

The Prevalence of Pathogenic Genetic Variants in a Cohort of Patients with Early-Onset and Severe Obesity

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Background

- Obesity is a multifactorial disease (Figure 1)
- 5-10% of patients with early onset obesity have a known genetic variant associated with obesity
- Genetic obesity can be syndromic (i.e. Prader-Willi, Bardet-Biedl) or non-syndromic which can be monogenic, polygenic, or chromosomal
- Hundreds of obesity related genes but 8 genes are known to cause obesity: *LEP*, *LEPR*, *POMC*, *PCSK1*, *MC4R*, *SIM1*, *BDNF*, *NTRK2*

Methods

- Retrospective review at a single institution between January 2025 to August 2025
- Offered to patients >18 years old with history of childhood obesity and BMI > 40kg/m² or patients <18 with BMI >95th percentile
- Buccal swab sent to third party laboratory
- Patients grouped into three groups: no genetic variant, variant of unknown significance, and pathogenic variant
- Non-parametric Kruskal-Wallis tests were used

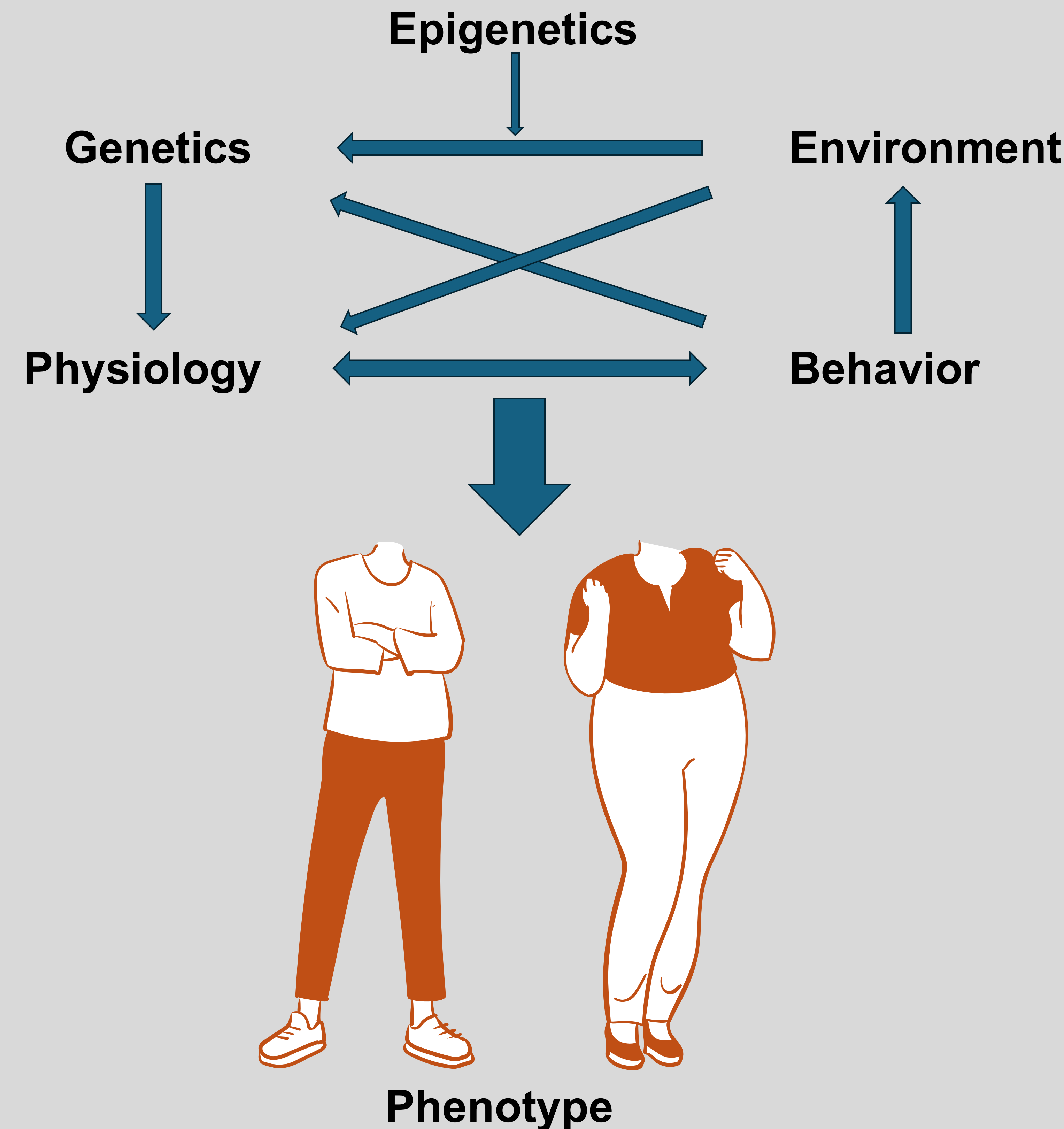


Figure 1. Obesity is multifactorial and is a result of the interplay of behavior, physiology, environment, and genetics. Figure based on "The Pathophysiology of Obesity and Obesity-Related Diseases" from the ASMBS Textbook of Bariatric Surgery.

Results

- 35 patients identified and tested
- 10 patients did not have any obesity related genetic variant
- 16 patients had variants of unknown significance
- 9 patients had pathogenic variants
- There was no significant difference in BMI between the groups (Table 1)

Table 1.

Differences between Variant Groups

Group	BMI Mdn (IQR)	p-value
No obesity-related genetic variant	48.9 (47.8 – 53.0)	
Variant of unknown significance	51.3 (44.4 – 61.6)	
Pathogenic variant	52.7 (46.3 – 54.5)	0.94

Note: BMI – body mass index, Mdn (IQR) – median (interquartile range)

Conclusion

- We identified pathogenic variants in 25% of our cohort by selectively testing
- While there is no statistically significant difference, BMI does progressively increase from the no variant group to the pathogenic variant group

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