

# Bardet-Biedl Syndrome: A Case Report

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## Abstract

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive ciliopathic human genetic disorder characterized by retinal dystrophy, truncal obesity, post-axial polydactyly, renal dysfunction, learning difficulties and hypogonadism. Many associated minor features can be helpful in making a diagnosis and are important in the clinical management of BBS. The diagnosis is based on clinical findings and can be confirmed by sequencing of known disease-causing genes in 80% of patients. BBS genes encode proteins that localize to the cilia and basal body and are involved in cilia biogenesis and function. Mutations lead to defective cilia accounting in part for the pleiotropic effects observed in BBS. We have presented a 11 years old female patient exhibiting characteristic features of Bardet Biedl syndrome (BBS) and then the literature is reviewed.

**Keywords:** Bardet-Biedl syndrome; Autosomal recessive inheritance; Ciliopathies; BBS genes.

## INTRODUCTION

The syndrome is named after Georges Bardet<sup>2</sup> and Arthur Biedl<sup>3</sup>. 14 genetic forms have been currently identified. In 1866, Laurence and Moon described a family of four siblings with retinal dystrophy, obesity, spastic paraparesis and cognitive deficit<sup>1</sup>. Bardet<sup>2</sup> and Biedl<sup>3</sup>. later reported separately on further similarly affected individuals who in addition had post-axial polydactyly and the condition was coined Laurence-Moon-Bardet-Biedl syndrome. The syndrome is often divided into two entities: Laurence-Moon syndrome and Bardet-Biedl Syndrome (BBS), but there is considerable phenotypic overlap, suggesting that they may be allelic<sup>4</sup>. BBS is now the standard term in common usage.

BBS is a pleiotropic genetic disorder with significant interfamilial and intra-familial variation<sup>5,6</sup>. Inheritance is traditionally considered autosomal recessive, although notable exceptions exist, whereby BBS may be an oligogenic disorder<sup>7,10</sup>.

In most of North America and Europe, Bardet-Biedl syndrome has a prevalence of 1 in 140,000 to 1 in 160,000 newborns. The condition is more common on the island of Newfoundland (off the east coast of Canada), where it affects an estimated 1 in 17,000 newborns. It also occurs more frequently in the Bedouin population of Kuwait, affecting about 1 in 13,500 newborns<sup>8</sup>.

## CASE SUMMARY

Miss. H, a 11 years old female patient hails from Chakaria, Chittagong admitted in Pediatric Medicine indoor ward of Chattagram Maa-Shishu O General Hospital with the complaints of generalized swelling of whole body, scanty micturation and dimness of vision. The swelling started from face then become generalized with scanty micturation for same duration. For last five years she was getting weight and developed dimness of vision. She has delayed developmental history with walking at the age of two years and talking at three years. She is the third child from a non-consanguineous marriage. Her parents are healthy, as are her other brothers and sisters. On examination she was found to be obese with a BMI of 28 (Figure-1), oedematous, hypertensive, Other findings were polydactyly of all four limbs (Figure-2,3), high-arched palate, low vision, retinitis pigmentosa and macular edema on funduscopy, ascites and renal insufficiency. There was no clinical evidence of spastic paraparesis (Table-1).

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**Figure 1 :** An 11 year old female BBS patient



**Figure 2 :** Polydactyly of feet



**Figure 3 :** Polydactyly of hands

Laboratory examination reveals Hb-6 g/dl, serum creatinine-8mg/dl, ABG-metabolic acidosis and high potassium level, ascites on ultrasonography of whole abdomen and thyroid function tests were found to be normal.

**Table-1:** Modified diagnostic criteria<sup>4</sup> and clinical manifestation in the case

Primary Features	Case
Rod-cone Dystrophy	+
Polydactyly	+
Obesity	+
Learning Disabilities	-
Hypogonadism in males	-
Renal Insufficiency	+
<b>Secondary Features</b>	
Speech disorder/Delay	+
Strabismus/cataracts/astigmatism	-
Brachydactyly/ syndactyly	-
Developmental delay	+
Nephrogenic diabetes insipidus	-
Ataxia/poor coordination/imbalance	-
Mild spasticity	-
Diabetes mellitus	-
High-arched palate	+
Dental crowding/hypodontia/small roots	-
Left ventricular hypertrophy/congenital heart disease	-
Hepatic fibrosis	-

## DISCUSSION

The BBS phenotype evolves slowly throughout the first decade of life, although there is a considerable variability. As a result, most patients are diagnosed in late childhood or early adulthood. Post-axial polydactyly is common and may be the only obvious dysmorphic feature at birth. This may affect all four limbs or only upper or lower limbs and may occur in conjunction with brachydactyly and/or syndactyly<sup>9</sup>. In the case, the patient has post-axial polydactyly in 4 limbs.

The most common diagnostic investigation for BBS is the development of rod-cone dystrophy. Primary loss of rod photoreceptors is followed by later demise of cone photoreceptors<sup>11</sup>. This presents as an atypical retinitis pigmentosa with early macular involvement<sup>12</sup>. The clinical manifestation is gradual onset of night blindness, followed by photophobia and loss of central and colour vision<sup>11</sup>. Symptoms usually develop in the first decade of life and most patients are legally blind by the second or third decade,<sup>1,3</sup> Other eye abnormalities such as cataracts and refractive errors are also prevalent in BBS. Our patient has low vision, retinitis pigmentosa and macular edema. Obesity is another major clinical finding which is present in our case. The incidence of obesity is reported to be 72–86% in the BBS population<sup>4,6, 14, 15</sup>. Birth weight is usually within the normal range. The development of type 2 diabetes is prevalent among patients. Hypogonadism may manifest as delayed puberty or hypogonadism in males and genital abnormalities in females<sup>4</sup>. Developmental delay and cognitive deficit are common in BBS. Renal abnormalities can be a major cause of morbidity and mortality in BBS<sup>14</sup>. The reported case is found to have significant chronic renal insufficiency that required peritoneal dialysis. Speech deficit has been reported in 60% of patients. Involvement of other organ systems such as the heart and gastrointestinal system are also observed. Cardiac abnormalities include valvular stenoses, patent ductus arteriosus and cardiomyopathies<sup>4</sup>. Hepatic involvement ranges from fibrosis to cystic dilatation of the bile duct, intrahepatic and extrahepatic tracts<sup>12</sup>. Hirschsprungs disease has been documented in BBS but the incidence of this association is unknown. Dental crowding and a high-arched palate are common. Other abnormalities include hypodontia, malocclusion and enamel hypoplasia<sup>5</sup>. Anosmia has been described following observations in a mouse model. Many affected individuals suffer from a degree of clumsiness and signs of ataxia and poor coordination<sup>4</sup>. BBS is usually not diagnosed before the patient starts to develop the visual problems characteristic of rod-cone

dystrophy. Although there are some distinctive dysmorphic features such as hypertelorism, midface hypoplasia and retrognathia, these are inconsistently present and can be subtle. Molecular confirmation of the diagnosis can be obtained in nearly 80% via direct sequencing of the BBS genes. The last decade has seen a rapid expansion in research into this syndrome, resulting in the discovery of 16 BBS genes accounting for approximately 80% of clinically diagnosed BBS. The majority of pathogenic mutations are found in BBS1 and BBS10, accounting for 23.2% and 20%, respectively,<sup>5</sup> although some regional variation in prevalence exists. Regarding management of BBS, multidisciplinary approach is required. Complications associated with BBS should be treated symptomatically as in the general population.

## CONCLUSION

Since the first gene for BBS was identified over a decade ago, there have been extensive developments within the field. A total of 16 disease-causing genes have now been discovered and our understanding of their functional properties has facilitated an insight into the molecular mechanisms underlying ciliary phenotypes in general and BBS in particular. In the coming years, it is likely that other disease-causing genes will be identified and that there will be further improvement of the clinical diagnostic services allowing for faster diagnosis and prenatal testing. Elucidation of the molecular pathogenesis of the clinical features of BBS and research into therapeutics may yield novel treatment options that target organ-specific aspects of the condition, such as renal cysts or rod-cone degeneration, or have a more general modulating effect on several aspects of the condition. But in a developing country like Bangladesh, the diagnosis of BBS depends on clinical assessment and conventional lab investigations, the genetic and molecular study of the syndrome will take more time to come into practice.

## REFERENCES

1. Laurence JZ, Moon RC: Four cases of 'retinitis pigmentosa' occurring in the same family, and accompanied by general imperfections of development. *Obes Res* 1995; 3: 400–403.
2. Bardet G: On congenital obesity syndrome with polydactyly and retinitis pigmentosa (a contribution to the study of clinical forms of hypophyseal obesity). *Obes Res* 1995; 3: 387–399.
3. Biedl A: A pair of siblings with adiposo-genital dystrophy. *Obes Res* 1995; 3: 404.
4. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA: New criteria for improved diagnosis of Bardet–Biedl syndrome: results of a population survey. *J Med Genet* 1999; 36: 437–446.
5. Waters AM, Beales PL: Bardet–Biedl Syndrome; GeneReviews [Internet]1993–2003 (Updated 2011).
6. Riise R, Andreasson S, Borgstrom MK et al. Intrafamilial variation of the phenotype in Bardet–Biedl syndrome. *Br J Ophthalmol* 1997; 81: 378–385.
7. Katsanis N, Ansley SJ, Badano JL et al. Triallelic inheritance in Bardet–Biedl syndrome, a Mendelian recessive disorder. *Science* 2001; 293: 2256–2259.
8. Farag TI, Teebi AS: High incidence of BardetBiedl syndrome among the Bedouin. *Clin Genet* 1989; 36: 463–464.
9. Green JS, Parfrey PS, Harnett JD et al. The cardinal manifestations of Bardet–Biedl syndrome, a form of Laurence–Moon–Biedl syndrome. *N Engl J Med* 1989; 321: 1002–1009.
10. Webb MP, Dicks EL, Green JS et al. Autosomal recessive Bardet–Biedl syndrome: first-degree relatives have no predisposition to metabolic and renal disorders. *Kidney Int* 2009; 76: 215–223.
11. Hamel CP: Cone rod dystrophies. *Orphanet J Rare Dis* 2007; 2: 7.
12. Baker K, Beales PL: Making sense of cilia in disease: the human ciliopathies. *Am J Med Genet C Semin Med Genet* 2009; 151C: 281–295.
13. Adams NA, Awadein A, Toma HS: The retinal ciliopathies. *Ophthalmic Genet* 2007; 28: 113–125.
14. Tobin JL, Beales PL: Bardet–Biedl syndrome: beyond the cilium. *PediatrNephrol* 2007; 22: 926–936.
15. Hjortshoj TD, Gronskov K, Philp AR et al. Bardet–Biedl syndrome in Denmark – report of 13 novel sequence variations in six genes. *Hum Mutat* 2010; 31: 429–436.