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Available online at: http://www.iajps.com *A Case Report*

LAURENCE MOON-BARDET BIEDL SYNDROME: A CASE REPORT OF A YOUNG FEMALE

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Abstract:

Laurence Moon-Bardet-Biedl syndrome is a rare autosomal recessive genetic disorder that mainly affects the limbs and eyes, with symptoms typically appearing during early childhood. The condition, like most other cases with an autosomal recessive genetic pattern, results from consanguineous marriage. The primary features of this syndrome include cone-rod dystrophy, polydactyly, obesity, learning disabilities, hypogonadism, renal anomalies, nystagmus, speech disorders, developmental delay, polyuria/polydipsia, ataxia, and poor coordination/clumsiness.

Diagnosing LM-BB syndrome involves careful clinical observation, and in 80% of cases, confirmation can be obtained through gene sequencing of known disease-causing genes. BBS genes encode proteins that play a crucial role in cilia biogenesis and function, localizing to the cilia and basal body. Mutations in these genes lead to defective cilia, which contribute to the diverse range of effects observed in individuals with LM-BBS.

We report a case of 13-year-old girl with all five recognised features of Laurence moon -Bardet Beidel syndrome: pigmentary retinopathy, polydactyly, obesity, mental retardation and hypogonadism. The patient presented with fatigue lasting for the last two weeks. Upon testing, her blood work revealed severe anemia, which was treated accordingly and found to be linked to poor food intake.

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INTRODUCTION:

Laurence-Moon-Bardet-Biedl syndrome (LMBBS) is a rare autosomal recessive disorder classified as a ciliopathy. It is known for its pleiotropic effects and often occurs in children born from consanguineous marriages. Typically, symptoms appear during the early years of life, with poor night vision being one of the initial signs [1]. The diagnosis of this condition is based on the presence of four primary features independently or three primary features combined with two secondary features. The primary features include cone-rod dystrophy, polydactyly, obesity, learning disabilities, hypogonadism in males, and renal anomalies. The secondary features encompass speech disorders, brachydactyly, developmental delay, polyuria/polydipsia, ataxia, poor coordination/clumsiness, diabetes mellitus, left ventricular hypertrophy, hepatic fibrosis, spasticity, and hearing loss. Additionally, other reported features include short stature, crowding of teeth, hypermobile or lax joints, and early osteoarthritis [2]. The classic pentad includes retinal dystrophy (93%), obesity (91%), retardation (87%), hypogonadism (74%), and polydactyly (73%).[3]

Diabetes mellitus type 2 is prevalent among individuals with this syndrome. One of the distinctive features is postaxial polydactyly, characterized by the presence of an extra digit in either the hand or the toe, which is a prominent and unique finding. Additionally, hypogonadism is another noteworthy manifestation, more commonly diagnosed early in males due to evident micropenis and small testes. In females, the disease may lead to underdeveloped uterus and fallopian tubes, accompanied by menstrual abnormalities, while delayed puberty is typical for both genders.[4]

Cognitive disorders and renal impairment are also frequent clinical manifestations. Patients may experience confusion, impaired memory, poor judgment skills, and uncoordinated, clumsy motor movements. Renal impairment remains a major cause of mortality, as end-stage renal disease is a frequent complication in these cases. Overall, LMBBS is a rare syndrome characterized by multi-organ involvement with varying degrees of complications and an unpredictable lifespan.[5]

We present a rare case of LMS syndrome presented to us with all the typical features of the LMS-BB Syndrome.

Case Presentation:

A 13-year-old girl with a previously diagnosed LMBBS presented to the outpatient department with complaints of fatigue and nausea lasting for two weeks. According to her mother, the patient was in her usual state of health before experiencing appetite loss and body aches. Initial laboratory tests, including complete blood count, urine analysis, and chest X-ray, revealed an RBC count of 2.23, Hb of 6.4, MCV of 90.3, and MCHC of 14g/dl, indicating anemia as the primary concern.

During her inpatient stay, further investigations were conducted, including VIT B12, basic metabolic panel, Malarial parasite, peripheral smear, thyroid levels, viral profile, ANA antibodies, urinalysis, Hba1c, clotting profile, TIBC, and serum ferritin. Raised ferritin levels and slightly elevated Hba1c (6.9) were noted, while other test results were within normal limits. Her ANA profile was also negative.

The patient's medical history revealed delayed developmental milestones, with the patient learning to walk and speak at the age of four. Additionally, the patient's brother also suffered from the same genetic abnormality, resulting in both children being mentally unfit. The mother mentioned that the patient was born out of a consanguineous marriage, and there were no complications during pregnancy or delivery.

Upon detailed clinical examination, the patient was found to be a young girl of short height and central obesity (BMI of 28 kg/m2). She displayed round facial features with frequent eye blinking and head nodding. Polydactyly was observed in right hand and both feet. CNS examination revealed a low Intelligent Quotient and a Glasgow Coma Scale score of 13/15, with intact gag and cranial reflexes. The patient exhibited bilateral nystagmus, and fundoscopy revealed retinitis pigmentosa. Genital examination showed hypogonadotropic features, including an underdeveloped vagina and absent pubic hairs. The chest examination revealed underdeveloped breasts.

Laboratory Findings: During her inpatient stay, repeat blood tests showed Hb of 6.6g/dl, mean corpuscular volume of 90.3, mean corpuscular haemoglobin concentration of 14g/dl, white blood cell count of 9.4g/dl, and platelet count of 150*103. The RBC morphology was normochromic with anisocytosis and normocytic. Iron studies revealed normal total iron binding capacity and raised ferritin. Vitamin B12 levels were normal, as were TSH studies and Beta HCG.

Management: The patient was hospitalized for four days, during which she received packed RBC transfusions, IV fluids, and nutritional support in the form of milk. The patient's symptoms improved, and she was discharged with a follow-up appointment in a week. The patient's mother was advised to adhere to a strict dietary plan for both her daughters and was provided with nutritional supplements, including vitamin A.

Conclusion: This case highlights the clinical presentation, laboratory findings, and management of a 13-year-old girl with Laurence-Moon Syndrome and Bardet-Biedl Syndrome. LMBBS is a rare genetic disorder that can lead to various physical and intellectual impairments. Early diagnosis and appropriate management can significantly improve the quality of life for affected individuals. Further research is needed to better understand the underlying pathophysiology and develop targeted therapies for this complex syndrome.

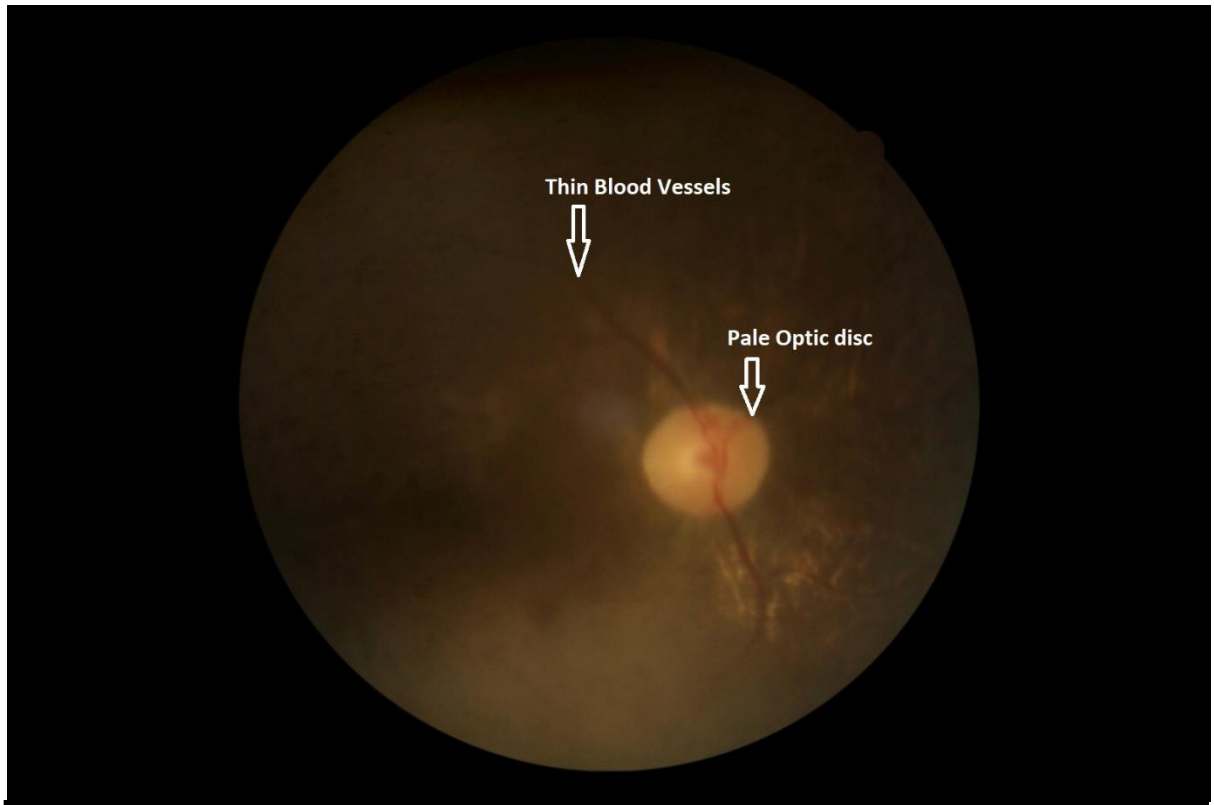

FIGURE:1 Fundoscopy showing **thin blood vessels** and **pale optic disc**

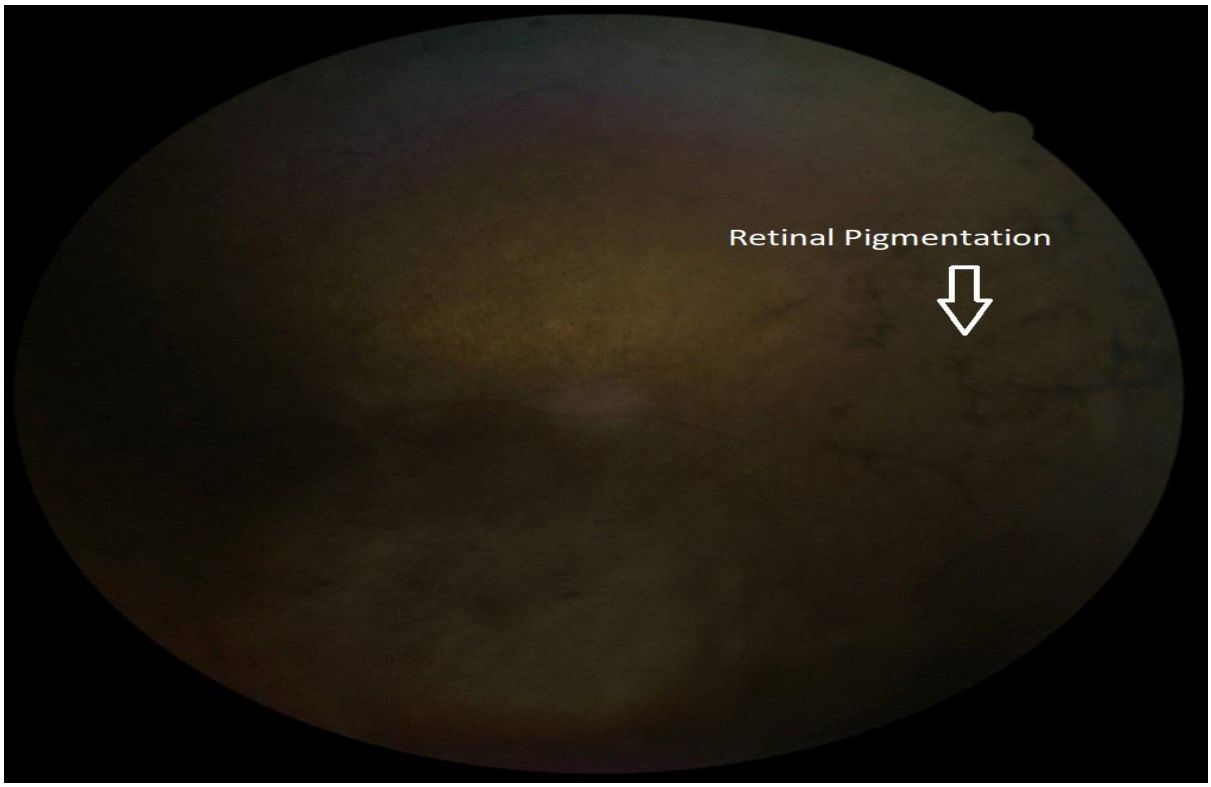

Figure:2 Fundoscopy showing **Retinal Pigmentation**

Fig.1 and Fig.2 are showing 'Features of Retinitis Pigmentosa"

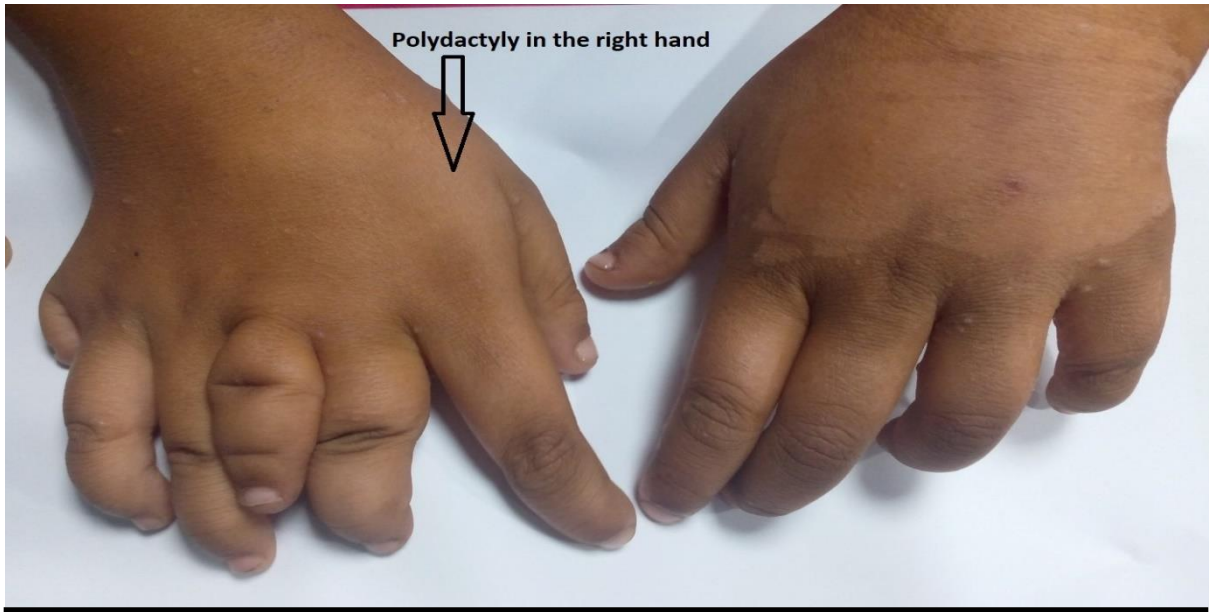

Fig.3: Showing **Polydactyly** in the right hand with normal left hand

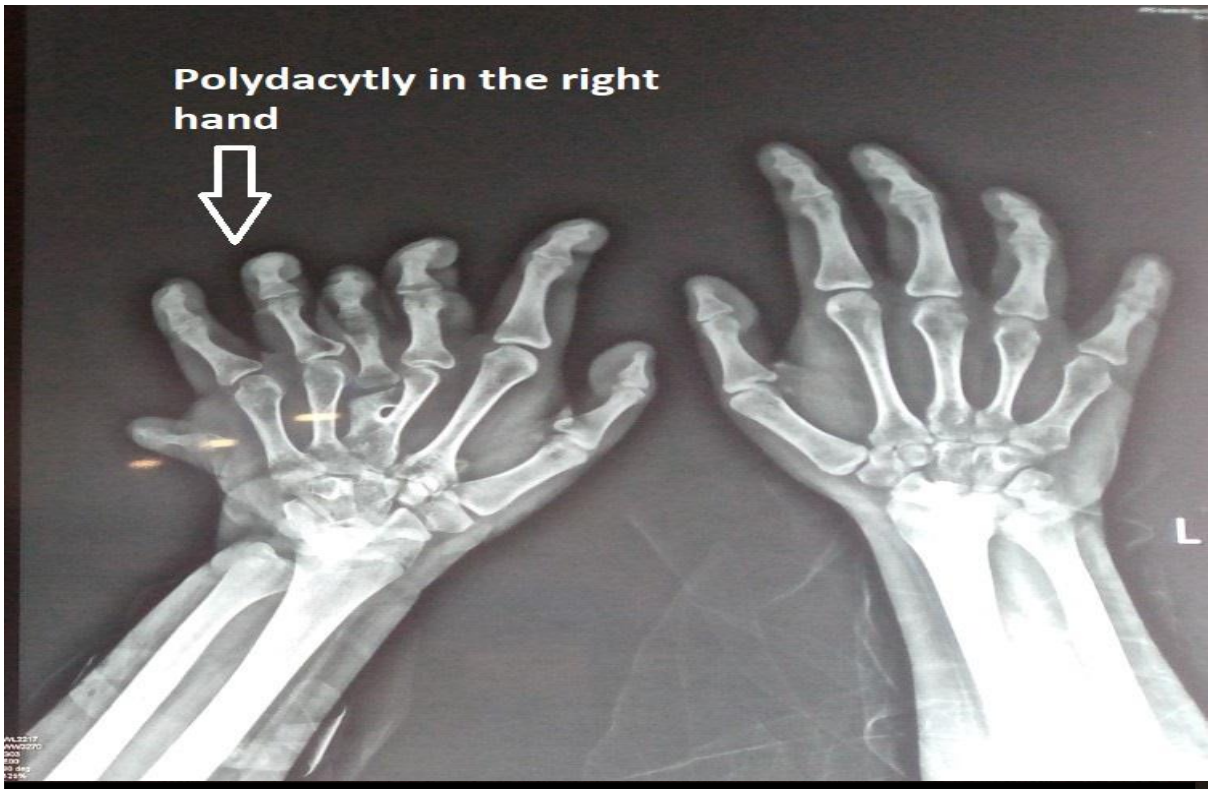

Figure:4 Showing radiograph of both hands, confirming the presence of **polydactyly** in right

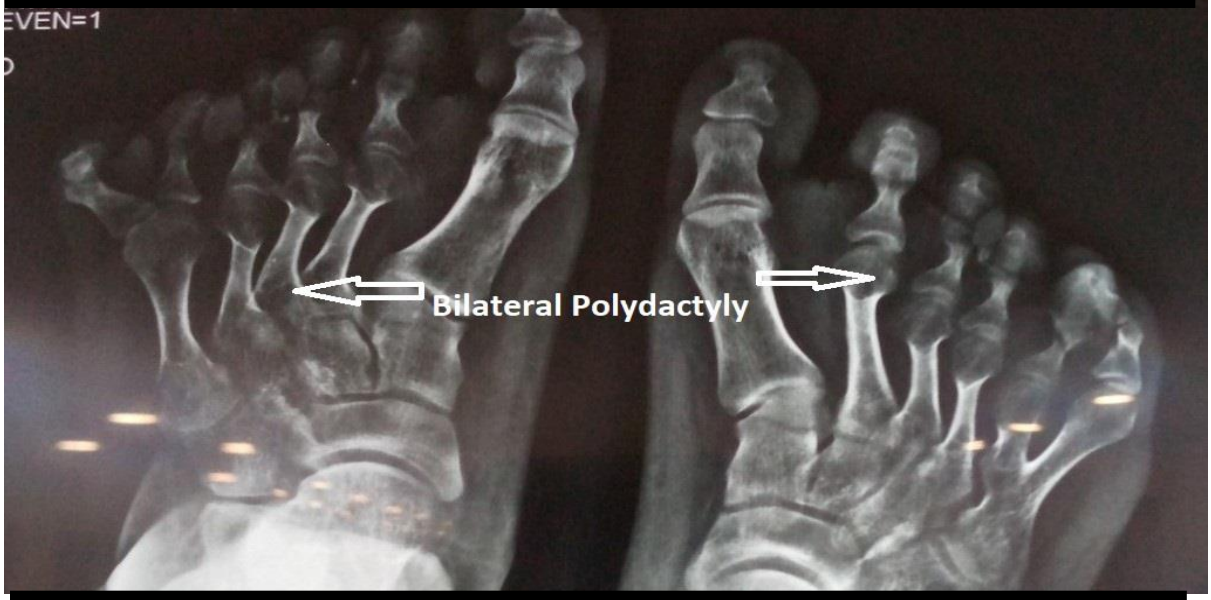

Fig:5 Radiograph showing bilateral polydactyly in the feet.

DISCUSSION:

Laurence-Moon-Bardet-Biedl syndrome (LMBBS) is a rare autosomal recessive genetic disorder that leads to various harmful manifestations affecting multiple organs.[**6]** Patients with LMBBS may experience a decline in the functioning of the brain, eyes, kidneys, hands, and feet. The syndrome's primary features encompass retinal dystrophy, polydactyly, obesity, hypogonadism, renal abnormalities, and mental retardation. In addition to these, LMBBS may also manifest with secondary abnormalities like speech disorder, developmental delay, ataxia, diabetes

insipidus, and dental crowding.**[7]** In clinical observation of the eye, key findings comprise pigmentary retinopathy, reduced visual acuity, and eventual vision loss. The impairment of photoreceptors in the retinal tissue, with macular involvement, results in initial night blindness, which often progresses to complete blindness in the majority of cases.**[8]** In individuals displaying a typical presentation of LMBBS, significant truncal obesity is a prominent feature, even though their birth weight is typically normal.[9] Laurence-Moon syndrome (LMS) and Bardet-Biedl syndrome (BBS) are two separate disorders sharing some similar characteristics with subtle differences. Research indicates that core features such as polydactyly and obesity are mostly present in BBS, while spasticity is more common in LMS. However, there is also evidence of an unclear phenotype-genotype correlation, suggesting that the two syndromes might be considered as closely related or potentially the same condition.[5] Consequently, to distinguish between the syndromes and achieve a precise diagnosis, it is essential to conduct a thorough genetic analysis, focusing on mutations in the molecular sequence. Unfortunately, due to financial constraints, we were unable to pursue this analysis, leading us to classify our patient under the term "Laurence-Moon-Bardet-Biedl syndrome" as a general descriptive label for the illness.[6] The incidence of the syndrome varies significantly, with rates ranging from 1:140,000 to 1:160,000 live births in North America and Europe, 1:65,000 in an Arab population, and higher prevalence in the Bedouin population of Kuwait and Newfoundland, affecting about 1:13,500 and 1:17,500 newborns, respectively [5]. This increase in prevalence in certain countries is thought to be linked to the tradition of consanguineous marriages, which is a common practice in the Middle East [10]. Although the exact prevalence of the syndrome in Pakistan is unknown, the cultural norms indicate that 60% of marriages are consanguineous, with first cousin marriages contributing approximately 80% of them. This highlights the likelihood of homozygous mutations in individuals with the recessive trait.[11] Our patient was born from a consanguineous marriage, which might have contributed to the development of this distressing condition. Notably, his sister also experienced similar symptoms, including retinitis pigmentosa, mental illness, hypogonadism, and polydactyly. These features were observed to worsen and progress over time.

To establish the diagnosis of the disease, a revised criterion with specific primary/major features and secondary/minor features is utilized. The primary set of symptoms includes polydactyly, retinitis pigmentosa, obesity, learning disability, and hypogonadism. In addition to these, the secondary features encompass ataxia, poor coordination, speech abnormalities, brachydactyly, diabetes mellitus, hearing loss, hepatic fibrosis, cardiovascular anomaly, and spasticity.[12] Forsythe and Beales concluded that the presence of either four major characteristics or three major characteristics along with two minor traits is adequate for a prompt diagnosis.[13]. Our patient exhibited a classic presentation of LMBBS, displaying all four major features along with some speech deficit. Patients commonly present with night blindness, photophobia, and blurred central vision as their chief complaints. These symptoms arise due to the loss of rod-cone photoreceptors, leading to retinal degeneration with macular involvement [5]. Our patient also experienced similar symptoms, and fundoscopic examination revealed classic findings consistent with retinitis pigmentosa.

Moreover, truncal obesity remains a cardinal symptom, prevailing in 72-86% of affected individuals, often associated with diabetes mellitus [5]. Our patient also displayed marked truncal obesity and slightly elevated HbA1c levels. Polydactyly, characterized by the presence of an extra finger or toe at birth, is the sole significant gross characteristic involving one or more limbs, found in approximately 69% of affected individuals.[10]. Our patient exhibited polydactyly in her left hand and both her left and right feet. Learning disability and cognitive impairment are essential components that can vary in their severity.[5]. Our patient experienced delayed milestones and displayed a significantly low IQ when assessed using an IQ testing scale. She faced challenges in following commands and exhibited intellectual disability, which was further verified through a DAP test. Hypogonadism is the last primary symptom, affecting about 59% of individuals, and it may be diagnosed during puberty with delayed development of secondary sexual characteristics.[8] During the clinical examination, we observed hypogonadism in our patient, along with the absence of pubic hair. This confirms the presence of all the major criteria necessary for diagnosing LMBBS.

Early diagnosis and a multidisciplinary approach are essential for effective management of this syndrome. Genetic counselling for the family to understand the disease's risks and raising awareness about consanguineous marriages can contribute to reducing the prevalence of this condition. Moreover, early detection through genetic analysis can aid in providing timely and more effective treatment, potentially

slowing down the progression of the manifestations. In later stages, conventional management is commonly employed based on the clinical presentation. While spectacles and visual aids are recommended to improve visual quality, they are not proven to be the definitive treatment of choice [5]. To mitigate the impact of cognitive impairment, it is crucial to conduct an educational evaluation, which should be assessed by a clinical psychologist. Additionally, the psychologist can address any mood-related symptoms that may arise as a consequence of this condition [13]. Regular counselling sessions with family members should be carried out to ensure optimal patient care at home. Engaging in regular physical exercise, adopting a low-calorie high-protein diet, and utilizing pharmacological interventions can be effective in reducing obesity and maintaining glucose and lipid levels within the normal range.[1] Moreover, it is essential for the community to embrace and accept individuals with rare conditions, avoiding any discrimination or prejudice. Creating an inclusive and accepting environment can significantly improve their quality of life [5].

CONCLUSION:

LMBB**S** poses significant morbidity and mortality risks, especially in children. Timely diagnosis is crucial for effective management, as the syndrome's rarity and multi-system involvement often lead to missed diagnoses, as observed in this case. Implementing comprehensive management plans can enhance the affected individuals' social integration and overall well-being. Additionally, genetic counselling is vital, especially for families with a history of consanguineous marriages, which is a significant contributor to LMBBS cases. Raising awareness about the possibility of having children with the condition and screening family members for clinical manifestations can help manage the condition effectively. Given the etiology, encouraging marriages outside of the family can help limit the incidence of LMBBS. It is essential for clinicians to stay updated on the diagnostic criteria and available therapeutic options to provide optimal care for individuals with LMBBS.

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