Proceedings of the 6th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/2026.37005

The Modifying Effect of Multimorbidity on the Association Between Edentulism and Frailty: Evidence from the Longitudinal Ageing Study in India (LASI)

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Abstract. Poor oral health, particularly edentulism, has been independently associated with frailty in older adults across Western and Chinese populations. Multimorbidity is also a well-established risk factor for frailty. Mechanistic studies generally posit a positive synergistic interaction, whereby edentulism and multimorbidity jointly increase frailty risk; however, an attenuating (ceiling) effect cannot be excluded. Whether these two risk factors interact—that is, whether the edentulism–frailty association depends on the level of multimorbidity—remains untested. This study aims to examine the independent and joint associations of edentulism and multimorbidity with frailty among middle-aged and older Indian adults, and to test whether multimorbidity modifies the edentulism–frailty relationship.Cross-sectional analysis of 71,876 adults aged ≥45 years from LASI Wave 1 (2017-2019). Frailty was assessed using a 32-item non-diagnostic frailty index (FI ≥ 0.25), constructed by excluding eight diagnosed chronic diseases to avoid construct overlap with the multimorbidity count (14 physician-diagnosed conditions). Logistic regression models with an edentulism × multimorbidity interaction term were fitted, adjusting for age, sex, residence, education, tobacco use, and alcohol consumption. The results showed that edentulism (OR = 1.21, 95% CI 1.13-1.30) and multimorbidity (OR = 1.58 per condition, 95% CI 1.56-1.61) each independently predicted frailty. The interaction was significant (β = -0.073, p = 0.016) and negative in direction. At 0 chronic conditions, the OR for edentulism was 1.32 (95% CI 1.19-1.45); this declined monotonically with increasing multimorbidity, becoming non-significant at ≥3 conditions (OR = 1.06, 95% CI 0.93-1.21). Sex-stratified analyses showed no significant three-way interaction (p = 0.232).The edentulism–frailty association is strongest when multimorbidity burden is low, and it is progressively diluted as chronic conditions accumulate — a pattern consistent with a ceiling effect. These findings suggest oral health may serve as a target for early frailty prevention, particularly before multimorbidity becomes established.

Keywords: edentulism, frailty, multimorbidity, LASI, India, interaction

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1. Introduction

India is undergoing rapid population aging alongside an escalating burden of non-communicable diseases and multimorbidity [1, 2]. Frailty — a geriatric syndrome characterized by diminished physiological reserve and increased vulnerability — affects approximately 30% of Indian adults aged ≥45 years [3]. Oral health deterioration, particularly complete tooth loss (edentulism), has emerged as a potentially modifiable risk factor for frailty. Cohort studies from the United Kingdom [4] and multi-cohort meta-analyses spanning China, the UK, and the United States [5] have demonstrated independent associations between edentulism and frailty. Proposed mechanisms include chronic systemic inflammation driven by periodontal pathogens [6] and compromised nutritional intake secondary to masticatory dysfunction [7].

Despite evidence that edentulism and multimorbidity each independently predict frailty [4, 5, 8], whether they interact synergistically — that is, whether being edentulous amplifies the deleterious effect of multimorbidity on frailty — has not been previously examined. To address this gap, the present study employed logistic regression with an interaction term using nationally representative data from the Longitudinal Ageing Study in India (LASI) Wave 1, with the aims of (1) confirming the independent associations of edentulism and multimorbidity with frailty in the Indian population, (2) testing their interaction, and (3) exploring sex differences in these associations. To our knowledge, this is the first study to test this interaction in any population; the findings contribute evidence from a low- and middle-income country setting where oral health services remain under-resourced, and may inform the timing of oral health interventions for frailty prevention.

2. Methods

2.1. Study design and population

This study used cross-sectional data from Wave 1 of the Longitudinal Ageing Study in India (LASI), conducted in 2017-2019 [9]. LASI is a nationally representative survey of adults aged ≥45 years and their spouses, employing a multi-stage stratified cluster sampling design. After applying exclusion criteria for frailty index (FI) construction (individuals missing >3 of 32 deficit items were excluded), the analytical sample comprised 71,876 participants; multivariable regression models were fitted on 71,799 participants with complete covariate data.

2.2. Frailty assessment (outcome)

Frailty was operationalized using the deficit accumulation approach [10, 11], consistent with recent Indian community-based evidence favouring the frailty index over phenotype-based measures and supporting the FI ≥ 0.25 cut-off [12]. A 32-item FI was constructed spanning six domains: general health (1 item), medical symptoms (4 items), mobility limitations (9 items), ADL/IADL disability (13 items), other deficits including depression screening (CES-D) and cataract surgery history (2 items), and physical measurements including BMI, grip strength (sex- and BMI-stratified), and gait speed (3 items), adapting the item-selection approach of a prior 32-item LASI-based index [13]. Critically, eight physician-diagnosed chronic diseases (hypertension, diabetes, psychiatric disorders, chronic lung disease, heart disease, stroke, arthritis, and asthma) were excluded from the FI to eliminate construct overlap with the multimorbidity count. Each deficit was scored between 0 and 1, and the FI was calculated as the sum of scores divided by the number of non-missing items, allowing up to three missing deficits. Frailty was defined as FI ≥ 0.25.

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2.3. Oral health and multimorbidity (exposure and effect modifier)

Edentulism was assessed via self-report (complete loss of all natural teeth: yes/no). Multimorbidity was operationalized as a continuous count (0-14) of physician-diagnosed chronic conditions, hypertension, diabetes, cancer, chronic lung disease, heart disease, stroke, arthritis, psychiatric disorders, hypercholesterolemia, thyroid disease, gastrointestinal disease, skin disease, osteoporosis, and asthma [1, 14]. The overlap between the 14-condition multimorbidity list and the 32-item FI was zero by design.

2.4. Covariates

All models were adjusted for age (continuous), sex (male/female), residence (rural/urban), educational attainment (categorical), tobacco use (never/former/current), and alcohol consumption (ever/never), selected based on prior LASI-based studies of frailty and oral health [3, 14].

2.5. Statistical analysis

Descriptive statistics were reported as means with standard deviations for continuous variables and frequencies with percentages for categorical variables. Three multivariable logistic regression models were fitted: Model 1 (edentulism → frailty), Model 2 (multimorbidity → frailty), and Model 3 (edentulism × multimorbidity interaction → frailty). Stratified odds ratios for edentulism at each level of multimorbidity (0-5 conditions) were computed from Model 3. Sex-stratified analyses were performed, and a three-way interaction term (edentulism × multimorbidity × sex) was tested. In addition, the original 40-item FI scale was used and the chronic disease diagnosis was retained for the sensitivity analysis.

3. Results

3.1. Sample characteristics

The mean age was 57.8 years (SD = 11.6), and 57.7% were female. The prevalence of edentulism was 6.22%, frailty (FI ≥ 0.25) was 31.03%, and multimorbidity (≥2 conditions) was 25.8%. Among dentate individuals, 29.7% were frail, compared with 50.6% among edentulous individuals. Frailty prevalence increased stepwise with multimorbidity: 20.3% (0 conditions), 32.3% (1), 42.0% (2), and 58.1% (≥3). (Table 1)

3.2. Main effects

In fully adjusted models, edentulism alone was independently associated with 21% higher odds of frailty (Model 1: OR = 1.21, 95% CI 1.13-1.30, $p < 0.001$), and each additional chronic condition alone was associated with 58% higher odds (Model 2: OR = 1.58, 95% CI 1.56-1.61, $p < 0.001$). Multimorbidity provided better model fit (AIC = 73,088) than edentulism (AIC = 76,476).

3.3. Interaction between edentulism and multimorbidity

The edentulism × multimorbidity interaction was statistically significant ($\beta = -0.073$, $p = 0.016$), but negative in direction — contrary to the hypothesized synergy (Table 1).

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Table 1. Interaction of edentulism and multimorbidity on frailty (n = 71,799)

Variable	β (SE)	OR	95% CI	P
Edentulism	0.274 (0.049)	1.315	1.195 - 1.448	< 0.001
Multimorbidity count	0.464 (0.008)	1.591	1.565 - 1.618	< 0.001
Edentulism × Multimorbidity	-0.073 (0.030)	0.930	0.877 - 0.987	0.016

Note: Adjusted for age, sex, residence, education, tobacco use, and alcohol consumption. β = log-odds coefficient; SE = standard error; OR = odds ratio; CI = confidence interval.

Stratified ORs for edentulism at each multimorbidity level revealed a monotonic decline: OR = 1.32 (95% CI 1.19-1.45) at 0 conditions; 1.22 (1.14-1.31) at 1 condition; 1.14 (1.04-1.24) at 2 conditions; 1.06 (0.93-1.21) at 3 conditions; and non-significant thereafter (Table 2).

Table 2. Stratified association of edentulism with frailty by number of chronic conditions

Number of chronic conditions	OR	95% CI	P
0	1.31	1.20-1.45	< 0.001
1	1.22	1.14-1.31	< 0.001
2	1.14	1.04-1.24	0.004
3	1.06	0.93-1.21	0.403
4	0.98	0.82-1.18	0.863
5	0.92	0.72-1.16	0.469

Note: ORs are for edentulism (edentulous vs. dentate) on frailty at each level of multimorbidity, derived from the interaction model, adjusted for age, sex, residence, education, tobacco use, and alcohol consumption. P for interaction (edentulous × multimorbidity) = 0.016.

The edentulism effect was thus diluted by approximately 7% per additional chronic condition (OR multiplier ≈ 0.93) and became undetectable at ≥3 conditions (Figure 1).

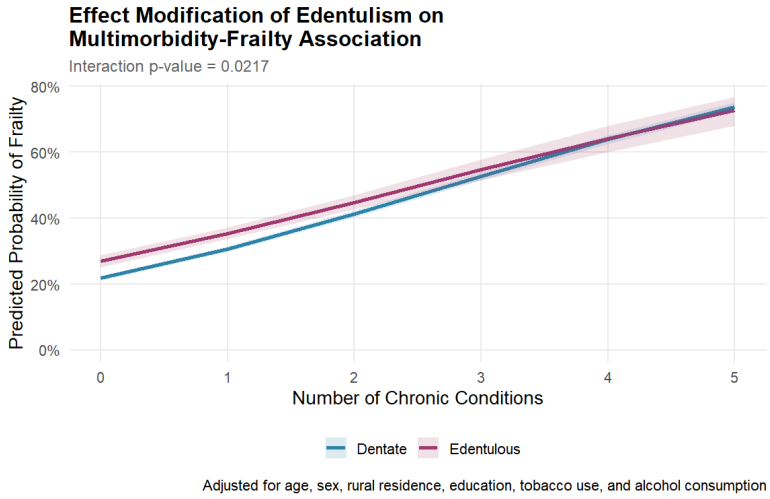

Figure 1. Predicted probability of frailty by number of chronic conditions, stratified by edentulism status

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3.4. Sex-stratified and sensitivity analyses

The three-way interaction (edentulism × multimorbidity × sex) was not significant (p = 0.232). However, the negative interaction was more pronounced in women (β = −0.104, p = 0.008) than in men (β = −0.032, p = 0.521), though this difference did not reach statistical significance — consistent with the observation of Gelman and Stern [15] that a significant effect in one group and a non-significant effect in another do not itself imply a significant difference between groups (Figure 2).

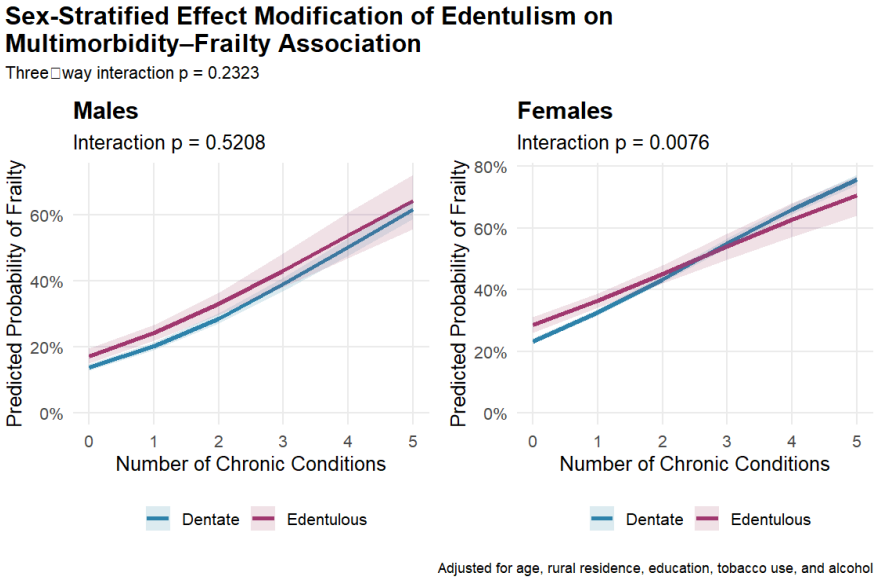

Figure 2. Predicted probability of frailty by number of chronic conditions and edentulism status, stratified by sex (three-way interaction p = 0.232)

To assess the robustness of the main findings with respect to the composition of the frailty index, we reconstructed a 40-item FI that additionally incorporated eight physician-diagnosed disease deficits (hypertension, diabetes, chronic lung disease, heart disease, stroke, arthritis, asthma, and psychiatric disorders), thereby deliberately reintroducing construct overlap with the multimorbidity count; all other variable definitions, covariate adjustment, and model specifications were identical to the main analysis (n = 71,792). Results were consistent with the main analysis. Edentulism remained independently associated with frailty (OR = 1.20, 95% CI 1.12-1.29), and multimorbidity remained a strong predictor (OR = 1.90 per condition, 95% CI 1.86-1.93). The edentulism × multimorbidity interaction remained negative and statistically significant (β = −0.095, p = 0.003), and was in fact stronger than in the main analysis (β = −0.073, p = 0.016). Stratified ORs for edentulism declined monotonically with increasing multimorbidity — 1.34 (95% CI 1.21-1.49) at 0 conditions, 1.22 (1.14-1.32) at 1, 1.11 (1.02-1.22) at 2, and 1.01 (0.88-1.16) at 3 conditions — again becoming non-significant at ≥3 conditions. The larger multimorbidity OR in this model reflects the reintroduced construct overlap between outcome and exposure that the 32-item FI was designed to avoid; the direction and significance of the interaction, however, were robust.

4. Discussion

The main effect finding — that edentulism independently predicts frailty in Indian adults — extends the generalizability of evidence previously confined to Western and Chinese populations [4, 5, 16].

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This cross-national consistency strengthens the case for oral health as a genuine frailty determinant rather than a setting-specific confound.

The negative interaction finding challenges the synergy hypothesis. Rather than amplifying the harm of multimorbidity, edentulism exerts its strongest independent effect when chronic disease burden is low — a pattern consistent with a ceiling or dilution effect. When systemic inflammation driven by multiple chronic conditions (via IL-1β, TNF-α, and other mediators [17]) already saturates the pathophysiological landscape, the additional inflammatory burden attributable to poor oral health may become negligible by comparison. Nutrition-mediated pathways [7] may also be more consequential when caloric and protein intake are not yet compromised by disease-related anorexia or metabolic dysregulation.

Methodologically, the deliberate exclusion of diagnosed chronic diseases from the FI represents a strength of this study, as it eliminates the circularity inherent in predicting an outcome with a variable constructed partly from the same items [10, 11]. This approach yields more conservative and interpretable estimates of the interaction.

These findings carry public health implications. They suggest that oral health interventions — including prosthodontic rehabilitation and periodontal treatment — may be most cost-effective at the pre-frailty stage or early in the chronic disease trajectory. Among individuals with established multimorbidity (≥3 conditions), improving oral health alone is unlikely to reverse frailty trajectories; comprehensive, multi-domain interventions would be required.

Limitations include the cross-sectional design (precluding causal inference [18]), self-reported oral health measures (likely underestimating true disease burden [19]), and the absence of data on denture use and oral hygiene behaviors. The relatively low prevalence of edentulism (6.22%) limited statistical power at higher multimorbidity levels. Future work using LASI Wave 2 will enable longitudinal analysis, and the composite oral health index may capture a broader spectrum of oral disease severity.

5. Conclusion

This study used nationally representative data from LASI Wave 1 to examine whether multimorbidity modifies the association between edentulism and frailty among middle-aged and older Indian adults. Three principal findings emerged.

First, both edentulism and multimorbidity independently predicted frailty after comprehensive covariate adjustment, confirming the oral–frailty link in a South Asian population for the first time with these methods.

Second, and more importantly, a significant negative interaction was identified: the effect of edentulism on frailty was strongest among individuals with low multimorbidity burden (OR ≈ 1.3 at 0 conditions, declining to ≈ 1.2 at 1 condition) and was progressively diluted as chronic conditions accumulated, becoming non-significant at ≥3 conditions. This finding — contrary to the hypothesized synergistic amplification — is most consistent with a ceiling effect, wherein the marginal pathogenic contribution of oral health is overwhelmed when multiple systemic diseases already drive frailty.

Third, the interaction pattern was directionally consistent across sexes, with no statistically significant three-way interaction, suggesting that the dilution effect generalizes across men and women.

These results carry two complementary implications. For clinical practice, these results identify a potential window of opportunity: oral health assessment and intervention may be most impactful in relatively healthy middle-aged and older adults, before multimorbidity becomes entrenched. Once

DOI: 10.54254/2753-8818/2026.37005

chronic disease burden is high, single-domain oral health interventions are unlikely to reverse frailty — advocating instead for integrated, multi-domain geriatric care. For research methodology, this study demonstrates the importance of eliminating construct overlap between exposure and outcome when testing interactions involving multimorbidity, a precaution not uniformly adopted in the existing literature.

Future research should leverage the longitudinal structure of LASI Wave 2 to establish temporal relationships, incorporate objective oral health measures where feasible, and explore whether specific chronic disease clusters (e.g., cardiometabolic vs. musculoskeletal) differentially interact with oral health in shaping frailty trajectories.

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