Nasal manifestations in patients with chronic renal failure on hemodialysis

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Background

Patients with end-stagerenal disease (ESRD) on regular hemodialysis (HD) show various otolaryngological manifestations owing to uremic toxins and electrolyte imbalance. Previous studies have reported epistaxis as the most common ENT manifestations of ESRD on HD as explained by bleeding tendency related to uremia or HD itself. Nasal crustation, septal perforation, and olfactory dysfunction were also observed in HD patients.

Objective

To evaluate the frequency of different nasal manifestations among nondiabetic prevalent HD patients.

Patients and methods

A cross-sectional study was conducted in Ain Shams University Hospital from March 2019 till September 2019. It included 68 eligible nondiabetic patients with ESRD on regular HD more than 6 m. All patients were subjected to full history and clinical examination. CT nose and sinus was done only if indicated. Complete blood count and routine chemistry (blood urea nitrogen, serum creatinine, urea reduction ratio, calcium, phosphorus, parathyroid hormone, and iron profile) were done.

Results

Most patients did not give a past history of epistaxis (94.1%). Overall, 44.1% of the patients experienced dry nasal mucosa and pale inferior turbinates, and 10.3% of the patients had congested nasal mucosa. Crustations were founded in 7.4% of the patients, although they were found in nearly double percentage in nasal septum (14.7%). The nasal septum deviation and ulceration were found in 2.9% each. Only one (1.5%) patient had nasal septum perforation. The mean level of hemoglobin (g/dl) concentration was 10.4 (range, 6.8–15 g/dl).

Conclusion

Modern adequate HD techniques have reduced epistaxis in patients with ESRD. The most common ENT manifestations were dry nasal mucosa and pale inferior nasal turbinate and to a lesser extent crustations on both nasal septum and inferior nasal turbinate.

Keywords:

end-stage renal disease, epistaxis, hemodialysis

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Introduction

Chronic renal insufficiency affects hemostasis by multiple pathways, resulting either in an anticoagulatory state characterized by bleeding episodes or in a procoagulatory state characterized by frequent thrombosis [1].

Bleeding disorders are due to inadequate platelet function, coagulation cascade, and/or activation of fibrinolytic system, whereas hypercoagulability is the product of regulatory coagulation disorders and hyperactivity of platelets [2].

Increased bleeding tendency in patients with renal failure may present clinically as gastrointestinal bleeding, retinal hemorrhage, subdural hematoma, epistaxis, hematuria, ecchymosis, purpura, bleeding from the gums, gingival bleeding, genital bleeding, hemoptysis, telangiectasia, hemarthrosis, and petechiae [3].

Interestingly, hemodialysis (HD) itself may predispose to bleeding disorders, not only because of the heparin administered but also because of continuous platelet activation at the dialyzer membrane with following decreased dialyzer activity [4]. On the contrary, HD has been shown to reduce platelet disorders, leading to decreased risk of bleeding because of uremic toxin removal [5].

In patients with renal failure, anemia directly affects the bleeding time [6,7]. Erythrocytes lead to accumulation of platelets along the vessel walls within the blood stream together with stimulating the release of platelet ADP and an inactivation of PGI2, thus activating platelet function [8].

Nasal septal perforation in uremic patients may occur owing to trauma from nasal catheters and impaired proliferation of mucosal cell. Moreover, disturbed innervation of the vessels in the nasal septum owing to autonomous nervous system neuropathy and ischemia secondary to arteriolar narrowing may play a role [9].

Infection is common among patients with end-stage renal disease (ESRD) undergoing HD, leading to hospitalization, with high rate of morbidity and mortality. The most frequently involved microorganism is *Staphylococcus aureus*, which is the most common endogenous organism in the anterior nares [10].

Autonomic dysfunction is highly encountered in chronic renal failure (CRF) and occurs in HD patients in a percentage that reaches ~50%. Autonomic outflow is disturbed, leading to sympathetic overdrive and declining parasympathetic activity. This sympathetic overdrive is potentially mediated by renal sensory afferents in damaged kidneys and is potentiated by impaired chemo sensory function, elevated circulating humoral and metabolic factors such as angiotensin II, and cardiovascular remodeling [11].

Olfaction may deteriorate in case of end-stage renal failure owing to malnutrition and impaired fluid intake [12]. Uremic neuropathy usually occurs owing to accumulation of uric acid, indoxyl sulfate, p-cresyl sulfate, interleukin 1 beta, interleukin 6, tumor necrosis factor-alpha, and parathormone, resulting in myelin sheath injury and axonal degeneration. Olfactory neuropathy may occur owing to uremia in patients with CRF [13,14].

Patients and methods

This cross-sectional study was conducted over a 6-month duration to evaluate the frequency of nasal affection among 68 prevalent HD patients in Ain Shams University Hospital. Eligibility criteria were age more than or equal to 18 years, patients were scheduled on regular thrice-weekly 4 h sessions of conventional HD, and adequate HD sessions more than 6 months before the study with a standard bicarbonate-containing dialysate, using biocompatible HD polysulfone low-flux dialyzer and heparin as anticoagulant. We excluded any patients who had diabetes mellitus, active autoimmune disease, advanced liver disease, or malignancy. Moreover, patients with previous nasal or sinus diseases were excluded.

All patients were subjected to full history and clinical examination with emphasis on demographic features, smoking, the etiology of renal failure, dialysis duration, vascular access, drug history, history of any diagnosed hereditary or acquired comorbidities, BMI, and blood pressure. ENT examination included close observation of any external nasal swellings, deformities, nasal versus mouth breathing, color of nasal mucosa, edema, hypertrophy, polyps, granulations, deviated or perforated nasal septum, discharge, or bleeding. Computed tomography (CT) nose and sinus was done only if indicated, as in patients with epistaxis, nasal obstruction, and recurrent sinusitis.

Laboratory investigations included blood hemoglobin level, blood urea nitrogen, serum creatinine, calcium, phosphorus, parathyroid hormone, iron study, and CRP titer. Urea reduction ratio=(U pre–U post)/U pre × 100%) (U pre is the predialysis urea level and U post is the postdialysis urea level) and K_t/V (K: dialyzer clearance, t: duration of dialysis, V: volume of bodily water) were measured to assess the adequacy of dialysis.

Statistical analysis

Statistical analysis of data was done by IBM computer using SPSS (Statistical Program for the Social Sciences, version 18, IBM SPSS USA). Quantitative data were presented as range, mean, and SD. Qualitative data were presented as number and percent. χ^2 test was used to compare qualitative variables between groups. Student t test was used to compare quantitative variables between two groups. One-way analysis of variance test was used to compare quantitative variables between more than two groups. P value less than 0.05 was considered significant.

Ethical considerations: all procedures performed in the study were in accordance with ethical standards of Ain Shams University Hospital Research Committee and with the ethical standards laid down in the 1964 Declaration of Helsinki. This study was approved by our institutional review board, and informed consent was obtained from all individuals enrolled in the study.

Results

A total of 68 eligible HD patients (35 males and 33 females), with a mean age of 52.1 ± 13.3 year and mean HD duration of 7.9 ± 5.58 years were included. The causes of renal failure were hypertension in 21 (30.9%) patients, chronic pyelonephritis in 11 (16.17%), amyloidosis in two (2.9%), analgesic nephropathy in seven (10.3%), lupus nephritis in two (2.9%), chronic obstructive uropathy in seven (10.3%), polycystic kidney in three (4.4%), and 15 (22.1%) patients of unknown etiology. Associated risk factors noticed in our studied patients are as follows: 16.2% of patients were smokers, 22 (32.4%) patients were hypertensive, and 26 (38.2%) patients with seropositive HCV. The parameters of adequacy of HD were the mean urea reduction ratio of 66.63 ± 10.21% and mean K_t/V of 1.37 ± 0.26 were parameters of adequacy of HD. Regarding medications, calcium dose (mg/day) had a mean of 2363.2 ± 950.3, the mean of vitamin D dose (μg/week) was 0.92 ± 1.02, and the mean of erythropoietin dose (IU/kg/week) was 53.4 ± 35.47. Demographic and clinical data are shown in Table 1 and laboratory results are shown in Table 2.

Nasal mucosa was normal in 45.6% of patients, whereas 44.1% of the patients experienced dry nasal mucosa. Only 10.3% of the patients had congested nasal mucosa. Inferior nasal turbinates in most of our patients (44.1%) were pale, whereas were normal in 35.3% and were hypertrophied in 13.2%. Crustations were found only in 7.4% of patients in the inferior turbinates, although they were found in nearly the double percentage in nasal septum (14.7%) (Table 3).

Most studied patients (77.9%) had normal nasal septum, whereas the most significant finding observed was nasal septum crustations in ~14.7% of patients and to a lesser extent the nasal septum deviation and ulceration, with 2.9% each. Only one (1.5%) patient had nasal septum perforation (Table 3).

Most patients did not give past history of epistaxis (94.1%). Mean hemoglobin level in patient with no evident epistaxis was 10.5 ± 1.7 g/dl versus 9.2 ± 1.6 g/dl in patients with epistaxis, with P value more than 0.05. Correlation between epistaxis and all parameters was statistically nonsignificant, except for sex, as none of our male patients experienced epistaxis during our study (P = 0.034) (Table 4).

Logistic regression analysis, after applying the forward method and entering some predictor variables such as the increase in disease duration, HD duration, smoking, and ferritin, shows an independent effect on increasing the probability of nasal mucosa abnormalities occurrence, with significant statistical difference (P < 0.05 each).

Logistic regression analysis, after applying the forward method and entering some predictor variables such as the decrease in transferrin saturation and albumin, shows an independent effect on increasing the probability of epistaxis occurrence, with significant statistical difference (P < 0.01 each).

Table 1 Demographic and clinical data among the studied hemodialysis patients

Variables	Mean±SD/*n* (%)
Age (years)	52.1±13.3*
Dry weight (kg)	67.27±16.2
BMI	26.25±4.8
MAP (mmHg)	93.7±16.7
Hemodialysis duration (year)	7.9±5.58
Sex	
Female	33 (48.5)
Male	35 (51.5)
Smoking	
Nonsmoker	57 (83.8)
Smoker	11 (16.2)
Hypertension	22 (32.4)
HCV seropositive	26 (38.2)

Table 2 Laboratory data among hemodialysis patients (*n*=68)

	Mean±SD
Urea reduction ratio (%)	66.63±10.21
Calcium (mg/dl)	11.0±13.07
Phosphorus (mg/dl)	4.33±5.19
Parathyroid hormone (ng/l)	465.4±407.1
TSAT (%)	41.37±19.89
TIBC (μg/dl)	197.3±45.81
Ferritin (ng/ml)	1737.0±541.1
Iron (μg/dl)	95.96±106.8
HB (gm/dl)	10.28±2.02
Albumin (g/dl)	3.65±0.45
Creatinine (mg/dl)	2.68±0.77

Hb, hemoglobin; TIBC, total iron-binding capacity; TSAT, transferrin saturation.

Table 3 Nasal manifestations among nondiabetic hemodialysis patients (*n*=68)

	n (%)
Nasal septum	
Normal	53 (77.9)
Crustation	10 (14.7)
Deviation	2 (2.9)
Ulceration	2 (2.9)
Perforation	1 (1.5)
Nasal mucosa	
Normal	31 (45.6)
Dryness	30 (44.1)
Congestion	7 (10.3)
Turbinate	
Normal	24 (35.3)
Pale	30 (44.1)
Crustation	5 (7.4)
Hypertrophy	9 (13.2)
Epistaxis (history)	
Negative	64 (94.1)
Positive	4 (5.9)

Discussion

Uremic patients display a bleeding diathesis that is primarily due to hemostasis abnormalities, particularly platelet dysfunction and impaired platelet-vessel

Table 4 Correlation between epistaxis and other parameters

	Epistaxis [n (%)]		χ^2	*P*	Significance
	Negative	Positive			
Sex					
Female	29 (45.3)	4 (100.0)	4.508(b)	0.034	S
Male	35 (54.7)	0			
Smoking					
Nonsmoker	55 (85.9)	2 (50.0)	3.586(b)	0.058	NS
Smoker	9 (14.1)	2 (50.0)			
Etiology HTN					
No	45 (70.3)	1 (25.0)	3.532(b)	0.060	NS
Yes	19 (29.7)	3 (75.0)			
Duration of CRF (years)					
0-5	25 (39.1)	2 (50.0)	2.942	0.568	NS
	14 (21.9)	2 (50.0)			
11-15	12 (18.8)	0			
16-20	10 (15.6)	0			
21-25	3 (4.7)	0			
Nasal septum					
Normal	51 (79.7)	2 (50.0)	4.338	0.362	NS
Crustation	8 (12.5)	2 (50.0)			
Deviation	2 (3.1)	0			
Ulceration	2 (3.1)	0			
Perforation	1 (1.6)	0			
Nasal mucosa					
Normal	31 (48.4)	0	5.383	0.068	NS
Dryness	26 (40.6)	4 (100.0)			
Congestion	7 (10.9)	0			
Turbinate					
Normal	24 (37.5)	0	5.383	0.146	NS
Pale	26 (40.6)	4 (100.0)			
Crustation	5 (7.8)	0			
Hypertrophy	9 (14.1)	0			

CRF, chronic renal failure; S, significant.

wall interaction. These patients, however, have a high prevalence of cardiovascular and thrombotic complications, despite the reduced platelet function [2].

Bleeding has been reported in 40–50% of patients with CRF or on HD [3]. A hospital-based study showed that the risk of attacks of bleeding increased twice in patients with renal failure [4].

Di Minno *et al.*[15] reported prolonged bleeding time to be more than 8 min in their study and explained this by abnormal platelet aggregation and thromboxane B2 formation and mentioned that these changes are corrected partially following dialysis. Kumar *et al.* [16], mentioned that the most common ENT manifestation of patients with CRF on dialysis is epistaxis, representing about 30%, and in most of these patients, epistaxis was arrested, immediately after correction of blood urea. Bleeding tendency can be reduced by using modern dialysis techniques and the use of erythropoietin to correct anemia [17]. Moreover, removal of uremic toxins after HD has been shown to improve platelet abnormalities, resulting in a reduced risk of bleeding [5]. These results may match our finding, as only 5.9% of our patients experienced epistaxis.

Patients with advanced renal failure may show clinical manifestations that affect both the hard and soft tissues. Occasionally, these manifestations may be owing to therapeutic measures that include the following: fluid restrictions; dietary changes; adverse effects of some medications; including antihypertensives, painkillers, diuretics, antidepressants, and anti-inflammatory drugs, which are commonly used in these patients; and dialysis and/or kidney transplantation patients [18]. One of these mucosal manifestations is dryness. Sadeghdehghanmehr *et al.*[19] found that the mean occurrence of dry mouth is seen in ~44.02% of their patients. Dry mouth in HD occurs owing to a variety of causes, such as limited intake of fluids at intervals between two dialysis [20]. In this study, we observed that the most common nasal manifestations in patients with CRF on regular dialysis are dry nasal mucosa and pale inferior nasal turbinates (44.1% each).

Mucociliary activity of the respiratory mucosal surfaces greatly affects its ability to eliminate foreign particles and pathogens and to keep mucosal surfaces moist and fresh. CRF and HD cause severe prolongation of mucociliary clearance time as reported by Sinan *et al.* [21].

In addition, Fan and Baiya [10], identified endogenous gram-positive cocci infection, in particular *S. aureus*, as the most common cause of hospitalization, morbidity, and mortality among patients with ESRD undergoing HD. The anterior nares are the most common endogenous SA carrier sites.

Nasal irrigation can activate the ciliary motility and decrease the bacterial adhesion, leading to increase in mucociliary clearance and decrease in mucous membrane inflammations, through flushing away inflammatory mediators, the crust, and other nasal discharges [22].

The second common nasal manifestation found in this study is the nasal septum crustations (14.7%), and then hypertrophied inferior nasal turbinates (13.2%), followed by congested nasal mucosa (10.3%). Crustations were founded in 7.4% of the inferior nasal turbinates of our patients, and nasal septal ulceration was found in 2.9%. These results may be explained by the study done by Kumar *et al.* [16], who mentioned that the high urea level with an average of 320 mg/100 ml, which was excreted in nasal secretions, is splitted by nasal bacteria, releasing ammonia, which leads to chemical rhinitis, the possible cause of congestion, ulceration of nose, and submucosal hemorrhages. In most of their patients, the lining of the mucous membrane returned to normal in 3–5 days after dialysis.

Nasal septal perforation was observed in only one patient in this study (1.5%). However, Adler and Ritz[9] reported spontaneous perforation of the nasal septum in eight (8.32%) of 104 patients and contributed this to local trauma after nasal catheterization postoperatively, impaired proliferation of mucosal cell, and autonomic neuropathy owing to disturbed innervation of the vessel wall in the nasal septum.

Although olfactory neuropathy was reported in patients with CRF [13,14] and the hypothesis of elevated odor thresholds was studied by Frasnelli *et al.* [12], who mentioned that 56% of the CRF patients were found to be anosmic or hyposmic, we did not observe such manifestation in our study.

Conclusions

The most common ENT manifestations were dry nasal mucosa and pale inferior nasal turbinates and to a lesser extent crustations on both nasal septum and inferior nasal turbinates. The incidence of epistaxis has been reduced in patients with ESRD on regular HD. Nasal septal ulceration and perforation are the least common ENT manifestation. No cases with olfactory neuropathy were reported in our study.

Recommendations

(1) Patients with CRF on HD should keep their nasal mucosa wet using regular saline irrigation and moisturizing agents such as gel and ointments.
(2) Correction of anemia and regular HD helps in decreasing bleeding tendency in uremic patients.

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Conflicts of interest

There are no conflicts of interest.

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