

Title: Obesity Among Patients with Chromosome 22q11 Duplication Syndrome

Introduction: Obesity is a known feature of chromosome 22q11 deletion syndrome, but there is scant literature about weight trends among patients with the reciprocal duplication. However, anecdotal evidence and rare reports suggest that obesity may also be associated with 22q11 duplication. We sought to describe pediatric patients followed at our institution who have 22q11 duplication syndrome and are overweight (body mass index [BMI] 85-95 centile) or obese (BMI \geq 95 centile).

Methods: Clinical databases of patients followed in the general genetics clinic or genetic obesity clinic at Texas Children's Hospital (TCH) were queried to identify patients with 22q11 duplication syndrome who are overweight or obese. In cases with available information, we further characterized the obesity onset as early (before age 5), childhood (between ages 5-12), or adolescent (between ages 13-19) and described the inheritance of the duplication and weight phenotype of the family members carrying the duplication.

We identified four individuals with 22q duplication and overweight or obesity.

Individual 1 is a six-year-old female with a maternally inherited 2.6Mb duplication of 22q11.21 (low copy repeat [LCR] A to LCR-D). She was born at the 30 centile for weight, became overweight at age nine months, and became obese at age 12 months. Her current BMI Z-score is 6.26. Her affected mother also has childhood-onset obesity.

Individual 2 is a four-year-old male with a paternally inherited 2.6Mb duplication of 22q11.21 (LCR-A to LCR-D). He was born at the 95 centile for weight, and became obese at 45 months. His current BMI Z-score is 1.74.

Results: There is no available information about his affected father's weight. Individual 3 is a three-year-old female with a 1.1Mb distal duplication of 22q11.21q11.22. She was born at the 86 centile for weight, became overweight at 15 months, and became obese at 18 months. Her current BMI Z-score is 2.10. Parental testing was not completed, thus inheritance status is unknown.

Individual 4 is a 17-year-old female with a maternally inherited 1.3Mb duplication of 22q11.23. She was born at the 1.5 centile for weight, became overweight at 15 months, and became obese at 28 months. Her current BMI Z-score is 3.54. Her affected mother has childhood-onset obesity. Her maternal half-brother carries the familial duplication but is neither overweight nor obese, with most recent BMI Z-score of -2.01.

Conclusions: Within our institution, we have identified four individuals with 22q11 duplication syndrome who exhibited childhood-onset obesity. Two individuals inherited the duplication from a parent with childhood-onset obesity. One individual inherited the duplication from a parent whose weight is not known. One individual has an affected sibling with the familial duplication and low weight. Further investigation is needed to determine the overall prevalence of obesity, overweight, and poor weight gain among individuals with 22q duplication syndrome. Notably, one of the individuals in this cohort first came to medical genetic attention for childhood-onset obesity, and initial recommendations for genetic testing included an obesity gene panel and did not include chromosomal microarray, thus initially missing the correct diagnosis. Future work may impact guidelines on genetic testing approaches for patients presenting with childhood-onset obesity.

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