Ministry of higher education and scientific research

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College of medicine

Otorhinological problems arising during the management of chronic renal failure

Submitted to

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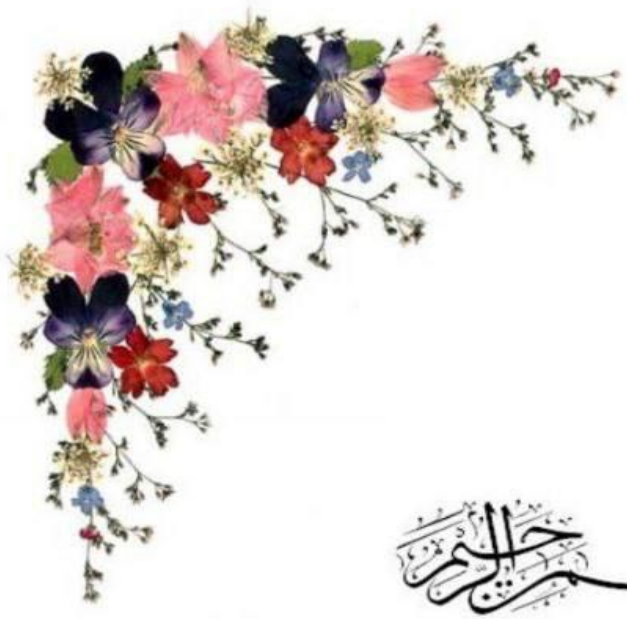


بسم الله الرحمن الرحيم

"يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا

الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ"

صدق الله العظيم

"سورة المجادلة-ايه 11"

Acknowledgement

At the outset, I would like to extend my sincere thanks to God, who enabled me to do this, to my mother and father, and to the supervising doctor, Qais Thank you very much, the supervising doctors for discussing the research. Thank you very much for your time and good listening.
I hope that it is sufficient and comprehensive for all the information that I would happily conclude my study trip with

Summary

Background : Otorhinological abnormalities are common complications of chronic kidney disease (CKD) and its treatment. The main aim of this study was to provide a brief and precise review of the current knowledge regarding CKD and its treatment-related influence on ear and nose .

Aim : The study was aimed at determining the prevalence, degrees and types of hearing impairment and complications and nose complications among Chronic kidney disease patients on haemodialysis in diyala.

Methods : the descriptive cross sectional study was conducted in baqubah general hospital / dialysis center . 65 case of end stage chronic kidney disease were collected . Statistical analysis of the results was done by using Windows based software device with Statistical Packages for Social Science(SPSS)version 20.

Result : Higher hearing thresholds were recorded across all the frequencies tested among the cases ($p < 0.05$) in both ears. Only sensorineural hearing loss was identified among the cases. The prevalence of hearing loss was 32% among the cases. No significant association was observed between hearing loss and duration of Chronic kidney disease ($p = 0.16$), gender of Chronic kidney disease patient and hearing loss ($p = 0.88$), and duration of Chronic kidney disease and degree of hearing loss ($p=0.31$).17 patient found to have tinnitus (26.1%) . 15 patient complained from vertigo (23%). 15 patient found to have epistaxis (23%).14 patient found to have nasal obstruction (21.5%) .no significant association was observed between nose complications and duration of chronic kidney disease {$p=0.14$}.

Conclusion : Our study showed that Chronic Kidney disease patients on haemodialysis are at higher risk of experiencing hearing loss, tinnitus ,vertigo and nose bleeding and obstruction .

Keyword : chronic kidney disease , hearing loss ,tinnitus ,vertigo , epistaxis , nasal obstruction .

Introduction

Chronic kidney disease (CKD) is a frequent condition currently defined as reduced kidney function expressed by glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m2 or markers of kidney damage that lasts at least 3 months irrespectively of the underlying cause . The overall prevalence of CKD in United States adult population reaches 14.8%, whereas in European countries the prevalence reaches up to 15.7%, depending on the country .

End-stage kidney disease (ESKD) is diagnosed when patients' GFR is less 15 ml/min/1.73 m2. At this stage, patients require renal replacement therapy, namely dialysis or kidney transplantation . The estimated number of ESKD cases in United States reaches 661,000 .

Many patients with CKD require kidney transplantation and subsequent immunosuppressive treatment for the rest of their lives to prevent organ rejection .

As the prevalence of CKD continues to rise worldwide, the number of patients with CKD-related systemic dysfunctions, including otorhinological, will presumably increase as well .

CKD-induced effects of the body systems is a result of the accumulation of nitrogenous waste products, so-called "uremic toxins", in various tissues, electrolyte imbalance, local chemical reactions due to ammonia, immunological, vascular and coagulation changes . Ototoxic and immunosuppressive drugs used in CKD therapy also lead to a number of systemic complications .

CKD affects a vast majority of organ systems, but the focus of this review will be on otorhinological complications of CKD.

-Sensorineural hearing loss (SNHL) Sensorineural hearing loss (SNHL) is a common otorhinolaryngological manifestation in patients with CKD . CKD is believed to be an important independent risk factor for SNHL . SNHL is usually bilateral in patients with CKD, and is more frequently observed in these individuals than in general the population . The prevalence of SNHL in CKD patients ranges from 28 to 77% . It was mainly diagnosed in long-lasting CKD patients and deteriorated over time . It was reported that the highest prevalence of SNHL occurred in individuals with estimated glomerular filtration rate (eGFR) above 45 ml/min/1.73 m2.

The high number of patients with CKD suffering from SNHL might result from several structural and functional similarities in kidney and in inner ear . The most important similarity is the active transportation of electrolytes and fluids carried out in the glomerular basement membrane and in the cochlear stria vascularis . It is a result of the presence of Na + K + ATPase pump and a carbonic anhydrase enzyme . Additionally, it was also found that the cochlea and kidney share similar antigenicity . To support that, there are some diseases and syndromes (e.g., Alport syndrome) that affect both, inner ear and kidney.

It was suggested that SNHL in patients with CKD could result from electrolyte disturbances, elevated serum urea and creatinine levels, treatment (ototoxic drugs, hemodialysis itself and prolonged treatment duration), hypertension or commonly coexisting DM . The most widely discussed ototoxic drugs used in managing CKD are aminoglycosides and furosemide . Vitamin D deficiency and reduction of Na+ K+ -activated ATPase were also implicated in SNHL.

It was suggested that inhibition of Na+ K+ -activated ATPase that is crucial in providing proper ionic gradient in the inner ear, could be the main cause of sensorineural hearing dysfunction in uremic patients . Another dysfunction predisposing to SNHL in patients with CKD is endolymphatic edema . It was previously described that endolymphatic hydrops was related to low-frequency SNHL and could explain hearing amelioration after hemodialysis .

-Tinnitus and vertigo : tinnitus is a perception of the sound in the absence of auditory stimulus from the outside, and is mainly a result of auditory pathology . It might be a coexisting symptom in SNHL . Tinnitus is an effect of downregulation of intracortical suppression that is linked to the cochlear damage, nevertheless the exact mechanisms leading to tinnitus in patients with CKD remain unclear . A population-based study on a large cohort conducted by Shin et al. revealed that CKD is an important and independent risk factor for tinnitus . The authors found that patients with CKD were 3.02-times more prone to develop tinnitus than general population, especially those with severe renal dysfunction . The risk was higher in females aged less than 30 years, and reached 4.5-increase in patients on hemodialysis . Tinnitus was also observed as a common accompanying symptom in patients with SSNHL on hemodialysis. Vertigo is a sensation of motion or spinning that is often described as dizziness. Several variables may contribute to the etiopathogenetic mechanisms of tinnitus and vertigo in CKD including factors related to the severity and duration of the disease, electrolyte disturbances, ototoxic drugs, age, comorbid conditions such as diabetes mellitus and hypertension, and hemodialysis .

-Nasal bleeding (epistaxis) is a common CKD-induced symptom . Nasal cavity is one of the most common sites of bleeding in patients with uremia. In patients with CKD, epistaxis is mainly caused by the collection of toxic elements that in healthy people are eliminated by kidneys in urine. Other factors predisposing to nasal bleeding in CKD are anemia and coagulation dysfunctions . It was suggested that urea was the most important cause of nasal bleeding . Patients presenting epistaxis had very high level of blood urea (320 mg/100 cc) that was eliminated by nasal discharge . In addition to that, epistaxis was exacerbated by bacteria that decompose urea to ammonia and colonize nasal cavity. It resulted in chemical rhinitis appearing as both, mucosal congestion and ulceration, and submucosal hemorrhages . It was also implied that nasal bleeding resolved immediately after blood urea level was normalized, thus indicating the definitive role of urea in triggering epistaxis.

-Nasal obstruction may be due to uremic deposit in the nasal mucous membrane leading to irritation, catarrh, edema, and nasal blockage. When catarrh is infected, there is associated crust formation, ulceration, and injury from nose picking.

Aim of the study

The main aim of this study was to provide a brief and precise review of the current knowledge regarding CKD and its treatment-related influence on ear and nose .

Methods

This cross sectional study was conducted from baqubah general hospital /dialysis center , from November 2022 to April 2023. The inclusion criteria were patients with chronic kidney disease. Ethical clearance and approval were respectively obtained. Pure tone audiometry was performed to determine the hearing acuity of the participants by presenting tones via both air and bone conduction .

Sampling technique

A multistage sampling technique was used to select participants. Study place was selected by simple random sampling . 65 patient were randomly selected. The patient were then stratified based on whose had symptoms of hearing loss , tinnitus , vertigo , nasal bleeding and obstruction . The detailed age , sex , presence of chronic disease (HTN,DM ,HF) are recoded .

Statistical methods

After collection, data were checked manually and analyzed by computer based program Statistical package of social science(SPSS) 20 version. Results were expressed as mean ± SD, or frequency or percentage.

Result

Majority (64%) of the participants in cases were males. The mean ages of the cases were 38.18 ± 8.32 years.

Table 1 etiology , duration of CKD and medications

Variable	Causes	n (%)
Etiology	Obstructive uropathy	2 (4.0)
	Hypertension	25 (50.0)
	Chronic glomerulonephritis	10 (20.0)
	Hypertension and Type 2 diabetes melitus	13 (26.0)
Duration of CKD	Less than 5 years	20 (40.0)
	5 years and above	30 (60.0)
Medica-tions	Supplements	50 (100.0)
	Anti-diabetics drugs	12 (24.0)
	Anti-hypertensives	38 (76.0)

Table 2 mean air conduction thresholds

Mean air conduction threshold (dBHL)

Frequency (Hz)	Ears	Cases
		Mean ± s.d
250	Right	27.60 ± 10.61
	Left	25.70 ± 7.83
500	Right	24.80 ± 7.21
	Left	24.10 ± 7.84
1000	Right	22.20 ± 6.86
	Left	20.90 ± 6.75
2000	Right	20.95 ± 7.74
	Left	22.80 ± 9.04
3000	Right	26.10 ± 10.07
	Left	26.80 ± 10.29
4000	Right	29.00 ± 11.65
	Left	28.20 ± 11.83
6000	Right	33.60 ± 11.02
	Left	32.90 ±16.04
8000	Right	37.50 ± 16.17
	Left	38.10 ± 17.46

Table 3 mean bone conduction threshold

Mean bone conduction thresholds (dBHL)

Frequency (Hz)	Ears	Cases
		Mean ± s.d
500	Right	7.20 ± 8.93
	Left	7.80 ± 10.41
1000	Right	7.70 ± 7.37
	Left	7.80 ± 6.93
2000	Right	9.10 ± 8.61
	Left	7.70 ± 6.93
3000	Right	10.90 ± 13.04
	Left	10.70 ± 11.87
4000	Right	14.00 ± 14.64
	Left	14.50 ± 14.37

Table 4 types and degree of hearing loss

Variable		n (Ears) (%)
Type of hearing loss	Normal hearing	39
	Conductive	-
	Sensorineural	26
	Mixed	-
	Total	65
Degree of hearing loss	Normal hearing	39
	Mild	20 (20.0)
	Moderate	4 (4.0)
	Moderately severe	2 (2.0)
	Total	65

The mean air conduction thresholds of the various frequencies among the CKD patients were used to plot an audiogram to ascertain the configuration of the hearing loss. A dome or tent-shaped configuration was observed in both ears.

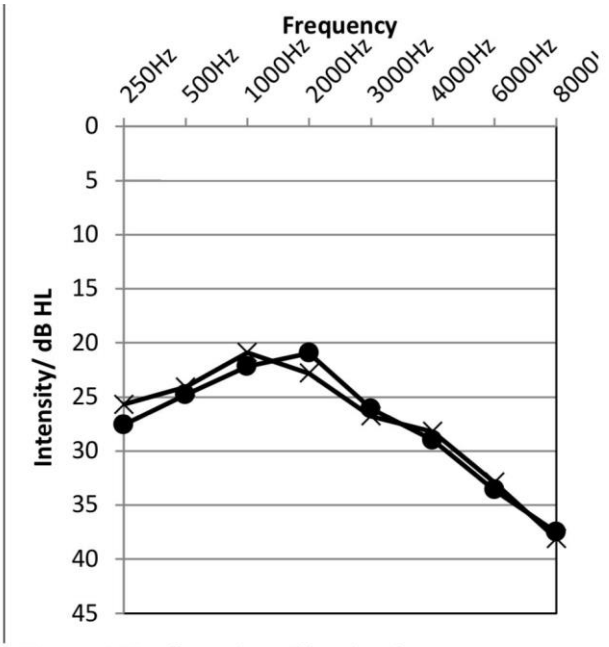


Figure 1 Configuration of hearing loss

The impairment was present in both ears among 10 of the cases while the remaining had unilateral losses. The only type of hearing loss present in this study population was SNHL. This was characterized by the presence of normal tympanogram and absence of air- bone gap across all the frequencies tested. The degree of hearing loss ranged from mild to moderately severe.

Association between duration of CKD and hearing loss was tested using chi-square at 95% CI. Statistically, there was no significant association between duration of CKD and hearing loss among this study population [$\chi 2$ (1, N = 50) = 0.035, p > 0.05], as shown in Table 5.

	Mild	Mod-erate	Moder-ately severe	To-tal	*p*-value
CKD duration					
<5 years	8	2	0	10	0.31
>5 years	10	14	2	16	

Although more male CKD patients (n =10) than females (n = 6) presented with hearing loss, the statistical analysis showed no significant association [X2(1, N= 50) = 0.02, p > 0.05] between gender and hearing loss among the study population.

_Tinnitus found in 17 patient and 15 patient found to have vertigo . 14 patient develop vertigo after > 5 years and 3 only < 5 years duration . 9 patient develop vertigo after >5 years and 6 patient found to have vertigo < 5 years . see figure 2

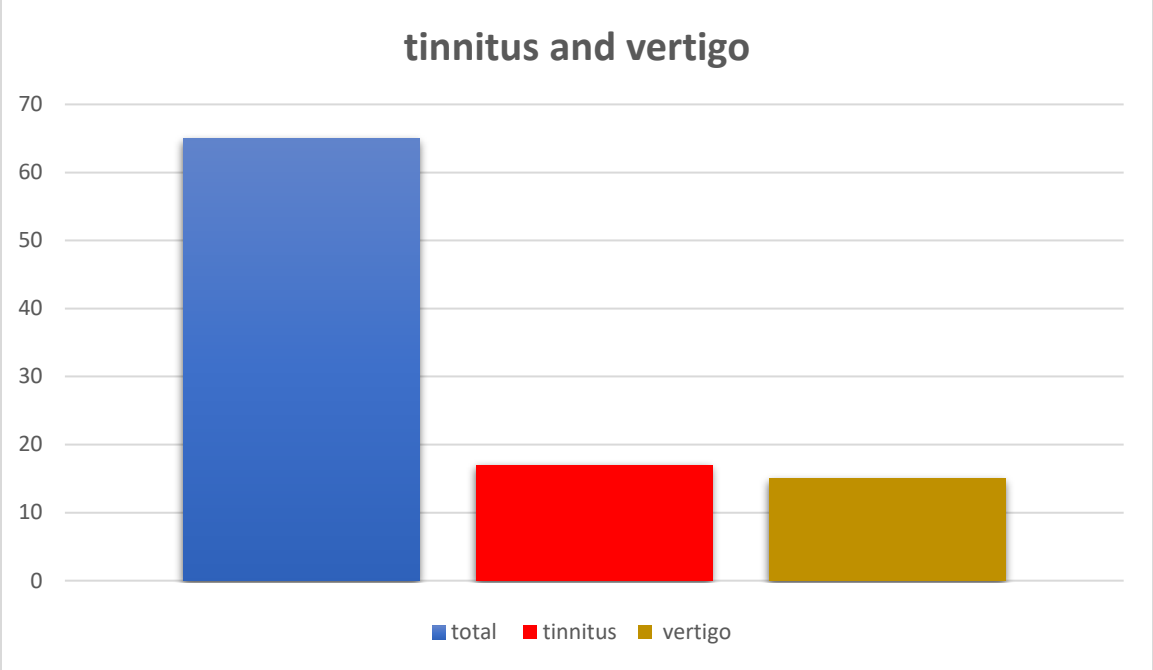


Figure 2

_Epistaxis found in 15 patient out of 65 . most cases develop in < 5 years duration of chronic kidney treatment (12 patient) and only 3 patient found to have epistaxis after > 5 years duration of treatment . see figure 3

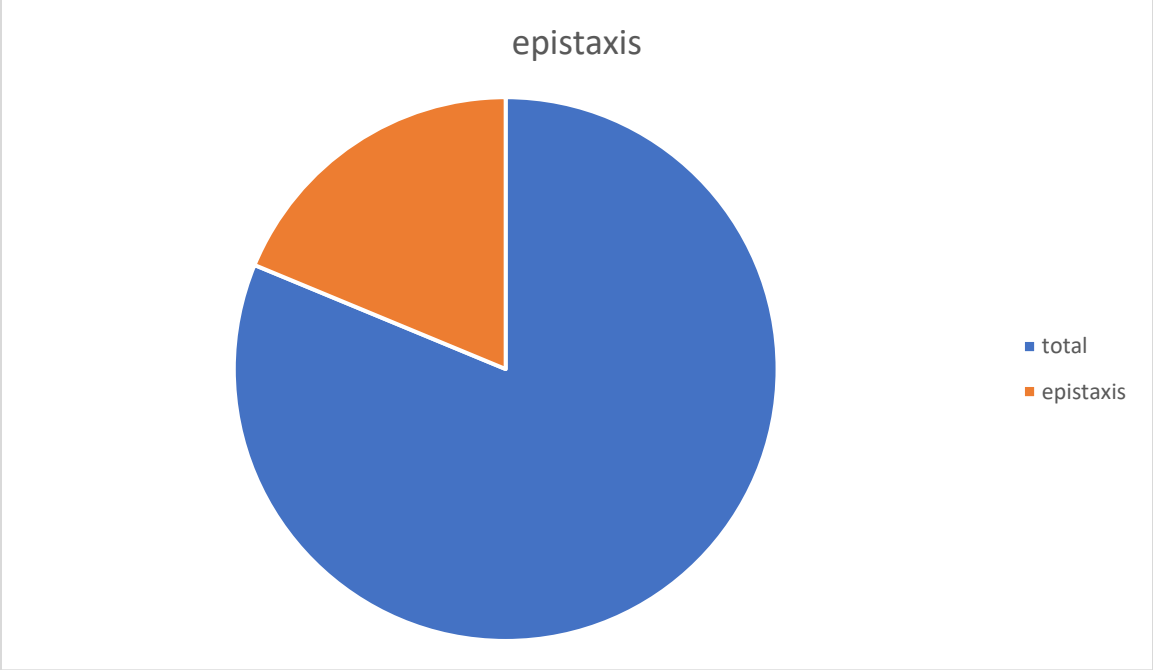
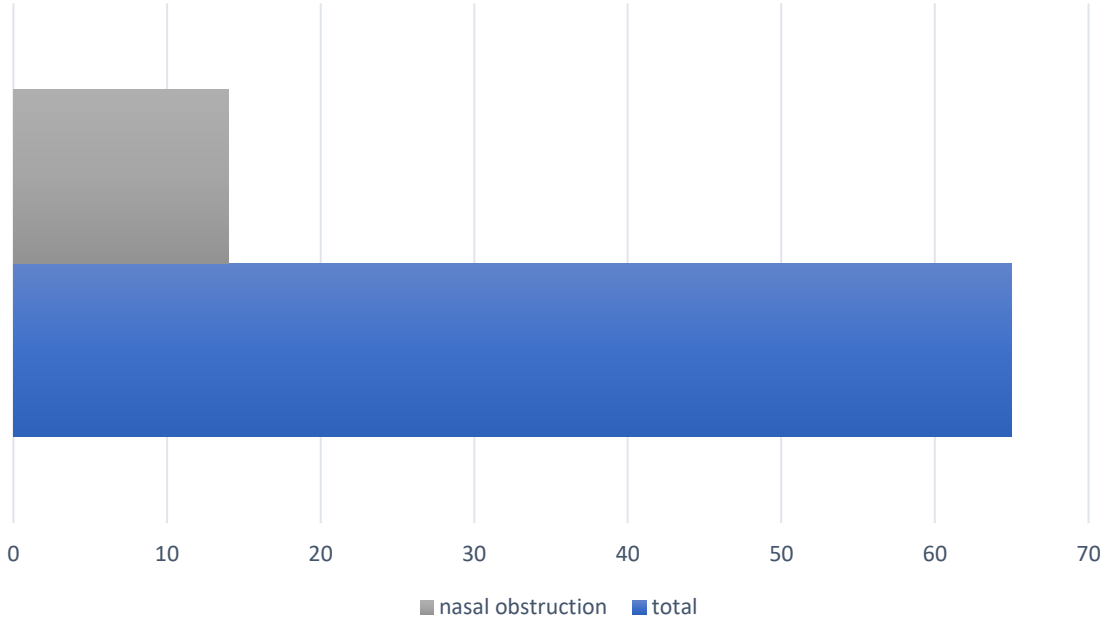


Figure 3

_ nasal obstruction in 65 patient was found in 14 patient . see figure 4



Discussion

CKD is associated with several complications. This study evaluated the hearing function of 65 CKD patients . It was postulated that there will be a significant difference between hearing thresholds of CKD patients and the non-CKD group. Several studies have reported significant difference in hearing thresholds between CKD patients and non-CKD individuals. In this study, higher hearing thresholds were recorded across all test frequencies among the cases .

Statistical analyses using unpaired t-test indicated that this difference was significant ($0.00 < p < 0.038$) at 95% confidence level in both ears. The difference could have been caused by the impact of electrolyte imbalance due to CKD or haemodialysis on the inner ear. The prevalence of hearing loss recorded in this study was 32.0% among the case. The difference in prevalence rates can be attributed to difference in sample size, inclusion and exclusion criteria, test protocols and hearing loss criterion. For instance, the addition of distortion product otoacoustic emission (DPOAE) test to pure tone audiometry raised the percentage of detected hearing loss in one study but the exact difference was not stated. However, DPOAE was not measured during this study. This may account for the relatively low prevalence recorded. The degree of hearing loss observed among the cases ranged from mild to moderately severe. Mild

hearing loss was most prevalent at 76.9%. The mean hearing thresholds in this study suggest that the low and high frequencies were more affected than the mid frequencies. The worse thresholds were recorded at high frequencies. This produced a dome-shaped audio- gram (Figure 1) for both ears. It is also important to note that increases in CKD durations imply increases in the patients' age. In a study involving 200 CKD patients in India, a significant correlation between duration of CKD and degree of hearing loss was recorded. Another author observed a relation between the two variables among 50 CKD patients but test for statistical significance was not stated. The results from the current study showed a weak positive correlation which was not significant at 95% confidence level.

Generally, men are more likely to suffer hearing loss than women. Odds of hearing loss was reported to be 5.5 times higher in men compared to women among the American population. This phenomenon has been attributed to lifestyle, nature of occupation and health seeking behaviour of men. Among CKD patients, this study as well as other authors observed no correlation between gender and hearing loss. This implies that CKD equally affects the auditory function of both men and women. Less than half of the population (48%) of CKD patients reported that they perceived reductions in their hearing level. However, hearing thresholds obtained were within normal in some cases. This may be attributed to limitations with respect to the test battery or response bias on the part of the patient. Most patients (60.0%) reported that the onset of the hearing loss was gradual, while the rest indicated reported it was sudden. More than half (56% and 60%) of the patients complained of fluctuating tinnitus and vertigo usually after dialysis. The tinnitus may be caused by hypertension since some of them described it to be pulsating. It can also be associated with the noisy environment of the dialysis unit. Uremic patients display a bleeding diathesis that is primarily due to hemostasis abnormalities, particularly platelet dysfunction and impaired platelet-vessel wall interaction. These patients, however, have a high prevalence of cardiovascular and thrombotic complications, despite the reduced platelet function .

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

Di Minno et al. 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.

, 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 . Moreover, removal of uremic toxins after HD has been shown to improve platelet abnormalities, resulting in a reduced risk of bleeding.

Nasal obstruction may be due to uremic deposit in the nasal mucous membrane leading to irritation, catarrh, edema, and nasal blockage. In this study we found 14 (21.5%) patient out of 65.

Recommendation

Based on the study outcomes, it is recommended that routine hearing assessments should be included in the protocol for managing patients with CKD. This will allow early detection of hearing loss for prompt intervention. Other studies to compare the hearing function of CKD patients before and after haemodialysis and also with those on other treatment regimens are also recommended. correction of blood urea and use of erythropoietin have a role in decrease the occurrence of epistaxis and both tinnitus and vertigo

Conclusion

This study therefore has concluded that CKD patients are at higher risk of experiencing hearing loss, vertigo, tinnitus ,epistaxis and nasal obstruction than non-CKD individuals. There was no significant association between duration of CKD, gender and hearing loss. There is no significant association between duration of CKD , gender and nose complications .

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