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Clinico demographic profile of chronic kidney disease patients and its manifestations on oral cavity and throat at a tertiary care centre in central India-original study

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***Abstract*---**With the aging of the population chronic kidney disease (CKD) has become one of the most common noncommunicable disease in the world as well as a leading cause of mortality. The present study was designed to describe the clinicodemographic profile of CKD patients and its manifestations on oral cavity and throat in central India, Madhya Pradesh (M.P.). This was a cross sectional, analytic study conducted in the Department of Medicine, Sanjay Gandhi Memorial Hospital (SHMH), associated with Shyam Shah Medical College (SSMC), Rewa, in the central India, M.P. between February

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2019 and August 2020.Data of 127 patients with CKD were recorded and studied. The mean age of patients was 50.86±17.28 yr, 70.07 percent males and 29.93 percent female's .84.70 percent were from rural area, mostly having >1 month of duration of CKD. 74.02% patients were in stage 5 of CKD, all on dialysis. 44.09% were associated with diabetes & 72.44% with hypertension. Most patients have Serum urea levels of >101 mg/dl with a mean level of 146.85 mg/dl, serum creatinine of >5mg/dl in most patients, serum hemoglobin levels of <7gm% in 54.33% and most have albuminuria. The oral cavity and throat manifestations includes pallor overall mucosa in 93.70 percent, xerostomia or dry mouth in 84.25%, uremic odour/halitosis in 72.44%, Sore throat in 64.56%, lip pigmentation in 63.77%, periodontitis in 48.81%. There was a significant correlation between Uremic odour with high urea levels ($p<0.00052$). Dry mouth was correlated with duration of dialysis i.e., for <1 year ($p<0.032$).CKD is associated with huge health system costs, especially in late stages, includes consistent episodes of dialysis and transplantation. Impact of CKD on oral cavity and throat plays important role in the progression of disease. Prevention of these manifestations decreases the morbidity and overall prognosis in the CKD patients.

***Keywords*---**chronic kidney disease, oral, throat, pharyngeal, xerostomia, pallor, halitosis.

Introduction

Chronic kidney disease (CKD) is a global health problem that increases the risk of noncommunicable illnesses such as cardiovascular disease.[1] CKD affects more than 322 million people worldwide,[2] and the number of patients with end-stage renal disease (ESRD) treated with dialysis or transplantation reaches 2.6 million. [3] CKD is also a primary cause of death, as the population ages. In the United States, half of the population is anticipated to acquire CKD at some point in their lives.[4]In the SEEK - India cohort study, the prevalence of CKD was 17.2 %.[5] The development of CKD has been linked to a number of risk factors. GFR below 60 ml/min/1.73 m2 is strongly linked to age, hence population ageing is virtually always accompanied with an increase in CKD burden. In multivariable-adjusted analyses, greater age is generally associated with a decreased risk of getting ESRD, despite the fact that ESRD incidence rates are highest among people over 65.[6,7] Women have a higher chance of developing CKD but a lower risk of developing ESRD than males.[8]Bad breath, i.e. halitosis, dry mouth or xerostomia, periodontal disease, dysgeusia, candidiasis, parotitis, abnormal lip pigmentation, a burning feeling in the mouth, and aphthous ulceration were all common oropharyngeal abnormalities of CKD patients.[8]

CKD risk is also influenced by socioeconomic variables. In the United States, those with lower socioeconomic class had a higher risk of CKD and a faster rate of GFR decrease, and this result has been confirmed in many other industrialized nations. [6, 9]. Diabetes mellitus and hypertension are frequently identified as key

contributors to CKD in the developed world, and a new research reveal that these factors are also present in the developing country.[6] Patients with CKD are also at risk of oral, dental and pharyngeal abnormalities constituted a significant proportion. Diabetes mellitus may have wedged the occurrence of pharyngeal/throat lesions in individuals with CKD.[10] In this study of CKD patients, clinicodemographic profile with its impact on oral cavity and throat were studied and investigated.

Material and Methods

This was a cross sectional, analytical study conducted in the Department of Medicine, Sanjay Gandhi Memorial Hospital (SGMH), associated with Shyam Shah Medical College (SSMC), Rewa, in the Vindhya region between February 2019 to August 2020 (15 months) with a sample population of 127 cases. The study was conducted for duration of 15 months on the patients with all diagnosed chronic kidney disease patients above the age of 18 years as inclusion criteria with willing to participate in the study. Detailed history about the patients' clinical and demographic information such as age and gender, the cause of renal failure, and the time duration on dialysis was retrieved. Most recent tests provided information on the patients' laboratory testing. After the process of history taking, detailed examination by expert in dentistry and ENT with routine instruments for manifestations of oral cavity and throat were examined and noted and then clinically assessed and ordered some baseline investigation like CBC, LFT, RFT, ABG, RBS, Serum Sodium, Serum Potassium and noted them for detailed discussion.

Patient's proforma was maintained which included the clinicodemographic particulars and the manifestations of oral cavity and throat. The study was approved by Ethical Committee of the institute and informed consent was obtained from every case. CKD was diagnosed by USG abdomen and eGFR measurement was done for staging of CKD by crockford-gault formula. Patients with < 18 years of age, who were not willing to participate in the study, associated malignancy, collagen vascular disorder, patients on steroid, patients with bleeding disorder and pregnancy were excluded from the study.

Statistical Methods

A total of 127 consecutive patients diagnosed with chronic kidney diseases with inclusion and exclusion criteria were selected for the study. Chi square test was used for statistical analysis. A p value <0.05 was considered significant.

Results

Table 1
Clinico demographic profile of CKD patients
(n= 127)

TABLE 1: CLINICODEMOGRAPHIC PROFILE OF CKD PATIENTS		
	No. Of Cases	Total %
AGE DISTRIBUTION OF PATIENTS		

17-29 yr	13	10.23%
29-41 yr	21	16.53%
41-53 yr	44	34.64%
53-65 yr	27	21.25%
65-77 yr	12	9.44%
77-89 yr	7	5.51%
89-101 yr	3	2.36%
GENDER DISTRIBUTION OF PATIENTS		
MALE	89	70.07
FEMALE	38	29.93
TOTAL	127	100.00
AREA DISTRIBUTION OF CKD PATIENTS		
URBAN	16	12.59
RURAL	111	87.40
TOTAL	127	100.00
1 month - 1 year	91	71.65
> 1 year	33	25.98
DIALYSIS DISTRIBUTION		
Dialysis	94	74.01
Non-dialysis	33	25.98
DURATION OF DIALYSIS		
< 1 month	16	17.02
1 month - 1 year	60	63.82
≥ 1 year	18	19.14
ASSOCIATED DIABETES		
PRESENT (+)	56	44.09
ABSENT (-)	71	55.90
ASSOCIATED HYPERTENSION		
PRESENT (+)	92	72.44
ABSENT (-)	35	27.55
SERUM UREA		
< 100	41	32.83
101 - 200	57	44.88
201 - 300	21	16.53
>300	8	6.29
DISTRIBUTION OF SERUM CREATININE		
< 5.0	38	29.92
5.0 - 15.0	68	53.54
> 15	21	16.53
HEMOGLOBIN LEVELS		
< 7 gm%	69	54.33
7.1-8.9 gm %	31	24.09
9-10.9 gm%	21	16.53
11 gm% or more	6	4.72
URINE ALBUMIN		

Traces	64	50.39
1+	24	18.89
2+	14	11.02
3+	20	15.74
Nil	5	3.93
DISTRIBUTION OF CASES BY ESTIMATED GLOMERULAR FILTRATION RATE (EGFR) AND STAGES OF CKD		
90+ /Stage 1	4	3.14
60-89 / Stage 2	7	5.51
45-59 / Stage 3A	3	2.3
30-44 / Stage 3B	5	3.93
15-29 / Stage 4	14	11.02
<15 / Stage 5	94	74.01
TOTAL	127	100.00

Table 2
Oral cavity and throat manifestations in CKD

TABLE 2 : ORAL CAVITY AND THROAT MANIFESTATIONS IN CKD							
MANIFESTATIONS	NUMBER (N=127)	%	MALES	%	FEMALES		%
Oral Cavity Manifestations							
Xerostomia	107	84.25	72	56.69	35		27.55
Lip Pigmentation	81	63.77	59	46.45	22		17.32
Pallor	119	93.70	82	64.06	37		29.13
Angular Chelitis	38	29.92	26	20.47	12		9.4
Gingivitis	23	18.11	15	11.81	8		6.29
Depapillated Tongue	60	47.24	47	37	13		10.2
Mucositis	52	40.94	36	28.34	16		12.59
Cracked Tongue	63	49.60	38	29.92	25		19.68
Cracked Lips	59	46.45	42	33.07	17		13.38
OSMF	14	11.02	7	5.51	7		5.51
Staining of teeth	36	28.34	30	23.62	6		4.7
Attrition of teeth	25	19.68	16	12.59	9		7.08

Periodontitis	62	48.81	43	33.85	19		14.96	
Missing Teeth	22	17.32	16	12.59	6		4.72	
Edentulism	45	35.43	33	25.98	18		14.17	
Dentatoalveolar abscess	40	31.49	31	24.40	9		7.08	
Throat Manifestations								
Halitosis	92	72.44	65	51.18	27		21.25	
Mucosal Ulceration	30	23.62	22	17.32	8		6.29	
Sore Throat	82	64.56	55	43.30	27		21.25	
Candidiasis	12	9.44	6	4.72	6		4.72	
Lichenoid changes/gingival overgrowth	6	4.7	5	3.93	1	0.78	0.78	

Table 3
Association between serum urea levels and halitosis

TABLE 3: ASSOCIATION BETWEEN SERUM UREA LEVELS AND HALITOSIS		
	Halitosis	
	Present	Absent
Serum Urea >146.85 mg/dl	47	6
Serum Urea <146.85 mg/dl	45	29
Total	92	35
P value - 0.00052(statistically significant)		

Table 4
Association between lichenoid changes/gingival growth vs dialysis status

Table 4: ASSOCIATION BETWEEN LICHENOID CHANGES/GINGIVAL GROWTH VS DIALYSIS STATUS			
	Present	Absent	
Dialysis	2	92	
Non-dialysis	4	29	
Total	6	121	
P value - 0.019(statistically significant)			

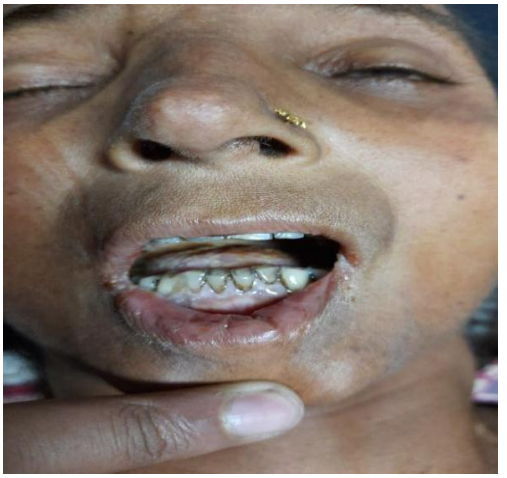

Fig 1. Clinical picture with Xerostomia and Oral Sub mucous Fibrosis

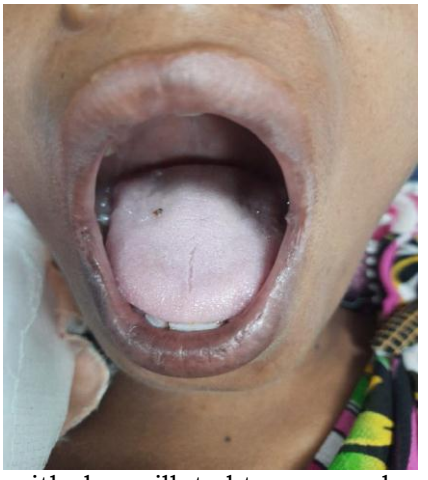

Fig 2. Clinical picture with depapillated tongue and cracked pigmented lips

Discussion

This was a cross-sectional study of patients in various stages of CKD were included, with a mean age of 50.86 years (ranged from 17-94 years). Predominantly patients were in age group 41-53 years (34.64%, with >65 years as 22.04%). Different studies showed that elderly (age >65 years) were predominantly affected. A study similarly showed age >65 years with 22.04% patients.[11]. Male predominance with 70.07% (89), with a male to female ratio of 2.34:1 was observed in the study. In a study, it was observed that males develop ESRD more quickly than females. [12]

Another study which was a meta-analysis has 65% males and 35% females on the rate of progression of renal disease women compared with men.13. Rural area has higher prevalence i.e., 87.40% (111) than the urban (12.59%) area. As the place of study was surrounded mainly by rural area and majority of population stays in rural area, there was higher prevalence among rural people than urban. Despite

the fact that the percentage prevalence was higher in more developed regions, predicted worldwide demographic shifts would increase the absolute number of persons in developing nations, where the population of the elderly will grow. In a developing economy, this rise will worsen the double burden of managing communicable and noncommunicable illnesses.[14]

The duration after disease for majority, i.e., 91 cases (71.65%) was between 1 month to 1 year, in 33 cases (25.98%) it was more than 1 year and in 3 cases (2.36 %) the duration after diagnosis was < 1 month. Out of 127 cases, 94 (74.01 percent, 66 males and 28 females) were having end stage renal disease/ stage 5 (eGFR of less than 15ml/min/1.73m2), stage 4 (eGFR of 15-29 ml/min/1.73m^2) constitute 14 cases (11.02% with 10 males and 4 females), stage 3B (eGFR of 30-44 ml/min/1.73m^2) constitutes 5 cases (3.93% with 4 males and 1 female),stage 3A (eGFR of 45-59 ml/min/m^2) constitutes 3 cases with 1 male and 2 females, stage 2 (eGFR of 60-89 ml/min/1.73m^2) constitutes 7 cases (5.51% with 5 males and 2 females) and stage 1 (eGFR of >90ml/min/m^2)constitutes 4 cases (3.14% with 3 males and 1 female). The bulk of the patients had end-stage renal disease, with 74 percent of them requiring dialysis. The majority of patients, 61.41 percent, had dialysis for more than one month. (Table 1)

Diabetes was common etiology in the patients of CKD in the study with 44.09 %(56) prevalence. In Diabetic patients there was a strong correlation of higher stages of CKD (stage 4 & 5) with the Anaemia taking the mean HB levels of 7.279, which came out to be highly significant (p=0.01). Similarly, there was also significant correlation between Urine albumin and Serum Creatinine levels when compared with the staging of CKD with p value as 0.03, 0.004 respectively. The growing worldwide prevalence of T2DM (type 2 diabetes mellitus) and chronic kidney disease (CKD) has encouraged research challenges to combat the epidemic DKD(diabetic kidney disease; additionally referred to as diabetic nephropathy). The fact that not all patients diagnosed with DKD have renal disease as a result of their diabetes mellitus may contribute to the limited success of many of these trials. Patients with CKD with diabetes mellitus (type 1 or type 2) may have frank DKD (in which CKD is a straight result of their diabetes status), NDKD (nondiabetic kidney disease) related with diabetes mellitus, or a blend of both NDKD and DKD. [15] Majority of patients of CKD have Hypertension in the study (72.44%) and 40 patients have both Hypertension and DM. (Table 1)

The serum urea level in the study of CKD patients ranged from 35 to 448 mg/dl with a mean of 146.8595. In this study of CKD patients, serum creatinine levels varied from 0.56 to 23.5 mg/dl. It was less than 5 mg/dl in 38 cases (29.92%), between 5-15 for 68 patients (53.54%) and more than 15mg/dl for 21 patients (16.53%). The hemoglobin level in the study of patients of CKD ranged from 2.1-15.8 gm % with a mean of 7.251 gm %. A total of 69 patients (54.33%) had a hemoglobin level of less than 7 gm%, indicating severe anemia. It was between 7.1-8.9 %(moderate anemia) for 31 patients(24.09%), 9-10.9 gm % (mild anemia) for 21 patients (16.53%) and 11 gm% or more for 6 patients (4.72%). (Table 1)

The Urine Albumin in this study of patients of CKD ranged from Nil-3+. Of these majority of 64 patients (50.39%) had Urine albumin in traces. It was 1+ for 24 patients(18.89%) , 2+ for 14 patients (11.02%) , 3+ for 20 patients (15.74%) and

nil for 5 (3.93%) patients. Normal albuminuria, moderately increased albuminuria, and substantially increased albuminuria were found to be 27.4–56.4 percent, 2.9–10.0 percent, and 0.4–3.2 percent, respectively, throughout GFR categories G2–5. 3.7–13.4 percent of individuals fell into the KDIGO 2012 moderate risk CKD group, 0.9–5.6 percent into the high-risk group, and 0.3–4.8 percent into the very high-risk group, based on GFR categories G2–5 and albuminuria categories A1–3.These findings are essentially similar with those of a recent cross-sectional study that assessed the global incidence of CKD stratified by the KDIGO 2012 categories using data from general population CKD screening programmes in China, Mongolia, India, Nepal, Iran, Nigeria, Moldova, and Bolivia .[16]

In this study out of 127 patients, 72 males (56.69%) and 35 females (27.55%) suffered from Xerostomia as seen in Fig. 1. The total prevalence in both sexes was 84.25% (107 cases). There was a strong association between dialysis duration and Xerostomia (p=0.032) as seen in Table 3, with greater manifestations when dialysis duration was less than one year. Other manifestations like lip pigmentation, pallor, angular cheitis, gingivitis, depapillated tongue, mucositis, cracked tongue, cracked lips and OSMF are not significantly very much linked with the duration of dialysis. Xerostomia was the most frequent mouth lesion among kidney transplant recipients. [18, 19] A meta-analysis showed that 48.4% of CKD patients had xerostomia. (17) According to Swapna et al., xerostomia occurred in 62 percent of non-diabetic CKD patients on hemodialysis compared to 78.7% of diabetic CKD patients on hemodialysis. As a result, the authors believe that individuals with CKD and DM had a greater prevalence of dry mouth than those with CKD alone. [20]

Lip Pigmentation was present in 81 patients (63.77%) as seen in Fig. 2. It was noted in 59 males (46.45%) and 22 females (17.32%). 82 males (64.06%) and 37 females (29.13%) had visible pallor and the total incidence is 93.70% (119 patients), Angular Cheilitis was noted in 38 patients (29.92%) totally. There were 12 females (9.4%) and 26 males among this group (20.47 percent). Gingivitis was present in 15 males (11.81%) and 8 females (6.29%). Depapillated tongue was noted in 47 male (37%) and 13 females (10.2%). Mucositis was observed in 52 patients (40.94%) totally. Of these 36 were males (28.34%) and 16 were females (12.59%).Cracked tongue was observed in 63 patients (49.60%) totally. Of these 38 were males (29.92%) and 25 were females (19.68 %). Cracked lips were observed in 59 patients (46.45%) totally. Of these 42 were males (33.07%) and 17 were females (13.38 %). OSMF was present in 14 patients (11.02%) totally with 7 patients (5.51%) in each sex.

Halitosis or foul breath was noted in 92 patients (72.44%) totally. There were 65 men (51.18 percent) and 27 women among them (21.25 percent). Minor & major aphthous ulceration was observed in 30 patients (23.62%) totally. Of these 22 were males (17.32%) and 8 were females (6.29 %). In a meta-analysis study 8.6% of patients with stage 5 CKD on hemodialysis had mucosal ulcerations.[17] In all, 82 individuals (64.56 percent) complained of a sore throat. Of these 55 were males (43.30%) and 27 were females (21.25 %). A study observed halitosis in 91% patients of CKD not having diabetes and were not on any dialysis, 90% of CKD on dialysis not having diabetes, in diabetics with CKD not on dialysis - 76 percentage

patients and 75% DKD on dialysis. Another study had 53.3% patients with bad odor which were on dialysis.[20]

Candidiasis was observed in 12 patients (9.44%) totally. Both sexes included 6 patients (4.7%) each. It was also observed in this study that the occurrence of candidiasis increased with the increase in duration of time on dialysis.[17] Gingival Bleeding was observed in 23 patients (18.11%) totally. Of these 15 were males (11.81%) and 8 were females (6.29 %). In a study , gingival overgrowth was seen in 85% patients who had transplanted their kidney and young patients were more susceptible to it .[20] Lichenoid changes/gingival overgrowth were observed in 6 patients (4.7%) totally. Of these 5 were males (3.93%) and single female (0.78%) depicted with lichen planus like Wickham's striae. There was a significant relationship (p value = 0.00052) between blood urea levels and halitosis, which was seen in 47 patients with higher-than-average serum urea levels (>146.85 mg/dl) compared to 29 patients with lower-than-average serum urea levels (146.85 mg/dl) as seen in Table 4.

Patients on dialysis for less than a year were more likely to have halitosis. Mucosal ulceration had an inverse relationship with dialysis time, with the greatest manifestation (18) occurring when dialysis lasted less than a year. Similarly, when dialysis was completed in less than a year, sore throats, Candidiasis, gingival bleeding, and lichenoid changes/gingival overgrowth were more common. There was a significant association (p value = 0.019) between the lichenoid changes / gingival growth vs. dialysis status which was present in 2 patients on Dialysis than the 29 patients in whom manifestation was not found in non-dialysis group.

A study found that 53.3 percent of CKD patients on hemodialysis had halitosis. [20] According to a meta-analysis mucosal ulcerations were observed in 8.6% of ESKD dialysis patients (n=832) and 1.3 percent of RTRs (n=453), respectively.[17] Patients with CKD often have pale gingivae with uncontrolled gingival bleeding, which is caused by anaemia, platelet failure caused by bacterial toxins, and is exacerbated by anticoagulant treatment and inappropriate vascular wall cell activity.[21] Oropharyngeal candidiasis is common in patients with CKD .[18]

Staining of teeth was observed in 36 patients (28.34%) totally. There were 30 men (23.62 percent) and 6 women among them (4.7 %). Total tooth attrition was reported in 25 individuals (19.68 percent). Of these 16 were males(12.59%) and 9 were females (7.08 %). Periodontitis was observed in 62 patients (48.81%) totally. Of these 43 were males(33.85%) and 19 were females (14.96 %). Missing Teeth was observed in 22 patients (17.32%) totally. Of these 16 were males(12.59%) and 6 were females (4.72 %). Edentulism was observed in 45 patients (35.43%) totally. Of these 33 were males(25.98%) and 18 were females (14.17 %). Dentatoalveolar abscess was observed in 40 patients (31.49%) totally. Of these 31 were males (24.40%) and 9 were females (7.08 %). Dentatoalveolar abscess significantly(p=0.001) correlated with the duration of dialysis, while others like attrition of teeth, periodontitis, missing teeth, edentulism and dentatoalveolar abscess are not significantly linked with the duration of dialysis. Other studies have verified that haemodialysis patients' periodontal health is poor, and that it is linked to indicators of malnutrition and inflammation. [22, 23]

Conclusion

CKD is associated with huge health system costs, especially in late stages, includes Dialysis and transplantation. The impact of CKD on the oral cavity was evidenced by significant changes, which pointed to an inter-relationship between oral health and CKD. This plays important role in the progression of disease. Prevention of these manifestations decreases the morbidity and overall outcome of the CKD.

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