CASE REPORT

A CASE REPORT OF BARDET-BIEDL SYNDROME: EMPHASIZING GENETIC COMPLEXITY AND MULTIDISCIPLINARY MANAGEMENT

Dua.B. Zaidi[1], Daayl Naim Mirza[2], Romesa Jamshed[2], Inshal Jawed[3]

[1]Karachi Institute of Medical Sciences, Karachi-Pakistan
[2]Ziauddin University, Karachi-Pakistan
[3]Dow University of Health Sciences, Karachi-Pakistan

Bardet-Biedl Syndrome (BBS) is a rare autosomal recessive ciliopathy presenting with multisystemic manifestations. We report a case of a 17-year-old female with BBS who presented with life-threatening kidney disease. The patient exhibited classic BBS features, including retinal dystrophy, polydactyly, obesity, and cognitive impairment. Genetic analysis revealed consanguinity, underscoring the link between familial history and increased disease likelihood. This case highlights the importance of early genetic studies, comprehensive multidisciplinary care, and genetic counseling for affected families to improve patient outcomes and guide subsequent pregnancies.

Keywords: Bardet-Biedl Syndrome (BBS); Ciliopathy; Autosomal recessive; Multisystemic manifestations; Genetic counseling; Chronic kidney disease

Citation: Jawed I, Zaidi DB, Mirza DN, Jamshed R. A case report of Bardet-Biedl Syndrome: Emphasizing genetic complexity and multidisciplinary management. J Ayub Med Coll Abbottabad 2025;37(2):254–8.

DOI: 10.55519/JAMC-02-13213

INTRODUCTION

Bardet-Biedl syndrome (BBS) is a rare pleiotropic autosomal recessive ciliopathy mostly occurring in children born from non-consanguineous marriages.[1] Primary features of rod-cone dystrophy, polydactyly, obesity, hypogonadism, kidney alteration, and behavioral dysfunction characterize it. Other manifestations include diabetes mellitus, heart disease, hepatic fibrosis, neurological features, and multiple pigmented nevi.[2]

The expression of BBS varies from person to person, so it was essential to establish a criterion for diagnosis, which was made by Forsythe and Beales, who derived that the existence of either four major characteristics or three majors, together with two minor traits, is sufficient to formulate the prompt diagnosis.[3]

In earlier years, Laurence-Moon-Bardet-Biedel (LMBBS) syndrome was the coined term for this genetic disorder, referred to as a single syndrome. Subsequent research showed that LMBBS comprised two disorders; Bardet-Biedl syndrome and Laurence-Moon syndrome which shared common features.[4] The overlapping features include pigmentary retinal degeneration, mental impairment, hypogonadism, and renal degeneration. Specifically, LMS primarily manifests with progressive spastic paraplegia and distal muscle weakness, while polydactyl and central obesity are predominately seen in BBS.[5]

The prevalence of Bardet-Biedl syndrome in most of North America and Europe is estimated to be 1 in 140,000 to 1 in 160,000 in northern European populations. It occurs more frequently in Newfoundland where it occurs 1 in 17,000 newborns, and even more frequently in the Bedouin population of Kuwait, where it affects about 1 in 13,500 newborns.[6] Renal dysfunction was established as a primary cause of high mortality rate in BBS.[7] BBS being a rare disease may have a delayed diagnosis and result in complications. Here, we present a case of a 17-year-old female, previously diagnosed with Bardet-Biedl syndrome, who presents to the clinic with advanced, life-threatening kidney disease.

CASE PRESENTATION

A 17-year-old female reported to the emergency department with complaints of severe headache, shortness of breath, nausea, and vomiting for one day. The patient's attendant recounted that just a day ago, she had been in her usual state of health, but then suddenly experienced a headache, sudden in onset, sharp, severe, continuous with increasing intensity, associated with nausea, vomiting, and loss of appetite, she also had shortness of breath, sudden, progressive in nature, at rest, associated with an overwhelming sense of apprehension.

This marked her third visit to the emergency room within a single month, each time with similar distressing complaints. Her arterial blood gas analysis unveiled a troubling picture of

metabolic acidosis, with a pH of 7.198, $cHCO_3$ of 7.4 mmol/L, PCO_2 of 19.4 mmHg, and PO_2 of 138.2.

According to her mother, she was born overweight, with polydactyly in both hands and had trouble reaching developmental milestones at times; she specifically mentioned that she learned to sit and walk at the age of 1 year and 2.5 years, respectively. She had trouble with vision from an early age; it was difficult to see in the dark. Despite starting school at 4, learning difficulties forced her to discontinue. She reached menarche at the age of 13 but had an irregular menstrual cycle. The parents have a consanguineous marriage; they had two other children born with polydactyly, and both died at the age of 4 months and 10 years, respectively, due to unknown reasons.

The clinical examination showed a young female of 153 cm in height and 60 kg weight falling into the overweight category with a BMI of 25.6. She was well-oriented with time, place, and person. Multiple hyperpigmented patches were observed on the face, neck, abdomen, and back [Figure 2], depressed nasal bridge and edematous face [Figure 3], postaxial polydactyly in both hands [Figure 1], short disfigured toes [Figure 4], central obesity. Neurological examination exposed a low intellectual quotient and a Glasgow Coma Score of 13/15.

Further examination unveiled ocular abnormalities—squints in both eyes and fundoscopy revealing bilateral white flakes with retinal atrophy and bony spicules, giving the impression of retinitis albipunctatus. The genital examination revealed adequately formed genitalia but a lack of pubic and axillary hair. BP and pulse were 100/80 mmHg and 100 bpm respectively.

To form a primary diagnosis, we carried out a few investigations, including a complete blood count, which revealed hemoglobin of 8.9 g/dL; renal function tests, showing urea and creatinine levels of 63 mg/dl and 5.45 mg/dl, respectively; Parathormone levels of 476 Pg/ml. Her thyroid profile was average, and viral markers were negative. [Table 1].

Ultrasound Abdomen showed bilateral echogenic kidneys leading to parenchymal changes and irregular margins. Echocardiography revealed mild Tricuspid Regurgitation and an ejection fraction of 71%. Based on this, we excluded our differential diagnosis of Renal Tubular Acidosis by the presence of polydactyly, developmental delays, vision problems, and other systemic abnormalities. We had Homocystinuria in mind, which could explain developmental delays, intellectual impairment, and ocular abnormalities. Still, the absence of typical findings such as thromboembolism and skeletal abnormalities also ruled it out.

Considering the patient's polydactyly, obesity, vision issues, and renal anomalies, we explored Bardet-Biedl Syndrome (BBS) as a potential diagnosis. Following insights from Forsythe and Beales[8] [Table 2], all these symptoms align with BBS characteristics, providing a basis for further investigation and management. The parents of the child were counseled and advised for urgent dialysis due to recurrent episodes of metabolic episodes, after which there was visible betterment in her health. Hence, the patient was discharged on conservative management and called for regular follow-up to observe whether any progressive renal changes developed.

Two weeks later, she was rushed back to the Emergency Room with complaints of severe headache and shortness of breath. Her Glasgow Coma Scale (GCS) was measured at 5 out of 15, blood pressure at 80/40 mmHg, pulse rate at 120 beats per minute, and oxygen saturation (SPO2) at 70%. Laboratory tests revealed severe metabolic acidosis. Her parents were counseled once again for immediate dialysis, and they agreed, but unfortunately, the patient passed away before treatment could begin.

Figure-1: Postaxial Polydactyly

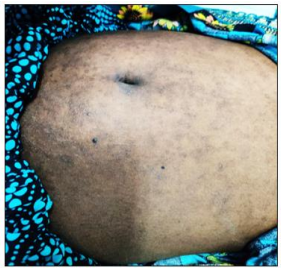

Figure-2: Hyper-pigmented patches on the abdomen

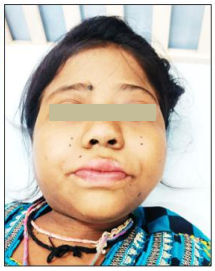

Figure-3: Facial edema and depressed nasal bridge

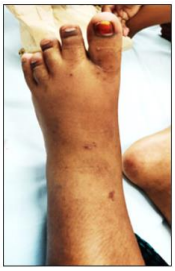

Figure-4: Disfigured toes

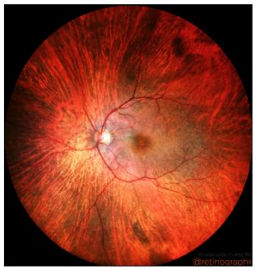

Figure-5: Fundus Albipunctatus

Table-1: Blood and Serum Laboratory Findings

Renal Function Tests	Patient Values	Reference Values
Serum Urea	63 mg/dl	10-50 mg/dl
Creatinine	5.45 mg/dl	0.8-1.3 mg/dL
Electrolytes		
Serum Sodium	139 mEq/L	136-149 mEq/L
Serum Potassium	4.2 mEq/L	3.8-5.2 mEq/L
Serum Chloride	117 mEq/L	98-107 mEq/L
Liver Function Tests		
Alanine aminotransferase	10 U/L	5-30 U/L
Alkaline Phosphatase	357 U/L	50-100 U/L
Total Protein A/G Ratio		
Total Protein	6.8 g/dl	6.6-8.7 g/dl
Albumin	2.9 g/dl	3.8-4.4 g/dl
Calcium	6.2 mg/dl	8.1-10.4 mg/dl
Phosphorus	5.2 mg/dl	2.5-4.8 mg/dl
C-Reactive Protein	1.1 mg/dl	<5.0mg/dl
Complete Blood Count		
Haemoglobin	8.9 g/dl	12-15 g/dL
Haematocrit	27.2%	36%-47%
M.C.V	86.9 fl	80-100 fL
M.C.H	28.4 pg	27-32 pg
M.C.H.C	32.7 g/dl	30-35 g/dl
RBC Count	3.13x10^12/L	4.0-5.5 x 10^12/L
Platelet Count	190x10^9/L	140-400 x1 0^9/L
Total Leukocyte Count	7.9x10^9/L	4-10 x 10^9/L
Neutrophils	64%	50-75%
Eosinophils	05%	01-06%
Lymphocytes	25%	25-40%
Monocytes	06%	02-10%

Table 2. Diagnostic Criteria of BBS

Diagnostic criteria	FEATURES
Primary features	Rod-cone dystrophy
	Polydactyly
	Obesity
	Learning disabilities
	Hypogonadism in males
	Renal anomalies
Secondary features	Speech disorder/delay
	Strabismus/cataracts/astigmatism
	Brachydactyly/syndactyly
	Developmental delay
	Polyuria/polydipsia (nephrogenic diabetes insipidus)
	Ataxia/poor coordination/imbalance
	Mild spasticity (significantly lower limbs)
	Diabetes mellitus
	Dental crowding/hypodontia/small roots/high-arched palate
	Left ventricular hypertrophy/congenital heart disease
	Hepatic fibrosis

DISCUSSION

Bardet-Biedl syndrome is associated with at least twenty genes (BBS1-BBS20) and follows an oligogenic inheritance pattern. The BBS protein present within centromeres is responsible for regulating the formation and functioning of cilia. In BBS, the functioning of systemic organs containing ciliated cells is compromised, leading to systemic manifestations.[9] About 25% of all cases of BBS stem from mutations within the BBS1 gene, while 20% result from a mutation in the BBS10 gene. The other BBS genes contribute to a smaller proportion of total cases; meanwhile, in one-fourth of patients, the precise cause remains unknown.[10]

There appears to be a greater incidence of BBS in regions with a customary practice of intra-familiar marriage.[3] The patient's parents had a consanguineous marriage, which significantly increases the likelihood of the disease. In addition to that, the patient whose two siblings died due to unexplained reasons also exhibited symptoms of polydactyly, indicating a potential genetic link. The BBS phenotype typically undergoes a slow progression over the first decade of a person's life, although some notable variabilities exist.[8] As a result,

most patients are diagnosed either in late adulthood or late childhood. The average age of diagnosis is nine years[11], although there are cases where the diagnosis was made in the second to the fifth decade of life. This late diagnosis speaks for the delayed manifestations of the symptoms. However, our patient was 17 years old when she presented to the hospital with fatal complications.

Our patient checked all the primary features of the disease, including some secondary features. She had central obesity, polydactyly in both hands, retinal findings, hypogonadism, and cognitive impairment with renal dysfunction. Retinal dystrophy is a hallmark of the disorder, occasionally manifesting during the first decade of the patient's life, but by the second decade, it is present in nearly all cases.[12] Our patient's ophthalmic evaluation concluded she had retinitis albipunctatus, which is a form of retinal dystrophy characterized by depositions of white or yellow flakes (punctate deposits, which are accumulations of lipofuscin) in the retina, resulting in the patient experiencing symptoms of night blindness. Typically, night blindness in patients with BBS results from degeneration of photoreceptors within the retina, primarily affecting the rods responsible for low light and night vision. Although retinitis pigmentosa is a more prevalent ophthalmologic clinical finding in a patient with Bardet-Beidel syndrome, it is to be noted that BBS exhibits a multifaceted genetic mutation that results in the manifestation of the entire syndrome. Her eye examination further revealed strabismus in both eyes, one of the disease's secondary features.

Obesity is another significant clinical finding in our patient, which is usually present in most patients with BBS, with the prevalence ranging from 72% to 86%.[3] Typically, patients with BBS present with an average birthweight, and after one year of age, they start getting obese. But there are cases where they are overweight from birth, just like our patient who had a high birth weight. Fat distribution is widespread in children and truncal in adulthood.[6] Secondary diabetes mellitus is also a common finding in patients. The patient had polydactyly in both hands along with short, disfigured toes. Post axial dactyl is present in 69% of patients by birth and other limb deformities of varying frequencies.[3] Moreover, learning disability and cognitive impairment are other important indicators of the syndrome. Additionally, her delayed developmental milestones prove further evidence for a lower IQ.

Hypogonadism is another significant finding, with it being more common in males than in females.[13] Our patient had a delay in the development of her secondary sexual characteristic, which was confirmed upon her genital examination when an absence of pubic hair (along with axillary hair) was observed. Furthermore, she had her menarche at 13 years of age with an irregular menstrual cycle. These findings are consistent with the characteristics portrayed in individuals having Bardet-Biedl Syndrome.[14]

Renal malformations have increased the incidence of BBS, with our patient presenting to the clinic with chronic end-stage renal failure.[13] The patient's lab suggests her CKD leads to the development of uremia and metabolic acidosis, which emerges as an essential contributor to heightened morbidity rate and premature mortality. Furthermore, the loss of calcium and phosphate through the urine due to renal insufficiency leads to the patient exhibiting high levels of PTH to restore the blood calcium. The patient underwent an assessment that determined the necessity for dialysis, leading to substantial improvement in her condition. She was discharged and sent home upon reaching a stable state. However, during a subsequent emergency visit to the hospital, her guardians were once again counseled for the urgent need for dialysis, to which they agreed. She away before her treatment process could begin.

Involvement of other organs is also likely. Cardiovascular manifestations are standard secondary features presented in patients with BBS. They are present in 50% of patients, so it's essential to do an EEG in all patients presenting with the syndrome.[15] The type of cardiovascular anomaly is variable; however, patients are more likely to have valvular stenosis, patent ductus arteriosus, and cardiomyopathies.[8] Our patient presented with mild tricuspid regurgitation and ejection fraction of 71%, which is an overall minor finding in the assessment of BBS since it's a relatively benign condition.

When treating Bardet-Biedl syndrome, a multidisciplinary approach is necessary to ensure the patient's good quality of life. The available treatments primarily focus on managing the manifestations of the condition.[16] Families should be offered genetic counseling to guide them about the risk of the disease in subsequent pregnancies. In the context of the patient, had a genetic study been conducted when her deceased siblings presented with similar conditions, it would have been easier for the parents to anticipate and understand the outcomes of the disease, providing them with valuable information.[13] Genetic testing is a costly process, and in a country where a substantial portion of the population struggles from poverty, assessing and affording such medical services becomes even more challenging.

CONCLUSION

In conclusion, Bardet-Biedl Syndrome (BBS) presents a complex clinical landscape, with at least twenty associated genes and an oligogenic inheritance pattern. The disorder, characterized by compromised systemic organ function due to ciliary regulation disruption, exhibits genetic heterogeneity, with BBS1 and BBS10 mutations being predominant. Consanguinity is linked to a higher incidence, as evident in cases like the one

presented here, where familial history and intra-familiar marriage increased disease likelihood. Clinical manifestations vary, with a slow progression over the first decade, late diagnoses, and the case of a 17-year-old patient highlighting the syndrome's diverse clinical course. The patient exhibited primary and secondary features, encompassing retinal dystrophy, obesity, polydactyly, cognitive impairment, hypogonadism, and renal dysfunction. Ophthalmologic, metabolic, limb and mental complications contribute to the multisystemic syndrome. The significance of genetic counseling, early genetic studies, and a multidisciplinary approach to management, including nephrological and cardiac evaluations, underscores the necessity for comprehensive care in addressing the challenges posed by BBS, guiding families, and improving the quality of life for affected individuals.

Declarations

Ethics approval and consent to participate: Ethical approval was not required to conduct it as this was a case report. Written informed consent was obtained from the patient's representative.

Consent for publication:

Consent for publication patient's pictures featuring characteristics disorder has been obtained prior submission.

Data availability:

The authors confirm that the data supporting the findings of this study are available within the case report.

Conflicts of interest:

There is no conflict of interest among the authors.

Funding:

N/A

Authorship Statement

Author (1) has made substantial contributions to the conception and design and Author (2) been involved in drafting the manuscript or revising it critically for important intellectual content; and Author (3) gives final approval of the version to be published; and Author (4) agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgments

N/A

REFERENCES

1. Fan Y, Rahman P, Peddle L, Hefferton D, Gladney N, Moore SJ, *et al*. Bardet–Biedl syndrome one genotype and obesity in the Newfoundland population. Int J Obes Relat Metab Disord 2004;28(5):680–4.
2. Karaman A. Bardet-Biedl syndrome: a case report. Dermatol Online J 2008;14(1):9.
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. J Med Genet 1999;36(6):437–46.
4. Moore SJ, Green JS, Fan Y, Bhogal AK, Dicks E, Fernandez BA, *et al*. Clinical and genetic epidemiology of Bardet–Biedl syndrome in Newfoundland: A 22-year prospective, population-based, cohort study. Am J Med Genet A 2005;132(4):352–60.
5. Parameswarappa DC, Das AV, Thakur PS, Takkar B, Multani PK, Padhy SK, *et al*. Retinitis pigmentosa in Laurence-Moon-Bardet-Biedl syndrome in India: Electronic medical records driven big data analytics: Report II. Indian J Ophthalmol 2022;70(7):2533–8.
6. Katsanis N, Lupski JR, Beales PL. Exploring the molecular basis of Bardet–Biedl syndrome. Human Mol Genet 2001;10(20):2293–9.
7. Williams B, Jenkins D, Walls J. Chronic renal failure; an important feature of the Laurence-Moon-Biedl syndrome. Postgrad Med J 1988;64(752):462–4.
8. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet 2013;21(1):8–13.
9. Priya S, Nampoothiri S, Sen P, Sripriya S. Bardet-Biedl syndrome: Genetics, molecular pathophysiology, and disease management. Indian J Ophthalmol 2016;64(9):620–7.
10. MedlinePlus. Bardet-Biedl syndrome [Internet]. Bethesda (MD): National Library of Medicine (US); 2013 [cited 2025 April 2]. Available from: https://medlineplus.gov/genetics/condition/bardet-biedl-syndrome/
11. Esposito G, Testa F, Zacchia M, Crispo AA, Di Iorio V, Capolongo G, *et al*. Genetic characterization of Italian patients with Bardet-Biedl syndrome and correlation to ocular, renal and audio-vestibular phenotype: identification of eleven novel pathogenic sequence variants. BMC Med Genet 2017;18(1):10.
12. Fulton AB, Hansen RM, Glynn RJ. Natural course of visual functions in the Bardet-Biedl syndrome. Arch Ophthalmol 1993;111(11):1500–6.
13. Qadar LT, Ahmed ZM, Munawar M, Hasan CA, Iqbal SU. Laurence-Moon-Bardet-Biedl Syndrome with Coexisting Abdominal Distension and Positive Fluid Thrill: A Rare Manifestation Reported in Karachi, Pakistan. Cureus 2019;11(6):e4885.
14. 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(15):1002–9.
15. Elbedour K, Zucker N, Zalzstein E, Barki Y, Carmi R. Cardiac abnormalities in the Bardet-Biedl syndrome: echocardiographic studies of 22 patients. Am J Med Genet 1994;52(2):164–9.
16. Khan BA, Shahid A, Nazir MB, Khan KS, Punshi A. Laurence-Moon-Bardet-Biedl syndrome: a case report. Cureus 2019;11(9):e5618.

Submitted: April 7, 2024	*Revised: June 19, 2024*	*Accepted: May 21, 2025*

Address for Correspondence:

Inshal Jawed, Dow University of Health Sciences, Karachi-Pakistan

Email: inshaljwd@gmail.com