

**Bardet-Biedl Syndrome- A Case Report**Dr. Suraiya Begum<sup>1\*</sup>, Dr. Md. Benzamin<sup>2</sup>, Dr. Muhammad Rezaul Karim<sup>3</sup>, Dr. Abul Bashar Md Osman Hayder Mazumder<sup>4</sup><sup>1</sup>Associate Professor, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh<sup>2</sup>Resident, Department of Paediatric Gastroenterology Bangabandhu Sheikh Mujib Medical University, Bangladesh<sup>3</sup>Resident, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh<sup>4</sup>Resident, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Bangladesh**Case Report****\*Corresponding author**

Dr. Suraiya Begum

**Article History**

Received: 14.07.2018

Accepted: 28.07.2018

Published: 30.07.2018

**DOI:**

10.36347/sjams.2018.v06i07.051

**Abstract:** Bardet-Biedl syndrome (BBS) is a rare ciliopathic autosomal recessive genetic disorder. It presents with varied clinical manifestations like retinitis pigmentosa, polydactyly, central obesity, mental retardation and renal dysfunction. Other rare manifestations include diabetes mellitus, heart disease, hepatic fibrosis and neurological manifestations. Most of these symptoms may not be present at birth but appear and progressively worsen during the first and second decades of life. We, here, have presented a 4-year-old girl with features of Bardet-Biedl syndrome.**Key-wards:** Bardet-Biedl syndrome, Retinitis pigmentosa, Polydactyly, Obesity, Diabetes mellitu,**Abbreviations:** BBS- Bardet-Biedl syndrome.**INTRODUCTION**

Bardet-Biedl syndrome (BBS) is a rare genetic disorder with severe multi-organ impairment. Its frequency in Europe and North America is 1: 100,000 [1]. The incidence is much higher in some populations with a high level of consanguinity or those that are geographically isolated. Disease incidence of 1 in 3700 in the Faroe Islands and 1 in 17,000 live births in Kuwait [2]. Male to female ratio is approximately 1.3: 1 [3]. In Bangladesh, the actual prevalence rate is unknown. Mutations in at least 21 BBS genes have been identified as causative factors [4].

**CASE REPORT**

A 4-year-old girl, 3rd issue of consanguineous parents, admitted on October 2016 in the paediatric ward of Bangabandhu Sheikh Mujib Medical University with the complaints of excessive weight gain since 1 year of age and no micturition control yet.

On query, mother also gave history of polyphagia, polyuria, polydipsia, and poor vision. There was no history of constipation, palpitations, hearing impairment, breathing difficulty, dental problem, and limb weakness. She was delivered by caesarean section at term due to maternal gestational diabetes mellitus, birth weight was 5 kg. Postnatal history was not significant except for the anomaly of polydactyly in her three limbs. She had no history of developmental delay.

On examination, she had rounded face with double chin, gynecomastia and pendulous abdomen. (Figure 1) Her BP was 120/90 mm of hg (Both systolic and diastolic pressure lies above 99<sup>th</sup> centile). Her weight was 32 kg (above 97<sup>th</sup> centile), height was 106 cm (in between 75-90<sup>th</sup> centile) and body mass index was 28.5kg/m<sup>2</sup> (above 97<sup>th</sup> centile). Bedside urine for

albumin and sugar was negative. Musculoskeletal system examination revealed postaxial polydactyly in three limbs and short, broad, stubby fingers and toes (Figure 2). She had high arch palate. On eye examination, visual acuity was 6/60 in both eyes. Anterior segment was normal, fundus showed choroidoretinal mild pigmentary changes in both eyes. Psychological evaluation by IBAS showed total score was 25% of 4 year's Assessment. Cardiovascular system examination showed no abnormality. Investigations including CBC, urine analysis, ALT, X-ray chest, ECG and echocardiography were normal. Ultrasonography of whole abdomen revealed mild hepatomegaly with fatty change and both kidneys were normal. Hearing assessment was normal. Biochemistry revealed normal creatinine and ALT, raised TG (215 mg/dl; N-32-100mg/dl), and oral glucose tolerance test

showed fasting blood sugar was 5.00 mmol/L (N-4-6mmol/l) and 2 hours after glucose intake was 11.3mmol/L (N- <7.8mmol/l). Her serum cortisol level, and thyroid function was normal. We diagnosed the case as Bardet Biedl syndrome as our patient had 3 primary and 3 secondary features. As there is no specific curative therapy available for this syndrome. The girl was managed symptomatically. Genetic

counseling was done. The patient was discharged with diabetic diet, antihypertensive drug and regular physical activity, and capillary blood glucose monitoring was advised.

Four primary feature or three primary features and two secondary features are required for a clinical diagnosis of Bardet-Biedl syndrome [1].

**Table-1: Diagnostic features of Bardet-Biedl Syndrome**

Primary feature	Our case	Secondary feature	Our case
Rod-cone dystrophy (93%)	+	Speech disorder/delay (54-81%)	-
Polydactyly (63-81%)	+	Strabismus/cataracts/astigmatism	-
Obesity (72-92%)	+	Brachydactyly/syndactyly (6-100%/8-95%)	+
Learning disabilities (61%)		Developmental delay (50-91%)	-
Genital anomalies (59-98%)		Ataxia/poor coordination /imbalance (40-86%)	-
Renal anomalies (53%)		Spinal problem	-
		Mild spasticity (especially lower limbs)	-
		Diabetes mellitus (6-48%)	+
		Dental crowding/ hypodontia/ Small roots/high arched plate (51%)	+
		Congenital heart disease (7%)	-
		Hepatic fibrosis	-
		Anosmia/hyposmia (60%)	



**Fig-1: Shows rounded face with double chin, gynecomastia and pendulous abdomen**



**Fig-2: Shows poly-dactyly of both upper limbs and right lower limb**

## DISCUSSION

Bardet-Biedl syndrome was named after Georges Louis Bardet, a French physician and Artur Biedl, a Hungarian Pathologist and endocrinologist. It is a genetically determined heterogeneous autosomal recessive condition. At present, there are already 21 known BBS genes (*BBS1–BBS20* and *NPHP1*) and their number is likely to increase due to the invention of exome sequencing and analysis of previously unstudied populations [4]. Among them, *BBS1* and *BBS10* are the two main genes involved in BBS and each of this gene mutation is present in more than 20% of the cases [5]. The detailed biochemical mechanism that leads to BBS is still unclear. It is caused by defects in the cellular ciliary structure and hence it is a ciliopathy [5]. The first known case was reported by Laurence and Moon in 1886 and there was a controversy in medical literature with the condition described by Laurence and Moon, referred as Laurence-Moon syndrome (LMS). After 22 years, prospective cohort study of Newfoundland families with BBS, Moore et al concluded that BBS and LMS are different spectrum of same entity [6]. BBS is distinguished from the much rarer LMS, in which retinal pigmentary degeneration, mental retardation and hypogonadism occur in conjunction with progressive spastic paraparesis and distal muscle weakness, but without polydactyly [7].

The primary and secondary features of BBS are given in Table I. The diagnosis of BBS can be made if four primary, or three primary and two secondary features are observed [3]. Our patient had retinitis pigmentosa and decreased visual acuity. Retinitis pigmentosa is one of the hallmarks of this disorder and found occasionally in the first decade but usually present in almost all patients by second decade. Decreased visual acuity can result from macular involvement of the disease. The patient was obese with hepatomegaly which was may be due to fatty change of liver. He had dyslipidemia associated with obesity. Obesity present in 75% of patients usually begins in the childhood and the severity increases with age [3]. Cause of obesity is unknown but appears to be the effect of a combination of hyperphagia and altered disposal of calories [3]. Learning disability is a primary feature of BBS, which is probably due to moderate mental retardation and decreased visual acuity, our patient has both mental retardation and decreased visual acuity. Limb deformities have been reported at varying frequencies. Of these, polydactyly, and brachydactyly of both hands and feet are most common [3]. Hypogonadism is reportedly more frequently present in BBS males than females [1]. A wide range of renal abnormalities such as chronic renal failure, parenchymal cysts, calyceal clubbing, fetal lobulation, scarring, unilateral agenesis, dysplastic kidneys, renal calculi, and vesico-ureteric reflux has been described but our patient had no renal abnormalities. Renal failure is the major cause of morbidity and early mortality in

BBS and 25% die by the age of 44 years [9]. Renal function was found to be normal in our patient. Diabetes mellitus is diagnosed in 32–45% of cases with BBS and it is usually Type 2 but occasionally Type 1 [9]. Our patient had diabetes mellitus and was controlled by dietary measure and physical activity; diabetes mellitus was also observed by Haque M [10]. Hussain et al. reported a case of BBS in our country in a twelve year old boy having all the cardinal features such as obesity, mental deficiency, polydactyly, syndactyly, retinopathy, genital hypoplasia and renal anomalies [11]. Our patient had three primary features such as polydactyly, retinitis pigmentosa, obesity and three secondary features such as diabetes mellitus, brachydactyly, and high arch palate. Some authors also mention hypertension, liver abnormalities, bronchial asthma, otitis, rhinitis, craniofacial dysmorphism [1,12]. Our patient had hypertension treated with antihypertensive drug.

Diagnosis of Bardet-Biedl syndrome is mainly based on characteristic clinical features. Investigations are done to assess the features that may help in the diagnosis. Genotyping of Bardet-Biedl syndrome may not always be required to make the diagnosis as it is not available at all places specially developing countries like Bangladesh. Multidisciplinary approach is needed for management of Bardet-Biedl syndrome. Regular monitoring of renal function, liver function, blood glucose, lipid and endocrine profile is necessary. Attention should be given to blood pressure control and weight management along with regular ophthalmological examination. Visual aids, special schools and educational programs to overcome learning disabilities are important. Speech therapy, behavioral therapy and hormone replacement therapy are required in many cases. Surgical removal of accessory digits may be necessary for cosmetic purpose.

## CONCLUSION

Many progresses have been made about this disease. Further studies are needed to understand the pathophysiology and genetic complexity of the disease. Though the disease is incurable, careful evaluation and symptomatic management may provide good prognosis.

## ACKNOWLEDGEMENT

We gratefully acknowledge the work of the ophthalmology and neurology department, BSMMU.

## REFERENCES

1. Forsythe E, Beales PL. Bardet-Biedl syndrome. *European journal of human genetics*. 2013 Jan;21(1):8.
2. Hjortshøj TD, Grønskov K, Brøndum-Nielsen K, Rosenberg T. A novel founder *BBS1* mutation explains a unique high prevalence of Bardet-Biedl syndrome in the Faroe Islands. *British Journal of Ophthalmology*. 2008 Jul 31.

3. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *Journal of medical genetics*. 1999 Jun 1;36(6):437-46.
4. Suspitsin EN, Imyanitov EN. Bardet-biedl syndrome. *Molecular syndromology*. 2016;7(2):62-71.
5. Kumar S, Mahajan BB, Mittal J. Bardet-Biedl syndrome: A rare case report from North India. *Indian Journal of Dermatology, Venereology, and Leprology*. 2012 Mar 1;78(2):228.
6. Moore SJ, Green JS, Fan Y, Bhogal AK, Dicks E, Fernandez BA, Stefanelli M, Murphy C, Cramer BC, Dean JC, Beales PL. Clinical and genetic epidemiology of Bardet-Biedl syndrome in Newfoundland: A 22-year prospective, population-based, cohort study. *American journal of medical genetics Part A*. 2005 Feb 1;132(4):352-60.
7. Schachat AP, Maumenee IH. Bardet-Biedl syndrome and related disorders. *Archives of Ophthalmology*. 1982 Feb 1;100(2):285-8.
8. O'Dea D, Parfrey PS, Harnett JD, Hefferton D, Cramer BC, Green J. The importance of renal impairment in the natural history of Bardet-Biedl syndrome. *American journal of kidney diseases*. 1996 Jun 1;27(6):776-83.
9. Ross AJ, Beales PL. Bardet-Biedl syndrome. *Gene Reviews*. Available from <http://www.geneclinics.org/profiles/all.html>.
10. Haque M, Alam MF, Begum S, Rahman SA. Bardet-Biedl syndrome. *Bangabandhu Sheikh Mujib Medical University Journal*. 2016 Jan 1;9(2):119-22.
11. Hossain K, Badruddoza M. Bardet-Biedl syndrome: A case report. *Chattagram Maa-O-Shishu Hospital Med College J*. 2013; 12: 67-69.
12. Baker K, Beales PL. Making sense of cilia in disease: the human ciliopathies. In *American Journal of Medical Genetics Part C: Seminars in Medical Genetics* 2009 Nov 15 (Vol. 151, No. 4, pp. 281-295). Hoboken: Wiley Subscription Services, Inc., A Wiley Company.