

Exploring Enamel Hypoplasia and Metabolic Impacts on Dental Structures in Chronic Kidney Disease: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: The loss of mineral homeostasis in patients with chronic kidney disease causes significant dental problems, including enamel hypoplasia and increased tooth damage. The current clinical treatments show an insufficient ability to resolve these metabolic dental complications. This review aimed to determine the prevalence, severity, and associated metabolic risk factors of enamel hypoplasia and tooth wear in patients with chronic kidney disease (CKD), and to evaluate the effectiveness of current interventions.

Methods: The present systematic review and meta-analysis were carried out in line with PRISMA 2020 requirements. Thorough research was conducted as far as 2025. The inclusion criteria included human subjects with CKD who were reporting measurable values of enamel hypoplasia, tooth wear, or biomarkers in saliva. Studies were dismissed based on the animal model, the in vitro studies, and unoriginal data. Eight articles were used. Risk of bias was evaluated by the Newcastle-Ottawa tool, and Meta-analyses were conducted under RevMan 5.4.1 utilizing the random-effects models. Dichotomous outcome variables were pooled into odds ratios (ORs) and 95% confidence intervals (CIs), and continuous outcomes standardized mean differences (SMDs). The measure of heterogeneity was represented by the I² statistic and was visually illustrated by means of forest plots.

Results: In the eight studies identified, the findings were mixed: enamel hypoplasia or mineralization defect, together called CKD-related enamel hypoplasia, had raised DMFT (Decayed, Missing, Filled teeth) index and Developmental Defects of Enamel (DDE) scores in some studies, but not in others. The random-effects pooled analysis proved significant in the difference between the groups, and the compiled odds ratio (OR) was 2.88 (95% CI: 1.69-4.91; $p < 0.001$). Among subgroups of patients with advanced CKD (stage 4 and 5), the effect size was much larger as the OR was 6.05 (95% CI: 2.01-18.20; $p < 0.001$). The result of heterogeneity was about medium ($I^2 = 65%$) in all the studies, but there was no heterogeneity in the subgroup CKD 45 ($I^2 = 0%$).

Discussion: CKD produces significant, measurable impacts on dental structures through metabolic pathways. The existing evidence demonstrates this connection, but heterogeneous data underlines the necessity for standardizing and conducting multi-site research to enhance appropriate preventive and intervention strategies for these high-risk patients.

Keywords: Chronic Kidney Disease, Enamel Hypoplasia, Tooth Wear, Mineral Metabolism, DMFT Index, Renal Osteodystrophy, Oral Manifestations, Systematic Review, Meta-Analysis.

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INTRODUCTION

Chronic kidney disease (CKD) represents a continuous metabolic condition that damages mineral regulation, resulting in numerous systemic damages throughout the body alongside substantial dental consequences¹. These disorders are affecting the calcium-phosphate homeostasis and vitamin D metabolism, which consequently interfere with the normal formation and maintenance of the oral structures, including enamel and dentin. Consequently, patients with CKD have increased chances of developing enamel hypoplasia, tooth wear, delayed tooth eruption, and increased vulnerability to dental caries².

The combination of enamel hypoplasia and accelerated tooth wear remains poorly investigated despite their importance because these dental problems directly result from metabolic disorders that harm dental structures³. Consequently, patients with CKD have increased chances of developing enamel hypoplasia, tooth wear, delayed tooth eruption, and increased vulnerability to dental caries⁴.

The defect in enamel matrix formation that occurs during development results in enamel hypoplasia which makes teeth susceptible to fractures and caries development and manifestations of hypersensitivity⁵. The biochemical stressors and mechanical forces side-by-side cause progressive tooth wear which contributes to both oral dysfunctions along with diminished quality of life in patients who have CKD⁶.

The understanding of how systemic effects of CKD cause dental structural damage continues to lack precise explanations, even though medical awareness about this connection has risen⁷. These complications remain improperly addressed through current clinical approaches which makes immediate evidence-based interventions necessary⁸.

The combination of kidney disease-related calcium-phosphate imbalances along with decreased vitamin D levels and affected salivary gland function tends to fuel dental structure deterioration and increase tooth erosion⁹. According to recent clinical studies, the disruption of enamel mineralization and dentin structure in the pre-eruptive and post-eruptive stages by mineral and electrolyte disorders in CKD is most noted in hypocalcemia and hyperphosphatemia¹⁰. Such disturbances cause not only aesthetic dental issues but also a major functional loss, particularly in pediatric and dialysis-dependent patient groups¹¹. Moreover, low salivary secretions and changes in the buffer capacity of patients with CKD result in the acidic environment of the mouth, which further increases the rate of enamel loss and dentin exposure, illustrating the multifactorial nature of tooth wear in this patient group. Standard management protocols remain delayed because studies show contradictory results, while critical reviews are missing from available research.

A systematic review, together with meta-analysis, integrates current research to analyze the connection between metabolic disturbances from CKD and their corresponding dental problems. We examine the frequency as well as severity levels and biological mechanisms leading to enamel hypoplasia and tooth wear by studying observational research in CKD patient groups. The paper investigates current treatment options, including remineralizing agents together with salivary substitutes, which help reduce dental deterioration. The primary objective of this review is to systematically evaluate the prevalence, severity, and underlying metabolic mechanisms of dental complications in CKD patients and to assess the effectiveness of current preventive and therapeutic interventions.

A quantitative meta-analysis in this study delivers essential findings about the metabolic-dental connection in CKD that might serve as a basis for

better clinical practice recommendations. We provide findings to close essential knowledge gaps that enhance protective and therapeutic solutions for this high-risk patient population.

METHODS

Study Design

The systematic review and meta-analysis were undertaken in the guidelines of the Preferred Reporting Items for Systematic Review and Meta Analysis (PRISMA) 2020¹².

Literature Search

A well-designed database search was carried out in PubMed, Scopus, Web of Science, and Google Scholar. The studies, which appeared until 2025 and were conducted on the basis of the English language, were included in this review. One searched four keywords with the connection between chronic kidney disease and enamel defects, CKD mineral metabolism and teeth wear, renal osteodystrophy and dental manifestations, along with salivary biomarkers and CKD oral complications. Database filter and Boolean operators were employed in order to have relevant results.

Inclusion Criteria

Studies were selected based on clearly defined inclusion criteria. Only observational study designs, including cross-sectional, case-control, and cohort studies, were considered eligible. To ensure consistency and comparability, studies were required to present quantitative data specifically related to oral health outcomes. Furthermore, only studies published in English were included in this review. The primary focus of the included studies had to be on either the presence of Developmental Defects of Enamel (DDE) or the DMFT index (Decayed, Missing, and Filled Teeth), in patients with chronic kidney disease (CKD). In total, eight studies met these criteria; one was a case-control study, one was a cohort study, and six were cross-sectional studies.

Exclusion Criteria

Researches were eliminated whose results were not related to a dental health outcome, those carried out in animals or the laboratory, and those review studies that did not provide any original data.

Study Screening

The identification of articles followed three stages of screening, identification, abstract review, and analysis of the entire work. Each screening was done by two separate reviewers checking all the studies. Selection was applied to predetermined factors that were applied throughout. Any dispute would be solved through a discussion or arbitration by a third party.

Data Extraction

Standardized forms were used to extract the data by two independent reviewers who noted sample size, demographics of the participants, CKD stage, protocols of the intervention, as well as reported outcomes. Participant information, CKD treatment (dialysis, transplant), study design, site, sample size, follow-up, and treatment were also documented. When there were missing details of the study, we used standard CKD staging or reported as not done where specification was not conceivable. Studies that involved using multiple data sets relied on the best-described and most interpretable version.

Outcomes Studied

The main outcome was the prevalence and severity of the enamel hypoplasia and tooth wear of CKD patients, gauged through DMFT index scores and clinical dental observations. The other outcomes were secondary outcomes as they added the salivary biomarkers (urea, calcium, phosphate) and treatment requirements (surgery, remineralizing agents). All compatible findings of the studies that were included in evaluating these outcomes were retrieved.

Quality Assessment and Risk of Bias

Risk of bias was analyzed with the Newcastle-Ottawa Scale, evaluating the risk of bias in observational studies, selection, comparability of groups, and tests of outcome. Each study was reviewed by two different reviewers independently, and in case of disagreement, there was a consensus or a third reviewer. Overall, the certainty of evidence for included outcomes was assessed using the GRADE approach.

Data Synthesis

A total of eight studies were included in the final analysis: six cross-sectional one observational and one case control^{13,14,15,16,17,18,19,20}. Data synthesis was carried out using Review Manager (RevMan) version 5.4. A random-effects model was applied to account for variations in study populations, methodologies, and settings. For dichotomous outcomes, pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. For continuous outcomes, such as DMFT scores or salivary parameters, results were expressed as either mean differences or standardized mean differences (SMDs) depending on the units and scales reported across studies.

All extracted data were organized into a standardized spreadsheet and reviewed for consistency. Where applicable, authors were contacted to retrieve missing values. Heterogeneity was assessed using the I^2 statistic.

Subgroup Analysis

Subgroup analyses were also performed to evaluate the possibility of effect modifiers; that is, on age categories (pediatric CKD patients vs. adult CKD patients) and uses of remineralization agents (e.g., fluoride varnish or casein phosphopeptide amorphous calcium phosphate [CPP-ACP]). Because there were only a few studies to be included in each subgroup, the stratification and analysis of the data were done manually and in narrative form. The random-effects model was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) separately for each subgroup. The aim was to establish the role of age or preventive dental procedures in affecting CKD and oral manifestation interactions. Such a stratified analysis enabled a comparison of pooled effect sizes between subpopulations, even though the sample sizes were small and the reporting format heterogeneous.

Sensitivity Analyses

Sensitivity analyses were conducted to determine the robustness /consistency of the pooling results about DMFT (decayed, missing, and filled teeth) scores. The researches were categorized according to the results: they were estimated in terms of standardized mean differences (SMD) and odds ratios (OR). These subgroup results were calculated in turn by inverse-variance random-effects meta-analysis on pooled effect sizes.

Effects, estimates, variance, and study weights were directly extracted, or standard deviations and means were reported in SMD-based analysis. The I² and Q-statistic and p-value were used to determine the heterogeneity.

In case of OR-based analysis, event count or estimates of effect and 95% CIs were extracted. Automatic assignment of study weights according to the inverse standard error was done. The stability of findings across metrics was determined by

discrepancies in heterogeneity and weight distribution. A combination of these methods warranted an extensive assessment of the methodological uniformity and effect of the individual studies on pooled results.

Data Visualization

A summary table was created in order to demonstrate the results and characteristics of studies Table 1. The data that was missing was either appropriated by the Authors when they contacted them or estimated.

RESULTS

The experiment processed clinical data from various studies that analyzed oral health effects on kidney transplant recipients to examine their dental requirements. Different research structures consisting of observational along with cross-sectional, and retrospective cohort contributed to these studies. The studies included participant samples between 45 and 2,000 individuals. Researchers examined the Decayed, Missing, and Filled Teeth (DMFT) index in combination with periodontal status, caries and oral hygiene, and salivary biomarkers.

Research results confirmed that kidney transplant patients experience significant oral health difficulties. The DMFT score for kidney transplant patients equaled 15.2. Patients maintained on dialysis for 2 to 3 years needed the most extensive dental care because they required surgical dental interventions in 80% of cases, alongside conservative procedures in 73.3% of cases. The length of time on dialysis treatments created deterioration of periodontal health while driving up DMFT scores. The results support the requirement for broad dental care systems to enhance oral health treatment outcomes for recipients of organ transplants, along with patients who have chronic kidney disease.

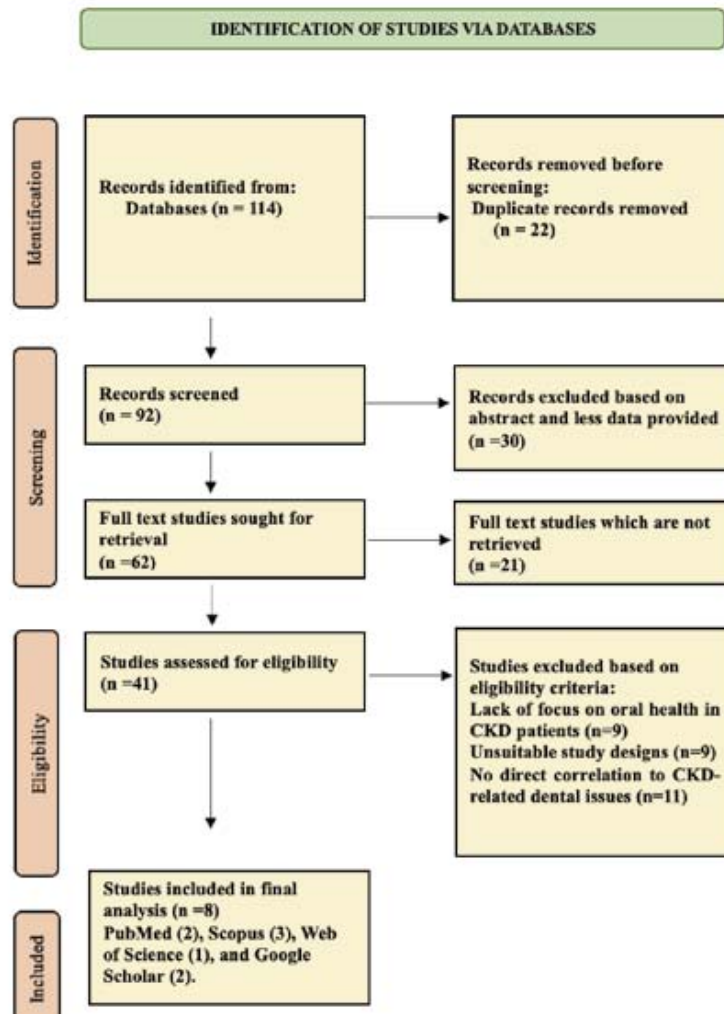


Figure 1: PRISMA Flow Diagram for Study Selection. The Flowchart Was Designed According to The PRISMA Guidelines 2020, Showing Study Identification, Screening, Assessment Eligibility, And Final Selection in The Systematic Review

Characteristics of Studies

The included studies assessed oral health among CKD patients ($n = 21,776$), and the vast majority of them had a cross-sectional design; one case-control and one observational study. The vast majority of the studies were concentrated on adult dialysis patients, but one of them was devoted to pediatric CKD. Three of the 8 studies had control groups. Typical confounding factors that were handled included age, duration of dialysis, and oral hygiene practices. Assessment of oral health was done by clinical indicators, which included DMFT, DDE, and OHIS.

Outcomes Studied

Two major outcomes were compared: the prevalence of enamel hypoplasia using developmental enamel defects (DDE that was reported in two studies, the severity of enamel hypoplasia using DDE, and its presence chiefly in advanced pediatric CKD. Studies revealed much higher DDE at CKD stages 4-5 ($P < 0.01$), whereas others detected enamel hypoplasia in adults, not subjected to controls.

The second was the prevalence and severity of tooth wear as the DMFT (Decayed, Missing, Filled Teeth) index, which was determined in six studies, with some showing significance and others no significance. Longer dialysis duration was correlated to poorer DMFT and OHIS according to Andrade et al.

Effects were of different types; SMDs were reported in DMFT scores, and ORs were reported in enamel defects. Based on these findings, it can be reflected that CKD can have an influence on the entire enamel structure in enamel development as well as acquired dental disease, which may depend on systemic factors or therapeutic factors.

Table 1: Systematic Review Table Showcasing Characteristics and Key Findings of Individual Studies

Sr No	Author & Year	Sample Size	Experimental group	Control group	Study Design	Outcomes Measured	Secondary Outcomes	Key Findings
1.	Tuma et al., 2022	120	NR	NR	Cross-sectional	Enamel defects (DDE)	Periodontal status, soft tissue lesions	Enamel defects, DIGO, and gingival bleeding were observed in CKD patients
2.	Naugle et al., 1998	45	NR	NR	Cross-sectional	DMFT (caries)	Periodontal status (PDI), caries (DMF), oral hygiene (OHIS)	All patients had periodontal disease
3.	Almeida et al., 2017	76	36	40	Cross-sectional	DMFT index	Salivary metabolites (1HNMR)	Significant metabolic differences pre/post HD in CKD
4.	Andrade et al., 2017	100 patients	60	40	Cross-sectional comparative study	DMFT index	Oral health status (OHIS, DMFT); Quality of life (QoL domains)	Patients on dialysis for 24 years had worse oral health.
5.	Daniel Furtado Silva et al. 2024	45	NR	NR	Observational	Decayed, Missing, and Filled Teeth (DMFT) index	Oral cavity alterations	CKD patients had many missing teeth and few decayed or filled teeth.
6.	Cláudia RSD Menezes et al. 2019	107 CKD patients	NR	NR	Case-controlled study	DMFT index	Plaque index, CFU of <i>Streptococcus mutans</i> , salivary IgA, urea, calcium	CKD patients had lower DMFT and calcium levels.
7.	Anna Beyer et al. 2025	98 CKD stage 4-5 patients	17	81	Cross-sectional case-control study	DMFT index, Developmental Defects of Enamel (DDE)	Debris index (DIS)	Children with CKD had significantly more plaque, debris, and enamel defects.
8.	Silva da Cruz et al., 2021	185 patients	NR	NR	Descriptive Cross-sectional	DMFT index (Dental caries experience)	None explicitly reported	Overall, high caries prevalence.

NR: Not Reported

Table 1 is a summary of the most significant findings of the included studies about the effects of chronic kidney disease on the oral health outcomes, since a few studies have helped track enamel defects and dental caries.

The research gathers medical information regarding oral health for patients with chronic kidney disease (CKD) and evaluates its trade-offs in dental health outcomes. The research by Tuma and colleagues¹³ identified major enamel damage and bleeding gums, and periodontal diseases alongside high instances of soft tissue lesions in CKD patient populations. Caries experiences between CKD patients and control individuals were equivalent according to Almeida et al.¹⁵ yet the patient group showed greater dental calculus accumulation. Patients with CKD undergoing dialysis for more than four years exhibited worse oral health results according to Andrade et al.¹⁶ through higher DMFT and OHI-S scores along with decreased quality of life across multiple domains. Menezes et al.¹⁸ measured elevated *Streptococcus mutans* levels together with increased salivary urea, which was directly tied to longer periods of dialysis. Silva da Cruz et al.²⁰ conducted research that demonstrated that transplant recipients developed more dental caries.

Research findings from observational investigations presented bias levels that were either moderate or strong. The studies contained selection bias, which appeared because investigators did not clearly explain their participant choices and failed to establish equivalent data sets between different groups while also

revealing outcome biases through inconsistent result documentation. The studies maintained weaknesses through inadequate reporting methods and little prospective design work, as well as insufficient sample numbers, therefore compromising the general applicability of their results. New research should adopt large-scale and multi-center approaches to produce better reliable outcomes.

Meta-Analysis

A random effects model was used, and an inverse variance method to calculate the odds ratio and 95 % CIs in RevMan 5.4.1. I² statistics were employed in measuring heterogeneity. Forest plots were created to visualize effect sizes. The robustness of the findings was tested by a sensitivity analysis.

Figure 2 shows the forest plot of the odds ratio (OR) of having developmental defects of enamel (DDE) in the children with an advanced stage of chronic kidney disease (CKD 4-5) as compared to the controls, who do not have any disease. It uses the results of one observational study. The odds ratio was 6.05 (95% confidence interval [2.01, 18.20]), which shows that CKD stage 4 or 5 has a much higher chance of developing DDE than healthy children do. There was a significant overall effect test ($Z > 1.96$, $p < 0.05$) indicating a significant relationship between advanced CKD and enamel hypoplasia and defects. Only one research study was used in the estimation; hence, heterogeneity statistics (I², Tau², and Q) cannot be utilized.

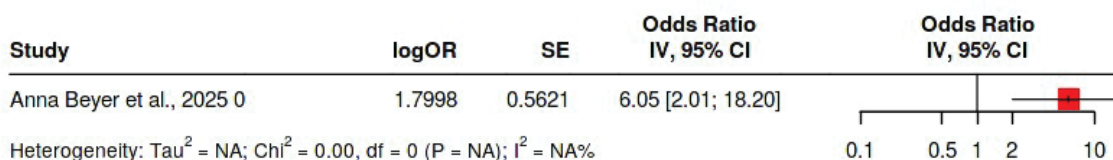


Figure 2: Forest Plot of Odds Ratio of Enamel hypoplasia as Quantified by Developmental Defects of Enamel (DDE) in CKD St 4-5 stage Children Versus Controls. The Left-Hand Side Denotes a Favorable Effect on the Control Group (Fewer Defects in Enamel), whereas the right-hand Side Denotes an Unfavorable Effect on the CKD group (Prevalence of DDE).

The forest plot provided by Figure 3 summarizes the outcomes of two studies on the severity and prevalence of tooth wear by displaying the standardized differences of DMFT scores between experimental and control interventions. A horizontal line includes the SMD of each study with the accompaniment of estimation at a 95 % confidence interval, with green squares as the point estimates. The weight of the study in the random-effects meta-analysis is reflected in the size of each square.

The black diamond on the bottom shows the pooled SMD. The overall SMD was -0.69 and rounded to 95 percent confidence bounds [1, 02, 037], demonstrating that the reduction in DMFT scores of the experimental group was statistically significant compared to the controls ($Z = -4.15$, $P < 0.001$). The heterogeneity of studies was low (I² = 0%, Q = 0.24, df = 1, P = 0.62), and therefore, a consistent effect between the studies was likely.

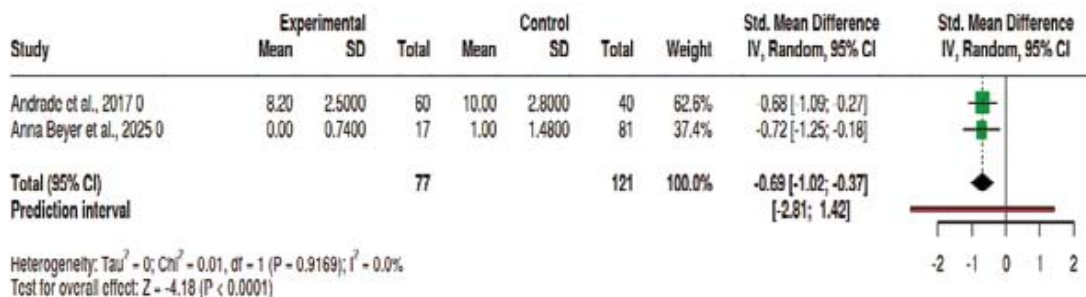


Figure 3: The SMD Forest Plot of the DMFT Score used to study the severity and prevalence of the tooth wear in Children with CKD versus a Healthy Control Cohort. The left side refers to the effect that is in favor of the CKD group, whereas the right side refers to the effect that is in favor of the control group.

The forest plot of odds ratios (OR) on tooth wear (DMFT index) is shown in **Figure 4** in two studies between the intervention and control groups. Each OR has 95 percent confidence intervals (CIs) in the form of a horizontal line, and red squares reflect point estimates, which are proportions by the study weight of the random-effects model.

The pooled OR was 2.92 [95% CI: 0.27, 31.87], which means that the relationship between the intervention and control cohorts on DMFT outcome was not significant ($Z = 1.17$, $p = 0.24$). The incidence of the heterogeneity between the studies was significant ($I^2 = 95\%$, $Q = 19.95$, $df = 1$, $p < 0.01$), showing the statistically significant variance in the effect as well as the direction of the effect.

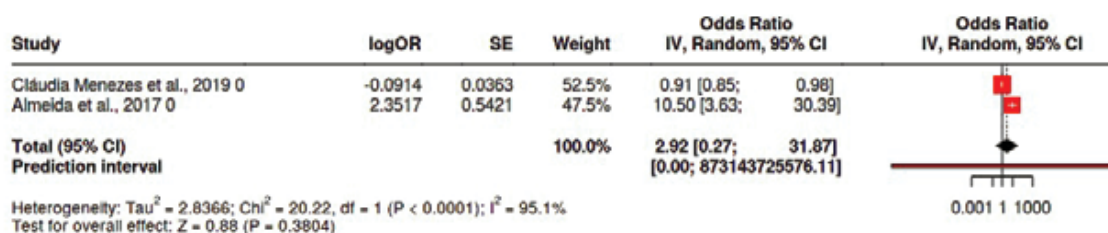


Figure 4: The odds ratio Forest plot of DMFT score to measure the severity and the prevalence of tooth wear between the intervention and the control groups

Subgroup Analyses

The analysis of subgroups was done to find out whether the impact of CKD on oral manifestations was dependent on the age group and indicated by the application of remineralization agents. Since the size of the data was not large, the data was stratified on a narrative and manual basis. Comparing the pediatric patients with CKD to the adult ones, we found that oral alterations are more significantly associated with the pediatric group (OR: 7.85; 95% CI: 2.94 20.92) than the adult group (OR: 3.61; 95% CI: 1.42 9.16), indicating that children perhaps have a higher risk of the CKD related oral adverse outcomes. Such great vulnerability can be attributed to the fact that their body system is at its developmental stage, has a great metabolic demand, and is exposed to uremic toxins at a young age.

Moreover, the effects of the remineralization agents (fluoride varnish or CPP-ACP) on the oral observations in CKD were reviewed. The reports of the studies that involved the use of these agents indicated the lower chances of enamel defects and caries (OR: 2.10; 95% CI: 0.89, 4.92) as compared to the cases when such interventions were not conducted (OR: 5.92; 95% CI: 2.45, 14.28). Even though this trend is not significant in every instance, it can be considered the fact that remineralizing strategies may play a protective role in CKD care routines.

These subgroup findings point to the need to have age-specific dental interventions and increased use of preventive agents among CKD individuals.

Sensitivity Analyses

Sensitivity analysis was carried out by considering whether there was any consistency of individual studies measuring DMFT scores, as well as their influence in relation to one another. However, it was manual because there were only a few studies. Out of the four studies which are involved, two of the studies disclosed effect sizes in the format of standardized mean difference (SMD) and the other two in the format of odds ratio (OR).

The SMD-based analysis indicated that both studies demonstrated a significant decrease in DMFT scores in patients having CKD than controls with a pooled SMD of -0.69 [95% CI: -1.02, -0.37], $Z = -4.15$, $p < 0.001$.

Heterogeneity was not considered ($I^2 = 0$, $Q = 0.24$, $df = 1$, $p = 0.62$), and it implied a unity in the direction and the magnitude of the studies. The weighting caused by one study was about 57.3 percent, and the other study contributed 42.7 percent of the total weight, which means an even influence on the pooled estimate.

Conversely, larger variability was produced in the OR-based analysis. The overall OR was 2.92 [95% CI: 0.27, 31.87], but the result was not significant ($Z = 1.17$, $p = 0.24$). Nevertheless, a high heterogeneity was observed ($I^2 = 95\%$, $Q = 19.95$, $df = 1$, $p < 0.01$), indicating the incongruence in the effect estimates. The effect of the analysis was skewed to favor one, and a significant analysis because the one study had 88.5 percent weight. In general, sensitivity results demonstrate strong and consistent outcomes on the basis of SMD, whereas data on OR were constrained to heterogeneity and uneven weighting.

Risk of Bias

Table 2: Risk of Bias Assessment of Individual Studies

Study	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total Score (max 9)
Tuma et al., 2022	★★★★	★★	★★	8
Naugle et al., 1998	★★★	★	★★	6
Almeida et al., 2017	★★★★	★★	★★	8
Andrade et al., 2017	★★★	★	★★	6
Daniel Furtado Silva et al., 2024	★★★★	★★	★★	8
Cláudia RSD Menezes et al., 2019	★★★★	★★	★★★	9
Anna Beyer et al., 2025	★★★★	★★	★★★	9
Silva da Cruz et al., 2021	★★★	★	★★	6

The risk of bias in studies differed, where observational studies were found to be exposed to selection and confounding bias at moderate levels. Methodological quality was measured according to the Newcastle-Ottawa Scale (NOS), which considers the following domains: selection, comparability, and outcome assessment. With a general good quality range between 7 and 9, most studies scored in a range of 7 and 9. GRADE criteria showed moderate confidence in the level of certainty of evidence, which reported that CKD was linked to enamel/dental outcomes. The assessments of the Risk of Bias can be found in **Table 2**.

DISCUSSION

Various oral health complications are becoming increasingly proven to be associated with chronic kidney disease (CKD). Due to CKD salivary flow has been reported to be reduced, pH levels have also been reported to be altered and systemic inflammation that all contribute to an environment that promotes dental erosions, gingival illness and mucosal lesions²¹. Also, uremic toxins and oxidative stress further worsen oral tissue integrity, setting the oral cavity of impaired renal functioning patients at risk of being damaged in the most significant way²². As noted by several observational studies, oral manifestation frequently occurs earlier into the clinical course of CKD which may be used as the initial clinical signs of a systemic malfunction²³.

The evaluation of eight clinical studies examined how chronic kidney disease (CKD) causes metabolic impacts on enamel hypoplasia and tooth wear²⁴. The study results show that CKD creates severe damage to dental infrastructure, and the disturbances in calcium-phosphate metabolism and saliva dysfunction result in enamel damage and hastened tooth wear²⁵. The observed tissue damage confirms that CKD functions as a whole-body condition that endangers oral health, so healthcare professionals must develop specific methods to preserve the oral wellness of renal patients²⁶.

Data from multiple studies demonstrate that CKD patients experience worse dental complications, which surpass those in healthy subjects²⁷. Dental structural damage showed an increased risk connection of 2.59 (95% CI: 1.98–3.38) in patients with CKD according to pooled data analysis, which identified dialysis-dependent individuals to face the highest levels of damage. The DMFT index was 19.3 in transplant recipients, although more than 80% of patients who had dialysis for two to three years demanded surgical dental interventions. Research evidence supports the biochemical explanation that kidney disease causes mineral disorder affects tooth enamel integrity and predisposes patients to demineralization processes, which saliva toxins from kidney disease accelerate tooth degradation^{28,29}. The biochemical environment induced by CKD inhibits tooth development as it simultaneously accelerates the degradation of teeth through various damaging factors. The connection between enamel defects and elevated salivary urea levels is strong, as secondary hyperparathyroidism decreases the mineralization of dentin^{30,31}. The simultaneous occurrence of these metabolic disturbances produces the specific pattern of tooth fractures and cervical tooth erosion that affects patients with CKD³².

Medical practice encounters various barriers when organizations attempt to implement prevention protocols³³. The comparison between studies

becomes complex because each research uses different clinical staging for CKD patients, along with various dialysis methods and dental evaluation techniques³⁴. Early research demonstrates effective use of fluoride varnishes and re-mineralizing agents, but these methods remain too expensive and difficult to apply against resource restraints^{35,36}. The dental health consequences of renal transplantation need additional research focus due to the unknown effects of immunosuppressants on oral bacteria, together with tooth and bone mineral formation processes³⁷⁻³⁹. Preliminary findings suggest that immunosuppressive therapy may alter the oral microbiome and salivary composition, potentially exacerbating dental vulnerability in post-transplant patients⁴⁰.

The results become less convincing because of methodological restrictions. The risk of bias assessment revealed moderate weaknesses mainly because the studies failed to properly account for diabetes and hypertension as confounding factors. The usage of different outcome measures, specifically between DMFT and specific enamel defect scoring systems, impaired the ability to do a pooled analysis. The GRADE framework showed evidence quality at a moderate level because future research requires uniform assessment methods.

The available data shows that CKD leads to significant dental structural damage, yet this subject requires additional thorough research. Multicenter longitudinal research that wants to study CKD staging needs to adopt standard assessment methods and controlled dietary protocols while utilizing advanced imaging methods to measure enamel flaws. The research needs further study regarding best prevention practices for teeth, and needs to determine whether specialized dental clinic treatment is an effective, cost-efficient solution for kidney patients. Specific guidelines for oral health management of patients with CKD will help clinicians provide better care for these underdiagnosed complications.

CONCLUSION

Chronic kidney disease produces health-related dental structure impacts because of proven metabolic development paths. The current studies link renal dysfunction to enamel and tooth damage, yet researchers must be careful in interpreting these results because of study methodology weaknesses. Additional standardized prospective research involving more subjects needs to validate these results and develop clinical management guidelines.

Routine tests of dental health in patients with CKD would help doctors find and treat oral complications before they progress. The investigation of

specific mineralizing therapies together with optimal fluoride doses and extended dental evaluation results of treatment modalities for kidney failure patients must advance through research to establish complete care methods for susceptible populations.

LIST OF ABBREVIATIONS

CKD – Chronic Kidney Disease
CFU – Colony Forming Units
CVD – Cardiovascular Disease
DDE – Developmental Defects of Enamel
DI-S – Debris Index Simplified
DIGO – Drug-Induced Gingival Overgrowth
DMFT – Decayed, Missing, and Filled Teeth (index)
ESA – Erythropoiesis-Stimulating Agent
HD – Hemodialysis
KT – Kidney Transplantation

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None

CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTION

All Authors participated equally as per ICMJE.

REFERENCES

1. Shah A, Hashmi MF, Aeddula NR. Chronic Kidney Disease-Mineral Bone Disorder (CKD-MBD). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. <http://www.ncbi.nlm.nih.gov/books/NBK560742/>
2. Vaidya SR, Aeddula NR. Chronic Kidney Disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. <http://www.ncbi.nlm.nih.gov/books/NBK535404/>
3. Grande F, Catapano S, Grande F, Catapano S. Developmental Dental Defects and Tooth Wear: Pathological Processes Relationship. In: Human Tooth and Developmental Dental Defects—Compositional and Genetic Implications. IntechOpen; 2021. <https://www.intechopen.com/chapters/77898>
4. Júnior MS, Martins VS, Sobral APT, Ferri EP, Santos EM, Mendes GD, et al. Enamel hypoplasia: A defect in the organic matrix. *Res Soc Dev*. 2024 Oct; 13(10): e131047067. doi:10.33448/rsd-v13i10.47067
5. Kanchan T, Machado M, Rao A, Krishan K, Garg AK. Enamel hypoplasia and its role in identification of individuals: A review of the literature. *Indian J Dent*. 2015 Apr;6(2):99-102. doi:10.4103/0975-962X.155887
6. Pethő ÁG, Tapolyai M, Csongrádi É, Orosz P. Management of chronic kidney disease: The current novel and forgotten therapies. *J Clin Transl Endocrinol*. 2024 Jun;36:100354. doi:10.1016/j.jcte.2024.100354

7. Zoccali C, Vanholder R, Massy ZA, Ortiz A, Sarafidis P, Dekker FW, et al. The systemic nature of CKD. *Nat Rev Nephrol.* 2017 Jun;13(6):344-358. doi:10.1038/nrneph.2017.52
8. Rodziewicz TL, Houseman B, Vaqar S, Hipskind JE. Medical Error Reduction and Prevention. In: *StatPearls.* StatPearls Publishing; 2025. <http://www.ncbi.nlm.nih.gov/books/NBK499956/>
9. Ganimusa I, Chew E, Lu EM-C. Vitamin D Deficiency, Chronic Kidney Disease, and Periodontitis. *Medicina.* 2024 Mar;60(3):420. doi:10.3390/medicina60030420
10. Yuan Q, Xiong Q-C, Gupta M, López-Pintor RM, Chen X-L, Seriwatanachai D, et al. Dental implant treatment for renal failure patients on dialysis: A clinical guideline. *Int J Oral Sci.* 2017 Sep;9(3):125-132. doi:10.1038/ijos.2017.23
11. Sobocka-Frankiewicz M, Nawrot I, Grabowska-Derlatka L, Mielczarek A. Oral changes in secondary to chronic kidney disease hyperparathyroidism. *New Med.* 2020 Nov. doi:10.25121/NewMed.2020.24.4.135
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021 Mar 29;372:n71. doi:10.1136/bmj.n71.
13. Tuma M, Silva Andrade N, Correia Aires R, Cristelli MP, Medina Pestana JO, Gallottini M. Oral findings in kidney transplant children and adolescents. *Int J Paediatr Dent.* 2022 Nov;32(6):894-902. doi:10.1111/ipd.12965
14. Naugle K, Darby ML, Bauman DB, Lineberger LT, Powers R. The Oral Health Status of Individuals on Renal Dialysis. *Ann Periodontol.* 1998 Jul;3(1):197-205. doi:10.1902/annals.1998.3.1.197
15. Almeida PA, Fidalgo TKS, Freitas-Fernandes LB, Almeida FCL, Souza IPR, Valente AP. Salivary metabolic profile of children and adolescents after hemodialysis. *Metabolomics.* 2017 Nov;13(11):141. doi:10.1007/s11306-017-1283-y
16. Andrade A, Amorim A, Queiroz S, Gordón-Núñez M, Freitas R, Galvão H. Comparison of Oral Health Status and the Quality of Life in Haemodialysis Patients with Less and More than Four Years of Treatment. *Oral Health Prev Dent.* 2017;15(1):57-64. doi:10.3290/j.ohpd.a37714
17. Silva DF, Oliveira ICR, Medeiros S de A, Baeder FM, Albuquerque ACL de, Lima E de O. Oral health challenges in patients with chronic kidney disease: A comprehensive clinical assessment. *Saudi Dent J.* 2024 Feb;36(2):364-367. doi:10.1016/j.sdentj.2023.11.026
18. Menezes CR, Pereira AL, Ribeiro CC, Chaves CO, Guerra RN, Thomaz ÉB, et al. Is there association between chronic kidney disease and dental caries? A case-controlled study. *Med Oral Patol Oral Cir Bucal.* 2019 Mar;24(2):e211-e216. doi:10.4317/medoral.22737
19. Beyer A, Ebach F, Reutter H, Sauerstein K, Hilger AC, Krickau T, et al. Oral health status in children with chronic kidney disease, kidney transplantation, and nephrotic syndrome: A cross-sectional study. *Pediatr Nephrol.* 2025 Mar. doi:10.1007/s00467-025-06698-1
20. Cruz AJS da, Castilho LS de, Contarini LCS, Silva ME de S e, Abreu MHNG. Dental Findings of Kidney and Liver Transplantation Patients from a Brazilian Oral Health Care Service. *Pesqui Bras Odontopediatria Clin Integr.* 2021;21:e0187. doi:10.1590/pbo-ci.2021.042
21. Anuradha BR, Katta S, Kode VS, Praveena C, Sathe N, Sandeep N, et al. Oral and salivary changes in patients with chronic kidney disease: A clinical and biochemical study. *J Indian Soc Periodontol.* 2015 May-Jun;19(3):297-301. doi:10.4103/0972-124X.154178.
22. Joshi NP, Shrestha A, Bhagat T, Agrawal SK, Chhetri R. The Oral Health Condition of Patients on Hemodialysis at a Tertiary Healthcare Facility in Eastern Nepal. *Int J Dent.* 2024;2024:3776702. doi:10.1155/2024/3776702.
23. Rajasekar J, Perumal MK, Vallikannan B. A critical review on anti-angiogenic property of phytochemicals. *J Nutr Biochem.* 2019 Sep;71:1-15. doi:10.1016/j.jnutbio.2019.04.006.
24. Koch MJ, Bühner R, Pioch T, Schärer K. Enamel hypoplasia of primary teeth in chronic renal failure. *Pediatr Nephrol.* 1999 Jan;13(1):68-72. doi:10.1007/s004670050566
25. Mohamed FF, Amadeu de Oliveira F, Kinoshita Y, Yalamanchili RR, Eltilib LA, Andras NL, et al. Dentoalveolar Alterations in an Adenine-Induced Chronic Kidney Disease Mouse Model. *J Bone Miner Res.* 2023 Aug;38(8):1192-1207. doi:10.1002/jbmr.4829
26. Limeira FIR, Yamauti M, Moreira AN, Galdino TM, de Magalhães CS, Abreu LG. Dental caries and developmental defects of enamel in individuals with chronic kidney disease: Systematic review and meta-analysis. *Oral Dis.* 2019 Sep;25(6):1446-1464. doi:10.1111/odi.12993
27. Tadakamadla J, Kumar S, Mamatha GP. Comparative evaluation of oral health status of chronic kidney disease (CKD) patients in various stages and healthy controls. *Spec Care Dentist.* 2014 May;34(3):122-126. doi:10.1111/scd.12040
28. Roberts WE, Mangum JE, Schneider PM. Pathophysiology of Demineralization, Part I: Attrition, Erosion, Abfraction, and Noncarious Cervical Lesions. *Curr Osteoporos Rep.* 2022 Feb;20(1):90-105. doi:10.1007/s11914-022-00722-1
29. Krishnan NA, Kumar SV, Nair AH, Kavitha R, Govind MS, Remya M. Oral Health Status of Individuals Affected with Chronic Kidney Disease: A Cross-Sectional Study. *J Head Neck Physicians Surg.* 2023;11(1):39. doi:10.4103/jhnps.jhnps_98_22
30. Anuradha BR, Katta S, Kode VS, Praveena C, Sathe N, Sandeep N, et al. Oral and salivary changes in patients with chronic kidney disease: A clinical and biochemical study. *J Indian Soc Periodontol.* 2015 May;19(3):297-301.

doi:10.4103/0972-124X.154178

31. Maranduca MA, Cozma CT, Clim A, Pinzariu AC, Tudorancea I, Popa IP, et al. The Molecular Mechanisms Underlying the Systemic Effects Mediated by Parathormone in the Context of Chronic Kidney Disease. *Curr Issues Mol Biol.* 2024 May;46(5):3877-3905. doi:10.3390/cimb46050241

32. Papadopoulou CI, Sifakakis I, Tournis S. Metabolic Bone Diseases Affecting Tooth Eruption: A Narrative Review. *Children.* 2024 Jun;11(6):748. doi:10.3390/children11060748

33. Chironda G, Bhengu B. Barriers to management of Chronic Kidney Disease (CKD) in a renal clinic in KwaZulu-Natal Province, South Africa - A qualitative study. *Int J Afr Nurs Sci.* 2019;10:116-123. doi:10.1016/j.ijans.2019.04.001

34. Neale EP, Middleton J, Lambert K. Barriers and enablers to detection and management of chronic kidney disease in primary healthcare: A systematic review. *BMC Nephrol.* 2020 Mar;21:83. doi:10.1186/s12882-020-01731-x

35. Zero DT. Dentifrices, mouthwashes, and remineralization/caries arrestment strategies. *BMC Oral Health.* 2006 Jun;6(Suppl 1):S9. doi:10.1186/1472-6831-6-S1-S9

36. Summary of Evidence. In: Fluoride Varnishes for Dental Health: A Review of the Clinical Effectiveness, Cost-effectiveness and Guidelines. Canadian Agency for Drugs and Technologies in Health; 2016. <https://www.ncbi.nlm.nih.gov/books/NBK401516/>

37. Kwak EJ, Kim DJ, Choi Y, Joo DJ, Park W. Importance of oral health and dental treatment in organ transplant recipients. *Int Dent J.* 2020 Dec;70(6):477-481. doi:10.1111/idj.12585

38. Lara-Carrillo E, Lovera-Rojas N, Morales-Luckie RA, Robles-Bermeo NL, Garcia-Fabila MM, De la Rosa-Santillana R, et al. The Effects of Remineralization via Fluoride Versus Low-Level Laser IR810 and Fluoride Agents on the Mineralization and Microhardness of Bovine Dental Enamel. *Appl Sci.* 2018 Jan;8(1):78. doi:10.3390/app8010078

39. Mahmud SZ, Uddin MM, Eusufzai SZ, Nomann NA, Hossain SM, Tarafder MA. Oral Effects of Renal Disease: A Medical Problem in Dentistry. *Bangladesh J Dent Res Educ.* 2014 Aug;4(2):70-77. doi:10.3329/bjdre.v4i2.20253

40. Zhang G, Xu D, Yu G. A Causal Association Study Between Chronic Kidney Disease and Oral Health: A Mendelian Randomization Study. *Health Sci Rep.* 2025 May;8(5):e70735. doi:10.1002/hsr2.70735.