

Absence of tongue papillae as a clinical criterion for the diagnosis of generalized recessive dystrophic epidermolysis bullosa types



To the Editor: Classifying epidermolysis bullosa (EB) in the new-born period is important because each subtype has different morbidities and prognoses, and diagnostic tests take time to complete and might not be available worldwide. Denuded tongue, which is the complete absence of tongue papillae on the dorsal tongue surface, can be observed in patients with the generalized severe recessive dystrophic type (RDEB-gen-sev).¹⁻⁴ Our aim was to study the diagnostic accuracy of absent tongue papillae for predicting the RDEB subtypes.

This prospective study included all 223 consecutive patients with an EB diagnosis⁵ confirmed by mutation analysis seen at DEBRA Chile between 2015 and 2018. Ethic committee approval and informed consent was obtained. The diagnostic criteria analyzed were complete absence, partial absence, and normal tongue papillae, also including normal papillae with a localized chronic ulcer (Fig 1). Age ranged from 2 hours to 75 years, the male-to-female sex ratio was 0.89. The distribution of EB type, subtype, gene affected, absence of tongue papillae, and patient flow diagram can be observed in Supplemental Tables I and II and Supplemental Fig 1 (available via Mendeley at <https://doi.org/10.17632/j7fm33t6j2.2>).

Absence of tongue papillae in RDEB. Tongue papillae were absent in 68 of 79 patients with RDEB (60 complete and 8 partial). All patients with RDEB-gen-sev (n = 52) and 66.7% of those with generalized intermediate RDEB (RDEB-gen-intermed) (n = 24) had some tongue depapillation. No patients with RDEB-localized (n = 3), EB simplex (n = 84), junctional EB (n = 23) or Kindler syndrome (n = 1) had absent tongue papillae. Only 11 patients with RDEB presented normal tongue papillae. Absence of tongue papillae had a positive predictive value (PPV) of 100% and negative predictive value (NPV) of 93% for RDEB (Table I).

Complete absence of tongue papillae in RDEB-gen-sev. Of patients with complete absence of tongue papilla, 87% had a diagnosis of RDEB-gen-sev (PPV). All patients with RDEB-gen-sev presented complete absence of tongue papillae (NPV, 100%).

Partial absence of tongue papilla in RDEB-gen-intermed. Only patients with RDEB-gen-intermed presented partial absence of tongue papillae, with a PPV of 100% and no false discovery rate. However, patients with this subtype can also present complete absence of papillae or normal papillae (sensitivity, 33%).

The results are consistent with previous reports.² A limitation in our study was the lack of patients with the uncommon RDEB-inversa subtype, which could present absence of tongue papillae.¹ Previous reports have not divided complete and partial absence of tongue papillae as different categories.

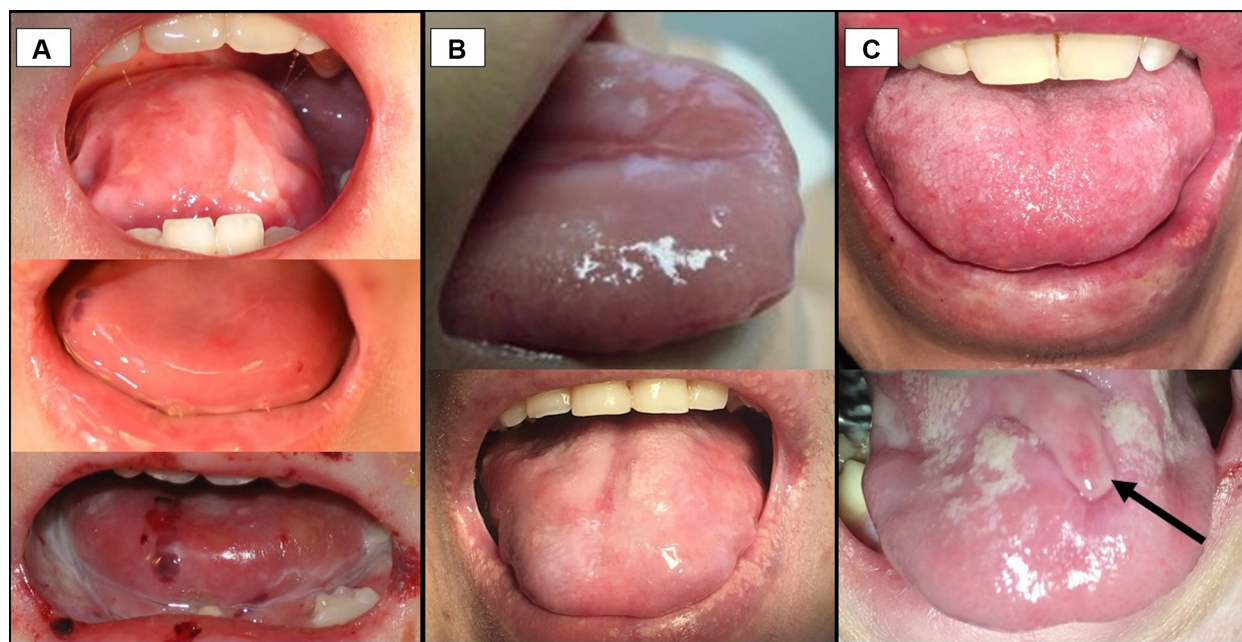


Fig 1. Tongue papillae phenotypes in epidermolysis bullosa. **A**, Complete absence of tongue papilla. **B**, Partial absence of tongue papilla. **C**, Normal tongue papilla. Lower image shows normal tongue papilla with a well-defined area of granulation tissue (arrow).

Table I. Summary of diagnostic estimates

Estimate	Absence of tongue papillae (partial or complete) in RDEB % (95% CI)	Complete absence of tongue papillae in RDEB-gen sev % (95% CI)	Partial absence of tongue papillae in RDEB-gen intermed % (95% CI)
Positive predictive value	100	87 (76.77-92.75)	100
Negative predictive value	93 (88.33-95.77)	100	93 (90.36-94.29)
Sensitivity	86 (76.45-92.84)	100 (93.15-100.00)	33 (15.63-55.32)
Specificity	100 (97.47-100.00)	95 (90.99-97.96)	100 (98.16-100.00)
Accuracy	95 (91.35-97.51)	96 (93.05-98.44)	93 (88.61-95.84)

CI, Confidence interval; RDEB, recessive dystrophic epidermolysis bullosa; RDEB-gen intermed, generalized intermediate recessive dystrophic epidermolysis bullosa; RDEB-gen sev, generalized severe recessive dystrophic epidermolysis bullosa.

This innovative categorization revealed a feature present only in RDEB-gen-intermed with a PPV of 100%. Multicenter studies should be encouraged to include more EB phenotypes and genotypes to strengthen and complement our results. Summarizing, our results suggest that:

1. RDEB-localized, EB simplex, junctional EB, dominant dystrophic EB, and Kindler syndrome subtypes can be ruled out if a newborn with EB has absence of tongue papillae.
2. Patients with complete absence of tongue papillae have an 87% probability of having RDEB-gen-sev and 13% probability of RDEB-gen-intermed.
3. Patients with partial absence of tongue papillae will develop RDEB-gen intermed.

Tongue examination is a simple, accessible, noninvasive, inexpensive, and highly reliable method of subclassification of EB before confirmatory genetic results are available.

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Belimumab for refractory manifestations of cutaneous lupus: A multicenter, retrospective observational study of 16 patients



To the Editor: Belimumab is a fully humanized monoclonal antibody against B-lymphocyte stimulator approved for systemic lupus erythematosus (SLE). A post hoc analysis of the 2 pivotal phase 3 studies showed that belimumab led to a better improvement than placebo on mucocutaneous