Rhythm PHARMACEUTICALS

DISEASE EDUCATION

Bardet-Biedl Syndrome

Solomon, living with BBS

What is BBS?

Bardet-Biedl syndrome (BBS) is a rare ciliopathy, resulting from genetic variants within the BBS family of genes. This heterogeneous genetic disease presents with a variety of symptoms that evolve over time, including:[1-3]

- **Early-onset, severe obesity and Hyperphagia**
- **Visual impairments**
- **Renal disease**
- **Cognitive impairment**
- **Polydactyly**
- **Genital anomalies**

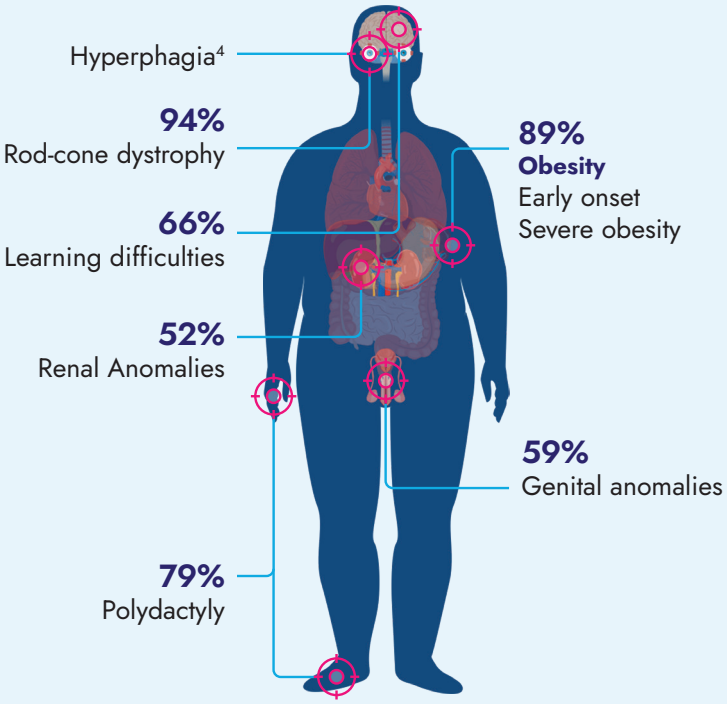
Common Clinical Features of BBS[2]

Prevalence:

Canada = ~1 in 140-160,000 individuals[5]

Newfoundland = ~1 in 17,500 individuals[6]

Prevalence estimates may increase as more healthcare professionals become aware of the clinical features of BBS and genetically test to aid in clinical diagnosis[7,8]



Percentages represent frequency of feature appearance among individuals diagnosed with BBS.

Bardet-Biedl Syndrome

How is BBS diagnosed?

More than 20 genes associated with BBS are involved in the melanocortin-4 receptor (MC4R) pathway.[1,2,9-12] Genetic testing can help provide additional diagnostic information and can confirm a clinical diagnosis.[13]

The following criteria have been used to help diagnose BBS. According to these criteria, diagnosis is based on the presence of a combination of features.[1,14]

Common features

- Rod-cone dystrophy
- Polydactyly
- Obesity
- Genital anomalies
- Renal anomalies
- Learning difficulties

Other features

- Speech delay or speech impairments
- Developmental delay
- Diabetes mellitus
- Dental anomalies
- Left ventricular hypertrophy or congenital heart disease
- Mild spasticity (especially lower limbs)
- Brachydactyly or syndactyly
- Strabismus, cataracts, or astigmatism
- Ataxia or poor coordination
- Anosmia or hyposmia
- Polyuria or polydipsia
- Hepatic fibrosis

BBS patients are treated and monitored based on individual symptoms[1,2]

BBS has a highly variable phenotype with common features that evolve over time[13,15,16]

	Birth	First years of life (0-5 years)	Early childhood (>5 years)
Postaxial polydactyly[2,13,17-19] (63%-81%)	Extra digits (postaxial)	Typically surgically removed	
Renal anomalies[2,13,20] (52%)	Anatomical malformations	Progressive kidney diseases	Polyuria/ Polydipsia
Obesity[3,4,13] (72%-86%)	Normal birth weight	Rapid weight gain Unusual food seeking	Severe obesity Hyperphagia persists
Cognitive impairment[13,14] (>50%)		Developmental delay	Learning difficulties
Visual impairment[13,21] (93%)			Progressive vision loss Night blindness

Obesity in BBS

- Obesity can begin in childhood and can increase in severity with age[2]
- Obesity may have a detrimental impact on long-term health, due to its association with increased morbidity, social stigma, and reduced quality of life[22]
- Hyperphagia may contribute to obesity in patients with BBS[4,23]

Hyperphagia is generally characterized by the following:[4,24]

Insatiable hunger

- Heightened and prolonged hunger
- Longer time to reach satiation
- Shorter duration of satiety

Excessive drive to eat

- Severe preoccupation with food
- Persistent food-seeking behaviors (eg, stealing food, night eating, eating food from the trash)

Distress and functional impairment due to denial of food

Mean Body Mass Index (BMI) of Patients With BBS by Age[25]

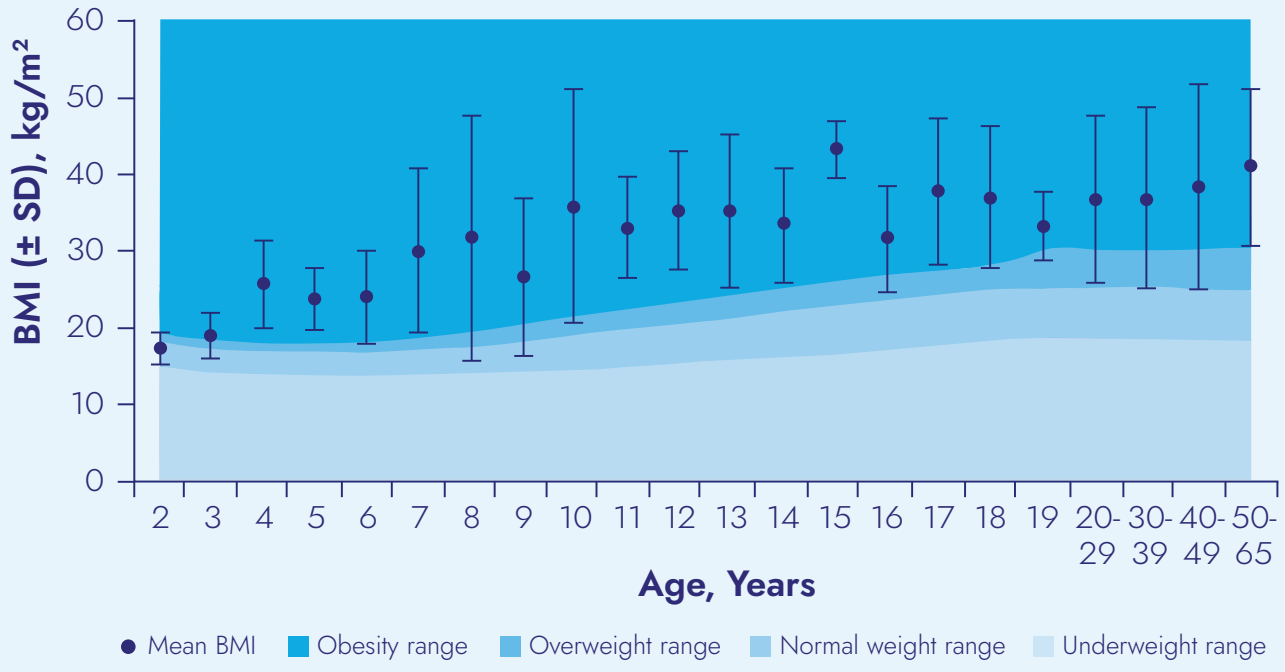


Figure adapted with permission from Marshfield Clinic Research Institute, the research division of Marshfield Clinic Health System.

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