Table 4:Unpopular coexisting symptoms in patient with CKD under hemodialysis

Female		Male		Decreased Level Of Consciousness	Decreased Level Of Consciousness	Weakness , Malaise , Fatigue	Weakness , Malaise , Fatigue	Leg Restleness Syndrome	Leg Restleness Syndrome	Sleep Disorder	Sleep Disorder	Muscular Cramp	Muscular Cramp	Headache	Headache	Nause Vomiting	Nause Vomiting	Anorexia	Anorexia	Coexisting symtoms/symptoms
percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	
23.53	*8*	*285.71*	*20*	10.71428571	3	82.14285714	23	21.42857143	6	57.14285714	16	78.57142857	22	39.28571429	11	50	14	60.71428571	17	(Pruritus)
41.18	*14*	*471.43*	*33*	12.76595745	6	78.72340426	37	17.0212766	8	53.19148936	25	76.59574468	36	38.29787234	18	51.06382979	24	57.44680851	27	(Xerosis)
38.24	*13*	*442.86*	*31*	13.63636364	6	79.54545455	35	20.45454545	9	59.09090909	26	77.27272727	34	36.36363636	16	47.72727273	21	56.81818182	25	(Uremic Pigmentation)
26.47	*9*	*214.29*	*15*	20.83333333	5	83.33333333	20	4.166666667	1	54.16666667	13	66.66666667	16	25	6	33.33333333	8	58.33333333	14	(Skin Atrophy)
35.29	*12*	*285.71*	*20*	15.625	5	87.5	28	12.5	4	62.5	20	78.125	25	40.625	13	53.125	17	62.5	20	(Dry Mouth)
26.47	*9*	*300.00*	*21*	13.33333333	4	80	24	13.33333333	4	50	15	73.33333333	22	30	9	43.33333333	13	53.33333333	16	Varicosity
17.65	*6*	*214.29*	*15*	19.04761905	4	76.19047619	16	4.761904762	1	61.9047619	13	76.19047619	16	33.33333333	7	47.61904762	10	47.61904762	10	subungual hyperkeratosis
29.41	*10*	*185.71*	*13*	21.73913043	5	82.60869565	19	17.39130435	4	52.17391304	12	60.86956522	14	26.08695652	6	43.47826087	10	56.52173913	13	Lentigo
14.71	*5*	*171.43*	*12*	17.64705882	3	88.23529412	15	11.76470588	2	52.94117647	9	70.58823529	12	29.41176471	5	47.05882353	8	52.94117647	9	(Half & Half Nail)
38.24	*13*	*428.57*	*30*	13.95348837	6	81.39534884	35	16.27906977	7	51.1627907	22	79.06976744	34	37.20930233	16	46.51162791	20	62.79069767	27	sclera discoloaration
8.82	*3*	*285.71*	*20*	4.347826087	1	69.56521739	16	21.73913043	5	60.86956522	14	73.91304348	17	34.7826087	8	56.52173913	13	52.17391304	12	dental discoloration
17.65	*6*	*100.00*	*7*	23.07692308	3	69.23076923	9	23.07692308	3	53.84615385	7	76.92307692	10	38.46153846	5	15.38461538	2	53.84615385	7	(Purpura)
8.82	*3*	*57.14*	*4*	0	0	42.85714286	3	0	0	57.14285714	4	57.14285714	4	28.57142857	2	14.28571429	1	42.85714286	3	sebation gland discoloration
2.94	*1*	*71.43*	*5*	16.66666667	1	100	6	16.66666667	1	100	6	83.33333333	5	50	3	50	3	66.66666667	4	chrinic diseases anemia skin manifestation
2.94	*1*	*100.00*	*7*	0	0	75	6	0	0	50	4	62.5	5	12.5	1	37.5	3	62.5	5	Vitiligo
2.94	*1*	*42.86*	*3*	0	0	50	2	50	2	50	2	75	3	0	0	25	1	50	2	(Acnea)
0.00	*0*	*71.43*	*5*	0	0	80	4	20	1	60	3	60	3	0	0	40	2	40	2	Shin Spot
2.94	*1*	*42.86*	*3*	25	1	75	3	0	0	50	2	100	4	50	2	75	3	75	3	(Hypertrichosis)
2.94	*1*	*57.14*	*4*	0	0	60	3	0	0	60	3	60	3	0	0	0	0	20	1	(Seborrheic Wart)
2.94	*1*	*14.29*	*1*	0	0	100	2	100	2	50	1	100	2	100	2	50	1	100	2	(Bullous Dermatitis)
2.94	*1*	*42.86*	*3*	25	1	75	3	25	1	75	3	75	3	50	2	50	2	75	3	scar repairing prolongation
0.00	*0*	*42.86*	*3*	0	0	100	3	0	0	33.33333333	1	33.33333333	1	0	0	66.66666667	2	33.33333333	1	(PityriasisVersicolor)
11.76	*4*	*42.86*	*3*	14.28571429	1	71.42857143	5	28.57142857	2	71.42857143	5	71.42857143	5	28.57142857	2	14.28571429	1	42.85714286	3	Skin Tag
0.00	*0*	*42.86*	*3*	0	0	66.66666667	2	0	0	0	0	33.33333333	1	0	0	33.33333333	1	33.33333333	1	fungal mucocutaneous manifestation
0.00	*0*	*42.86*	*3*	0	0	66.66666667	2	33.33333333	1	33.33333333	1	100	3	33.33333333	1	66.66666667	2	100	3	gingival hyperplasia
30.61	*15*	*69.39*	*34*	14.89	7	85.11	40	19.15	9	55.32	26	80.85	38	38.3	18	48.94	23	61.7	29	total

Table 5: Levels of lab data in CKD patient under hemodialysis

lab data / Symptoms	TIBC LOW		SERUM IRON low		hemoglobin								FBS				CHOL HIGH		T.G.				CALCIUM							
					< 7 (gr/dl)		7 - 9 (gr/dl)		9 - 11 (gr/dl)		→ 11 (gr/dl)		High		Extremely High				High		Extremely High		High		Upper limit Normal		Lower Limit Normal		Low	
	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person	percent	person
(Pruritus)	25	4	33.33333333	1	100	3	56.25	9	62.5	10	37.5	6	62.5	5	66.66666667	2	50	1	50	3	50	1	100	1	80	4	84.62	11	40	2
(Xerosis)	31.25	5	100	3	100	3	93.75	15	118.75	19	62.5	10	87.5	7	100	3	100	2	83.33	5	100	2	100	1	100	5	100	13	80	4
(Uremic Pigmentation)	37.5	6	100	3	100	3	93.75	15	106.25	17	56.25	9	75	6	66.66666667	2	50	1	66.67	4	100	2	100	1	100	5	100	13	80	4
(Skin Atrophy)	12.5	2	100	3	33.33333333	1	37.5	6	81.25	13	25	4	50	4	66.66666667	2	50	1	50	3	0	0	0	0	60	3	61.54	8	40	2
(Dry Mouth)	25	4	100	3	100	3	62.5	10	81.25	13	37.5	6	75	6	66.66666667	2	50	1	33.33	2	50	1	100	1	60	3	84.62	11	40	2
Varicosity	18.75	3	66.66666667	2	33.33333333	1	62.5	10	87.5	14	31.25	5	50	4	66.66666667	2	100	2	66.67	4	0	0	100	1	80	4	69.23	9	40	2
Subungual hyperkeratosis	18.75	3	66.66666667	2	100	3	25	4	56.25	9	31.25	5	37.5	3	33.33333333	1	50	1	50	3	0	0	0	0	60	3	69.23	9	40	2
Lentigo	6.25	1	100	3	33.33333333	1	37.5	6	75	12	25	4	62.5	5	33.33333333	1	50	1	16.67	1	50	1	0	0	60	3	53.85	7	40	2
(Nail & Half Nail)	18.75	3	66.66666667	2	33.33333333	1	25	4	56.25	9	18.75	3	50	4	0	0	0	0	16.67	1	0	0	100	1	40	2	23.07	3	40	2
sclera discoloration	37.5	6	100	3	100	3	87.5	14	106.25	17	56.25	9	62.5	5	66.66666667	2	50	1	66.67	4	50	1	100	1	100	5	92.31	12	80	4
dental discoloration	31.25	5	0	0	100	3	68.75	11	37.5	6	18.75	3	25	2	33.33333333	1	100	2	33.33	2	0	0	100	1	60	3	46.15	6	60	3
(Purpura)	6.25	1	66.66666667	2	33.33333333	1	37.5	6	31.25	5	6.25	1	25	2	0	0	0	0	0	0	0	0	0	0	60	3	38.46	5	0	0
sebation gland discoloration	6.25	1	0	0	33.33333333	1	12.5	2	18.75	3	6.25	1	25	2	33.33333333	1	0	0	0	0	50	1	0	0	20	1	7.69	1	20	1
chrinic diseases anemia skin manifestation	6.25	1	0	0	33.33333333	1	6.25	1	18.75	3	6.25	1	12.5	1	33.33333333	1	0	0	0	0	50	1	0	0	40	2	7.69	1	20	1
(Vitiligo	0	0	0	0	33.33333333	1	12.5	2	25	4	6.25	1	0	0	0	0	50	1	16.67	1	0	0	0	0	20	1	23.07	3	0	0
(Acnea)	6.25	1	0	0	0	0	6.25	1	6.25	1	12.5	2	0	0	33.33333333	1	50	1	16.67	1	0	0	0	0	0	0	0	0	20	1
Skin Spot	0	0	0	0	0	0	6.25	1	12.5	2	12.5	2	37.5	3	33.33333333	1	50	1	33.33	2	0	0	0	0	20	1	15.38	2	0	0
(Hypertrichosis)	6.25	1	0	0	0	0	12.5	2	6.25	1	6.25	1	0	0	0	0	0	0	0	0	0	0	100	1	0	0	7.69	1	0	0
(Seborrheic Wart)	0	0	0	0	33.33333333	1	6.25	1	12.5	2	6.25	1	0	0	0	0	50	1	16.67	1	0	0	0	0	20	1	15.38	2	20	1
(Bullous Dermatitis)	0	0	0	0	0	0	6.25	1	0	0	6.25	1	0	0	0	0	0	0	0	0	50	1	0	0	20	1	0	0	0	0
scar repairing prolongation	0	0	0	0	0	0	12.5	2	6.25	1	6.25	1	12.5	1	0	0	0	0	0	0	50	1	0	0	40	2	7.69	1	0	0
(PityriasisVersicolor)	0	0	0	0	0	0	0	0	18.75	3	0	0	25	2	0	0	0	0	16.67	1	0	0	0	0	0	0	15.38	2	0	0
Skin Tag	0	0	0	0	33.33333333	1	12.5	2	25	4	0	0	0	0	33.33333333	1	0	0	0	0	50	1	0	0	20	1	15.38	2	20	1
fungal cutaneous manifestation	0	0	33.33333333	1	0	0	6.25	1	6.25	1	6.25	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7.69	1	20	1
gingival hyperplasia	6.25	1	0	0	0	0	12.5	2	0	0	6.25	1	0	0	0	0	0	0	16.67	1	0	0	0	0	0	0	7.69	1	20	1
total	12.24489796	6	6.382978723	3	6.12244898	3	32.65306122	16	40.81632653	20	20.40816327	10	33.33333333	8	12.5	3	4.545454545	2	13.63636364	6	4.545454545	2	2.040816327	1	10.20408163	5	26.53061224	13	10.20408163	5

Table 6: Some of the skin manifestations were fully linked to the patients' laboratory data

	100%of patients who had the mentioned laboratory data showed the following skin symptoms.
Hg>11	Xerosis
Hg<7	Pruritus, xerosis, uremic pigmentation, dry mouth, sclera discoloration
Low TIBC	Uremic pigmentation, sclera discoloration
Low level serum iron	xerosis, uremic pigmentation, dry mouth, sclera discoloration , skin atrophy,