2023 Annual Research Day Poster Sessions – April 19th, 2023

| Session/Poster# | Presenter |
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| A47 | Ilham Farhat<br>Pediatric Resident |

Advisor(s): Dr. Vivian Chin, Pediatric

**Screening for Rare Genetic Diseases of Obesity in Children**

Background: Genetic screening for variants in the MC4R pathway which regulates central control over hunger and in obesity syndromes is recommended for individuals with early onset severe obesity. We identified genetic variants in our cohort of pediatric patients with early onset obesity.
Design/Methods: We report results and features for 20 patients with severe obesity (BMI >97%) screened using RhythmÂ® Genetics Test panel, a clinically approved free buccal test targeting 79 genes and 1 chromosomal region.
Results: Thirteen (65%) of the 20 patients, including 7 females and 6 males, tested positive for genetic variants, mostly variants of uncertain significance (VUS). Six (46%) had only one genetic mutation found, while 7 (53%) had two or more. All reports were VUS due to the lack of solid functional and genetic evidence, with the exception of MC4R likely pathogenic. The most frequently noted clinical feature was autistic spectrum disorder with learning disability in 5 (38%), followed by extreme hyperphagia in 3 (23%). PCNT is the most common variant found in 4 (30%), followed by SEMA3 in 3 (23%), MC4R in 2 (15%), BBS in 2 (15%), SDCCAG8 in 2 (15%) and PLXNA1 in 2 (15%). Pathogenic PCNT is found in microcephalic osteodysplastic dwarfism type 2, short stature and insulin resistance, while MC4R variants are associated with severe early-onset obesity with hyperphagia. SDCCAG8 variants are associated with Bardet-Biedl syndrome. PLXNA1 is associated with developmental delay, and brain/eye anomaly.
Conclusion(s): Targeted genetic screening for children with early onset obesity is easy, free, and clinically important in detecting variants in early onset obesity. Since introduction into our clinical practice, we were able to identify several variants and a likely pathogenic variant in MC4R. Identification of variants can guide further therapy. A majority of patients had one or more VUS which warrants further investigation.