# Bardet Biedl Syndrome

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**Abstract**

Bardet Biedl syndrome is a rare autosomal recessive condition with a wide spectrum of clinical features. The accepted major criteria for diagnosis include obesity, polydactyly, male hypogonadism, mental retardation, retinal dystrophy, adrenal dysfunction. We have presented a 14 year old male patient exhibiting characteristic features of Bardet Biedl syndrome (BBS), admitted into Community Based Medical College Hospital.

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**Key Words:** *Bardet Biedl Syndrome, obesity, polydactyly.*

## Introduction

Bardet Biedl syndrome (BBS) is a rare autosomal recessive disorder. BBS was first described by Bardet and Biedl in the 1920[1]. The principal manifestations are rod-cone dystrophy (retinitis pigmentosa), postaxial polydactyly, central obesity, mental retardation, hypogonadism, and renal dysfunction. Other features not always present include hepatic fibrosis, diabetes mellitus, neurological, speech and language deficits, behavioral traits, facial dysmorphism, dental anomalies and developmental delay[2,3]. There is widespread controversy whether Bardet Biedl syndrome and Laurence-Moon syndrome are separate entity or whether they are simply phenotypic variation of the same disorder. We are presenting here a case of BBS which is rarely encountered in clinical practice.

## Case report

Babul Mia, a 14 years old mentally retarded and obese boy with polydactyly, hailing from Trishal, Mymensingh admitted into Community Based Medical College Hospital, Mymensingh, presented with flaccid paralysis followed by episodes of vomiting for one day, increase frequency of scanty micturition with fever associated with chills and rigor for two days. The mother of the patient complained he is gaining weight, gradual impairment of vision especially at night, small genitalia, learning disability for last few years. There was no history of trauma, back pain, recent respiratory tract infection, loose motion, prolonged intake of steroid, cold intolerance, constipation, voice change, skin infection, high colour urine and leg swelling. He was elder of the two brothers; his younger one was normal and healthy. There is no history of such type of illness in his family. His father & mother are alive and healthy. No history of consanguineous marriage. He was born at home as a big baby with polydactyl. On general examination, he looked obese (BMI 30.5), face was rounded, moon like but not plethoric. There were polydactyly involving six fingers on both feet and right hand. Five fingers on left hand. Lipomastia of both breasts and striae on the lower abdomen and thighs. Genitalia and both testes were smaller in size. He was mildly anemic, non icteric, non cyanosed. There was mild pedal oedema, no clubbing, koilonychia and leukonychia. No bruise and proximal myopathy.

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Thyroid gland and lymph nodes were normal. Pulse-96/min, regular, Blood Pressure-140/70 mm of Hg, Temperature: 100 F, Respiratory rate: 18/min. On nervous system examination patient was conscious and oriented but low intelligence. Speech was normal but delayed response. All cranial nerves function were normal except optic nerves, where acuity of vision was 6/60. Ophtalmoscopic examination revealed features suggestive of retinitis pigmentosa. All sensory modalities were normal. Cardiovascular, respiratory, alimentary and other systemic examination revealed normal findings. Laboratory examination including complete blood count showed patient was mildly anaemic (Hb 8.3 gm/dl), ESR was high(130 mm in 1 hour), Chest X-ray revealed normal findings. Urinalysis revealed mild proteinuria (+), pus cell upto 30/HPF, no RBC and cast. Serum creatinine was 4.6mg/dl. Serum electrolyte revealed severe hypokalaemia ($K^+$ 1.78 mmol/L, $Na^+$ 137.7 mmol/L, $Cl^-$ 111.6 mmol/L Ultrasonography revealed features suggestive of chronic kidney disease) . Serum testosterone was at the lower level of normal range. Thyroid function test were normal.

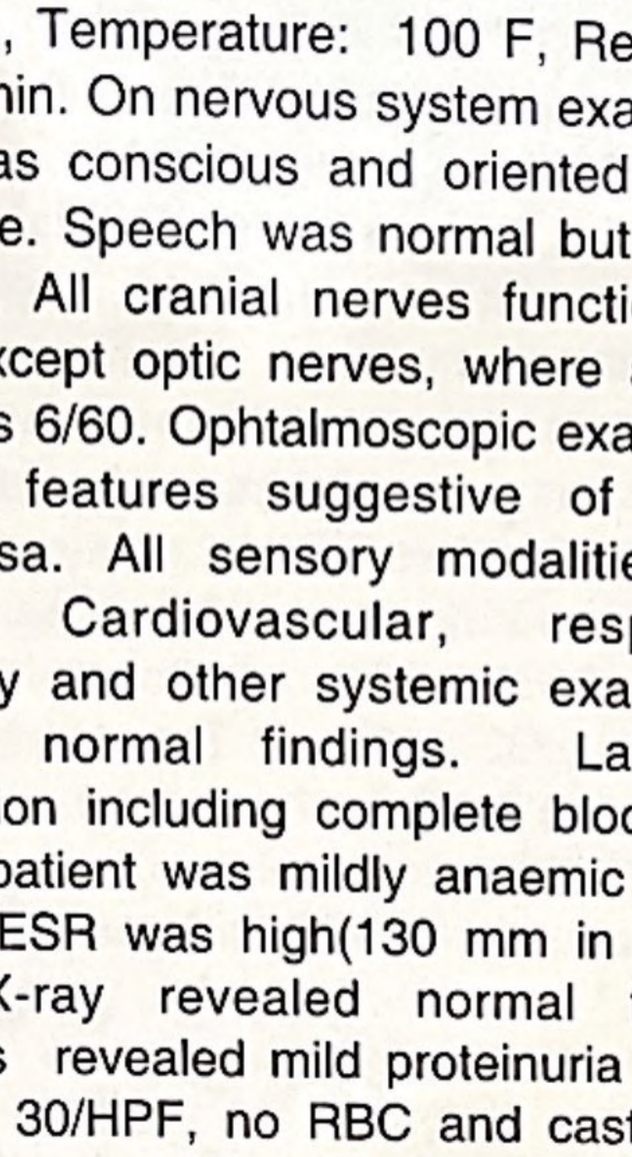

Figure 1: Full size profile picture of the patient

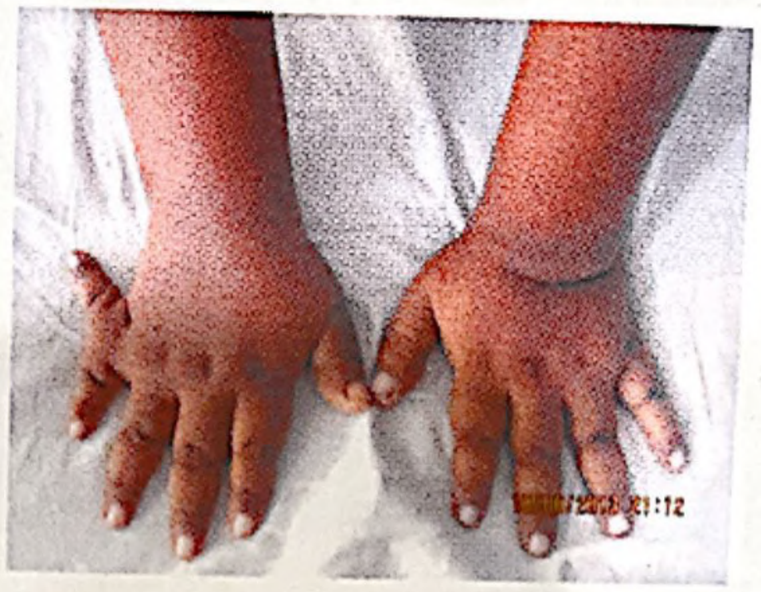

Figure 2: X-ray right hand showing extra digit

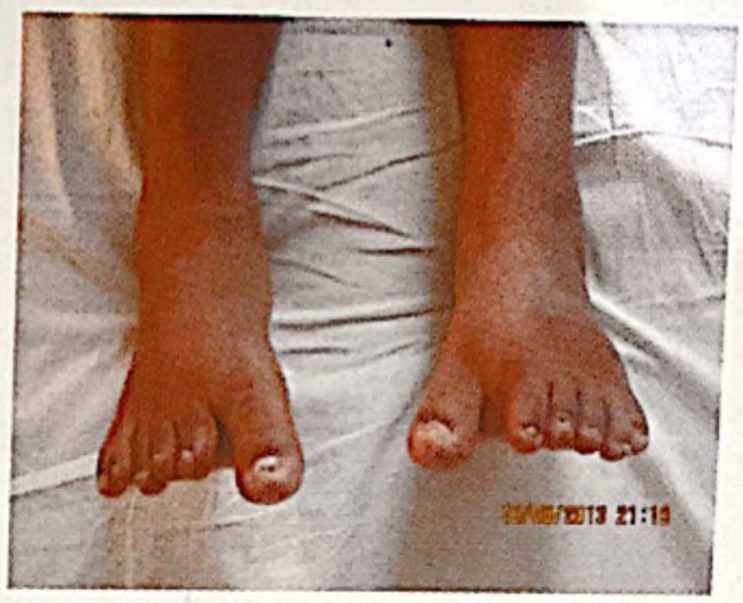

Figure 3: Extra digit on the patient's both feet.

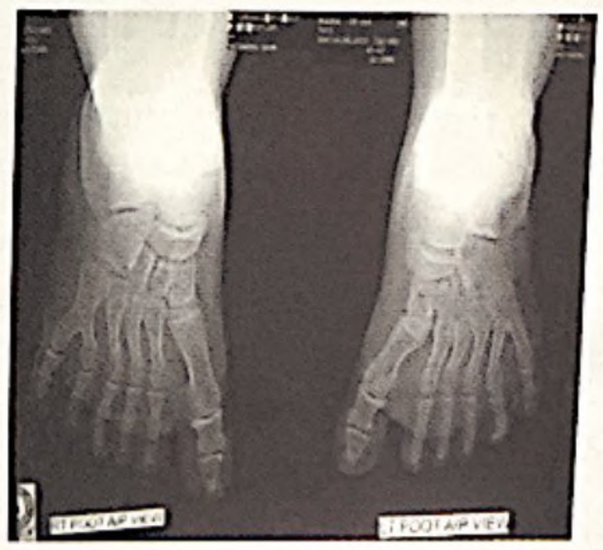

Figure 4: X-ray both feet showing extra digits

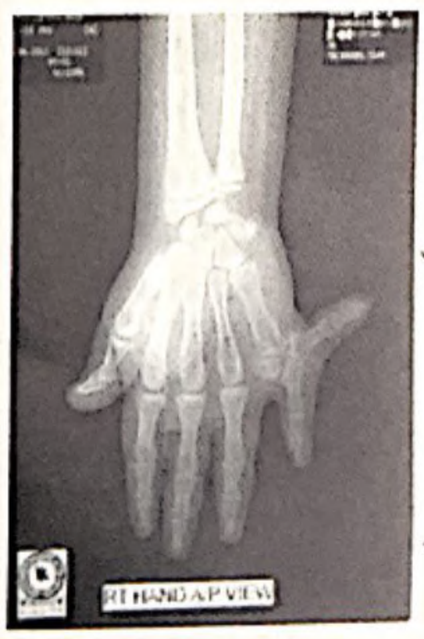

Figure 5: X-ray right hand showing extra digits

**Table-1: Modified diagnostic criteria and clinical manifestation in case[3].**

| Major features | Features present in case |
|---|---|
| Polydactyly | + |
| Obesity | + |
| Learning disabilities | + |
| Hypogonadism in males | + |
| Rod-cone dystrophy | + |
| Renal impairment | + |
| **Minor features** | |
| Speech disorder/Delay | + |
| Strabismus/cataracts/astigmatism | – |
| Brachydactyly/ syndactyly | – |
| Developmental delay | + |
| Nephrogenic diabetes insipidus | – |
| Ataxia/poor coordination/imbalance | + |
| Mild spasticity | – |
| Diabetes mellitus | – |
| Dental crowding/hypodontia/small roots | – |
| Left ventricular hypertrophy/congenital heart disease | – |
| Hepatic fibrosis | – |

## Discussion

The syndrome was described by Bardet Biedl in the 1920. It was later erroneously coupled with another disorder described by Laurence and Moon in 1866 and was consequently referred to as Laurence- Moon-Biedl syndrome. BBS is distinguished from the much rarer Laurence- Moon syndrome, in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly[4,5]. The prevalence of BBS is 1:160000 in Europe and North America[6], although higher incidence has been reported in the isolated populations of Newfoundland [1:13000][2] and Kuwait [1:17000][7]. Retinal dystrophy (100%) is the first major feature of the disorder. It is found occasionally in the first decade but present in almost all patients by the second decade[8]. Obesity is the second major feature of BBS, with a frequency of 72-96 percent depending on measurement criteria. Obesity usually begins in childhood and the severity increases with age, with the majority of cases exhibiting symptoms within the first year of life[3]. Limb-abnormalities are the third major feature of BBS. Limb deformities have been reported at varying frequencies[3,9]. Of these, post-axial polydactyly, polydactyly, and brachydactyly of both hands and feet are most common. Partial syndactyly, fifth finger clinodactyly, and a prominent gap between the first and second toes are sometimes associated[3]. Mental retardation is a more disputed feature of BBS. Recently, objective IQ tests determined that only a minority of patients are mentally retarded. An IQ of 79 or below is found in 44 percent of BBS patients. The decrease in IQ level correlates with the presence of visual handicap[3,9]. Hypo-genitalism is reportedly more frequently in BBS males than females[3]. In BBS females, genital abnormalities encompass a wide range, including hypoplastic fallopian tubes, uterus, and ovaries, partial and complete vaginal atresia, absent vaginal orifice, and absent urethral orifice[10,11]. Bardet-Biedl syndrome males have small penis and testes (88%)[9]. Renal failure is the major cause of morbidity and early mortality in BBS. A wide range of renal abnormalities has been described (chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, vesico-ureteric reflux. Mild to moderate mental retardation and learning difficulties are additional features of the syndrome[2,3]. In 1999, modified diagnostic criteria were defined after a study conducted in England in 109 BBS patients[3]. Patients who had 4 major characteristics or 3 major and 2 minor criteria were identified as BBS (Table 1) .Our case had six major and three of the minor criteria, thus fulfilling the diagnostic criteria of Bardet-Biedl syndrome. BBS is an autosomal recessive disorder characterized by non-allelic heterogeneity. BBS is genetically heterogeneous, with four loci mapped to date. These are BBS1 (11q13)12, BBS2 (16q22)13, BBS3 (3p13)14, and BBS4 (15q21)15. We have recently shown that the BBS1 locus is involved in ~45% of affected white families[3]. The BBS4 locus appears to be the next most common[16], but there are several families of Middle Eastern and Asian origin which do not

show linkage to any known locus. Genotype-phenotype correlations between the various loci do not show obvious differences, with the possible exception of minor effects on growth[3]. The most plausible hypothesis regarding a shared function for BBS proteins is that they assist microtubule-related transport and cellular organization processes, in particular relating tociliary/flagellar and centrosomal activities. This hypothesis is supported by several studies using different model organisms[17,18,19]. Some of the phenotypes exhibited by BBS proteins, including retinal degeneration, skeletal anomalies and renal cysts/malformations bear resemblance to human diseases associated with abnormal cilia function[20].

## Conclusion

Though a lot of progress has been made about this rare disease, there are still lots more things need to be known about its pathophysiology. Further large scale studies are required to understand the genetic complexity of Bardet-Biedl Syndrome. The disease is incurable, and therefore, persists as a chronic condition. However, timely symptomatic treatment ensures a good prognosis.

## References


1. *Bardet G. Sur un syndrome d'ob sit infantile avec polydactyly et r tinitepigmentaire. Thesis, University of Paris, France, 1920.*
2. *Green JS, Parfrey PS, Harnett JD, Farid NR, Cramer BC, Johnson G, et al. The cardinal manifestations of Bardet-Biedl syndrome, a form of Laurence-Moon-Biedl syndrome. N Engl J Med 1989; 321:1002-1009.*
3. *Beales PL, Elcioglu N, Woolf AS, Parker D, FlinterFA. New criteria for improved diagnosis of Bardet- Biedlsyndrome: results of a population survey. J Med Genet 1999; 36:437-446.*
4. *Laurence JZ, Moon RC. Four cases of retinintispigmentosa occurring in the same family, and accompanied by general imperfections of development. Obes Res 1995; 3:32-41.*
5. *Schathat AP, Maumenee IH. Bardet-Biedlsyndrome and related disorders. Arch Ophthal.1982. 100:285-288.*
6. *Fulton AB, Hansen RM, Glynn RJ. Natural course of visual functions in the Bardet-Biedl syndrome. Arch. Ophthalmo 1993; 111: 1500-1506.*
7. *Farag, T.I. and Teebi, A.S Highbincidence of BardetBiedl syndrome among the Bedouin. Clin Genet 1989; 36:463-464.*
8. *Croft JB, Morrell D, Chase CL and Swift M. Obesity in heterozygous carriers of the gene for the Bardet- Biedl syndrome. Am J Med Genet 55:12-15,1995*
9. *Kenneth lyons Jones. Bardet-Biedl syndrome: Smith's Recognizable Patterns of Human Malformation 5th edition, saunders company; 1997;590-591*
10. *Mehrotra N, Taub S, Covert RF. Hydrometrocolposas a neonatal manifestation of the Bardet-Biedlsyndrome. Am J Med Genet 1997; 69: 220.*
11. *Stoler JM, Herrin JT, Holmes LB. Genital abnormalities in females with Bardet-Biedlsyndrome. Am J Med Genet 1995; 55: 276-278.*
12. *Leppert M, Baird L, Anderson KL, et al. Bardet-Biedl syndrome is linked to DNA markers on chromosome 11q and is genetically heterogeneous.Nat Genet 1994; 7:108-12*
13. *Kwitek-Black AE, Carmi R, Duyk GM, et al. Linkage of Bardet-Biedl syndrome to chromosome 16q and evidence for non-allelic genetic heterogeneity. Nat Genet 1993; 5:392-6.*
14. *Sheffield VC, Carmi R, Kwitek-Black A, et al. Identification of a Bardet-Biedl syndrome locus onchromosome 3 and evaluation of an efficientapproach to homozygosity mapping. Hum MolGenet 1994; 3:1331-50.*
15. *Carmi R, Rokhlina T, Kwitek-Black AE, et al. Use of a DNA pooling strategy to identify a human obesity syndrome locus on chromosome 15. Hum MolGenet 1995; 4:9-13.*
16. *Bruford EA, Riise R, Teague PW, et al. Linkage mapping in 29Bardet-Biedl syndrome families confirms loci in chromosomal regions 11q13, 15q22.3-q23, and 16q21 Genomics 1997; 41:93-9.*
17. *Ansley SJ, BadanoJL, Blacque OE, Hill J, Hoskins BE, Leitch CC, et al. Basal body dysfunction is a likely cause of pleiotropic Bardet-Biedl syndrome. Nature 2003; 425:628-633.*
18. *Li JB, Gerdes JM, Haycraft CJ, Fan Y, TeslovichTM, May-Simera H, et al. Comparative genomics identifies a flagellar and basal body proteome that includes the BBS5 human disease gene. Cell 2004; 117:541-552.*
19. *Blacque OE, Reardon MJ, Li C, McCarthy J, Mahjoub MR, Ansley S, et al. Loss of C. elegans BBS-7 and BBS-8 protein function results in cilia defects and compromised intraflagellar transport. Genes Dev 2004; 18:1630-1642.*
20. *Pazour GJ, Rosenbaum JL. Intraflagellar transport and cilia-dependent diseases. Trends Cell Biol2000;12:551555.*