Screening for syndromic causes of obesity

Sanjay Kalra,[1] Saurabh Arora,[2] Nitin Kapoor[3]

Abstract

Syndromic obesity is sometimes encountered in clinical practice, but may often be misdiagnosed. This is more often seen in the south Asian region due to higher rates of consanguinity. This article simplifies the clinical features which should prompt a high index of clinical suspicion, and ensure a detailed assessment for syndromic obesity including a genetic test. This manuscript lists various aspects of history and physical examination in an alliterative manner.

Keywords: Childhood obesity, Dysmorphic obesity, Endocrine obesity, Obesity, Overweight, Paediatric obesity, Syndromic obesity.

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Introduction

Obesity has become a major concern across the world and even in south Asian countries.[1] Most discourse on this syndrome focus on adult obesity, neglecting the unique aspects of weight homeostasis in childhood and adolescence. Even when paediatric obesity is discussed, it is approached through a monochromatic prism of environmental and behavioural factors.[2,3] Public health messaging emphasizes the need to curtail caloric intake and increase energy expenditure, without analysing various biological causes of weight gain. At times, these children also present in adult endocrine clinics with morbid obesity, which has not been addressed in childhood.[4]

There are multiple genetic syndromes and endocrine conditions which can cause obesity in children (Table-1).[5] The physician should keep a high index of clinical suspicion for these, and refer to colleagues with expertise in managing such patients. In this article, we list the various causes of obesity in children, and provide a simple framework to help identify cases which will benefit from a detailed workup.

[1]Department of Endocrinology, Bharti Hospital, Karnal, [2]Department of Endocrinology, Dayanand Medical College and Hospital, Ludhiana, [3]Department of Endocrinology, Diabetes and Metabolism, Christian Medical College, Vellore, India, and Non-Communicable Disease Unit, The Nossal Institute for Global Health, Melbourne School of Population and global health, University of Melbourne, Victoria, Australia.

Correspondence: Sanjay Kalra. Email: brideknl@gmail.com

Table-1 Causes of obesity in children.

Endocrine syndromes
• Hypothyroidism
• Growth hormone deficiency
• Cushing's syndrome
• Hypogonadism
• Insulinoma
Hypothalamic syndromes
• Injury
• Surgery
• Congenital malformation
Leading to
• Deranged production of an(orexigenic) peptides
• Hypothalamic increased binding of gut messengers to hypothalamic receptors
Monogenic obesity (mutations of homeostatic pathways)
• Leptin deficiency
• Leptin receptor resistance
• Pro-opiomelanocortin deficiency
• Prohormone convertase 1 deficiency
Genetic syndromes
• With developmental delay
• Prader Willi syndrome
• Bardet-Biedl syndrome
• WAGR syndrome
• Fragile X syndrome
• Without developmental delay
• Alstrom syndrome

Clinical Suspicion

Table-2A and 2B offer a simple, yet comprehensive, checklist to assist in clinical screening for syndromic obesity. Any clinical feature, listed in the tables, should prompt a detailed assessment, and referral, if necessary.

Cues can be gleaned from the medical history dietary habits, and family history. In particular family history is important not only with respect to the number of people with obesity in the family but also the age of onset of obesity in them. Consanguinity is another important factor.[6] In a paper from Pakistan, it was shown that about one-third of children born to consanguineous populations could have a syndromic monogenic cause of obesity when tested for 3 common genes.[7] A general physical examination also reveals hints about the nature of obesity. Endocrine causes of obesity are usually associated with slow growth velocity, symptoms/signs suggestive of the specific endocrinopathy, and swift response to correction of the underlying abnormality.

Table-2A: Checklist-Screening for Syndromic obesity.

- Developmental delay
- Diminished intelligence quotient
- Diet abnormality: hyperphagia
- "Dynastic" history (family history)
- Dysmorphism: digit anomalies (poly/syn/brachy-dactyly)
- Dysmorphism: dome of head (macro/acro-cephaly

Table-2B: Checklist-Screening for Syndromic obesity.

"Swift" onset of obesity (<5years of age)
Severe (morbid) obesity
"Sweet tooth" (hyperphagia)
Sibling (family) history
Sanguine marriages (history of consanguinity)
Suboptimal response to medical nutrition therapy
Slow development
Sight (visual) impairment
Size of head (macro/acro-cephaly)

Dysmorphic features such as macro/acro-cephaly, altered shape of eyes, ears or mouth, change in shape of jaw, skeletal dysplasia, muscular hypotonia, and macro-orchidism are suggestive of some syndromic causes of obesity. Retinitis pigmentosa and optic atrophy can help pinpoint the diagnosis in other cases.[5]

Confirmation

The diagnosis of syndromic obesity is confirmed by genetic studies. In many health care settings, however, such laboratory support is not available. A careful assessment of the phenotype can suffice, in these situations, to explain the prognosis and plan the course of therapy. Considering the rapid increase in prevalence of childhood obesity, and the need to characterize patients accurately, we call for strengthening genetic laboratories across the world. Moreover with the next generation sequencing platform, these tests are now available at a much subsidised cost and have a rapid turnaround time.[8]

Clinical Significance

It is of utmost importance to identify syndromic obesity, as well as other reversible causes of the disease. Obesity is associated with significant social stigma and psychological stress. Peers, parents and the public at large, all are guilty of "bullying" children living with obesity, and body-shaming then. Identification of, and empathic explanation about, a "genetic" or "endocrine" or "inherited" etiopathology is the key to blunting such nagging and bullying. All medical professionals should be sensitized to these psychosocial aspects of living with obesity.[9] Non-judgmental language and tone must be used to ensure that children with obesity, especially syndromic obesity, are provided with a supportive and happy environment.[2,10]

Conclusion

A clinical assessment of children presenting with obesity helps identify persons at high risk of having syndromic obesity. The screening aids shared in this communication will help practitioners in referring such patients to centres with expertise in caring for them.

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