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Rubinstein–Taybi syndrome in diverse populations

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Abstract

Rubinstein-Taybi syndrome (RSTS) is an autosomal dominant disorder, caused by loss-of-function variants in CREBBP or EP300. Affected individuals present with distinctive craniofacial features, broad thumbs and/or halluces, and intellectual disability. RSTS phenotype has been well characterized in individuals of European descent but not in other populations. In this study, individuals from diverse populations with RSTS were assessed by clinical examination and facial analysis technology. Clinical data of 38 individuals from 14 different countries were analyzed. The median age was 7 years (age range: 7 months to 47 years), and 63% were females. The most common phenotypic features in all population groups included broad thumbs and/or halluces in 97%, convex nasal ridge in 94%, and arched eyebrows in 92%. Face images of 87 individuals with RSTS (age range: 2 months to 47 years) were collected for evaluation using facial analysis technology. We compared images from 82 individuals with RSTS against 82 age- and sex-matched controls and obtained an area under the receiver operating characteristic curve (AUC) of 0.99 ($p < .001$), demonstrating excellent discrimination efficacy. The discrimination was, however, poor in the African group (AUC: 0.79; $p = .145$). Individuals with EP300 variants were more effectively discriminated (AUC: 0.95) compared with those with CREBBP variants (AUC: 0.93). This study shows that clinical examination combined with facial analysis technology may enable earlier and improved diagnosis of RSTS in diverse populations.

Keywords: Africa; Asia; Latin America; Middle East; Rubinstein-Taybi syndrome; facial analysis technology.

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