



Biological Pathways of Oral Health Inequality: A Longitudinal Analysis of Stunting, Enamel Defects, and Salivary Immunity on Caries Trajectories in Indonesian Children

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ABSTRACT

Introduction: The syndemic of stunting and Early Childhood Caries (ECC) constitutes a major public health crisis in developing nations. While an association is established, the specific biological mechanisms remain poorly quantified. This study aimed to longitudinally determine the direct and indirect effects of early childhood stunting on caries increment, testing the mediating roles of enamel hypoplasia and salivary immunity after controlling for key confounders. **Methods:** We conducted a 3-year prospective cohort study of 542 two-year-old children in West Java, Indonesia. Stunting at baseline was defined as a height-for-age Z-score (HAZ) < -2 SD. The primary outcome was the 3-year increment in decayed, missing, and filled primary tooth surfaces ($\Delta dmfs$). Putative mediators—enamel hypoplasia and salivary secretory immunoglobulin A (s-IgA) and lactoferrin—were assessed. Longitudinal mixed-effects models and structural equation modeling (SEM) were used to analyze the pathways, adjusting for socio-demographic factors and fluoride exposure. **Results:** At baseline, 31.4% of children were stunted. After adjusting for confounders including fluoride exposure, stunting remained a powerful predictor of accelerated caries increment (an additional 1.95 surfaces/year; $p < 0.001$). SEM analysis revealed the total effect of stunting on $\Delta dmfs$ was substantial (Standardized $\beta = 0.45$, $p < 0.001$). This effect was significantly mediated by enamel hypoplasia (indirect effect $\beta = 0.17$, accounting for 37.8% of total effect) and suppressed salivary s-IgA levels (indirect effect $\beta = 0.10$, accounting for 22.2% of total effect). The direct effect of stunting, independent of these mediators, remained significant ($\beta = 0.18$, $p < 0.001$). **Conclusion:** Stunting in early life is a critical determinant of a high future caries burden, an effect that persists even after accounting for fluoride exposure. This relationship is substantially driven by two major biological pathways: compromised tooth structure (enamel hypoplasia) and impaired oral mucosal immunity (suppressed s-IgA). Public health strategies must integrate nutritional support within the first 1,000 days of life with oral health promotion to disrupt these pathways and combat the dual burden of stunting and ECC.

1. Introduction

The concurrent global epidemics of childhood malnutrition and dental caries represent a syndemic of profound public health significance, particularly in

low- and middle-income countries (LMICs).¹ Stunting, a manifestation of chronic undernutrition resulting in impaired linear growth, affects over 149 million children under five globally. It is a devastating

condition that serves as an integrated marker of past nutritional deficiencies, poverty, and recurrent infection. Its consequences extend far beyond physical stature, predicting a future of diminished cognitive development, poor academic performance, and an elevated risk of chronic diseases in adulthood.² Concomitantly, Early Childhood Caries (ECC), the most prevalent chronic non-communicable disease of childhood, affects millions worldwide, causing pain, infection, and diminished quality of life. In nations like Indonesia, the prevalence of both stunting and severe ECC is among the highest in Southeast Asia, creating a substantial and interconnected burden on the healthcare system and limiting the potential of future generations.^{3,4}

A robust body of epidemiological evidence, largely from cross-sectional studies, has established a strong association between stunting and ECC, with stunted children consistently exhibiting a higher prevalence and severity of dental caries.⁵ This association is often attributed to shared socio-behavioral risk factors, including low socioeconomic status, high-sugar diets, and suboptimal hygiene practices. While these determinants are undeniably important, they do not fully elucidate the biological plausibility of a direct causal link. The compelling hypothesis that chronic malnutrition directly compromises host susceptibility to caries through deep-seated physiological and structural alterations requires rigorous longitudinal investigation to establish temporality and delineate the precise mechanisms involved. Such an understanding is critical to move beyond simply managing risk factors to developing interventions that target the root biological causes.^{6,7}

Two primary biological pathways are postulated to mediate the effect of stunting on caries susceptibility. The first pathway involves permanent defects in tooth development and structure.⁸ The development of primary dentition occurs from in utero through early childhood—a critical window that precisely overlaps with the period of greatest vulnerability to the nutritional insults that cause stunting. Amelogenesis (enamel formation) and dentinogenesis (dentin formation) are metabolically demanding processes that require an adequate supply of essential nutrients,

including protein, vitamins A and D, calcium, and phosphorus. Chronic deficiencies disrupt the function of ameloblasts and odontoblasts, leading to developmental defects, most notably enamel hypoplasia. This condition manifests as visible pits, grooves, or missing enamel, creating a structurally compromised tooth surface. These imperfections act as niches for bacterial plaque accumulation and, due to their reduced mineral content and disorganized prism structure, offer significantly less resistance to acid demineralization, thereby accelerating cavity formation.⁹

The second proposed pathway involves the impairment of the host's immune system, particularly within the oral cavity. The salivary immune system is the first line of defense against cariogenic pathogens like *Streptococcus mutans*. Saliva contains a host of antimicrobial proteins and immunoglobulins that maintain oral homeostasis. Among these, secretory immunoglobulin A (s-IgA) is paramount. As the principal immunoglobulin in mucosal secretions, s-IgA functions by agglutinating bacteria in the fluid phase, preventing their adhesion to tooth surfaces and neutralizing their virulence factors. Another key protein, lactoferrin, exerts bacteriostatic effects by sequestering iron essential for bacterial metabolism. Malnutrition is a well-documented cause of systemic immune suppression, with a particular impact on mucosal immunity. It is therefore biologically plausible that stunting, as an integrated marker of chronic malnutrition, leads to reduced production and secretion of critical salivary proteins, thereby crippling the oral cavity's defense capacity and fostering a dysbiotic environment conducive to caries.¹⁰

Despite the strong theoretical basis for these pathways, prior research has been limited by cross-sectional designs, which cannot disentangle cause and effect. Furthermore, few studies have simultaneously investigated the mediating roles of both enamel structure and salivary immunity within a single, comprehensive longitudinal framework, and almost none have done so while accounting for the powerful confounding effect of fluoride exposure. This represents a critical knowledge gap, as understanding the relative contribution of these specific mechanisms

is essential for designing targeted and effective interventions.

Therefore, the primary aim of this 3-year longitudinal cohort study was to determine the association between stunting at age two and the subsequent increment of dental caries by age five in a population of preschool children in West Java, Indonesia. The novel secondary aim was to quantify the mediating effects of developmental enamel hypoplasia and salivary s-IgA concentration in the pathway from stunting to caries development, after adjusting for a comprehensive set of socio-behavioral confounders, including fluoride exposure. We hypothesized that stunting would be a significant predictor of an accelerated rate of caries accumulation and that this effect would be substantially, though perhaps not entirely, mediated by an increased prevalence of enamel hypoplasia and suppressed levels of salivary immune components.

2. Methods

This study utilized a prospective cohort design with assessments at baseline (T0) and two subsequent annual follow-ups (T1 and T2). The study was conducted in several rural sub-districts within the Bandung Regency of West Java, Indonesia, a region selected for its high prevalence of childhood stunting and ECC and its stable population. Participant recruitment occurred from January to March 2021. Children were eligible if they were 24-30 months of age, were permanent residents, and their legal guardians provided written informed consent. Exclusion criteria included diagnosed systemic diseases affecting growth, congenital craniofacial syndromes, severe acute malnutrition requiring hospitalization, or use of medications known to affect salivary flow.

A multi-stage cluster sampling method was employed. First, ten sub-districts were randomly selected, from which 30 integrated health posts (Posyandu) were chosen. All eligible children attending these Posyandu during the recruitment period were invited to participate. The sample size was calculated to detect a clinically significant difference in the 3-year caries increment between stunted and non-stunted

children. Based on prior regional data, we anticipated a mean 3-year dmfs increment of 8 (SD=6) in the stunted group and 5 (SD=5) in the non-stunted group. With a statistical power of 90% ($\beta=0.10$) and a two-sided alpha of 0.05, a minimum of 163 children per group was required. To account for a cumulative attrition rate of approximately 30% over 3 years, we aimed to recruit a total sample of at least 540 children.

Data were collected at baseline (T0; age ~2 years), and at two annual follow-ups (T1; age ~3 years and T2; age ~4 years), with the final outcome reflecting the caries increment by age 5. Children's standing height was measured to the nearest 0.1 cm using a portable stadiometer (Seca 213, Germany) by a trained anthropometrist. The Height-for-Age Z-score (HAZ) was calculated using WHO Anthro software based on the 2006 WHO Child Growth Standards. Stunting, the primary exposure, was defined as HAZ < -2 standard deviations (SD) at baseline.

The primary outcome was the 3-year increment in the decayed, missing (due to caries), or filled primary tooth surfaces (Δ dmfs). Oral examinations were performed by two calibrated dental examiners using a dental mirror, a WHO-CPI probe, and a portable LED headlamp. Caries was diagnosed at the cavitation level (D3), corresponding to codes 5 and 6 of the International Caries Detection and Assessment System (ICDAS II). The Δ dmfs was calculated as (dmfs at T2 - dmfs at T0). Inter- and intra-examiner reliability was excellent (weighted Kappa > 0.88). The presence of developmental enamel hypoplasia was recorded at baseline using the modified Developmental Defects of Enamel (DDE) Index. A child was classified as having enamel hypoplasia if at least one primary tooth exhibited a clear pit, groove, or missing enamel. Unstimulated whole saliva samples were collected at each time point (T0, T1, T2) in the mid-morning, at least 90 minutes postprandial. Samples were immediately placed on ice, centrifuged within two hours, and the supernatant stored at -80°C. Concentrations of salivary s-IgA and lactoferrin were quantified using commercial enzyme-linked immunosorbent assay (ELISA) kits (Abcam, Cambridge, UK). The final concentrations were expressed in μ g/mL.

A structured questionnaire administered to the primary caregiver collected data on potential confounders: (1) Socio-demographics: Parental education (years of schooling), household income (Indonesian Rupiah/month); (2) Dietary habits: Frequency of sugary snack and beverage consumption, categorized as ≤ 1 time/day or > 1 time/day; (3) Oral hygiene: Frequency of daily tooth brushing, categorized as < 2 times/day or ≥ 2 times/day; (4) Fluoride Exposure: This was operationalized as a composite variable. Children were classified as having 'Adequate' exposure if the caregiver reported consistent (≥ 2 times/day) brushing with a fluoridated toothpaste. All other patterns were classified as 'Inadequate'.

Analyses were performed using Stata v17.0. Descriptive statistics were calculated, and baseline differences were assessed using t-tests and chi-squared tests. A linear mixed-effects model was constructed to analyze the longitudinal effect of stunting on dmfs scores over the three time points (T0, T1, T2). The model included stunting, time, and a stunting-by-time interaction term as primary predictors, adjusting for all covariates (parental education, income, sugar intake, brushing frequency, and fluoride exposure). A random intercept for each child accounted for repeated measures.

The mediation pathways were evaluated using structural equation modeling (SEM). The model tested the direct and indirect pathways from baseline stunting (exogenous variable) to the 3-year dmfs increment (Δ dmfs; outcome). Enamel hypoplasia (baseline) and average salivary s-IgA/lactoferrin concentrations (averaged across T0-T2) were the mediators. All paths were adjusted for the full set of covariates. Model goodness-of-fit was assessed using the CFI, TLI, RMSEA, and SRMR indices. The significance of indirect effects was determined using bootstrapping with 5,000 replications to generate 95% confidence intervals (CIs).

The study protocol was approved by the Health Research Ethics Committee of the CMHC Research

Center, Indonesia. Written informed consent was obtained from each child's parent or guardian. All participants received oral hygiene education and free dental care as needed at each visit.

3. Results and Discussion

Of the 580 children invited, 542 (93.4%) were enrolled. Over the 3-year period, 61 (11.3%) were lost to follow-up. The final analysis included 481 children who completed all assessments. There were no significant baseline differences between study completers and those lost to follow-up (all $p > 0.20$). At baseline, the mean age was 26.8 (± 2.1) months, and 170 children (31.4%) were classified as stunted.

Table 1 presents the baseline characteristics stratified by stunting status. Compared to non-stunted children, stunted children were from families with significantly lower income and parental education ($p < 0.001$). Behaviorally, they had a higher frequency of sugar intake, less frequent tooth brushing, and significantly lower rates of adequate fluoride exposure ($p < 0.001$). Clinically, the prevalence of enamel hypoplasia was over four times higher in stunted children (78.2% vs. 17.5%, $p < 0.001$). Stunted children also exhibited significantly lower mean concentrations of salivary s-IgA and lactoferrin ($p < 0.001$).

The gap in caries experience between the groups widened progressively over time. The 3-year dmfs increment (Δ dmfs) was 12.4 ± 6.8 for stunted children and 5.7 ± 4.1 for non-stunted children. The results of the fully adjusted linear mixed-effects model are presented in Table 2. After adjusting for all confounders, adequate fluoride exposure was strongly protective, associated with a reduction of 1.12 dmfs surfaces per year ($p < 0.001$). Crucially, the stunting-by-time interaction remained a powerful and highly significant predictor ($\beta = 1.95$, $p < 0.001$). This indicates that even after accounting for fluoride and other factors, children who were stunted at baseline accumulated nearly two additional carious surfaces per year compared to their non-stunted peers.

Table 1. Baseline Characteristics of the Study Cohort

Stratified by Stunting Status (n=542)

Characteristic	Total (N=542)	Non-Stunted (N=372)	Stunted (N=170)	P-Value
Socio-demographics				
Maternal Education (years, mean±SD)	9.1 ± 2.8	9.8 ± 2.5	7.6 ± 2.9	<0.001
Paternal Education (years, mean±SD)	9.5 ± 3.1	10.3 ± 2.8	7.9 ± 3.0	<0.001
Household Income (million IDR/month, mean±SD)	2.8 ± 1.5	3.2 ± 1.6	1.9 ± 0.9	<0.001
Behavioral Factors				
Sugar Intake >1 time/day, n(%)	315 (58.1)	188 (50.5)	127 (74.7)	<0.001
Brushing <2 times/day, n(%)	288 (53.1)	160 (43.0)	128 (75.3)	<0.001
Clinical & Biological Variables				
HAZ Score (mean±SD)	-1.48 ± 1.1	-0.71 ± 0.6	-2.98 ± 0.5	<0.001
dmfs Score (mean±SD)	1.0 ± 1.9	0.6 ± 1.1	1.8 ± 2.5	<0.001
Enamel Hypoplasia, n(%)	198 (36.5)	65 (17.5)	133 (78.2)	<0.001
Salivary s-IgA (µg/mL, mean±SD)	103.5 ± 32.4	115.6 ± 30.8	78.4 ± 25.1	<0.001
Salivary Lactoferrin (µg/mL, mean±SD)	18.5 ± 6.5	20.5 ± 6.2	14.2 ± 4.9	<0.001

Table 2. Fully Adjusted Linear Mixed-Effects Model

Dependent Variable: dmfs Score Over 3 Years

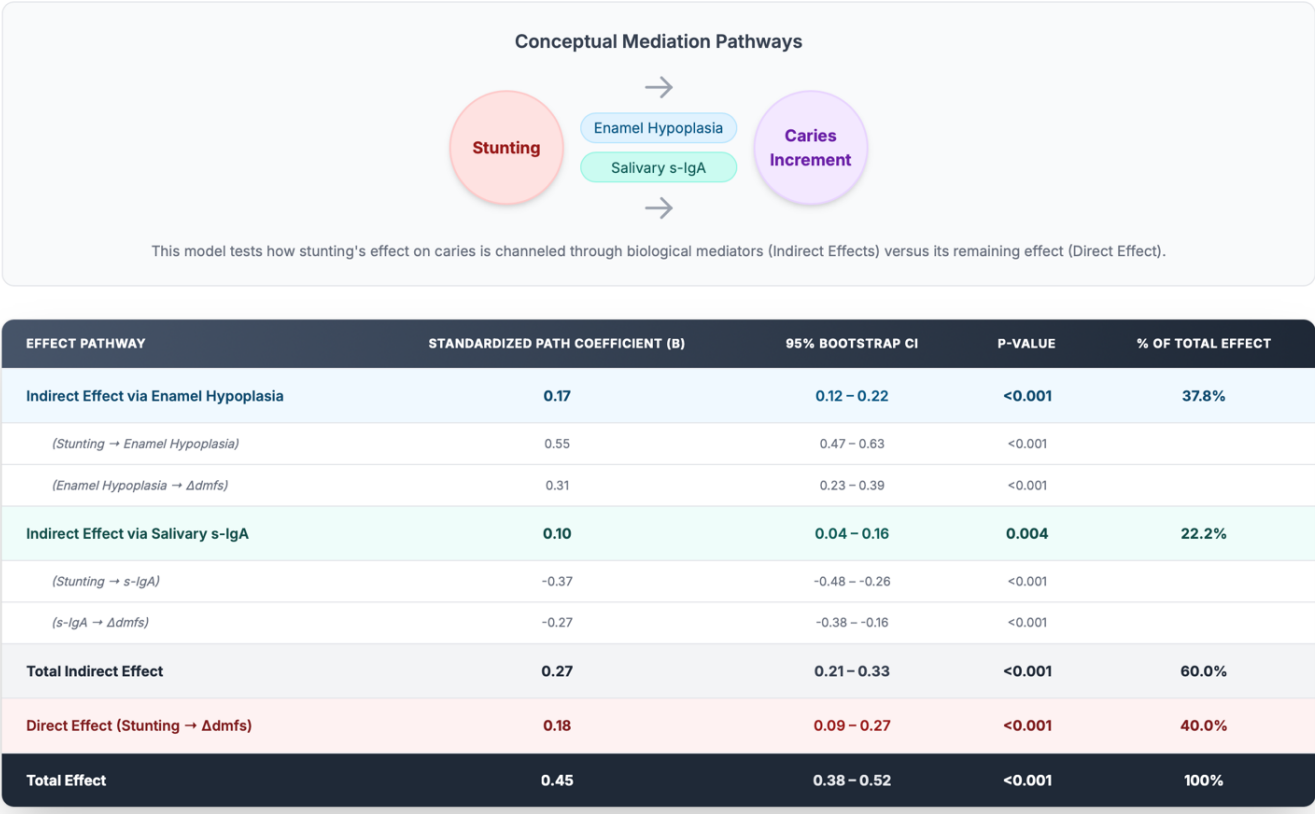
Variable	Coefficient (B)	95% Confidence Interval	P-Value
Fixed Effects			
Time (years)	+1.79	1.57 – 2.01	<0.001
Stunting (Stunted vs. Non-stunted)	+1.03	0.68 – 1.38	<0.001
Time × Stunting Interaction	+1.95	1.68 – 2.22	<0.001
Maternal Education (per year)	-0.09	-0.17 – -0.01	0.025
Household Income (per million IDR)	-0.21	-0.36 – -0.06	0.007
Sugar Intake >1 time/day	+0.81	0.49 – 1.13	<0.001
Brushing <2 times/day	+0.75	0.41 – 1.09	<0.001
Adequate Fluoride Exposure	-1.12	-1.45 – -0.79	<0.001
Intercept	0.51	0.18 – 0.84	0.003

● Key Interaction Term ● Risk Factor (β > 0) ● Protective Factor (β < 0)

The final SEM, adjusted for all confounders including fluoride, demonstrated an excellent fit to the data (CFI=0.98, TLI=0.97, RMSEA=0.038, SRMR=0.031). The standardized path coefficients are broken down in Table 3. The total effect of stunting on caries increment remained strong and significant (Standardized Total Effect β = 0.45; $p<0.001$). Two significant indirect pathways were confirmed: (1) Enamel Hypoplasia Pathway: Stunting was a strong predictor of enamel hypoplasia ($\beta=0.55$), which in turn was a strong predictor of higher $\Delta dmfs$ ($\beta=0.31$). The standardized indirect effect was 0.17, accounting for

37.8% of the total effect; (2) Salivary s-IgA Pathway: Stunting was associated with lower average salivary s-IgA ($\beta=-0.37$), and lower s-IgA was associated with higher $\Delta dmfs$ ($\beta=-0.27$). The standardized indirect effect was 0.10, accounting for 22.2% of the total effect. The pathway through salivary lactoferrin was not statistically significant in the multivariable model ($p=0.18$) and was removed. After accounting for the two significant mediators, the direct effect of stunting on $\Delta dmfs$ remained statistically significant (Standardized Direct Effect β = 0.18; $p<0.001$), accounting for the remaining 40.0% of the total effect.

Table 3. Structural Equation Model Results
Effects of Stunting on 3-Year dmfs Increment ($\Delta dmfs$)



This 3-year longitudinal study provides robust, mechanistically detailed evidence that stunting in early childhood is a powerful determinant of an accelerated and severe caries trajectory. By employing a comprehensive analytical approach that adjusted for key confounders, including the potent anti-caries effect of fluoride exposure, our findings move beyond

the well-documented epidemiological association to quantify the specific biological pathways that underpin the stunting-caries nexus. The results confirm our central hypothesis: the detrimental effect of chronic malnutrition on oral health is not merely a reflection of correlated socio-behavioral disadvantages but is substantially mediated through the dual,

synergistic pathways of compromised tooth structural integrity and impaired local mucosal immunity. The critical finding that these profound biological relationships persist after accounting for fluoride exposure underscores a pivotal public health message: while fluoride is an essential tool for population-level caries prevention, its protective mechanisms cannot fully compensate for the deep, developmental disadvantages embedded by chronic malnutrition during the most critical periods of a child's life.^{11,12}

The most significant and novel contribution of this investigation is the statistical and biological quantification of the mediating pathways, which together explain a majority of the total effect of stunting on future caries burden. Our structural equation model revealed that developmental enamel hypoplasia was the single most powerful mediator, explaining nearly 38% of the total effect of stunting on the 3-year caries increment. This finding provides compelling empirical validation for the "biological embedding" hypothesis, which posits that systemic insults experienced during critical developmental windows can become permanently inscribed into an organism's structure and physiology. The formation of primary tooth enamel—a process known as amelogenesis—begins in utero and continues through the first few years of postnatal life, a timeframe that precisely overlaps the period of maximum vulnerability to the nutritional deficiencies and recurrent infections that lead to stunting. Amelogenesis is a metabolically intense and exquisitely orchestrated process driven by specialized epithelial cells called ameloblasts. These cells require a consistent and adequate supply of essential substrates, including proteins for the organic enamel matrix scaffold (amelogenin and enamelin), Vitamin A for epithelial cell differentiation and function, and Vitamin D for the regulation of calcium and phosphate homeostasis, which are the fundamental mineral components of hydroxyapatite crystals. Chronic malnutrition, for which stunting serves as an integrated, cumulative marker, systematically deprives these developing cellular systems of their necessary building blocks. This deprivation disrupts both the secretory phase of amelogenesis, where the matrix is laid down, and the

subsequent maturation phase, where the matrix is resorbed and replaced by dense, well-organized mineral crystals. The pathological consequence is the formation of defective, or hypoplastic, enamel. At a microscopic level, this manifests as disorganized enamel prisms, reduced crystal density, and a higher proportion of organic material—a structure that is inherently weaker and more porous than healthy enamel. Clinically, these microscopic defects present as macroscopic pits, deep grooves, and patches of missing enamel on the tooth surface. These structural imperfections serve as a lifelong Achilles' heel for the tooth, initiating a pathological cascade that profoundly elevates caries risk. The pits and grooves act as ideal retention sites for food debris and microorganisms, fostering the development and maturation of cariogenic biofilms in locations that are physically shielded from the cleansing actions of saliva and toothbrushing. Furthermore, the hypomineralized nature of the affected enamel means that it has a higher critical pH—the pH at which demineralization begins—making it far more susceptible to dissolution in the face of the acid challenges produced by the cariogenic biofilm. Our data, by quantifying this pathway, confirm that enamel hypoplasia is not merely a co-occurring condition but a primary biological bridge that mechanistically connects systemic malnutrition in early life to localized, progressive oral disease in later childhood.^{13,14}

Equally important to the structural argument was the confirmation of the salivary immunity pathway, which accounted for over 22% of the total effect of stunting on caries increment. This finding illuminates a critical functional consequence of malnutrition, demonstrating how systemic nutritional status directly modulates the host's first line of immunological defense in the oral cavity. The mucosal immune system of the mouth is a dynamic and vital barrier, with saliva acting as its primary effector fluid. Secretory immunoglobulin A (s-IgA) is the cornerstone of this defense system and the predominant immunoglobulin class in all mucosal secretions. Produced by local plasma cells in the salivary glands, s-IgA is actively transported into saliva, where it performs its critical function of immune exclusion. Its

primary anti-caries mechanism involves preventing the initial attachment of planktonic *Streptococcus mutans* and other cariogenic bacteria to the pellicle-coated tooth surface. By binding to bacterial adhesins, s-IgA molecules agglutinate the bacteria into large clumps in the fluid phase of saliva; these clumps are too large to adhere effectively and are subsequently cleared by swallowing. This immunological rinsing is fundamental to preventing the establishment of a critical bacterial mass necessary for pathogenic biofilm formation. Our results demonstrate that stunted children have significantly lower concentrations of this crucial protective protein. This finding is consistent with the broader concept of Nutritionally Acquired Immune Deficiency Syndrome (NAIDS), where chronic malnutrition, particularly deficiencies in protein, zinc, vitamin A, and folate, systematically impairs immune function. These nutrients are essential for the proliferation, differentiation, and function of lymphocytes, especially the B-cells that mature into antibody-producing plasma cells. The resulting reduction in salivary s-IgA effectively lowers the oral cavity's immunological surveillance, creating a permissive environment where cariogenic bacteria can colonize tooth surfaces more freely and proliferate with less opposition. This immunological vulnerability tips the delicate ecological balance of the oral microbiome towards dysbiosis, favoring the overgrowth of acidogenic and aciduric species and thereby directly increasing the risk of caries initiation and progression.^{15,16}

The true clinical and public health significance of these findings is revealed in the devastating synergy between these two pathways. Our analysis suggests that stunting creates a "two-hit" model of caries susceptibility that powerfully explains the dramatically accelerated disease trajectory observed in affected children. In a healthy, well-nourished child, the oral defense system exists with a degree of redundancy: a robust and intact enamel structure can withstand minor or temporary fluctuations in immune function, while a highly effective salivary immune system can often protect minor structural imperfections from becoming carious. Stunting dismantles this redundancy. It simultaneously results

in a structurally weaker, more vulnerable tooth (via enamel hypoplasia) and a functionally less effective local defense system (via suppressed s-IgA). A compromised tooth structure requires a more potent defense to remain healthy, yet it is precisely this defense system that is also crippled by the same underlying state of chronic malnutrition. This two-pronged biological assault provides a compelling pathophysiological explanation for the non-linear, rapidly diverging caries rates observed between stunted and non-stunted children, and clarifies why these children remain at high risk even when exposed to the protective effects of fluoride.¹⁷

Interestingly, while salivary lactoferrin concentrations were significantly lower in stunted children at baseline, this pathway did not emerge as a statistically significant mediator in the final multivariable model. This null finding, in the context of the strongly significant s-IgA pathway, may reflect the distinct and perhaps hierarchical roles of these immune components. Lactoferrin's primary antimicrobial action is bacteriostatic—it sequesters free iron from the environment, depriving bacteria of a mineral essential for their metabolic processes and growth. In contrast, s-IgA's primary role is anti-adherence, a mechanism that acts at the very first stage of colonization. It is plausible that in the context of the oral environment, particularly one with frequent high-sugar challenges, preventing bacterial attachment *ab initio* (the role of s-IgA) is a far more critical rate-limiting step for caries development than merely slowing bacterial growth (the role of lactoferrin). The powerful, direct effect of s-IgA in preventing biofilm establishment may have therefore statistically overshadowed the smaller, secondary effect of lactoferrin in our comprehensive model.¹⁸

Finally, the observation of a significant and substantial direct effect of stunting, which accounted for the remaining 40% of the total effect, strongly suggests that our two-mediator model, while comprehensive, does not capture the full, complex scope of malnutrition's deleterious impact on oral health. This large residual effect points towards other unmeasured biological mechanisms that likely contribute to the stunting-caries relationship. One

probable pathway involves direct alterations to saliva itself, beyond specific immune proteins. Chronic protein-energy malnutrition can lead to atrophy of the salivary glands, resulting in a reduced salivary flow rate (hyposalivation). This diminishes the physical cleansing of tooth surfaces and, more critically, reduces the delivery of bicarbonate, the principal buffering agent in saliva. A compromised buffering capacity severely impairs the oral cavity's ability to neutralize acid produced by plaque bacteria, leading to more frequent and prolonged drops in pH below the critical threshold for enamel demineralization. Another potential mechanism involves the direct influence of a child's systemic metabolic and inflammatory state on the composition of the oral microbiome. Stunting is associated with chronic, low-grade systemic inflammation and altered host metabolism. These systemic conditions may create a selective pressure within the oral environment that favors the growth of more acidogenic and acid-tolerant bacterial species, independent of the host's immune response. Lastly, stunting is known to be associated with delayed physical development, including delayed eruption of the primary dentition. While this might initially seem protective by reducing the time teeth are exposed to the oral environment, it can be detrimental if the teeth erupt into an oral milieu that is already highly cariogenic and at a developmental stage when the child's oral hygiene cooperation is still poor. The enamel of newly erupted teeth is also less mature and more permeable, making it especially vulnerable during this period. The combination of these unmeasured factors—impaired salivary function, direct microbial selection, and altered developmental timing—likely constitutes a significant portion of the direct effect observed in our model, highlighting fruitful avenues for future research.^{19,20}

While this study has significant strengths, including its longitudinal design and advanced statistical modeling, certain limitations should be acknowledged. First, our diagnostic threshold for caries was cavitation (ICDAS 5-6). This is a specific but insensitive measure that excludes non-cavitated enamel lesions. It is possible that the effects of stunting are even more pronounced on caries

initiation, and thus our results may underestimate the true magnitude of the association. Second, key behavioral variables, including diet and fluoride use, were based on caregiver self-report, which is subject to recall and social desirability bias. Finally, our findings are from a specific rural population in Indonesia and may not be generalizable to all settings.

4. Conclusion

In conclusion, this longitudinal study provides compelling evidence that stunting in the first two years of life is a critical risk factor for an accelerated and severe trajectory of Early Childhood Caries. This relationship is not a statistical artifact of socio-behavioral confounding but is underpinned by tangible biological mechanisms. Chronic malnutrition, marked by stunting, predisposes children to a higher caries burden by causing permanent defects in enamel structure and by suppressing essential components of the salivary immune system. These findings have profound implications for public health, demonstrating that fluoride-based strategies, while essential, are insufficient to protect children whose biological defenses have been compromised by malnutrition. Policy and practice must dismantle the silos between nutrition and dental health, promoting integrated interventions that ensure adequate nutrition in the first 1,000 days of life as a fundamental strategy for lifelong oral health.

5. References

1. Nurmawi Y, Mahsalisa F. Analysis of health literacy with dental caries and stunting in toddlers in Jambi City in 2023. *Ris Inf Kesehat*. 2024; 13(1): 24.
2. Rafilia YN, Sukmasari S, Setiawan AS, Indriyanti R. Connection of Oral Health Related Quality of Life with Caries in Children with Stunting: descriptive study. *Padjadjaran J Dent Res Students*. 2024; 8(2): 144-52.
3. So M, Ellenikiotis YA, Husby HM, Paz CL, Seymour B, Sokal-Gutierrez K. Early childhood dental caries, mouth pain, and malnutrition in the Ecuadorian Amazon region. *Int J Environ Res Public Health*. 2017;

- 14(5).
4. Kadiwala AI, Hun V, Patel E. A study to assess the prevalence of malnutrition & its association with dental caries among pre-schoolers at selected anganwadies of Vadodara city. *Int J Nurs Educ.* 2019; 11(4): 5.
5. Folayan MO, Arije O, El Tantawi M, Kolawole KA, Obiyan M, Arowolo O, et al. Association between early childhood caries and malnutrition in a sub-urban population in Nigeria. *BMC Pediatr.* 2019; 19(1): 433.
6. Zahid N, Khadka N, Ganguly M, Varimezova T, Turton B, Spero L, et al. Associations between child snack and beverage consumption, severe dental caries, and malnutrition in Nepal. *Int J Environ Res Public Health.* 2020; 17(21): 7911.
7. Singh A, Purohit BM. Malnutrition and its association with dental caries in the primary and permanent dentition: a systematic review and meta-analysis. *Pediatr Dent.* 2020; 42(6): 418–26.
8. Mahmood MK, Lan R, Tassery H, Tardivo D. Association between malnutrition and dental caries in Iraqi Kurdish children. *Dent J.* 2023; 11(6): 141.
9. Fasna K, Khan SY, Ahmad A, Sharma MK. Exploring the association between early childhood caries, malnutrition, and anemia by machine learning algorithm. *J Indian Soc Pedod Prev Dent.* 2024; 42(1): 22–7.
10. Fathallh A, Al-Sudani F, Almuhsen S, Hassoon S. The impact of malnutrition on dental health of 12-year-old children: a study on permanent teeth caries, cariogenic bacteria and salivary IgA. *Folia Med (Plovdiv).* 2024; 66(4): 515–20.
11. Wang D, Wang X, Zhao C, Ma S, Zhang Y, Shi H. Study on the association between malnutrition, early childhood caries and caries activity among children aged 3–5 years. *BMC Oral Health.* 2024; 24(1): 1035.
12. Folayan MO, El Tantawi M, Schroth RJ, Vukovic A, Kemoli A, Gaffar B, et al. Associations between early childhood caries, malnutrition and anemia: a global perspective. *BMC Nutr.* 2020; 6(1): 16.
13. Simorangkir EA, Panggabean SP, Sudaryati E. Relationship between caries experience and food intake with stunting among 6–8-years old of elementary school at Pantai Labu in 2018. *Bioex.* 2020; 2(1): 313–9.
14. Achmad H, Ramadany S, Fajriani, Sukmana BI, Hanan N, Hartami E, et al. A review of stunting growth in children: Relationship to the incidence of dental caries and its handling in children. *Syst Rev Pharm.* 2020; 11(06).
15. Husain Akbar F, Pratwi R, Hulwah N. Differences in quality of life of stunting children based on caries status in Indonesia. *Braz Dent Sci.* 2020; 23(3).
16. Large J, Marshman Z. Does dental caries lead to stunting and wasting in children? *Evid Based Dent.* 2022; 23(4): 144–5.
17. Tedjosasongko U, Marwah A, Dewi AM. Salivary sIgA as a predictor of caries risk in stunting children. *World J Adv Res Rev.* 2022; 14(2): 052–6.
18. Putri TN, Indriyanti R, Setiawan AS. A descriptive study on oral hygiene practice and caries increment in children with growth stunting. *Front Oral Health.* 2023; 4: 1236228.
19. Sari RP, Rahayuwati L, Setiawan AS. Eating behavior and caries experience in children with growth stunting. *Eur J Dent.* 2024; 18(1): 161–7.
20. Marlindayanti M, Maris GW. Milk feeding patterns on the incidence of caries in stunting children. *JDHT Journal of Dental Hygiene and Therapy.* 2024; 5(1): 25–31.