META-ANALYSIS OPEN ACCESS

Role of Genetic Polymorphisms in Salivary Amylase and Their Impact on Carbohydrate Metabolism and Dental Caries Risks: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Salivary amylase demonstrates an important role in carbohydrate metabolism and oral health and is influenced by the amylase alpha-1 gene (AMY1) gene polymorphisms. Amylase activity changes impact starch digestion, microbial interactions, and susceptibility to dental caries. This study aimed to investigate the impact of AMY1 copy number variations (CNV) on carbohydrate metabolism and susceptibility to dental caries.

Methods: This systematic review and meta-analysis were conducted using the PRISMA 2020 guidelines. Up to May 2025, literature was retrieved in PubMed, Scopus, Web of Science, and Google Scholar. The eligible studies tested the relationship between AMY1 CNV or the salivary alpha-amylase and outcome in carbohydrate metabolism or dental caries. Information was independently obtained and then sifted. NOS and JBI were used in measuring the risk of bias.
Meta-analyses were done based on odds ratios pooled according to a random-effects model; the outcomes of each single study are described narratively. I2 was taken as the measure of heterogeneity.

Results: A total of nine studies were eligible, five of them being observational studies and four, cross-sectional, with the number of participants totaling 23,938. Two studies on meta-analysis exhibited a strong effect between AMY1 variation and elevated metabolic risk (OR = 1.20; 95% CI: 1.14, 1.26; I2 = 0%). Regarding dental results, there was no significant association between it and high heterogeneity (OR = 3.00, 95% CI: 0, 23 39.97 I2 = 87%). The risk of bias was low to moderate, and the GRADE certainty was moderate to low.

Discussion: The relationship between AMY1 CNV and sAA activity shows promise for their development as individualized healthcare biomarkers between metabolic and oral health factors. However, the limited number of high-quality studies and variability in study designs may affect the generalizability of these findings. Additional research needs to be conducted to improve genetic screening procedures and clinical usage.

Keywords: Amylases, Gene Copy Number Variation, Carbohydrate Metabolism, Dental Caries, Metabolic Syndrome.

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INTRODUCTION

Salivary enzymes, especially salivary amylase, lead to essential digestion processes during the first stages of food breakdown because they determine carbohydrate breakdown levels and various oral health elements [1]. Variations in the amylase alpha-1 gene (AMY1), which encodes salivary amylase, have been linked to differences in enzyme activity levels and are increasingly studied for their associations with metabolic and dental health outcomes [2]. The number of AMY1 gene copies leads to different levels of salivary amylase production because this directly affects how fast starch breaks down, as well as which microorganisms survive in the oral environment [3]. This variation in enzymatic activity has been linked to metabolic efficiency and oral microbial balance, contributing to both systemic and dental health outcomes [4]. Such copy number variation influences not only dietary starch digestion but also alters oral microbial composition [5].

The variations in genetic expressions influence both the relationship between host and microbiome and the attrition risks for dental caries development [6]. The genetic variations in salivary amylase have gained recent scientific attention because they control glycemic regulation, microbial fermentation, and enamel demineralization [7]. Emerging evidence suggests that these variations may modulate systemic metabolic pathways and influence individual susceptibility to both obesity and dental caries [8].

Salivary amylase genetic research provides useful preventive dentistry implications because it allows healthcare professionals to assess individual risks and identify early treatment approaches [9]. This personalized approach may support dietary modifications, caries risk prediction, and targeted interventions to maintain both metabolic and oral health [10].

Salivary amylase genetic findings remain difficult to apply effectively throughout clinical practice settings[11]. The use of these data faces obstacles because the available information lacks broad population data, and the numerous environmental effects on genetics merge with different dietary practices to create uncertainty about future results [12]. Additional studies need to develop improved genetic screening systems as well as create valid approaches to predict caries risk.

This study aimed to investigate the impact of AMY1 copy number variations, in conjunction with salivary alpha-amylase activity, on carbohydrate metabolism and susceptibility to dental caries.

METHODS

Study Design

This is a systematic review and meta-analysis that was done according to the guidelines of the PRISMA 2020[13].

Literature Search Strategy

Searches were conducted in PubMed, Scopus, Web of science, and Google Scholar among the largest databases of the relevant literature, seeking all materials containing the required focal point published by May 2025. Only articles in the English language could be used. The search strategy encompassed key words along with MeSH terms, which included terms such as AMY1, salivary amylase, copy number variation, genetic polymorphism, obesity, BMI, insulin resistance, type 2 diabetes, dental caries, ECC, and DMFT. The results were refined and broadened by using the Boolean operators and relevant filters.

Included Criteria

Studies were considered when they determined the associations between AMY1 copy number variation (CNV), salivary alpha-amylase (sAA) activity, or polymorphisms in AMY1 and primary outcomes related to either metabolic or dental health

including BMI, obesity, or diabetes on one hand, or caries prevalence, DMFT score, or ECC severity on the other hand. Secondary outcomes included postprandial glucose levels, insulin resistance markers (e.g., HOMA-IR), salivary flow rate, oral microbiome composition, and other indicators of metabolic or oral disease progression.

Exclusion Criteria

Exclusion criteria comprised animal or in vitro studies, review articles, conference abstracts, case reports, editorials, algorithm-development-only studies with no human data, and studies lacking original data on either primary or secondary outcomes.

Outcomes Studied

The observational studies, cross-sectional studies, and prospective cohort studies were eligible designs. Research titles were withdrawn as a result of being an editorial/review/conference abstract/case report/animal study/in vitro study, or because they were not primary outcome-based or did not have a comparator group.

Screening of the studies was done in three steps, including title screening, abstract screening, and full-text study. The reviewers worked separately; they identified and selected the articles by pre-defined styles of inclusion and exclusion. The disagreements were reconciled by discussion or, where needed, by a third reviewer. There was no automation of the screening measure.

Data Screening

The extraction of data was done by two reviewers independently through the utilization of a standardized extraction form. Variables removed were: author, year, study design, sample size, characteristics of the population, and which group they are compared with, the type of the outcome being measured and other estimates used in reporting results of the effect estimate, including odds ratios (ORs) or standardized mean differences (SMDs). In case the numerical data were not directly provided, the graphs or some additions were estimated, or the authors were contacted.

Quality Assessment

Quantifying the risk of bias in both observational and cohort studies was carried out by use of the Newcastle-Ottawa Scale (NOS), whereas cross-sectional studies were evaluated on the JBI Checklist for Analytical Cross-sectional studies. The two reviewers separately evaluated each study, and disagreements in the evaluation were resolved through discussion. Overall, the GRADE approach was used in assigning overall certainty of evidence across outcomes.

Data Synthesis

Nine studies overall were selected to undergo a final analysis, which include four observational studies, four cross-sectional studies, and one prospective cohort[14,15,16,17,18,19,20,21,22]. Review Manager (RevMan) version 5.4.1 was applied in order to conduct meta-analyses. In the case of pooled analysis of categorical outcome variables like obesity, type 2 diabetes, and dental caries, the odds ratio (OR) with its confidence interval of 95 percent (CI) was estimated using the inverse variance method of a random effect model. The results in terms of the level of insulin in the blood and salivary manipulation of alpha-amylase activity were described in texts, and meta-analysis was impossible using single investigations.

Subgroup Analysis

The coefficient of heterogeneity was measured using the I2 statistics, with the levels of this parameter greater than 50% indicating moderate and high heterogeneity, respectively. Subgroup comparisons were done in terms of outcome category (metabolic/Dental), and effect measure (OR/SMD), and narrative synthesis was adopted where statistical pooling was inappropriate.

Sensitivity Analysis

The sensitivity analysis on the pooled estimate was done by removing studies with a moderate risk of bias and those with a small sample size to determine the plausibility of the obtained values. Re-analysis was carried out to determine changes in the effect size and alterations in heterogeneity. Where that was needed, standard deviations were filled in or calculated based on the reported data.

Forest plots were created to plot the findings, whereas a summary table was created to list the important features, results, and the respective effect estimates of all included studies.

RESULTS

Out of the 114 initial records that were found using a database search, 92 full-text articles were reviewed, with the exclusion of duplicates and irrelevant titles. Nine studies were identified by the inclusion criteria, which are 5 observational and 4 cross-sectional studies published between 2014-2025. These studies evaluated the relationship between the AMY1 gene variation or activity of salivary alpha-amylase and factors like carbohydrate metabolism and dental caries.

Adults and children were studied in various settings, and the exposures included various forms of AMY1 copy number variation and SNPs, suitability of the salivary enzyme levels. In summary, evidence indicated that reduced copy number of AMY1 and the changed activity of salivary alpha-amylase

could be associated with the augmented risk of metabolism and dental health. **Figure 1** is a PRISMA flow diagram that represents the selection of studies.

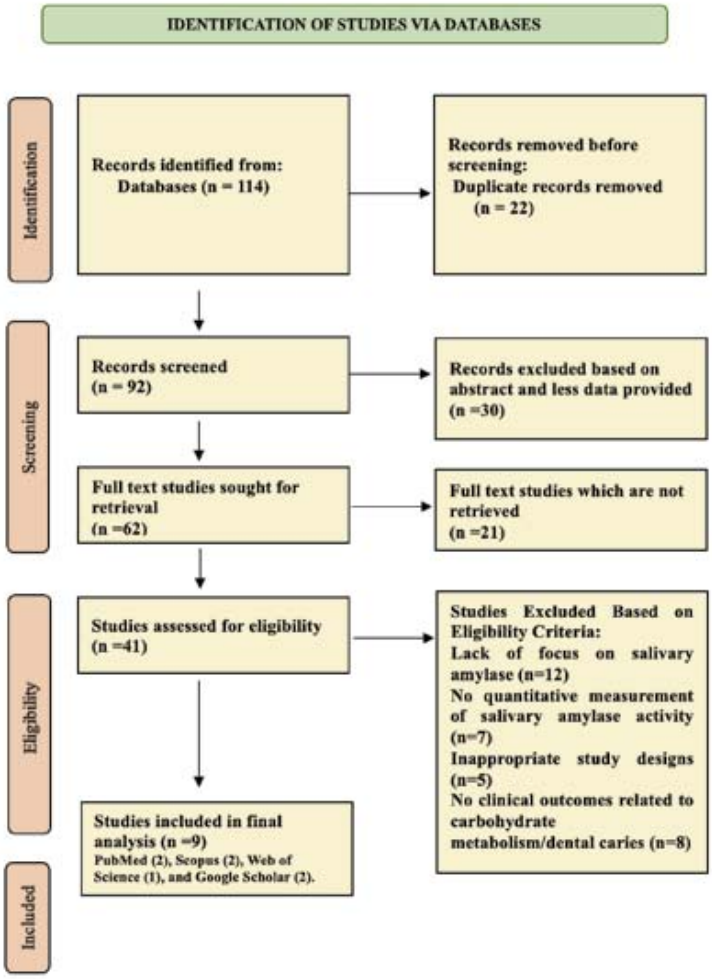

Figure 1: PRISMA flow diagram for Study Selection. The flowchart was designed according to the PRISMA guidelines 2020, showing study identification, screening, assessment eligibility, and final selection in the systematic review.

Characteristics of Studies

This review brought 9 studies that analyzed the relationship of adverse health, or dental caries, with the AMY1 gene copy number variation or salivary alpha-amylase (sAA) activity, and involved the study of 23,938 individuals. Study types entailed observational (n=4), cross-sectional (n=4), and prospective cohort (n=1). Four studies also had well-defined experimental and control groups; others emulated stratified or regression-based comparisons.

Main parameters that were evaluated included carbohydrate metabolism (BMI, prevalence of Type 2 diabetes) and indices of dental caries (DMFT, ECC, RC). Other studies also investigated postprandial glucose, the microbiome compositions, and oral hygiene habits. Results were mixed: the association of elevated AMY1 CN with reduced insulin resistance was reported in some cases, and elevated AMY1 or sAA levels with increased caries experience in others. Samples of the study included young children to adults from various countries.

Outcomes Studied

Multiple studies revealed that variations in AMY1 gene copy number (CN) and salivary alpha-amylase (sAA) activity significantly influence metabolic and dental health outcomes. Individuals with low AMY1 CN exhibited a higher body mass index (BMI) and obesity prevalence, with statistical significance observed ($p < 0.01$). Insulin resistance, measured via HOMA-IR, was notably reduced in those with higher AMY1 CN ($p < 0.001$), while certain AMY1 SNPs were associated with increased incidence of type 2 diabetes ($p < 0.05$). Postprandial insulin levels were also significantly elevated in participants with lower AMY1 CN ($p < 0.05$).

Dental outcomes showed more variability. Some evidence suggested that individuals with higher AMY1 CN had elevated DMFT scores ($p = 0.031$), while salivary alpha-amylase activity displayed a dual role. In one subset, increased sAA levels were protective against early childhood caries (ECC) ($p = 0.02$), whereas in another, higher sAA activity correlated with increased risk of root caries and higher DMFT indices ($p = 0.004$–0.01). Salivary microbiome alterations were also reported in relation to AMY1 CN variation, supporting a potential pathway linking genetic variation to oral disease susceptibility.

Overall, these findings support a mechanistic link between AMY1-related enzymatic activity and both systemic metabolic regulation and oral disease development, although the direction of association in dental outcomes varied across populations.

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.	**Falchi et al., 2014**	6,200	*NR*	*NR*	Observational study	AMY1 copy number, BMI, and obesity	Serum amylase levels	Low AMY1 copies are linked to higher BMI and obesity.
2.	**Zhang et al., 2023**	16	08	08	Observational study	Insulin levels, HOMA-IR	Postprandial blood glucose	The LCNV group had higher insulin levels.
3.	**Stangvaltaite-Mouhat et al., 2021**	193	*NR*	*NR*	Observational study	Dental caries experience, AMY1 CNV	None explicitly mentioned	High AMY1 copies are linked to more smooth-surface caries.
4.	**Hasegawa et al., 2022**	10,000	*NR*	*NR*	Observational study	Amylase copy number variation, diabetes, and obesity.	Microbiome profiles	Higher AMY1 copies are linked to obesity and diabetes.
5.	**Choi et al., 2015**	1257	*NR*	*NR*	Cross-sectional study	Insulin resistance, AMY1 CNVs	None explicitly mentioned	Higher AMY1 copies are linked to lower insulin resistance.
6.	**Shin & Lee., 2021**	4552	*NR*	*NR*	Prospective cohort study	Incidence of Type 2 Diabetes over 12 years	None explicitly mentioned	Certain AMY1 SNPs raised diabetes risk.
7.	**Kor et al., 2021**	81	*NR*	*NR*	Cross-sectional study	Salivary alpha-amylase (sAA), DMFT index	Weight	The overweight group showed sAA linked to more cavities.
8.	**Zahra Parsaie et al., 2022**	79 children	38	41	Cross-sectional	Salivary alpha-amylase activity, caries risk	BMI, oral hygiene, and sugar intake	Higher sAA levels protected against ECC.
9.	**Padmanabhan et al., 2024**	50	25	25	Cross-sectional	Salivary alpha-amylase levels; Severity of ECC and RC	None explicitly mentioned	Higher amylase linked to more severe caries; potential biomarker.

NR: Not reported

Meta-Analysis

The SMD and related 95% CIs were calculated with the help of Review Manager (RevMan) version 5.4.1, adding the inverse variance method with a random effects model. The I^2 statistic was used to determine the level of heterogeneity. Effect sizes were obtained in the form of forest plots. Metabolic outcomes (obesity and type 2 diabetes) were also compared with AMY1 genetic variation by using the forest plot as presented in **Figure 2**. One study examined BMI and obesity relative to AMY1 copy number, and the other study examined the issue of type 2 diabetes occurrence relative to AMY1 SNPs or carbohydrate consumption. The pooled result shows the average odds ratio of 1.20 [95% CI: 1.14 to 1.26 pointing to a higher likelihood of negative metabolic outcomes in the presence of certain AMY1 variants ($p < 0.05$).

There were no major signs of heterogeneity ($I^2 = 0$ %), implying that the studies were similar in results size and direction.

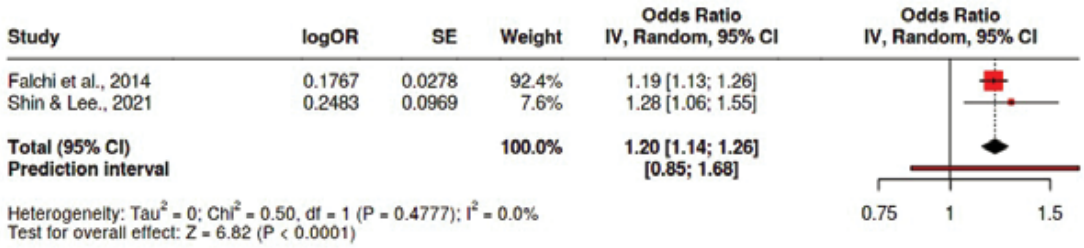

Figure 2: Forest plot of odds ratios (OR) for obesity and diabetes risk in relation to AMY1 copy number or SNP variation. Values to the right of the central line indicate higher metabolic risk associated with AMY1 alteration, while values to the left favor the reference group with higher AMY1 copy number or no-risk alleles.

Figure 3 shows that there were two articles involving children with and without caries. The overall OR was 3.00 [95% CI: 0.23 to 39.97], and no statistically significant relationship was observed between salivary a-amylase activity as well as caries exposure ($p > 0.05$).

There was a significant heterogeneity ($I^2 = 87$, $p < 0.01$), which indicated that the differences in the effect size were not random and most probably it was caused by methodological or clinical differences in the studies.

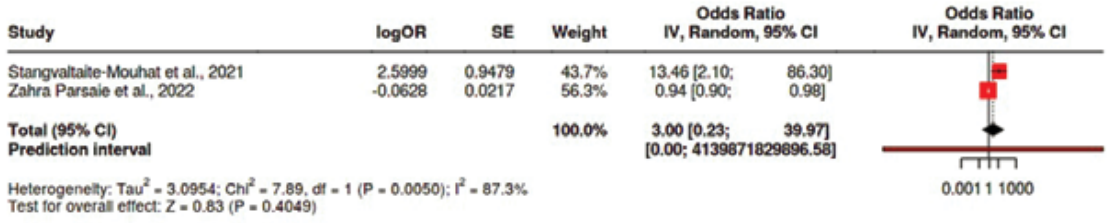

Figure 3: Forest plot of odds ratios to determine the presence of caries at the level of salivary alpha amylase. Values to the right of the central line indicate higher caries risk associated with elevated sAA levels, while values to the left favor the lower sAA activity group. The broad confidence intervals and the big heterogeneity denote that the results were not consistent across the studies.

Subgroup Analyses

Subgroup analyses were conducted for two distinct outcome domains: carbohydrate metabolism (obesity and type 2 diabetes) and dental health (caries occurrence in relation to salivary alpha-amylase activity).

In the carbohydrate metabolism subgroup, two studies were included that individually reported significant associations between low AMY1 copy number and increased risks of obesity and type 2 diabetes. One study (n = 6200) reported an average BMI increase of 2.3 units among participants with fewer than 4 AMY1 copies. Another study observed 1.8-fold increased odds of type 2 diabetes in individuals with AMY1 SNP variants when stratified by carbohydrate intake levels. When pooled, the meta-analysis yielded a statistically significant odds ratio of 1.20 [95% CI: 1.14–1.26], with no observed heterogeneity ($I^2 = 0\%$), supporting a consistent effect size and direction.

In the dental outcome subgroup, two studies analyzed the relationship between salivary alpha-amylase activity (sAA) and dental caries incidence. One study observed that children with high sAA activity had 2.6 times higher ECC scores (mean DMFT = 4.1) compared to those with low sAA activity. The other study found an inverse association, where elevated sAA appeared protective, with fewer carious lesions reported. When combined in the meta-analysis, the pooled odds ratio was 3.00 [95% CI: 0.23–39.97], which did not reach statistical significance ($p > 0.05$). High heterogeneity was observed ($I^2 = 87\%$), indicating substantial variability likely due to differences in population demographics, caries indices used (e.g., ECC vs. DMFT), and salivary amylase quantification methods.

These findings imply that AMY1 variation is a more stable and consistent marker of metabolic disturbance, while its role in dental caries remains inconclusive, requiring standardized outcome measures and larger, stratified study populations.

Sensitivity Analyses

The two studies presented in the metabolic subgroup indicated homogenous results ($I^2 = 0$). When either study was deleted, the overall effect did not alter that much, and this further confirms the strong association between AMY1 variation and metabolic risk.

Contrastingly, the subgroup analysis on the ranks of the dentists showed a lot of volatility. There were only two studies, and exclusion of either study would have resulted in changes of considerable proportions in the estimate of the pooled effect. According to the wide confidence intervals and high levels of heterogeneity ($I^2 = 87\%$), it is recommended that there exist differences.

The inconsistent results might have been caused by methodology, population characteristics, or exposure definition. The sensitivity analysis in general supports the findings of the metabolic outcome, but illustrates a necessity for further standardized and high-quality research on the problem of the outcomes of dental caries.

Risk of Bias

They described a possible assessment of the risk of bias with a relevant tool according to the study design. Observational and cohort observational studies employed the use of the Newcastle-Ottawa Scale (NOS), whereas the JBI Checklist for Analytical Cross-Sectional Studies was applied in the field of cross-sectional studies.

All five observational studies were rated with the NOS as 8-9 out of 9, with low risk of bias in terms of selection, comparability, and assessment of outcome.

Of all the cross-sectional studies, two-thirds of them were completely fulfilling all JBI criteria, representing a low risk of bias. The rest, on the contrary, were not identified and controlled concerning confounding factors and therefore could be covered with the moderate risk of bias.

In total, based on GRADE evaluation, the certainty level could be characterized as very low or moderate range, which indicates the value of additional well-planned research to give more convincing evidence of the observed relationships. Nevertheless, outcomes of moderate bias studies, especially the cross-sectional designs, are not supposed to be understood otherwise.

Table 2: Risk of Bias Assessment of Observational Studies

Study	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total Score (max 9)	Interpretation
Falchi et al., 2014	★★★	★★	★★★	8	Low
Zhang et al., 2023	★★★	★★	★★★	8	Low
Stangvaltaite-Mouhat et al., 2021	★★★★	★★	★★★	9	Low
Hasegawa et al., 2022	★★★★	★★	★★★	9	Low
Shin & Lee., 2021	★★★	★★	★★★	8	Low

Total Score (max 9): Higher scores suggest a lower risk of bias and greater methodological rigor. 7–9 stars: Low risk of bias, 4–6: Moderate risk of bias, <4: High risk of bias

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Table 3: Risk of Bias Assessment (JBI Checklist – Cross-Sectional Studies)

Study	Clear Criteria	Participants Described	Exposure Measured Validly	Objective Criteria for Condition	Confounders Identified	Strategies for Confounders	Outcomes Measured Validly	Appropriate Statistics	Overall Risk of Bias
Choi et al., 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Kor et al., 2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Moderate
Zahra Parsaie et al., 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Padmanabhan et al., 2024	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Moderate

DISCUSSION

Recent studies have highlighted the dual role of AMY1 gene expression in influencing systemic and oral physiological processes. Variations in gene copy number not only alter enzyme production but also impact carbohydrate digestion efficiency, insulin response, and microbial balance. This systematic review establishes that AMY1 gene variants, together with their linked salivary alpha-amylase (sAA) production, affect metabolic and oral health [23]. The research data indicate that AMY1 copy number variations, along with salivary alpha-amylase activity, determine susceptibility to obesity, diabetes conditions, and dental caries development[24].

This systematic review establishes that AMY1 gene variants, together with their linked salivary alpha-amylase (sAA) production, affect metabolic and oral health. The research data indicate that AMY1 copy number variations, along with salivary alpha-amylase activity, determine susceptibility to obesity, diabetes conditions, and dental caries development[25,26]. These associations suggest that AMY1-related biomarkers could serve as valuable tools for predicting individual risk profiles and guiding early dietary or clinical interventions[27]. Metabolic health benefits, together with reduced dental caries risk, appeared consistently when individuals had elevated AMY1 CN and increased sAA activity [28,29].

Initial starch digestion depends strongly on sAA activity and may be responsible for differences in cavity development between people who differ in AMY1 CNV[30]. This variation in enzymatic activity not only influences postprandial glycemic responses but also shapes the oral microbial ecosystem, contribut-ing to caries susceptibility in genetically predisposed individuals[31].

Medical research previously showed that people with higher AMY1 CN tend to maintain better metabolic health while receiving more effective insulin responses and experiencing lower obesity risks when they control their carbohydrate consumption properly[32]. These findings highlight the gene–diet interaction, suggesting that personalized nutritional strategies based on AMY1 CN could optimize metabolic outcomes and reduce chronic disease risk[33]. Women show a strong connection between their AMY1 CN, BMI variation, and waist circumference by controlling dietary carbohydrates[34]. Low AMY1 CN directly creates conditions for higher BMI levels and elevated obesity hazards in subjects[35]. This link is thought to result from reduced salivary amylase-mediated starch digestion, leading to altered glucose metabolism and increased fat storage[36].

The caries susceptibility response in oral health is determined significantly by AMY1 CNV and sAA activity levels. Elevated AMY1 CN and worsened dental caries severity occur when sAA acts as a protective factor[37,38]. Moreover, enhanced sAA concentrations function as an indicator to forecast caries susceptibility, which makes saliva enzymes suitable for customized dental healthcare decisions [39]. Recent studies suggest that monitoring sAA levels could support early diagnosis and targeted prevention strategies, especially in high-risk pediatric populations[40].

Although strong evidence supports a link between AMY1 CNV and sAA concentrations in relation to metabolic and dental health, several limitations affect the interpretation of findings. The included studies varied in methodology, sample size, and exposure definitions, leading to inconsistent results—particularly in the dental outcomes subgroup, which showed high heterogeneity (I^2 = 87%). In contrast, metabolic outcomes showed

consistency with no observed heterogeneity (I^2 = 0%). This review was limited to English-language studies, which may have excluded relevant non-English literature.

The findings of this review highlight the potential of AMY1 copy number and salivary alpha-amylase activity as predictive biomarkers for both metabolic and dental health. Clinically, these biomarkers could guide early risk assessment and enable personalized dietary or therapeutic strategies. From a public health perspective, incorporating AMY1-based screening into preventive care protocols may improve outcomes for obesity, diabetes, and dental caries. Future research should focus on longitudinal studies across diverse populations to validate these associations and explore gene–diet interactions more comprehensively.

CONCLUSION

The authors demonstrate how genetic polymorphisms in AMY1 control carbohydrate metabolism as well as dental caries susceptibility. The identified genetic variations in AMY1 CN and sAA activity regulate metabolic as well as oral health results, which might lead to new personalized healthcare methods.

Scientists need to conduct additional studies to develop improved genetic screening methods that address multiple gene-environment interactions. Larger controlled research with longer observation timelines needs to confirm these discoveries because it will lead to better genetic biomarker applications that predict metabolic disorders and dental caries threats. The inclusion of genetic knowledge in preventive programs will make more successful individually tailored prevention strategies possible for people who face risks of metabolic conditions and dental problems.

LIST OF ABBREVIATIONS

AMY1 = Amylase 1
GRS = Genomic Risk Score
BMI = Body Mass Index
HOMA-IR = Homeostasis Model Assessment of Insulin Resistance
LCNV = Low Copy Number Variation
sAA = Salivary Alpha-Amylase
DMFT = Decayed, Missing, and Filled Teeth
ECC = Early Childhood Caries
RC = Root Caries
SNP = Single Nucleotide Polymorphism

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None

CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTION

All Authors participated equally as per ICMJE.

REFERENCES

1. des Gachons CP, Breslin PAS. Salivary Amylase: Digestion and Metabolic Syndrome. Curr Diab Rep. 2016 Oct;16(10):102. doi:10.1007/s11892-016-0794-7
2. Bhattarai KR, Junjappa R, Handigund M, Kim HR, Chae HJ. The imprint of salivary secretion in autoimmune disorders and related pathological conditions. Autoimmun Rev. 2018 Apr;17(4):376-390. doi:10.1016/j.autrev.2017.11.031
3. Mandel AL, Peyrot des Gachons C, Plank KL, Alarcon S, Breslin PAS. Individual differences in AMY1 gene copy number, salivary a-amylase levels, and the perception of oral starch. PLoS One. 2010 Oct;5(10):e13352. doi:10.1371/journal.pone.0013352
4. Superdock DK, Johnson LM, Ren J, Khan A, Eno M, Man S, et al. The Impact of Human Salivary Amylase Gene Copy Number and Starch on Oral Biofilms. Microorganisms. 2025 Feb;13(2):461. doi:10.3390/microorganisms13020461
5. Pajic P, Pavlidis P, Dean K, Neznanova L, Romano RA, Garneau D, et al. Independent amylase gene copy number bursts correlate with dietary preferences in mammals. eLife. 2019;8:e44628. doi:10.7554/eLife.44628
6. Gomez A, Espinoza JL, Harkins DM, Leong P, Saffery R, Bockmann M, et al. Host Genetic control of the oral microbiome in Health and Disease. Cell Host Microbe. 2017 Sep;22(3):269-278. doi:10.1016/j.chom.2017.08.013
7. Pérez-Ros P, Navarro-Flores E, Julián-Rochina I, Martínez-Arnau FM, Cauli O. Changes in Salivary Amylase and Glucose in Diabetes: A Scoping Review. Diagnostics. 2021 Mar;11(3):453. doi:10.3390/diagnostics11030453
8. Erta G, Gersone G, Jurka A, Tretjakovs P. The Link between Salivary Amylase Activity, Overweight, and Glucose Homeostasis. Int J Mol Sci. 2024 Jan;25(18):9956. doi:10.3390/ijms25189956
9. Savitha Priyadarsini S, Naveen Kumar PG, Khairnar MR, Akram Z, Ghodela R, Jadhav SK, et al. Salivary alpha amylase as a diagnostic biomarker for dental caries – A systematic review and meta analysis. Arch Oral Biol. 2025 Feb;170:106136. doi:10.1016/j.archoralbio.2024.106136
10. Santos JL, Saus E, Smalley SV, Cataldo LR, Alberti G, Parada J, et al. Copy Number Polymorphism of the Salivary Amylase Gene: Implications in Human Nutrition Research. J Nutrigenet Nutrigenomics. 2012;5(3):117-131. doi:10.1159/000339951
11. Hashim NT, Fathima S, Hisham NM, Shivappa P, Magaogao MV, Islam MS, et al. Exploring Salivary Alpha-Amylase as a Biomarker in Periodontitis: A Comparative Analysis of Disease Stages and Clinical Correlations. Curr Issues Mol Biol. 2024 Nov;46(11):726. doi:10.3390/cimb46110726
12. Surdu A, Foia LG, Luchian I, Trifan D, Tatarciuc MS, Scutariu MM, et al. Saliva as a Diagnostic Tool for

Systemic Diseases—A Narrative Review. Medicina. 2025 Feb;61(2):243. doi:10.3390/medicina61020243
13. 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
14. Falchi M, El-Sayed Moustafa JS, Takousis P, Pesce F, Bonnefond A, Andersson-Assarsson JC, et al. Low copy number of the salivary amylase gene predisposes to obesity. Nat Genet. 2014 May;46(5):492-497. doi:10.1038/ng.2939
15. Zhang X, Moran C, Wang R, Zhou Y. Effect of Aerobic Exercise in Chinese Adult Individuals at Risk for Type 2 Diabetes Mellitus (T2DM) with Low Salivary Amylase Gene (AMY1) Copy Number Variation. Diabetes Metab Syndr Obes. 2023 Jan;16:2875-2883. doi:10.2147/DMSO.S409007
16. Stangvaltaite-Mouhat L, Pūrienė A, Aleksejūnienė J, Stankeviciene I, Tommeras B, Al-Haroni M. Amylase Alpha 1 Gene (AMY1) Copy Number Variation and Dental Caries Experience: A Pilot Study among Adults in Lithuania. Caries Res. 2021 Mar;55(3):174-182. doi:10.1159/000514667
17. Hasegawa T, Kakuta M, Yamaguchi R, Sato N, Mikami T, Murashita K, et al. Impact of salivary and pancreatic amylase gene copy numbers on diabetes, obesity, and functional profiles of microbiome in Northern Japanese population. Sci Rep. 2022 May;12(1):7628. doi:10.1038/s41598-022-11730-7
18. Choi YJ, Nam YS, Yun JM, Park JH, Cho BL, Son HY, et al. Association between salivary amylase (AMY1) gene copy numbers and insulin resistance in asymptomatic Korean men. Diabet Med. 2015 Dec;32(12):1588-1595. doi:10.1111/dme.12808
19. Shin D, Lee KW. Dietary carbohydrates interact with AMY1 polymorphisms to influence the incidence of type 2 diabetes in Korean adults. Sci Rep. 2021 Aug;11(1):16788. doi:10.1038/s41598-021-96257-z
20. Kor M, Pouramir M, Khafri S, Ebadollahi S, Gharekhani S. Association between Dental Caries, Obesity and Salivary Alpha Amylase in Adolescent Girls of Babol City, Iran-2017. J Dent (Shiraz). 2021 Mar;22(1):27-32. doi:10.30476/DENTJODS.2020.84190.1070
21. Parsaie Z, Rezaie P, Azimi N, Mohammadi N. Relationship between Salivary Alpha-Amylase Enzyme Activity, Anthropometric Indices, Dietary Habits, and Early Childhood Dental Caries. Int J Dent. 2022;2022:2617197. doi:10.1155/2022/2617197
22. Padmanabhan V, Islam MS, Rahman MM, Goud MBK, Alshehhi LMSA, Hamed HMA, et al. Salivary alpha-amylase activity and its association with early childhood caries and rampant caries experience: a cross-sectional study. Front Med. 2024;11:1480139. doi:10.3389/fmed.2024.1480139
23. Perry GH, Dominy NJ, Claw KG, Lee AS, Fiegler H, Redon R, et al. Diet and the evolution of human amylase gene copy number variation. Nat Genet. 2007 Oct;39(10):1256-1260. doi:10.1038/ng2123
24. Hatipoğlu Ö, Saydam F. The role of AMY1 gene copy number variation in dental caries susceptibility: Insights from a Turkish population. BMC Oral Health. 2025;25:722. doi:10.1186/s12903-025-06074-3
25. Venkatapoorna CMK, Ayine P, Parra EP, Koenigs T, Phillips M, Babu JR, et al. Association of Salivary Amylase (AMY1) Gene Copy Number with Obesity in Alabama Elementary School Children. Nutrients. 2019 Jun;11(6):1379. doi:10.3390/nu11061379
26. Selvaraju V, Venkatapoorna CMK, Babu JR, Geetha T. Salivary Amylase Gene Copy Number Is Associated with the Obesity and Inflammatory Markers in Children. Diabetes Metab Syndr Obes. 2020 May;13:1695-1701. doi:10.2147/DMSO.S251359
27. Devarakonda SLS, Ren J, Poole AC. The association between salivary amylase gene copy number and enzyme activity with type 2 diabetes status. medRxiv. 2025 Mar 31;2025.03.31.25324922. doi:10.1101/2025.03.31.25324922
28. Khalifa O, Al-Akl NS, Arredouani A. Differential expression of cardiometabolic and inflammation markers and signaling pathways between overweight/obese Qatari adults with high and low plasma salivary α-amylase activity. Front Endocrinol. 2024;15:1421358. doi:10.3389/fendo.2024.1421358
29. Spatafora G, Li Y, He X, Cowan A, Tanner ACR. The Evolving Microbiome of Dental Caries. Microorganisms. 2024 Jan;12(1):121. doi:10.3390/microorganisms12010121
30. Farrell M, Ramne S, Gouinguenet P, Brunkwall L, Ericson U, Raben A, et al. Effect of AMY1 copy number variation and various doses of starch intake on glucose homeostasis: Data from a cross-sectional observational study and a crossover meal study. Genes Nutr. 2021 Nov;16(1):21. doi:10.1186/s12263-021-00701-8
31. Rukh G, Ericson U, Andersson-Assarsson J, Orho-Melander M, Sonestedt E. Dietary starch intake modifies the relation between copy number variation in the salivary amylase gene and BMI. Am J Clin Nutr. 2017 Jul;106(1):256-262. doi:10.3945/ajcn.116.149831
32. Zhan F, Chen J, Yan H, Wang S, Zhao M, Zhang S, et al. Association of Serum Amylase Activity and the Copy Number Variation of AMY1/2A/2B with Metabolic Syndrome in Chinese Adults. Diabetes Metab Syndr Obes. 2021 Dec;14:4705-4714. doi:10.2147/DMSO.S339604
33. Al-Akl NS, Thompson RI, Arredouani A. Reduced odds of diabetes associated with high plasma salivary α-amylase activity in Qatari women: A cross-sectional study. Sci Rep. 2021 Jun;11(1):11495. doi:10.1038/s41598-021-90977-y
34. Tayhan F, Helvacı G, Yabancı Ayhan N. Obesity Parameters in Women Is Associated With AMY1 Gene Copy Number, Nesfatin-1 Level, and Dietary Intake: A Case-Control Study. Mol Nutr Food Res. 2024;68(4):e70049. doi:10.1002/mnfr.70049

35. Rossi N, Aliyev E, Visconti A, Akil ASA, Syed N, Aamer W, et al. Ethnic-specific association of amylase gene copy number with adiposity traits in a large Middle Eastern biobank. NPJ Genom Med. 2021 Feb;6(1):1-9. doi:10.1038/s41525-021-00170-3
36. Yang ZM, Chen LH, Zhang M, Lin J, Zhang J, Chen WW, et al. Age Differences of Salivary Alpha-Amylase Levels of Basal and Acute Responses to Citric Acid Stimulation Between Chinese Children and Adults. Front Physiol. 2015 Oct;6:340. doi:10.3389/fphys.2015.00340
37. Mauricio-Castillo R, Valdevit A, Gonzalez-Davalos L, Dominguez-Perez RA, Garcia-Solis P, Vazquez-Martinez O, et al. Dental caries prevalence and severity positively associate with AMY1 gene copy number. Clin Oral Investig. 2023 Dec;28(1):25. doi:10.1007/s00784-023-05435-y
38. Carpenter D, Mitchell LM, Armour JAL. Copy number variation of human AMY1 is a minor contributor to variation in salivary amylase expression and activity. Hum Genomics. 2017 Feb;11(1):2. doi:10.1186/s40246-017-0097-3
39. Stankeviciene I, Puriene A, Brukiene V, Mieliauskaite D, Bække S, Tommeras B, et al. AMY1 gene copy number associated with xerostomia and Sjögren's syndrome: A cross-sectional study. BMC Oral Health. 2025 Feb;25(1):239. doi:10.1186/s12903-025-05595-1
40. Poole AC, Goodrich JK, Youngblut ND, Luque GG, Ruaud A, Sutter JL, et al. Human Salivary Amylase Gene Copy Number Impacts Oral and Gut Microbiomes. Cell Host Microbe. 2019 Apr;25(4):553-564. doi:10.1016/j.chom.2019.03.001