

PHENOTYPIC AND GENOTYPIC PROPERTIES OF CHILDREN WITH SUSPICION OF MONOGENIC OBESITY

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Introduction

- Monogenic obesity is a rare form of obesity that occurs early in life due to mutation of one of the genes in the leptin-melanocortin pathway.
- Mainly;
 - Leptin (LEP)
 - Leptin receptor (LEPR)
 - Proopiomelanocortin (POMC)
 - Proprotein converting protein subtilisin / kexin-type 1 (PCSK1)
 - Melanocortin 4 receptor (MC4R)
- Numerous different genetic variants have been shown to cause monogenic forms of obesity in these genes.

Aim

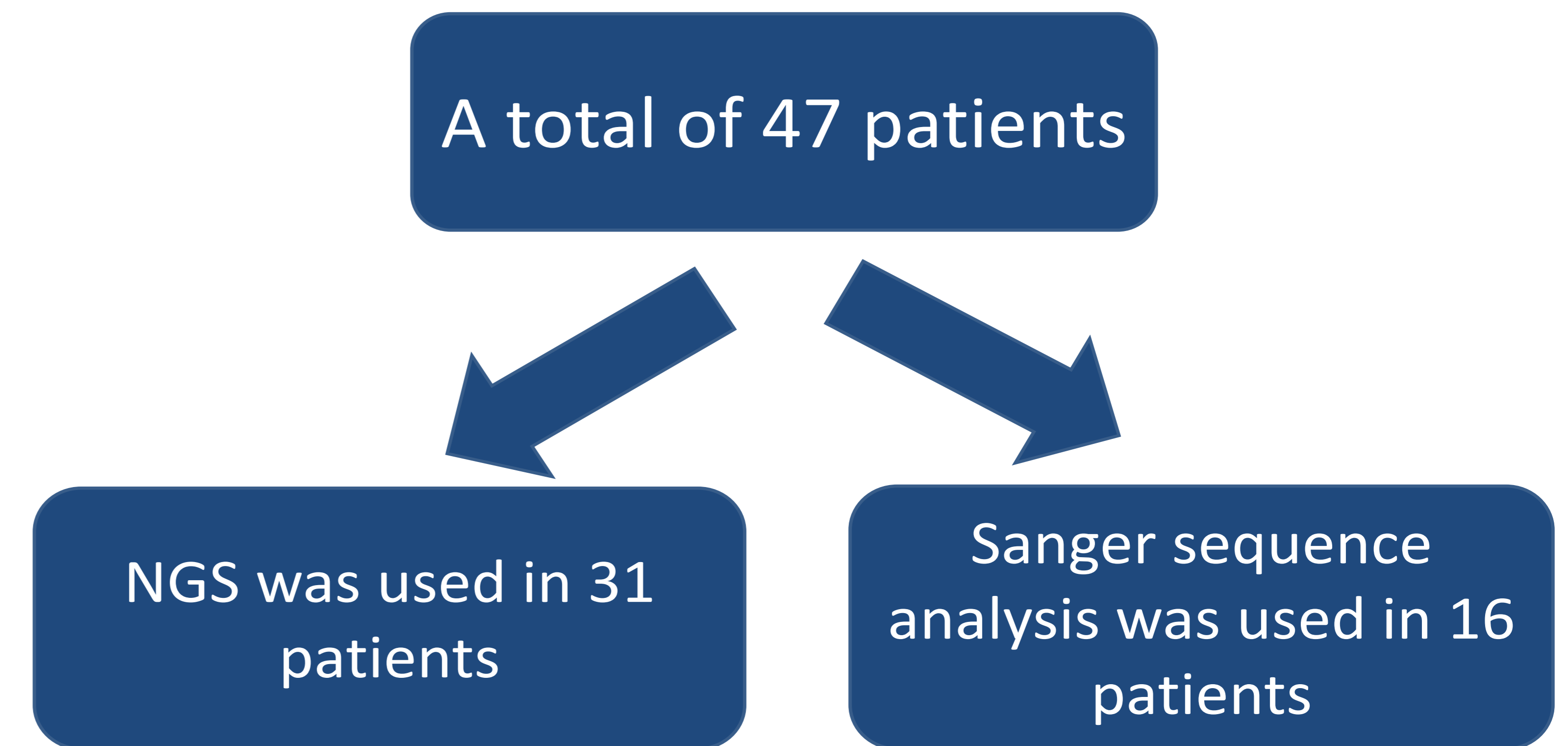
The aim of this study was to evaluate the phenotypic features and the molecular genetic results in children with a diagnosis of monogenic obesity.

Table 1. Clinical and demographic characteristics of the cases with monogenic obesity

	MC4R (Case 1)	MC4R (Case 2)	MC4R (Case 3)	LEPR
Age (year)	7.99	10.94	9.12	16.4
Obesity Onset age	From birth	From birth	From birth	From birth
Sex	Male	Female	Female	Male
Puberty	Prepubertal	Pubertal	Prepubertal	Pubertal
Obesity in parents	Yes	Yes	Yes	Yes
Weight (kg)	68.4	95	51.7	97.4
Weight (SDS)	4.63	4.43	2.79	2.3
Height (cm)	140.1	162	133	166
Height (SDS)	2.48	2.5	0.03	-1.25
BMI (kg/m ²)	34.8	36.2	29.2	35.3
BMI-SDS	3.8	3.45	2.89	2.7

Method

- Patients who underwent molecular genetic analysis for monogenic obesity in our clinic between years 2016-2018 were included in the study.
- Presence of at least 2 of below mentioned criterias was considered as indication for genetic analysis for monogenic obesity.
 1. Severe Obesity (BMI SDS) >3)
 2. Early-onset obesity (<6 years)
 3. At least one of the parents with obesity
 4. Consanguinity between parents
- Molecular genetic analysis was performed by Sanger sequence analysis of the *MC4R* gene or by next generation sequencing of *MC4R*, *LEP*, *LEPR* and *POMC* genes.



Results

- Pathogenic variant in *MC4R* was detected in 3 cases.
- In one patient, a novel heterozygous variant was detected in *LEPR* which was predicted to be pathogenetic in in-silico analysis.
- Frequency of sequence variant was 6.3% for the *MC4R* gene, and frequency of the sequence variant for the *LEPR* gene was 2.1%.
- Clinical and demographic characteristics of cases with sequence variants are summarized in **Table 1**

Conclusion

Sequence variant was found in 8.5% (n = 4) of the children who were examined for suspected monogenic obesity. Obesity developed in the first year of life in all cases and at least one of the parents had obesity. Obesity was severe in 2 of 4 cases. Monogenic obesity should be investigated in the presence of severe obesity, obesity with an onset in the first year of life, and obesity in parents.

