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Genetics of obesity in consanguineous populations – A road map to provide novel insights in the molecular basis and management of obesity

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Further to the recent paper published by Schneeberger M in this journal, wherein the author described the utility of GWAS in identifying the genetic associations of obesity and the innovation of Irx3 as a novel determinant of body mass index and body composition, we would like to highlight here the importance of evaluating obesity related genetic information from highly consanguineous populations and its role in providing novel insights in understanding the pathogenesis of obesity [1].

Obesity has attained epidemic proportions in many South Asian countries, affecting about 15% of the Asian population, and is largely considered a familial disorder [2]. Genetics is responsible for about 45 to 75% of the inter-individual variations in body mass index [3]. These heritable factors are likely to operate through a range of potential pathophysiological pathways and several candidate genes have been proposed to not only elicit the cause but also predict management strategies based on the genetic makeup of an individual [4].

Given that obesity is a widespread disorder in South Asian countries and has a significant genetic component, especially so in the morbidly obese, it would be useful to study the genetic characteristics in Indian and other Asian populations. These populations not only harbour a unique obese phenotype with high rates of consanguinity but currently has minimal published literature on this subject. This is concordant with the call made by Sadia et al., for more genetic work in the field of obesity from consanguineous populations, with which we strongly agree [5]. So far understanding the genetic basis of obesity has been essentially through identification of monogenic causes of this disease leading to identifying pathogenic pathways and possible therapeutic options. However, since this work is carried out at a limited number of locations and involves a small number of patients, future collaborative work from such centres is likely to provide the foundational data required to design future diagnostic and therapeutic protocols [6].

Genetic factors are more pronounced in extreme forms of obesity and studying the genetic makeup of morbidly obese individuals is more likely to improve the understanding of the genetic architecture of this disorder [7]. Previously published literature in another consanguineous population has demonstrated that genetic variants in only 3 genes could attribute towards nearly 30% of the causes of morbid obesity [8].

Those individuals who have an underlying genetic cause of obesity are likely to have early onset obesity and therefore a large number of affected years. In our multi-disciplinary bariatric clinic located in a tertiary care hospital located in southern India, we have found that subjects with young onset obesity are more likely to have associated psychiatric disorders underscoring the clinical implications and need for prioritization in this field [9].

With recent advances in the genetic sequencing technology using next generation sequencing, there has been tremendous progress in identifying the underlying genetic aetiology of several disorders in a cost effective and scalable way [10].

Therefore, future research in this area will not only increase the understanding of this disease but also have significant potential utility in clinical practice including patient-specific aetiological analysis, planning on customized management strategies and conceivably individualized prognostic opinions.

Author declaration

The authors declare no conflict of interest.

Author contribution

NK wrote the manuscript. AC provided inputs to the genetic analysis domain. JF, SH and TVP approved the main conceptual ideas and proof outline. NT and BO provided critical feedback to the final manuscript. All authors provided final edits and approved the manuscript.

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