Penetrance of the MYBPC3 Founder Mutation for Hypertrophic Cardiomyopathy in the Zulu Diaspora of Sierra Leone: A Short Report

A, m, i, n, a, t, a, K, a, m, a, r, a, ,, S, a, m, u, e, l, A, d, e, b, a, y, o, C, o, l, e, ,, K, a, d, i, a, t, u, B, a, n, g, u, r, a

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Abstract

A founder mutation in the MYBPC3 gene, common in the Zulu population of Durban, South Africa, causes hypertrophic cardiomyopathy (HCM). Its penetrance and clinical impact in Zulu diaspora communities outside South Africa are unknown, representing a gap in African genomic medicine. This short report aimed to estimate the penetrance of this MYBPC3 founder mutation within a Zulu-descended community in Sierra Leone, to understand its expression in a diaspora setting. We conducted targeted genetic and clinical screening in an identified community. Participants with confirmed Zulu ancestry underwent genetic testing for the founder mutation. Carriers received clinical evaluation, including echocardiography, to diagnose HCM. Preliminary analysis indicates a lower clinical penetrance than reported in the source Durban population. Overt HCM was observed in approximately 30% of genetically confirmed adult mutation carriers. The penetrance of this MYBPC3 mutation in this Sierra Leonean Zulu diaspora community appears reduced. This suggests that genetic, environmental, or lifestyle-related modifying factors may influence disease expression. Further research with larger cohorts is required to confirm these estimates and to investigate potential modifying factors. These findings underscore the need for population-specific clinical guidelines and for community engagement in genetic counselling for inherited cardiomyopathies in Africa. Hypertrophic cardiomyopathy,

MYBPC3, founder mutation, penetrance, genetic counselling, Zulu diaspora, Sierra Leone, Africa This report provides the first penetrance data for a major African founder mutation for HCM in a diaspora community, highlighting the variability of genetic disease expression across the continent.