ISSN 2515-8260 Volume 08, Issue 04, 2021

ORIGINAL RESEARCH

Study of oral manifestations in chronic kidney disease in vindhya Region

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ABSTRACT

Background: Normal kidney secretes nitrogenous waste product, regulate volume and acid /base balance of plasma and synthesize erythropoietin, 25-$(OH)_2$- cholecalciferol and renin. Chronic kidney disease (CKD) is caused by a progressive and irreversible decline in the number of nephrons. A wide variety of oral manifestations occurs in CKD patients. Determination and identification of these manifestations will improve the quality of life in these patients.

Methods: Thus, this cross-sectional study was 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 and August 2020.

Results: Out of 127 patients, maximum prevalence of oral manifestations occurring was pallor (93.70%), xerostomia (84.25%), halitosis (72.44%), sore throat (64.56%), lip pigmentation (63.77%), periodontitis (48.81%). High Urea levels were found to be highly significant when correlated with halitosis ($p<0.00052$). Xerostomia was found significant when correlated with duration of dialysis (<1 year) with $p<0.032$.

Conclusions: Manifestations of CKD are common during the progression of uremia. In the patients studied, the impact of CKD on the oral cavity was evidenced by significant changes, which pointed to an inter-relationship between oral health and CKD.

Keywords: Chronic Kidney disease, oral, xerostomia, periodontitis.

BACKGROUND

CKD is caused by a progressive and irreversible decline in the number of nephrons.[1] Clinical involvements at prior stages of CKD can effectually slow, halt or in some cases reverse the development to ESRD. The likelihood of avoiding early-stage CKD from emerging into kidney failure denotes a still-unfolding zone of revolution in nephrology, and real treatments for prior stages of CKD are still developing.[2]

The rising importance on CKD rather than ESRD alone has stood epidemiological encounters.[3] The prevalence of CKD was 17.2 percent in the SEEK-India cohort.[4] CKD affects all races, but, in the United States, a significantly higher incidence of ESRD exists in blacks than in whites; The black incidence rate is nearly four times that of whites.[5]

Prevalence is affected by regional factors such as demographic composition, comorbidity, smoking, and obesity. While the debate over which method of GFR estimation is the most accurate continues, it is undeniable that the introduction of KDOQI definitions, flaws and all, has created a simplified framework for conducting comparative epidemiological studies at the regional and international levels.[6] Bad breath/ halitosis, xerostomia, periodontal disease, dysgeusia, candidiasis, parotitis, aberrant lip pigmentation, a burning feeling in the mouth, and ulcerations were all common oral abnormalities in CKD patients.[7] Patients with CKD are also at risk of dental abnormalities, which constituted a significant proportion of all oral findings. Other comorbidities, such as diabetes mellitus, may have impacted the incidence of oral lesions in individuals with CKD.[8]

We wanted to study the oral manifestations of CKD patients with their clinical and demographical profile.

METHODS

This was a cross sectional study conducted in the Department of Medicine, SGMH, associated with SSMC, Rewa, in the vindhya region between February 2019 to August 2020 (15 months) with sample size was 127 cases. The study was conducted for duration of 15 months on the patients with following inclusion criteria –

- ✓ all diagnosed chronic kidney disease patients above the age of 18 years.
- ✓ patients who are willing to participate in the research.

Thorough history about the patients was taken and their records, demographic information such as age, gender, the etiology of renal failure and the length of time on dialysis was retrieved. The most current tests provided information on the patients' laboratory testing. After the process of history taking, detailed dental examination was done by dental expert in a location with adequate light on dental chair with routine diagnostic investigations for oral manifestation examination. After clinical examination some baseline investigations like CBC, LFT, RFT, ABG, RBS, Serum Sodium, Serum Potassium were advised.

The study was approved by the institutional ethical committee. Patient's informed consent was obtained and proforma was maintained which included questionnaire for oral manifestations with clinical and demographic particulars. CKD was diagnosed by USG abdomen and eGFR measurement for staging was done by Cockcroft-gault formula.

EXCLUSION CRITERIA INCLUDES

- ❖ Patients with < 18 years of age,
- ❖ Patients not willing to participate in the study,
- ❖ Malignancy,
- ❖ Collagen vascular disorder,
- ❖ Patients on steroid,
- ❖ Patients with bleeding disorder and
- ❖ Pregnant females.

STATISTICAL METHODS

Chi square test was used to find the association. A p value <0.05 was considered significant.

A total of 127 consecutive patients abiding with the inclusion and exclusion criteria were selected for the study.

ISSN 2515-8260 Volume 08, Issue 04, 2021

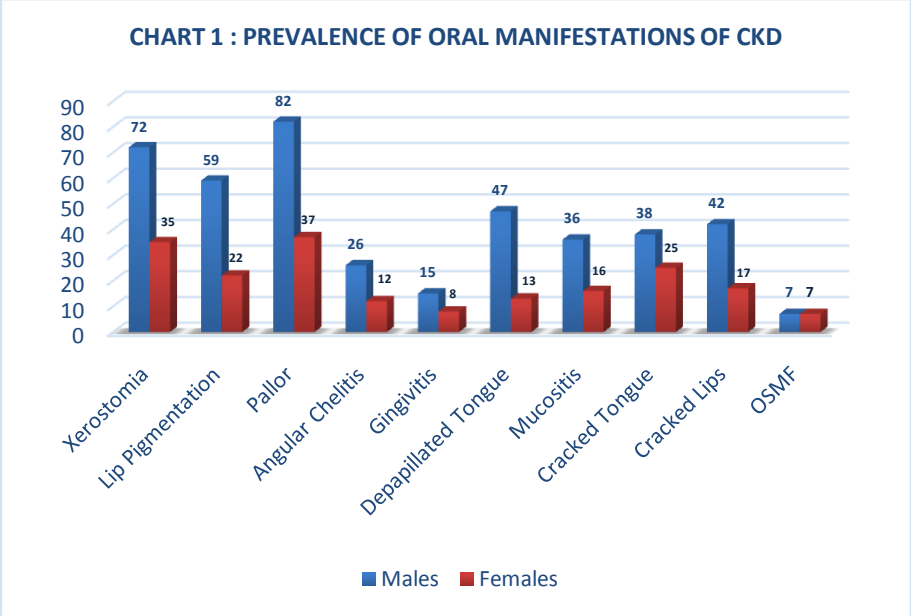
RESULTS

Table 1: Age distribution of cases			
Age in years	**No of patients**		**Total**
			NO.%
17-29	13		10.23%
29-41	21		16.53%
41-53	44		34.64%
53-65	27		21.25%
65-77	12		9.44%
77-89	7		5.51%
89-101	3		2.36%
Total	**127**		**100%**
Mean ± SD	50.86±17.28		
Range	17-94 years		

Table 2: Habitat distribution of cases		
Habitat area	**Number of patients**	**Total %**
Urban	16	12.59
Rural	111	87.40
TOTAL	127	100.00

Table 3 : Oral and dental manifestations in chronic kidney disease						
Manifestations	**Number(n=127)**	**%**	**Males**	**%**	**Females**	**%**
Oral manifestation						
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 cheilitis	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
Dentalmanifestations						
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

ISSN 2515-8260 Volume 08, Issue 04, 2021



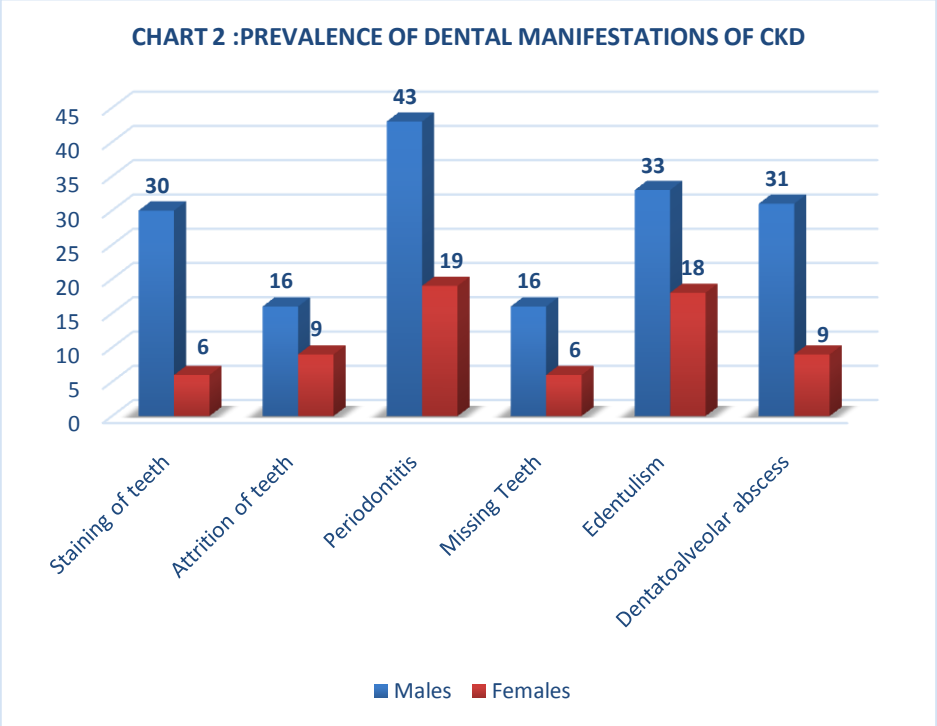


TABLE 4 : Distribution of cases by estimated glomerular filtration rate (EGFR) and stages of CKD

eGFR	Stage of CKD	No. of cases in males	No. of cases in females	Total No of cases	% of total cases
90+	1	3	1	4	3.14
60-89	2	5	2	7	5.51
45-59	3A	1	2	3	2.3
30-44	3B	4	1	5	3.93
15-29	4	10	4	14	11.02

<15	5	66	28	94	74.01
TOTAL		89	38	127	100.00

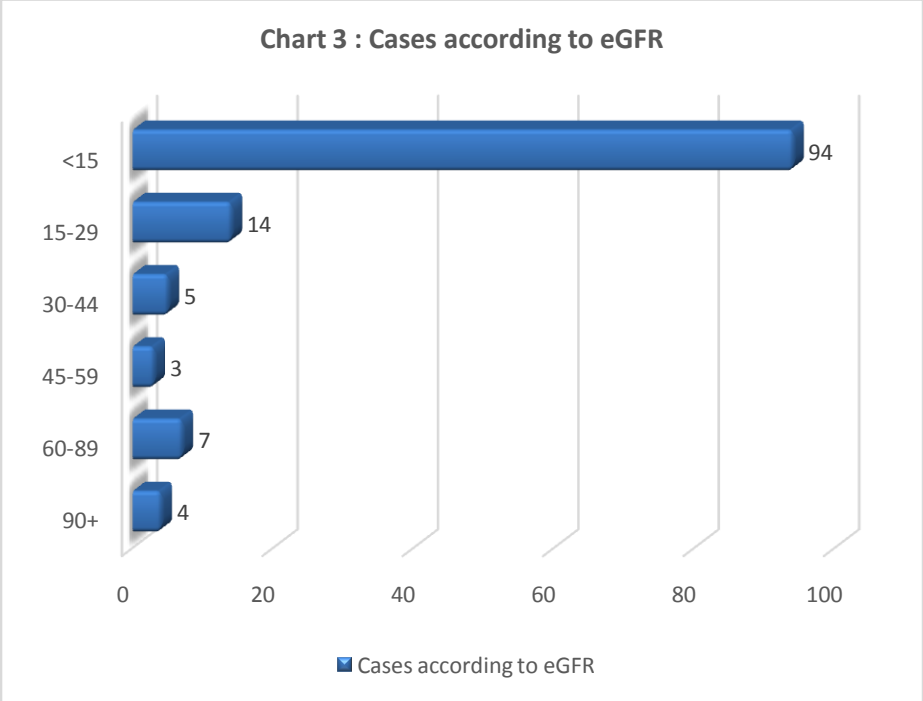


Table 5: clinical profile of chronic kidney disease patients		
Duration of ckd	**No of cases**	**%**
< 1 month	3	2.36
1 month - 1 year	91	71.65
> 1 year	33	25.98
Dialysis distribution		
Dialysis	94	74.01
Non-dialysis	33	25.98
Duration of dialysis		
< 1 month	16	17.02
1 month - 1 year	60	63.82
≥ 1 year	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

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> 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

Table 6: Correlation between serum urea levels and halitosis

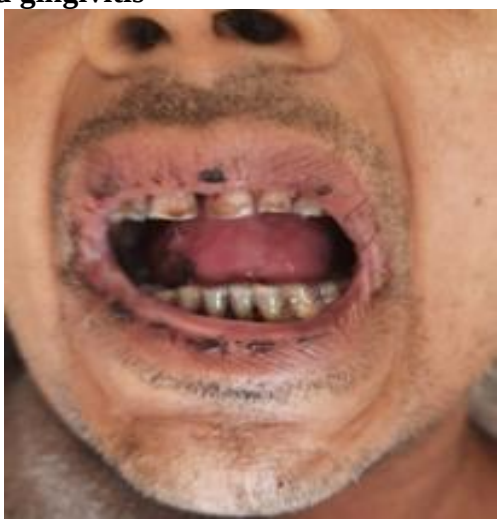
	Halitosis		
	Present	**Absent**	
Urea >146.85 mg/dl	47	6	
Urea <146.85 mg/dl	45	29	
Total	92	35	
P value = 0.00052			

Table 7: Correlation between lichenoid changes/gingival growth vs dialysis status

	Present	**Absent**	
Dialysis	2	92	
Non-dialysis	4	29	
Total	6	121	
P value - 0.019			

Figure1: A CKD patient with Periodontitis, angular cheilitis, depapillated tongue, xerostomia and generalised attrition of teeth

Figure 2 : A CKD patient with Grade 3 sub mucous fibrosis, black discoloration of teeth and mucosa and generalised gingivitis



DISCUSSION

Patients in various stages of CKD were included in this cross-sectional study, with a mean age of 50.86 years (ranged from 17-94 years) (Table no, 1). With aging the prevalence of CKD increases. A Japanese study founded the prevalence of CKD in elderly (>65 years) to be as many as 20%.[16] Our study revealed the similar results with maximum number of cases i.e. 22.04% patients were >65 years (34.64% in the age group of 41-53 years). The prevalence of CKD as calculated by the CKD-EPI equation is 46.8% in participants 70 years and more in the earlier study done under NHANES (National Health and Nutrition Evaluation Survey), compared to 6.71 percent in those 40–59 years of age.[17]

The present study has male predominance with 70.07% (89 patients), with a male to female ratio of 2.34:1. According to Joel et al in a study, males develop CKD more quickly than females.[18] Tazeen et al study have 65% males and 35% females in the meta-analysis on the rate of progression of renal disease women compared with men. [19]

The majority of the patients, i.e., 87.40% (111) were from rural area so much more than from the urban background (12.59%). Majority, i.e., 91 cases (71.65%) the duration after diagnosis 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 less than 1 month. 94 (74.01 percent, 66 males and 28 females) of the overall patients have an eGFR of less than 15ml/min/1.73m2, 15-29 ml/min/1.73m^2 constitute 14 cases (11.02% with 10 males and 4 females), 30-44 ml/min/1.73m^2 constitutes 5 cases (3.93% with 4 males and 1 female), 45-59 ml/min/m^2 constitutes 3 cases with 1 male and 2 females, 60-89 ml/min/1.73m^2 constitutes 7 cases (5.51% with 5 males and 2 females) and eGFR of >90ml/min/m^2 constitutes 4 cases (3.14% with 3 males and 1 female). Stage 5 CKD include 94 cases (74.02%), stage 4 includes 14(11.02%), stage 3B includes 5(3.93%), stage 3A includes 3(2.3%), stage 2 includes 7 (5.51%) and stage 1 includes 4 cases (3.14%) of total 127 cases. 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.

Diabetes was strongly associated with the patients of CKD in the study with 44.09% (56) incidence. Majority of patients of CKD have hypertension (HTN) in the study (72.44%) and 40 patients have both HTN and DM. The growing worldwide prevalence of T2DM (type 2 diabetes mellitus) and 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. [(34)] In a study, the incidence of self-reported HTN was 86 percent in the chronic renal insufficiency (CRIC) cohort, which comprised 3612 people with CRF (moderate to late stage), compared to 29 percent in the general population. [35,36]

The serum urea level in the study of CKD patients ranged from 35 to 448 mg/dl with a mean of 146.85. In a 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 7.25 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%). The pooled endpoint rate was substantially greater in patients with Hb 10 g/dl compared to Hb 1012 g/dl, although Hb 10 g/dl was solely associated with an elevated risk of CVD and mortality in G3 [Hazard Ratio (HR) 4, 49, (95 percent Confidence Interval (95 percent CI) 2069.80] Only G4 [HR 3.08 (95 percent CI 1.406.79)] and G5 [HR 1.43 (95 percent CI 1.012.05)] were shown to have a risk of CKD with Hb 10 g/dl. No greater risks were found with higher Hb values**.** **(33)**

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.

In this study out of 127 patients, 72 males (56.69%) and 35 females (27.55%) suffered from xerostomia. The total prevalence in both sexes was 84.25% (107 cases). Xerostomia was the most frequent mouth lesion among kidney transplant recipients. [7,9] A meta-analysis by Ruospo et al. showed that 48.4% of CKD patients had xerostomia. [10] 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. [11]

Lip Pigmentation was present in 81 patients (63.77%). It was noted in 59 males (46.45 %) and 22 females (17.32%). The most frequent oral lesion seen in our CKD patients, abnormal lip pigmentation, was not widely documented among renal patients in previous investigations. [20, 21] In renal patients, oral and cutaneous hyperpigmentation is caused by the kidney's failure to eliminate excess beta melanocyte stimulating hormone (b-MSH), which accumulates and stimulates melanocytes in the basal layer of the mouth epithelium. [22] The overuse of conventional or orthodox medications for the treatment of renal illness or other disorders might be one of the causes for the increased prevalence of hyperpigmentation in our environment.

Most common oral manifestation encountered in patient with CKD was generalized pallor in oral mucosa owning to low hemoglobin levels due to anemic status of patients. It was seen in 119 patients. 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 %). It was a not so common manifestation of CKD.

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%) due to presence of fissures on dorsum of tongue. Of these 38 were males(29.92%) and 25 were females (19.68 %). Cracked lips was

observed in 59 patients (46.45%) in our study. 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 was noted in 92 patients (72.44%). Of these 65 were males(51.18%) 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. [21] Another study had 53.3% patients with bad odor which were on dialysis. [12]

There was a significant association (p value = 0.00052) between the serum urea levels and halitosis which was present in 47 patients of more than the mean serum Urea levels (>146.85 mg/dl) group than the 29 patients in whom halitosis was not found in less than the mean serum urea levels (<146.85 mg/dl) group. Halitosis was found predominant in the patients whose dialysis duration was <1 year.

According to a meta-analysis done by Ruospo et al., mucosal ulcerations were observed in 8.6% of ESKD dialysis patients (n=832) and 1.3 percent of RTRs (n=453), respectively. [10]

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. [13] Oropharyngeal candidiasis is common in patients with CKD. [7]

Staining of teeth was observed in 36 patients (28.34%) which led to generalized gingivitis. There were 30 men (23.62 percent) and 6 women among them (4.7 percent). Total teeth 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%) denoted as generalized gingival recession and pocket formation. Of these 43 were males β3.85%) and 19 were females (14.96 %). In CKD patients, oral health, particularly destructive periodontitis, is linked to poor prognostic variables such as malnutrition, the protein-energy wasting syndrome, and inflammation, [22,23,24] and may predict progression of renal disease.[25] Endothelial dysfunction, [26] athero-sclerosis, [27] thrombosis, [28] vascular damage and endotoxemia [29] and chronic inflammation [30,31] are physiologically plausible mechanisms that promote severe outcomes in CKD.

Missing Teeth were observed in 22 patients (17.32%) totally. Of these 16 were males (12.59%) and 6 were females (4.72 %). In a meta-analysis decayed missing teeth were found in 14.5% patients.[32]

Partial edentulism was observed in 45 patients (35.43%) owing to debilitating periodontal status of dentition. 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 %). Other studies have verified that in hemodialysis patients, the periodontal health is poor, and that it is linked to indicators of malnutrition and inflammation. [14,15]

CONCLUSION

CKD can lead to huge socioeconomic burden on society. Manifestations of CKD are common during the progression of uremia. The impact of CKD on the oral cavity was evidenced by significant changes, which pointed to a significant inter-relationship.

So, by countering these manifestations at various levels of prevention, we can decrease the progression of CKD and its overall outcomes.

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