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Comorbidity of hypertension and chronic renal failure and their impact on oral complications: A cross-sectional study.

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Abstract

The present study aimed to investigate the influence of both end-stage renal diseases (ESRD) and hypertension (HTN) on the various oral manifestations and periodontal condition, to evaluate and compare the oral manifestations and periodontal health status in hypertensive patients with ESRD versus control, and to explore any possible correlation of the oral findings with systemic disease status. This was a cross-sectional study which included two equal groups of patients, Group I were hypertensive patients with ESRD and Group II were hypertensive patients only. All patients were hypertensive and were on antihypertensive medications. Regarding the incidence of oral lesions in both groups, a substantially higher proportion of cases in ESRD group had xerostomia, burning sensation, and altered taste ($p<0.05$). In addition, significantly higher proportion of cases in hypertensive group with ESRD group had stages (III) and (IV) periodontitis, while significantly higher proportion of cases in the hypertension group without ESRD had stages (I) and (II) ($p<0.001$). For gingivitis and lichenoid reaction, there was no meaningful difference between both groups ($p>0.05$). In the current study hypertensive patients with ESRD had a significantly higher prevalence of oral manifestations as xerostomia, burning sensation, and altered taste sensation, and were affected by more severe stages (III and IV) of periodontitis than HTN patients indicating the powerful influence of ESRD comorbidity on oral health. HTN and ESRD are closely connected systemic diseases with a high burden of oral manifestations especially when they occur concomitantly.

Keywords: Hypertension, ESRD, Lichenoid reactions, Periodontitis.

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1. Introduction

Management of patients with complex medical problems is one of the important challenges facing oral health care specialists. Renal disease is one of the systemic conditions closely linked to oral health and it is a major cause of morbidity and mortality worldwide [1-2]**.** Renal failure and hemodialysis treatment cause diverse systemic and oral complications including xerostomia, changes in salivary composition, bad breath, increased occurrence of caries, erosions, fungal and viral infections, as well as periodontal disease [3-5]. HTN is a very common disease affecting 20% to 30% of adults, and 2 -5% of children and adolescents in developed countries [6-9]. Anti -hypertensive medications can cause several oral complications which include lichenoid reactions, mucosal burning, xerostomia altered taste, gingival enlargement, bleeding, and angioedema [10-12].

HTN is a significant risk factor for chronic kidney disease (CKD) advancement to ESRD and for cardiovascular diseases associated mortality and morbidity [13-14]. The cause effect association concerning oral and systemic diseases is an important aspect in management of medically complex patients, as proper treatment of oral lesions is reported to be associated with significant improvement in the underlying systemic condition also sufficient knowledge of systemic conditions and their impact on oral health is of paramount importance to successful management of patients with underlying systemic diseases [15]. Moreover, periodontal diseases, oral ulcers, pulpitis, and different dental interventions may be associated with bacteremia which may cause substantial morbidity and sometimes mortality in renal failure patients, particularly those on hemodialysis [16-17].

Comprehensive knowledge of the oral manifestations of various systemic disorders including CKD patients is important as these oral symptoms could help in properly diagnosing or monitoring the underlying systemic disease. All precautions must be properly implemented to avoid the occurrence of bacteremia with its serious complications in such liable patients [18]. Likewise, more attention should be paid to the oral health attributes in hypertensive patients [19]. As prevalent complications and prolonged therapeutic etiquette of HTN are potential causes of the oral complications seen in hypertension. Therefore, more attention to oral wellbeing in systemically compromised patients is required especially in the developing countries where oral health aspect is often neglected leading to further decline of prognosis of the underlying systemic disease and overall health.

Thus, increasing oral and dental awareness among medically complex patients and other medical specialists as well as encouraging the collaboration between medical and dental professionals is essential [20]. The current research was carried out to investigate the influence of both ESRD and hypertension on the various oral manifestations and periodontal condition, to assess and compare the oral manifestations and periodontal health status in hypertensive patients with ESRD versus control, and to explore any possible correlation of the oral findings with systemic disease status.

2. Materials and Methods

2.1. Sample size

A power analysis was planned to have suitable power to apply a 2-sided statistical test of the null hypothesis that there is no difference between dissimilar tested groups concerning prevalence of oral lesions in hypertensive patients with and without ESRD. By adopting an alpha (α) level of 0.05 (5%), a beta (β) level of 0.2 (i.e. power=80%), and a critical (z) value of (1.96) founded on a previous study's result[1]; the expected sample size (n) was a total of (270) cases (i.e. 135 cases per group). Sample size estimation was executed via G*Power version 3.1.9.7[2].

2.2. Study design and patient selection

This was a cross-sectional study which included two equal groups of patients, Group I were hypertensive patients with ESRD and Group II were hypertensive patients only. All patients included in this investigation were hypertensive and were on antihypertensive treatment protocol.

2.2.1. Groups

2.2.1.1. Group I

Group I include 135 hypertensive patients with ESRD.

Inclusion criteria were hypertensive patients of both genders with any age above 20 and clinically diagnosed of having end stage renal disease.

Exclusion criteria were patients with previous malignancy or with transplanted kidney, smoking, patients with early stages of kidney diseases that don't require hemodialysis, and patients who may have any underlying systemic diseases rather than hypertension.

2.2.1.2. Group II

Group II include 135 hypertensive patients without ESRD.

Inclusion criteria were hypertensive patients of both genders with any age above 20.

Exclusion criteria were patients who have renal disease or any history of renal disorder, smoking.

2.2.2. Patient Selection

The research approval was acquired from the related Ethics Committee in the British University in Egypt. The trial was clarified to the patients who signed an informed consent. All personal data was kept private by coding & filing systems that were only accessible to the main investigator. Comprehensive oral evaluation was performed to all eligible patients. Data was collected by means of a structured questionnaire, followed by an oral examination. The form included mainly:

2.2.2.1. History taking

History taking includes:

1. Individual history, age, gender, occupation and marital status.
2. Chief complaint.
3. Medical condition.
4. Drug history; current prescribed drugs, formulations, duration, doses, frequencies, routes of administration, previous drug hypersensitivity reactions and adherence to therapy.
5. History of renal hemodialysis (from 6 months up to 2 years), frequency and duration.
6. Hemoglobin level.
7. Subjective clinical symptoms as changes in the sense of taste, burning mouth, xerostomia was recorded by asking patients in the questionnaires.

2.2.2.2. Intra oral Examination

Oral mucosa was examined carefully for any abnormalities. The primary investigator (A.A) did a careful oral examination to detect common oral manifestations such as gingivitis, periodontitis, lichenoid reactions, altered taste, burning sensation and xerostomia [21]. Periodontitis and gingivitis were diagnosed according to Russell's periodontal index, and xerostomia was confirmed by interrogating the subjective symptoms of patients; asking if they feel their mouth dry, if they sip liquids to help swallow dry food, if their mouth feel dry when eating a meal, and weather they think there is too little saliva in their mouth [22]. While the

[1]Madathil, Jinisha, et al. "Prevalence of oral lesions in patients with type 2 diabetes in north Kerala population." *Journal of Diabetology* 11.1 (2020): 32-38.

[2]Faul, Franz, et al. "G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences." *Behavior research methods* 39.2 (2007): 175-191.

other investigators, S.A. collected the data then D.G analyzed it.

2.3. Clinical periodontal examination

The primary investigator made a complete mouth periodontal examination, charts and radiographs to detect the periodontal condition and stage conferring to the recent of periodontal diseases classification (2017) for all the participants [23-24].

2.4. Statistical analysis

Categorical information was displayed as frequency and percentage values and was investigated using chi-square test. Statistical data were represented as mean and standard deviation values. Shapiro-Wilk's test was utilized to assess normality. Data were normally distributed and evaluated by independent t-test. The level of significance was set at $p<0.05$ for all tests. R statistical analysis software version 4.3.1 for Windows was used for analysis.

3. Results

The present study was conducted on 286 cases (134 cases in each group). Most of group I cases had grade (3) hypertension, while most of the cases in group II had grade (2) hypertension. For other parameters, the differences were not statistically significant ($p>0.05$) as shown in **Table 1.**

The intergroup comparisons of incidence of oral lesions revealed that substantially higher proportion of cases in group I had xerostomia, burning sensation, and altered taste sensation ($p<0.05$). In addition, meaningly higher proportion of cases in group I had stages (III) and (IV) periodontitis, and significantly lower proportion of cases with stages (I) and (II) than the group II ($p<0.001$). For gingivitis and lichenoid reaction, no significant difference was found between both groups ($p>0.05$) as shown in **Table 2.**

Correlating the incidence of oral lesions with the severity of hypertension revealed that in group II xerostomia, altered taste sensation, and lichenoid reaction were significantly associated with grade (2) hypertension. Periodontitis cases having stages (II), (III) and (IV) periodontitis were also significantly associated with grade (2) hypertension. while gingivitis was significantly associated with grade (1) hypertension. On the other hand, no substantial association was found between the occurrence of oral lesions and severity of hypertension in group I. There was no substantial association between the occurrence of oral lesions and duration of hypertension in either group I or group II.

4. Discussion

Hypertension is perhaps the most significant health problem in developed nations. Approximately one fourth of the world's adult residents have clinical hypertension but only 70% are alert to their condition and fewer than 20% are properly treated. The long-standing therapy and various complications caused by hypertension are underlying causes for the oral signs and symptoms encountered in hypertensive patients [19]. The recognized oral lesions associated with hypertension include gingival swelling, periodontitis, xerostomia, taste alteration, burning sensations, erythema multiforme, salivary gland swelling, paresthesia, and lichenoid drug reactions [19, 21].

The co-existence of other systemic diseases as echoed in the etiopathogenesis of secondary hypertension may contribute to oral complications [21]. Some of the frequent reasons of secondary hypertension such as CKD, diabetes mellitus, neoplasms, and thyrotoxicosis have established oral manifestations. CKD is one of the most common and important causes of secondary hypertension, and hypertension is a significant risk factor for developing CKD and an important leading cause of ESRD [25]. Therefore, HTN is both a reason and consequence of CKD, and its occurrence rises with progression of CKD. The incidence of uncontrolled HTN in patients with ESRD is as high as 80–90% [26]. Patients affected by ESRD have a high burden of oral symptoms that are either related to the disease itself or the hemodialysis treatment including, xerostomia, ammonia-like smell, dental erosions, mucosal pallor, gingivitis, tooth mobility and lesions as lichenoid reactions [5, 27]. Oral health represents a potential and preventable cause of poor health outcomes and is linked with more mortality in patients with systemic diseases such as ESRD and HTN due to their relation to infection, inflammation, and malnutrition [28]**.** Hence, proper management of the associated oral lesions in systemic diseases would improve the response to therapy of the underlying systemic disorder and the quality of life in such people [19].

Accordingly, this study was conducted to evaluate the oral changes in ESRD and HTN patients and to assess the influence of ESRD on the various oral manifestations encountered in hypertensive patients, and to explore any possible correlation of the oral findings with systemic disease status. Xerostomia is the most prevalent oral complication found in hypertensive patients, and it is associated with a persistently high blood pressure and with antihypertensive medications especially with diuretics [21, 12]**.** As well, dry mouth is extremely common in CKD and ESRD patients, which could be resulting from the fluid restricted diet, side effect of multiple medication use, the hemodialysis process, and salivary gland atrophy and fibrosis [29-32]. Experiencing dry mouth may lead to taste alterations, bigger hazard of infections as oral candidiasis, halitosis, difficulty in speaking, chewing, and swallowing, swiftly developing caries and periodontitis, and higher fluid consumption with interdialytic weight gain, eventually leading to poor quality of the patient's life [33-35]. Results of the present study showed that a significantly higher percentage of cases in group I had xerostomia, burning sensation, and altered taste ($p<0.05$) when compared to group II. This was comparable to a previous study which reported an increased frequency of taste disorders, xerostomia, and burning sensation in ESRD patients [36]**.**

The significantly higher percentage of xerostomia encountered in group I could be attributed to the pronounced impact of ESRD on salivary flow rate. Composition of saliva is also affected. As upon comparison with saliva of healthy individuals, saliva from ESRD patients had increased viscosity, increased urea concentrations, potassium, sodium, phosphorus, and total protein, reduced levels of calcium, increased pH and decreased buffering capacity. These changes may increase the extent of oral complications of xerostomia and, possibly, reinforce the feeling of a dry mouth [37-38]. Burning mouth sensation is a relatively common intraoral condition with varying etiologies that has a substantial bearing on life quality.

Table 1: Demographic data

Parameter		Group I	Group II	Statistic	p-value
Sex [n (%)]	**Male**	86 (64.2%)	82 (61.2%)	**0.26**	**0.613**
	Female	48 (35.8%)	52 (38.8%)		
Age (years) [Mean± SD]		52.76±9.82	55.63±7.68	**2.67**	**0.008**
Duration of hypertension [n (%)]	**<18 months**	61 (45.5%)	60 (44.8%)	**0.02**	**0.902**
	≥18 months	73 (54.5%)	74 (55.2%)		
Hypertension grade [n (%)]	**1**	0 (0.0%)	58 (43.3%)	**147.37**	**<0.001***
	2	50 (37.3%)	76 (56.7%)		
	3	84 (62.7%)	0 (0.0%)		

*; significant (p<0.05)

Table 2: Intergroup comparisons of oral lesions

Parameter		***n (%)***		χ^2	***p-value***
		Group I	***Group II***		
Hyposalivation	***No***	44 (32.8%)	103 (76.9%)	**52.45**	**<0.001***
	Yes	90 (67.2%)	31 (23.1%)		
Burning sensation	***No***	90 (67.2%)	117 (87.3%)	**15.47**	**<0.001***
	Yes	44 (32.8%)	17 (12.7%)		
Altered taste	***No***	90 (67.2%)	106 (79.1%)	**4.86**	**0.027***
	Yes	44 (32.8%)	28 (20.9%)		
Gingivitis	***No***	107 (79.9%)	99 (73.9%)	**1.34**	**0.247**
	Yes	27 (20.1%)	35 (26.1%)		
Periodontitis	***No***	27 (20.1%)	35 (26.1%)	**35.15**	**<0.001***
	Stage (I)	11 (8.2%)	22 (16.4%)		
	Stage (II)	18 (13.4%)	44 (32.8%)		
	Stage (III)	47 (35.1%)	24 (17.9%)		
	Stage (IV)	31 (23.1%)	9 (6.7%)		
Lichenoid reaction	***No***	122 (91.0%)	128 (95.5%)	**2.14**	**0.143**
	Yes	12 (9.0%)	6 (4.5%)		

*; significant (p<0.05)

Xerostomia or an altered taste may be associated with the pain [39]. Regardless of its impact, BMS barely received attention from health care providers as well as the patients who usually fail to report the problem [40-42]. The complaint of burning mouth sensation has been reported in hypertensive patients in some studies [43-45]**.** And is mainly caused by the drugs used in treatment of HTN or because of xerostomia. Nevertheless, burning mouth sensation was reported to be significantly prevalent in CKD patients and this was a consistent finding of several studies [46-50]. This could be credited to the dry mouth, effects of medications, and peripheral nerves injury by the uremic toxins accumulating in the body of CKD and ESRD patients. The significant influence of this particular cause could explain the significantly higher prevalence of burning mouth sensation in ESRD group I (32.8%) when compared to group II (12.7%) that encountered in the present investigation. Altered taste sensation was found in the current study in 32.8% of group I and 20.9% in group II cases with a significantly high difference. This was in line with prior articles reporting a prevalence range of taste disorder from 31 to 95% among ESRD affected subjects [51-52]. A study by *Liu et al.,* reported an altered taste sensation ranging from 4.1 to 6.4 in hypertensive patients [53]. Altered taste sensation is one of the important factors influencing the poor nutritional status of many patients with CKD. Accumulation of toxins between dialyses sessions had resulted in more loss of taste sensation as they approached the next dialysis appointment [54]. Additionally, disorders of smell and taste have been commonly described in the elderly and in subject on medications, as antibiotics, antihypertensive, neurologic, endocrine and antihyperlipidemic drugs [55].

The significantly higher prevalence of altered taste sensation found in the present study in group I in comparison to group II is possibly attributable to the increase of uremic toxins in the saliva of ESRD patients, and the influences of those uremic toxins on the peripheral and central nervous system with the taste receptors [49, 56-58]. Periodontal disease is a widely prevalent inflammatory as well as infectious illness that often develops an upregulated inflammation with subversion of immune response. Recent evidence suggests a link between periodontitis and hypertension [59]. As they both have some mutual predisposing factors. Furthermore, presence of low-grade general inflammation was considered as a rational biologic connection of both diseases with raised risk of cardiovascular disease [60-61]. Moreover, a high frequency of periodontal disease was observed in CKD patients which could be attributed to genetic polymorphism or drug usage that modifies the immune response to periodontal pathogens or by increasing the host vulnerability to periodontal infection [62-63]. In the current study, a substantially higher proportion of cases in ESRD group in comparison to group II had stage (III) and (IV) periodontitis and significantly lower percentage of cases had stage (I) and (II) periodontitis. Furthermore, fewer periodontally healthy cases were found in group I compared to group II, indicating a stronger association of ESRD with more advanced periodontitis cases. This could be explained by the presence of micro- and macrovascular problems associated with ESRD [64].

The impairment of immune response, due to dysfunction of macrophages and lymphocytes, which disrupts the host-microbe homeostasis leading to microbial dysbiosis [65]. This dysbiosis causes the irreversible tissue damage in periodontitis [66-67]. These results agreed with prior research reporting a 99% prevalence of periodontitis in ESRD patients [68]. Likewise, a 100% incidence of periodontitis was reported in hemodialysis patients [69]. Other studies reported similar results in renal disease patients [70-71]**.** Additionally, a recent study reported that stages (III) and (IV) periodontitis were the most prevalent among ESRD patients [72]. On the other hand, in group II a substantially higher proportion of cases had stage (I) and (II) periodontitis. While stage (III) and (IV) periodontitis cases were significantly lesser than group I. Which is in agreement with prior research reporting that hypertensive patients were most commonly associated with stage II periodontitis [73]. The incidence of lichenoid reaction in the current results was found to be higher in group II (9.0%) than in group I (4.5%) with no significant difference. This was in line with earlier studies which reported the occurrence of lichenoid reactions in hypertensive patients [21, 12, 74]. Which is mainly resulting from the use of antihypertensive medications most commonly angiotensin converting enzymes inhibitors particularly captopril and the combined use of beta -blockers and angiotensin receptor blockers [21]**.** A few studies have investigated the oral manifestations found in hypertensive patients. Likewise, a limited number of studies researched the common oral lesions in ESRD patients, but none was done to discover the possible combined effect of both diseases on the extent and severity of the oral manifestations. The current research thus aimed to shed light on the impact of ESRD on the various oral manifestations encountered in hypertensive patients in Egyptian population where the burden of both hypertension and ESRD is continuously escalating.

In the current study the occurrence of oral symptoms as xerostomia, burning sensation, altered taste sensation and periodontal disease was substantially higher in the ESRD group (group I) than in the HTN group without ESRD (group II) denoting the substantial impact of ESRD on oral health which could be due to malnutrition, limited diets, neglecting oral hygiene, suppressed immunity, and drugs side effects [47]**.** But more importantly, this detrimental impact of ESRD is attributed to uremic toxins which are responsible for the various symptoms of uremia causing poor quality of life in ESRD patients on dialysis. However, despite many advances in dialysis procedure over the last decades, the occurrence of uremic complications is still the same as uremic toxins are not entirely removed by dialysis [58].

4. Conclusions

In the present study hypertensive patients with ESRD had a significantly higher prevalence of oral manifestations as xerostomia, burning sensation, and altered taste sensation, and were affected by more severe stages (III and IV) of periodontitis than HTN patients indicating the powerful influence of ESRD comorbidity on oral health. This could be related to impaired drug excretion, inflammation, impaired immunity, or to hemodialysis itself. Oral health represents a potential and preventable cause of poor health outcomes in patients with systemic comorbidity. Thus,

proper assessment and management of the associated oral lesions would enhance the general health and quality of life in such individuals. Therefore, dental and medical collaboration is of paramount importance for optimal patient care. The limitation of the current study was being single centered. HTN and ESRD are closely connected systemic diseases with a high burden of oral manifestations especially when they occur concomitantly.

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