META-ANALYSIS OPEN ACCESS

Defensin-Mediated Oral Immunity: A Systematic Review and Meta-Analysis of DEFB1 Expression in Preventive Dentistry Strategies

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ABSTRACT

Background: Human beta-defensin 1 (DEFB1), together with other defensins, serves as a fundamental immune protector for oral tissues since it suppresses harmful microbial growth and fosters healthy oral conditions. The research included two main purposes assessing the relationship between DEFB1 expression levels and genetic polymorphism with oral disease risks, and evaluating DEFB1's potential for oral disease prevention biomarker use.

Methods: This research performed a systematic review and meta-analysis on 11 observational studies using PubMed, Google Scholar, and Web of Science databases. The data extraction process concentrated on recording DEFB1 expression data together with clinical results and population characteristics. The risk-of-bias tools were done using the Newcastle Ottawa tool, while a random-effects model was applied for meta-analysis due to heterogeneity in the studies.

Results: Eleven studies that contained DEFB1 gene polymorphisms and expression were considered. Rs11362 and rs1799946 polymorphisms and low levels of DEFB1 gene/protein were linked to increased risks of oral diseases, such as caries and periodontitis. The effect sizes were noted as 2.26 (95% CI: 0.90 -5.67) and -0.59 (95% CI: -1.28 to 0.09). Subgroup and sensitivity analyses showed the same direction of effect. Nonetheless, the significant heterogeneity was recorded (I2 > 90 percent), and the overall certainty of evidence was low because of the study design, inconsistency, and imprecision.

Discussion: Research findings show that DEFB1 demonstrates potential as an indicator of susceptibility to diseases, although specific studies exhibit some variation in their results. Additional research needs standardized approaches to advance knowledge.

Keywords: β-Defensins, Oral Mucosal Immunity, Gene Polymorphism, Dental Caries, Periodontitis, Preventive Dentistry

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INTRODUCTION

Human beta-defensins (HBDs) demonstrate a vital role in dental healthcare transformation because they provide new preventive measures for dentistry through innate immunity mechanisms according to research findings [1]. Research shows oral tissues receive strong protection through DEFB1 defensins because these peptides maintain epithelial integrity while continuously preventing microbial ingress to sustain oral health [2].

DEFB1 expression within oral tissues provides three essential benefits, which reduce pathogenic bacteria numbers and direct immune cell behavior while accelerating tissue repair to stop dental caries and periodontitis development [3]. Studies of DEFB1 biological properties strengthen its potential use in oral health evaluation while helping develop person-centered preventive dental practices. Clinicians could develop specific prevention strategies for oral disease reduction by profiling patients according to their disease risks through biological markers [4]. Researchers performed this study to gather and analyze emerging molecular evidence about DEFB1 in oral immunity while assessing its clinical effects for preventive dentistry practices.

The clinical use of DEFB1 remains restricted because of diverse detection techniques and unclear relationships between genetics and environment, and defensins, while standard protocols are needed for defensin-based preventive measures [5]. The field requires more education and clinical validation research about molecular diagnostics because practitioners need better training about their place in preventive care [6]. Current research about DEFB1 in preventive dentistry studied its clinical value together with the factors preventing its broad clinical implementation [7]. Defensin-mediated immunity has transformative power for the prevention of oral healthcare, but the domain is underexplored [8].

The research included two main objectives: assessing the relationship between DEFB1 expression levels and genetic polymorphism with oral disease risks, and evaluating DEFB1's potential for oral disease prevention biomarker use. The research conducted a detailed investigation of how these molecular elements affect dental caries and periodontal diseases, and oral cancer concerning different populations.

METHODS

The research process which investigated DEFB1 expression in preventive dentistry strategies followed PRISMA 2020 guidelines throughout every step of the systematic review process[9]. The analysis concentrated on examining DEFB1 expression in oral tissue while evaluating its effects on dental prevention outcomes from dental caries to periodontitis and oral mucosal infections.

The researchers performed an extensive search of electronic databases starting from publication year 2012 till 2023 and limited to English-language articles within PubMed, Google scholar, and Web of Science databases. The research adopted the keywords "Human Beta Defensin 1" OR "DEFB1" and the terms "Oral Immunity" OR "Oral Mucosa Defense" and "Preventive Dentistry" OR "Dental Caries Prevention" OR "Periodontal Disease" while searching for observational studies along with case-control studies and cross-sectional studies. The search results went through Boolean operator filtering together with specific database adjustments to enhance their precision level.

Studies qualified for inclusion when they fulfilled these three requirements: DEFB1 expression assessment in human oral samples and fluids, connection between DEFB1 expression and preventive dentistry outcomes including dental caries and periodontal disease prevention, and they contained original quantitative clinical measurements. The evaluation excluded research which examined in vitro experiments, without clinical data or computational predictions, or review articles or case reports.

The key outcomes of interest were the correlation between the DEFB1 gene polymorphism and oral diseases, and the variation between the DEFB1 gene or protein expressions levels of the diseased and healthy groups. These outcomes were measured by genotypic (e.g. Single nucleotide Polymorphisms (SNPs) like rs11362 and rs1799946) and expression information (captured by reverse transcription polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assay (ELISA), or immunohistochemistry (IHC)). The secondary outcomes were subgroup comparisons (e.g., children versus adults, smokers versus non-smokers, persons with caries versus persons without, different levels of severity of the disease, e.g., mild vs. severe caries or periodontitis). In cases where subgroup data were reported on several stages of disease, most severe disease stage data were pulled out in order to have consistency. All pertinent results that were consistent with the specified domains of outcomes were searched and used, giving precedence to the most transparent case-control comparisons where multiple measures or time points were illustrated.

The evaluation procedure which includes study identification followed by title and abstract screening and full-text assessment adopted a three-phase methodology. A team of two

independent reviewers checked all articles at each point while a third senior reviewer mediated conflicts through consensus-based discussions. The researchers create a standardized data extraction table to record study design features, together with participant demographic information along with DEFB1 evaluation methods and expression levels and disease relationships and preventive outcome data. Information regarding genetic polymorphisms that impact DEFB1 expression levels was also documented when researchers presented it.

Quality assessment for observational and case-control studies employed the Newcastle-Ottawa Scale (NOS). The research team used the GRADE framework to determine the overall evidence certainty.

Meta-Analysis Online was used to analyze the statistical data for the study. A random-effects model generated pooled risk ratios (ORs) with 95% confidence intervals (CIs) for the relationship between DEFB1 expression and preventive oral health outcomes during quantitative synthesis. The I^2 statistic assessed study heterogeneity, while sequential study exclusion analyses determined the reliability of the results. The sensitivity analyses were also carried out when required.

The methodology created a framework to establish the clinical value of DEFB1 in dental prevention through assessment of methodological weaknesses and future research directions[10]. The review protocol underwent prospective registration as a measure to maintain methodological transparency before researchers started extracting data and conducting their analyses.

The analysis included eleven observational studies that met inclusion criteria for the research[11,12,13,14,15,16,17,18,19,20,21]. Meta-analysis was performed using Review Manager software version 5.4.0, which resulted in mean differences (MDs) and odds ratios (ORs) with 95% Confidence Intervals (CIs) for DEFB1 expression outcomes. The I^2 statistic was used to assess heterogeneity; moderate to high results were taken when it exceeded 50%. The study with the largest confidence interval was excluded from the sensitivity design analysis, also known as leave-one-out analysis. Subgroup analyses were performed on the subgroups, like age, smoking status, and severity of caries. Forest plots were generated using a random effects model.

RESULTS

A total of 11 research papers published from 2012 to 2023 analyzed both the oral immunity functions of DEFB1 and its significance for preventive dental care. The research included various types of observational studies, while utilizing sample sizes that ranged from small cohorts to large population numbers. Any study that lacked the primary aim was excluded. Figure 1 demonstrates the flow diagram for study selection.

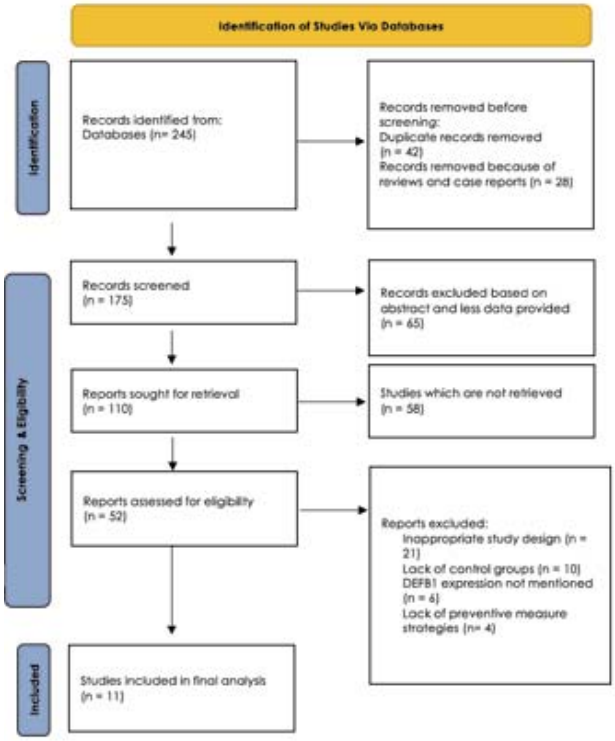

Figure 1: PRISMA Flow Diagram

This meta-analysis involved the utilization of 11 studies, published in the period 2012-2023. These experiments were carried out on varying groups of people in Africa, Asia, Europe, and South America, including children and adults. The majority of the studies were cross-sectional and case-control in design, and the most frequent oral health conditions were dental caries, periodontitis, gingivitis, and oral squamous cell carcinoma (OSCC). The evaluation of DEFB1 differed between studies, and evaluation was performed through genotyping of single-nucleotide polymorphisms (SNPs) (mainly through rs11362 and rs1799946) and measures of expression using ELISA, RT-PCR, or IHC. There were sample sizes as low as 18 and as high as 500 participants, and factors like smoking habits, age, and methods of maintaining oral hygiene were poorly reported. **Table 1** highlights the baseline characteristics of individual studies included in the meta-analysis.

Table 1: Characteristics at Baseline as Measured in the Included Studies

Study	Study Type	Country / Ethnicity	Total N (or Group N)	Age (Mean ± SD / Range)	Gender (M/F or %)	Smoking Status	Primary Oral Health Condition Studied
Ikuta et al., 2015	Human, Case-control	Japanese	105 (AgP: 21, Severe CP: 28, Moderate CP: 13, CP Control: 22, AgP Control: 21)	AgP group older than matched control ($p < 0.05$); other groups similar	Not fully detailed	Not reported	Periodontitis (Aggressive and Chronic)
Loo et al., 2012	Human, Cross-sectional	Chinese (Hong Kong and Sichuan)	Control: 108; Patients: 44	Control: 42.9 ± 9.7 (18–60); Patients: 49.3 ± 13.6 (18–74)	Control: 69M/39F; Patients: 26M/18F	Non-smokers in both groups	Chronic Periodontitis (moderate to advanced)
Nelson-Filho et al., 2022	Human, Cross-sectional	Brazilian (Manaus)	27 (Gingivitis: 10, No Gingivitis: 17)	Mean 9.92 ± 0.82 years (range 10–12)	Gingivitis: 6M/4F; No Gingivitis: 10M/7F	Not reported (children)	Gingivitis in children (plaque-induced)
Li et al., 2016	Human, Cross-sectional	Chinese	CP: 46; Healthy: 50	CP: 23–70 years; Healthy: 20–46 years	CP: 24M/22F; Healthy: 20M/30F	Not reported	Expression of hBD-1 to hBD-4 in gingival epithelia
Wu et al., 2020	Human, Association analysis (genetic factors)	Chinese (Gansu Province)	Total: 519 (265 controls, 254 caries-affected children)	Caries: 4.67 ± 0.55; Controls: 4.53 ± 0.67 (both 3–5 years)	Caries: 131M/123F; Controls: 135M/130F	Not reported (children)	Dental Caries (mild/moderate/severe, by dmft scores)
Han et al., 2014	Human, Tissue-based study with TMA	Chinese	62 tissue blocks + 175 OSCC TMA patients	OSCC patients: <60 yrs (n=85), ≥60 yrs (n=90)	OSCC: 125M/50F	Smokers (n=97), Non-smokers (n=78)	Oral Squamous Cell Carcinoma (OSCC) and oral leukoplakia
Salman et al., 2023	Human, Comparative-case	Iranian	48 (16 mild, 16 moderate, 16 severe caries)	Mean age ~4.4 to 4.56 years (all under 6)	Mild: 8M/8F; Moderate: 9M/7F; Severe: 8M/7F	Not reported	Early Childhood Caries (ECC/SECC)
Gürsoy et al., 2023	Human, Cross-sectional	Finnish	175 (Control: 17; PerioA: 55; PerioB: 33; PerioC: 29; Edentulous: 41)	Mean: 74.35 years (range 65–92); group-specific data in Table 1	Overall: 70M/105F	Smoking status reported by group: daily, occasional, former, never	Periodontal Disease and Tooth Loss in the elderly
Zupin et al., 2018	Human, Cross-sectional	Italian	Patients: 95; Controls: 178	Patients: mean 8 yrs (2–18); Controls: mean 8 yrs (6–12)	Controls: 85M/93F; Patients' gender not specified	Not reported (children)	Adeno-tonsillar hypertrophy (AH)

Wolgin et al., 2012	Human, Cross-sectional	German	Smokers: 9; Non-smokers: 9	Smokers: 45.3 ± 14.3 yrs; Non-smokers: 54.7 ± 15.2 yrs (range 21–80)	Smokers: 3M/6F; Non-smokers: 4M/5F	Smokers: ≥10 cig/day; Non-smokers: never smokers	Gene expression of hBD-1 and hBD-2 in gingival tissue
Rahmayanti et al., 2019	Human, Cross-sectional	Indonesian	Smokers: 44; Non-smokers: 24 (all male)	Overall: 20–55 years	All male (n = 68)	Grouped as smokers vs non-smokers; cigarette type/duration/frequency not differentiated	Salivary hBD-1 levels and oral health in tobacco smokers

Human beta-defensin 1 expression values, along with other important variables, are shown in **Table 2.**

Table 2: Expression data of Human Beta Defensin 1 in Included Studies

Author(s) & Year	Study Design	Sample Size	Measurement Type	Oral Disease	Genotype / Expression Data	Key Data Values	Confounders / Limitations
Ikuta et al., 2015	Case-control	105 (AgP, CP, Controls)	DEFB1 Genotyping & hBD-1 in GCF (ELISA)	Aggressive & Chronic Periodontitis	-44 CC genotype ↑ in CP; lower hBD-1 levels in CC genotype	CC genotype OR = 4.15 (1.113–15.304), $p < 0.05$	No link to AgP; role of NFκB needs clarification
Loo et al., 2012	Comparative	30 CP, 38 healthy	Genotype (DEFB1 -1654 G/A), salivary hBD-2 (ELISA)	Chronic Periodontitis	Genotype: G allele lower in patients; hBD-2 higher in patients	OR = 3.9474 (1.8697–8.3339)	Only one SNP analyzed; genotype-expression relationship not fully explored
Nelson-Filho et al., 2022	Cross-sectional	27 children (10 gingivitis, 17 controls)	Genotyping (TaqMan endpoint PCR)	Gingivitis	No significant SNP associations (rs1799946, rs11362)	rs1799946 OR = 0.87 (0.08–9.15); rs11362 OR = 0.94 (0.11–7.74); $p > 0.05$	Small sample size; genetic-environmental interaction unaccounted
Li et al., 2016	Comparative	21 CP, 21 healthy	RT-PCR & IHC (hBD-1–4)	Chronic Periodontitis	No significant differences in gene/protein expression	Median hBD-1: Healthy = 0.1; CP = 0.0 (relative units)	Advanced CP may mask early differences; population specificity
Wu et al., 2020	Association analysis	511 children (254 caries; 265 controls)	Genotyping (MassARRAY iPLEX)	Dental Caries	rs11362 (↑ with severity), rs1799946 (↓ with severity)	rs11362: OR = 2.447; severe OR = 3.234 (3.039–3.506); rs1799946 OR = 0.473 (0.347–0.789)	Genetic heterogeneity; explains partial heritability only
Han et al., 2014	Cross Sectional	62 tissues + 175 TMA + cell lines	IHC, ELISA, RT-PCR	OSCC & OLK	↓ hBD-1 in OSCC; ↑ hBD-1 in OLK	HR = 0.382 (0.238–0.615); $p = 0.001$	Contradiction with mRNA data; biological mechanism unclear

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Salman et al., 2023	Comparative (Cross-sectional)	48 children (16 per group)	Salivary hBD-1/-2 (ELISA)	ECC / SECC	↓ hBD-1 & hBD-2 with increasing caries severity	hBD-1: Mild = 1.255 ± 0.299 µg/mL; Severe = 0.067 ± 0.195 µg/mL	Nutrition and hygiene not controlled; literature shows variability
Gürsoy et al., 2023	Cross-sectional	175 elderly (≥65 yrs), 5 subgroups	Salivary hBD-1/-2/-3 (ELISA)	Periodontitis & Tooth Loss	No significant defensin differences across groups	hBD-1 median: Controls = 4500 pg/mL; Edentulous = 4600 pg/mL	No younger group; no power calculation
Zupin et al., 2018	Case-control	273 (95 AH patients, 178 controls)	DEFB1 Genotyping (TaqMan), mRNA (RT-PCR)	Adeno-Tonsillar Hypertrophy (AH)	Rare haplotypes ↑ in patients	Rare DEFB1 haplotypes OR = 9.90 (2.03–95.26); p = 0.001	No normal tonsil tissue for comparison; expression variability
Wolgin et al., 2012	Comparative	18 (9 smokers, 9 non-smokers)	Gingival hBD-1/-2 mRNA (RT-PCR)	Gingival Health & Smoking	~2.5-fold ↓ in expression in smokers	hBD-1: Smokers = 0.0008 ± 0.0026; Non-smokers = 0.0030 ± 0.0034	Small sample; no salivary validation
Rahmayanti et al., 2019	Cross-sectional	68 males (44 smokers, 24 non-smokers)	Salivary hBD-1 (ELISA)	Smoking-related Oral Health	Higher hBD-1 in smokers	Smokers = 5.65 (0.07–45.02) pg/mL; Non-smokers = 2.34 (0.04–16.76) pg/mL; p = 0.01	Small sample; potential selection bias

Polymorphisms and expression of the DEFB1 gene were found to have strong connections with oral disease. A rs11362 T allele was associated with a higher risk of caries with an odds ratio (OR) of up to 3.23, whereas the rs1799946 T allele was viewed to be protective (OR = 0.47). The level of hBD-1 in the saliva also ended up falling drastically along with the level of caries, 1.25 µg/ml (mild) and 0.07 µg/ml (severe). Studies identified that the -44 CC genotype was at an increased risk, which was over four times (OR = 4.15), accompanied by reduced DEFB1 levels in periodontitis; however, other studies did not show significant variations. HBD-1 expression in the gingiva of the smokers was 2.5-fold diminished, even though saliva levels were considerably augmented (p = 0.01). In OSCC, low DEFB1 expression was associated with unfavorable survival (HR = 0.38, p = 0.001), whereas in leukoplakia, the expression was high. Rare DEFB1 haplotypes were seen as risk factors of mucosal hypertrophy (OR = 9.9, p = 0.001).

Meta-analysis involved the two primary outcomes: the linkage of DEFB1 single-nucleotide polymorphisms (SNPs) to the risk of the oral disease and the expression of DEFB1 in diseased compared to healthy people. Two forest plots were created to represent these results.

Squares demonstrated effect sizes of the individual studies, and the diamond in the middle showed the combined estimate of the studies. The first forest plot compared five studies that estimated the odds ratios related to the SNP. Pooled odds ratio (OR) was 2.26 (95% CI: 0.90 -5.67), which showed that the relationship between DEFB1 variants and oral diseases is non-significant. The heterogeneity was high (I^2 = 92%, p < 0.01), indicating that there were different genetic effects across the studies. **Figure 2** demonstrates the forest plot for 5 studies included, of which two studies studied two SNPs; therefore, both values were added.

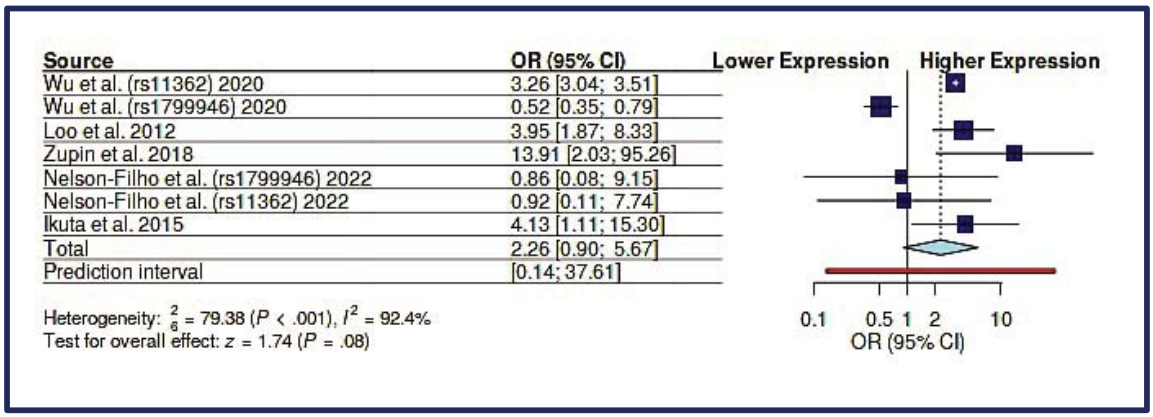

Figure 2: Human Beta Defensin 1 Single Nucleotide Polymorphism Expression Data in Oral Disorders

The second forest plot reviewed three publications that reported the levels of DEFB1 expression. The overall mean difference (MD) was -0.59 (95% CI: -1.28 to 0.09), and once again, this did not show any significant difference between diseased and control groups. A high level of heterogeneity (I2=99 %, p 0.01) was noted, indicating methodological inconsistency and varied disease settings along with the difference in scales used to calculate values. **Figure 3** highlights the forest of 3 studies pooled to study protein/gene expression data.

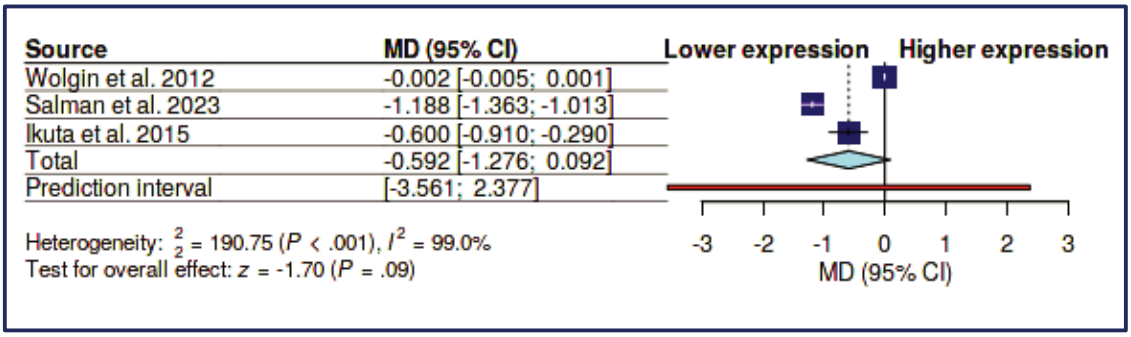

Figure 3: Human Beta Defensin 1 Protein/Gene Expression Data in Oral Disorders

The subgroup analyses were done according to three categories, namely, age, smoking, and the severity of disease. In case of the age-based analysis, the expression data was ripe in excess of 750 children and 175 elderly persons. The levels of median hBD-1 concentration in the elderly subjects were 3000-4600 pg/mL, which exhibited no significant trend as compared to children. Smokers (n = 44) in the smoking subgroup (n = 77) showed a mean value of hBD-1 of 5.65 pg/mL (min-max: 0.07-45.02) as opposed to non-smokers (n = 33) at 2.34 pg/mL (min-max: 0.04-16.76). Comparisons in mRNA expression revealed a 2.5-fold decrease in smokers as compared to non-smokers. In caries subgroups (n = 48), HBD-1 concentrations among subgroups of caries (n = 48) were lower in severe caries as compared to mild cases (0.067 +/- 0.195-ug/mL, versus 1.255 +/- 0.299-ug/ mL, respectively). These figures indicated that DEFB1 expression depends upon disease progression as well as lifestyle influences, but that variation between studies should be taken with caution.

Leave-one-out was done in order to determine the effects of the individual studies on the pooled estimates and the heterogeneity. In SNP-based meta-analysis (based on odds ratios), the original heterogeneity was I2 = 92.4%. By systematically removing studies one by one, the pooled effect size did not change direction, and the I2 varied between 84.7% and 92.4% which means that no specific study contributed to heterogeneity alone.

In the gene/protein expression meta-analysis (mean difference as base), the initial heterogeneity was I2 = 99%, which indicated extreme inter-study heterogeneity. After leave-one-out analysis, the heterogeneity slightly varied yet remained high (I2 range: 97.2% to 99%), and the pooled MD still favored the DEFB1 reduction in diseased populations. These results indicate that the outcomes are qualitatively strong but have a quantitative influence of substantial heterogeneity, probably as a consequence of differences in methodology and populations in the included studies.

Risk of Bias

Most observational studies within the scope of DEFB1 expression in oral immunity and preventive dentistry exhibit a low to moderate risk of bias based on total scores ranging between 5 and 7 out of 9. The studies properly selected their participants and measured outcomes, but some surveys demonstrated restricted comparability resulting from possible confounding variables. The results of the risk of bias are shown in Table 3.

Table 3: Risk of Bias Assessment of Individual Observational Studies

Study	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Total Score (max 9)
Ikuta et al., 2015	★★★	★★	★★	7
Loo et al., 2012	★★★	★★	★★	7
Nelson-Filho et al., 2022	★★	★	★★	5
Li et al., 2016	★★★	★★	★★	7
Wu et al., 2020	★★★	★★	★★	7
Han et al., 2014	★★	★★	★★	7
Salman et al., 2023	★★★	★★	★★	6
Gürsoy et al., 2023	★★★	★★	★★	7
Zupin et al., 2018	★★★	★★	★★	7
Wolgin et al., 2012	★★★	★★	★★	7
Rahmayanti et al., 2019	★★★	★★	★★	7

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

Overall, the body of evidence showed low levels of certainty because the heterogeneity among studies, sample sizes, observational designs, and methodological limitations was high.

DISCUSSION

The review analyzes existing evidence about human beta-defensin 1 (DEFB1) function in oral immunity, together with its applications for preventive dental care. DEFB1 acts as a major antimicrobial peptide that maintains automatic expression within oral epithelial tissue, which plays a fundamental role in defending against microbial invaders [22]. The expression changes of DEFB1 play a part in oral health conditions including periodontitis and oral squamous cell carcinoma (OSCC) because decreased levels indicate weakened defense mechanisms and suppressed tumor regulation [23]. The DEFB1 expression level suffers from environmental influences which include tobacco smoking and results in diminished oral immunity. Research on dental caries associations with DEFB1 gene polymorphisms has focused on two specific variants rs11362 and rs1799946 [24,25].

Research on different populations gave significant findings on the influence of DEFB1 expression and genetic variation on oral disorders [26]. For example, the presence of polymorphisms in rs11362 and rs1799946 had been illustrated to predispose children to dental caries, whereas DEFB1-1654 G/A and -44 C/G polymorphisms were associated with the severity of periodontitis in adult patients [27]. Studies in smokers showed that the gingival innate defense was highly impaired with remarkable reduction of DEFB1 expression, and this showed repression of innate oral defenses under tobacco exposure[28]. Correspondingly, there was reduced antimicrobial activity in salivary DEFB1 in aged individuals with edentulism or oral health problems with severe periodontal disease, indicating a connection between low levels of defensins with less protection against oral degradation [29]. Additionally, comparisons of children and adults also indicated that there was a developmental variation in the expression of the defensins, which might be a reason why diseases were susceptible based on age [30].

At the transcriptional level, DEFB1 was found to be

downregulated in OSCC relative to normal mucosa, which meant that it played a role in maintaining epithelial tumor surveillance [31]. The significance of this tumor-suppressive role might be connected with the effect on epithelial integrity and immune modulation [32]. Conversely, precancerous lesions, including oral leukoplakia, had been seen to have high DEFB1 expression, perhaps as a compensatory antiprotective response [33]. The ELISA-based salivary measurements had indicated a uniform decline in hBD-1 amounts in caries and periodontitis patients as opposed to healthy controls [34]. The additional factors that affected expression differences include smoking, age, and oral hygiene practices [35]. Meta-analytic estimates demonstrated that DEFB1 gene and protein expression were consistently reduced in oral disease, except with large inter-study variance [36]. These results promoted the possibility of using DEFB1 as a biomarker as well as the future personal plans of prevention, depending on explicit heredity and expression portrait [37].

The research data demonstrates that DEFB1 plays an important role in oral immunity and disease risk but multiple factors need consideration. The inconsistent findings might result from differences in sample size distribution, combined with research design aspects together with DNA sequencing techniques alongside population variable elements [38,39]. Research findings are affected by the unknown effects of publication bias as well as by the absence of standardized methods for testing DEFB1 expression levels [40]. The review has limitations because of inconsistent research designs along with small participant numbers and non-uniform methods for DEFB1 expression evaluation. Future research must use bigger and more diverse population sets together with standardized protocols to study functional DEFB1 behavior and develop its dental disease prevention applications.

CONCLUSION

The analyzed research demonstrates that changes in DEFB1 gene expression levels determine dental caries and periodontal disease risk thus making DEFB1 a potential marker for oral health risk evaluations. The current research results remain inconclusive because of inconsistent research designs together with differing sample sizes and methodologies that need standardization. Future research needs to perform extensive longitudinal studies which study populations representing different groups across diverse environments to test DEFB1's practical value in dental clinics. The inclusion of DEFB1 analysis during standard dental evaluation procedures may develop patient-specific preventive practices which would optimize oral health outcomes. A partnership between clinical practitioners and researchers remains central for converting these study results into professional preventive dental applications.

LIST OF ABBREVIATIONS

HBD-1/DEFB1: Human Beta Defensin 1
OSCC: Oral squamous cell carcinoma
SNPs: Single-nucleotide polymorphism
NOS: New Castle Ottawa Scale

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None

CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTIONS

All contributed equally as per ICMJE.

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