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PRUNE BELLY SYNDROME: INSIGHTS INTO PATHOGENESIS AND MANAGEMENT

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ABSTRACT Prune Belly Syndrome (PBS), also known as Eagle-Barrett Syndrome, is a rare congenital disorder characterized by a triad of abdominal wall musculature deficiency, severe urinary tract abnormalities, and bilateral cryptorchidism in males. The etiology remains unclear, with proposed genetic, mesodermal development, and fetal urinary obstruction hypotheses. PBS predominantly affects males, with an incidence of 2 to 4 per 100,000 live births. Diagnosis is established prenatally via ultrasound or postnatally through clinical and imaging evaluations. Management strategies include prophylactic antibiotics, surgical correction for cryptorchidism and abdominal wall defects, and reconstructive urinary tract procedures. Patients with severe renal dysfunction may require dialysis or kidney transplantation. Advances in fetal interventions, surgical techniques, and assisted reproductive technologies have improved outcomes, yet PBS remains associated with significant morbidity, including renal insufficiency, respiratory complications, and infertility. This review explores the latest insights into PBS pathogenesis, clinical presentation, diagnosis, and therapeutic approaches to optimize patient management and long-term outcomes.

KEYWORDS : Prune Belly Syndrome, Congenital Abnormalities, Urinary Tract Malformations, Cryptorchidism, Abdominal Musculature Deficiency

INTRODUCTION

Prune Belly Syndrome (PBS), also known as Eagle-Barrett Syndrome, is a rare congenital disorder characterized by a triad of clinical manifestations: severe abdominal muscle deficiency, significant urinary tract abnormalities, and bilateral cryptorchidism in males. The term "prune belly" refers to the wrinkled appearance of the abdominal wall due to muscle hypoplasia or aplasia. However, PBS is a multisystem disease, often associated with cardiopulmonary, gastrointestinal, and musculoskeletal anomalies, affecting overall morbidity and mortality (1).

PBS primarily affects males, with an estimated incidence of 2 to 4 cases per 100,000 live births (2). Although the exact pathogenesis remains unclear, several genetic and developmental hypotheses have been proposed, including mesenchymal tissue maldevelopment and urethral obstruction leading to secondary organ abnormalities (3). Early diagnosis and intervention are essential to prevent severe complications such as renal failure and recurrent infections (3).

This review aims to provide an updated analysis of the pathogenesis, clinical presentation, diagnosis, and management strategies of PBS. A systematic review of the literature was conducted to consolidate current evidence regarding this complex congenital disorder.

Methods

A comprehensive literature review was performed using four major databases: PubMed, Scopus, Embase, and Web of Science. The search strategy included the following keywords: "Prune Belly Syndrome," "Eagle-Barrett Syndrome," "Congenital Abdominal Musculature Deficiency," "Cryptorchidism," and "Urinary Tract Anomalies." Studies published within the last 15 years were included, prioritizing systematic reviews, clinical trials, and evidence-based guidelines.

The inclusion criteria encompassed studies discussing epidemiology, pathogenesis, diagnostic approaches, and treatment modalities of PBS.

A total of 15 studies were selected for analysis, ensuring a comprehensive understanding of this rare syndrome and its clinical implications.

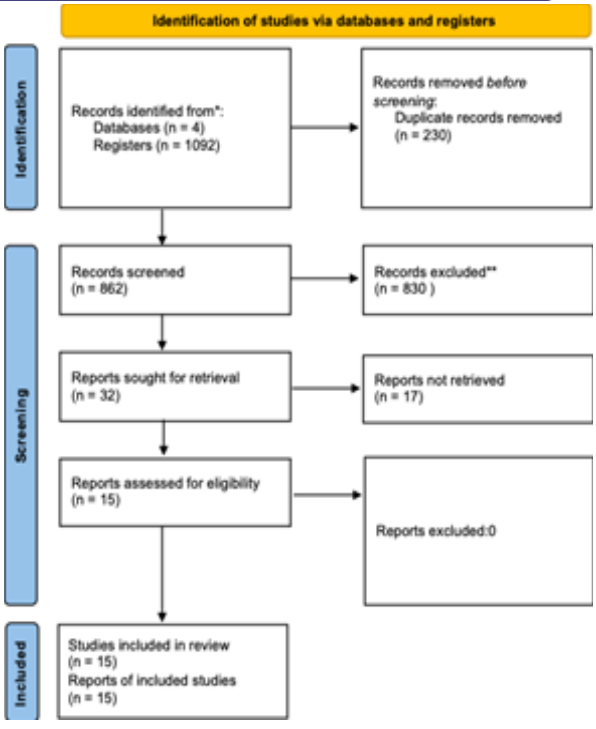

Figure 1. Prisma.

Epidemiology

Prune Belly Syndrome (PBS) is a rare congenital disorder with an estimated incidence ranging between 2 and 4 cases per 100,000 live births. The condition predominantly affects males, accounting for over 95% of reported cases. However, there are rare occurrences in females, typically presenting with milder phenotypic manifestations and less severe urinary tract abnormalities (4).

Epidemiological studies suggest potential variations in prevalence among different populations, with some reports indicating a higher frequency in specific ethnic groups. However, definitive genetic or environmental risk factors have not been clearly established (5). The etiology of PBS remains uncertain, though it is believed to involve abnormal mesodermal development affecting both the urinary and musculoskeletal systems.

Advancements in prenatal imaging, particularly ultrasound and fetal magnetic resonance imaging, have improved the early detection of PBS. This has facilitated early postnatal management and intervention strategies, significantly impacting patient outcomes. Despite these advances, the overall prognosis varies based on the severity of associated renal dysfunction and the presence of other congenital anomalies (5). Continued research into the genetic and developmental mechanisms of PBS is essential to enhance early diagnosis and optimize long-term management strategies.

Pathogenesis

The pathogenesis of Prune Belly Syndrome (PBS) remains incompletely understood, though several genetic and developmental mechanisms have been proposed.

Genetic Factors

A potential X-linked inheritance pattern has been suggested, given the overwhelming male predominance of PBS. However, this hypothesis does not account for all cases, as rare occurrences in females have been documented (6). PBS has also been associated with chromosomal abnormalities, including trisomies 13, 18, and 21, further supporting a genetic basis for the syndrome (7). Additionally, mutations in genes involved in mesodermal development, such as HNF1B, FLNA, BMPR1B, and MYOCD, have been implicated in PBS pathogenesis. These genes play essential roles in renal, muscular, and mesenchymal tissue differentiation, and their dysfunction may contribute to the phenotypic abnormalities observed in PBS (7).

Defective Mesenchymal Development

PBS has been linked to impaired mesenchymal development, affecting multiple structures, including the abdominal musculature, mesonephric and paramesonephric ducts, and urinary organs. Disruptions in mesodermal tissue differentiation result in hypoplasia or aplasia of abdominal muscles, leading to the characteristic lax abdominal wall appearance. Concurrently, anomalies in Wolffian and Müllerian duct derivatives contribute to the genitourinary malformations commonly seen in PBS (8).

Early Urethral Obstruction Hypothesis

An alternative theory suggests that early fetal urinary tract obstruction leads to secondary defects in muscle differentiation and renal development. Impaired urine outflow in utero may increase intra-abdominal pressure, disrupting normal muscular and organogenesis processes. This hypothesis is supported by findings of urinary tract dilation and renal dysplasia in PBS patients, indicating a strong relationship between urinary tract anomalies and the syndrome's phenotypic spectrum (8).

Clinical Manifestations

Prune Belly Syndrome (PBS) is characterized by a classic triad of findings: severe abdominal wall laxity, cryptorchidism, and urinary tract anomalies. However, PBS is a multisystem disorder with varying degrees of involvement in different organ systems.

Genitourinary System

Renal and urinary tract abnormalities are central to PBS. Patients frequently present with renal dysplasia, hydronephrosis, and vesicoureteral reflux, predisposing them to recurrent urinary tract infections and progressive renal dysfunction. Additionally, bladder abnormalities, including a dilated, poorly contractile bladder, contribute to voiding dysfunction and urinary stasis (9). Male patients exhibit hypoplastic or absent prostates, further affecting urinary function and fertility potential (9).

Musculoskeletal System

The most visually striking feature of PBS is the deficiency or absence of abdominal musculature, resulting in a wrinkled, lax abdominal wall. This muscular hypoplasia can also affect respiratory function due to impaired diaphragmatic support. Other musculoskeletal abnormalities include scoliosis, clubfoot (talipes equinovarus), and limb hypoplasia, further impacting mobility and posture (10).

Respiratory System

Severe cases of PBS may be complicated by pulmonary hypoplasia, a consequence of oligohydramnios due to fetal urinary obstruction. Impaired lung development can result in neonatal respiratory distress, which is a major determinant of early morbidity and mortality (10).

Gastrointestinal System

Gastrointestinal abnormalities are common in PBS and may include intestinal malrotation, anal atresia, and chronic constipation. These anomalies can necessitate surgical intervention to prevent complications such as volvulus or bowel obstruction (11).

Cardiovascular System

Congenital heart defects are rare but have been reported in PBS patients. These include atrial and ventricular septal defects, patent ductus arteriosus, and other structural anomalies, which may contribute to increased morbidity in affected individuals (11).

Diagnosis

Prenatal Diagnosis

Prune Belly Syndrome (PBS) can often be identified prenatally through fetal ultrasound, typically between the 20th and 30th weeks of gestation. Key sonographic findings include a distended bladder (megacystis), bilateral hydronephrosis, and severe oligohydramnios, which is indicative of impaired fetal urine output. The presence of these features, particularly in male fetuses, should prompt further evaluation and close prenatal monitoring (12).

Postnatal Diagnosis

The diagnosis of PBS is confirmed postnatally through clinical examination and imaging studies. The characteristic triad of abdominal muscle deficiency, cryptorchidism, and urinary tract anomalies facilitates early recognition. Renal and bladder ultrasonography is the initial imaging modality used to assess urinary tract abnormalities, while voiding cystourethrography (VCUG) is essential for detecting vesicoureteral reflux and urethral anomalies. Magnetic resonance urography (MRU) provides further anatomical detail and helps in surgical planning (13).

Differential Diagnosis

Several congenital conditions present with overlapping features and must be distinguished from PBS. Posterior urethral valves can also cause bladder distention and hydronephrosis but have a distinct pathophysiology involving anatomic obstruction. The megacystis-microcolon-intestinal hypoperistalsis syndrome is another important differential, characterized by severe gastrointestinal dysmotility in addition to bladder dysfunction. Other congenital muscular dystrophies may also mimic PBS but lack the hallmark genitourinary anomalies (13).

Management And Treatment

Prenatal Management

In severe cases of PBS with oligohydramnios, vesicoamniotic shunting may be considered to improve pulmonary prognosis by facilitating fetal urine drainage and preventing lung hypoplasia. However, this intervention remains controversial due to variable outcomes and potential procedure-related complications (14).

Postnatal Management

Urological Treatment

Early management focuses on preserving renal function and preventing urinary tract infections. Prophylactic antibiotics are commonly prescribed to reduce the risk of recurrent infections. In severe cases, urological interventions such as urethrotomy, cystostomy, or urinary diversion may be necessary to manage obstructive uropathy and maintain adequate bladder drainage (14).

Surgical Treatment

Surgical correction plays a crucial role in the management of PBS. Early orchidopexy is recommended to prevent infertility and reduce the risk of malignancy. Abdominoplasty is performed to enhance abdominal wall stability, improve respiratory function, and reduce the risk of musculoskeletal deformities such as scoliosis. In patients with severe urinary dysfunction, reconstructive surgery, including bladder augmentation or urinary diversion, may be required to optimize continence and renal preservation (15).

Renal Failure Management

For patients with progressive renal insufficiency, peritoneal dialysis is often the preferred modality in pediatric cases. In end-stage renal disease, kidney transplantation remains the definitive treatment, offering improved long-term outcomes and quality of life (15).

Prognosis And Quality Of Life

Neonatal mortality in PBS is approximately 30%, primarily due to pulmonary insufficiency secondary to oligohydramnios. Long-term outcomes are highly variable, with renal dysfunction, mobility issues, and infertility being common concerns. In adulthood, most male patients experience infertility due to azoospermia; however, advances in assisted reproductive technologies have provided successful outcomes in selected cases (15).

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