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Analyzing the factors that contribute to the development of embryological classical type of bladder exstrophy

Ria Margiana[1,2,3,*], Widya Juwita[1,*], Khoirul Ima[2,3], Zakiyatul Faizah[1,4], Supardi Supardi[1]

[1]Andrology Program, Faculty of Medicine, Airlangga University, Surabaya, [2]Master's Program in Biomedical Sciences, Faculty of Medicine, University of Indonesia, Jakarta, [3]Department of Anatomy, Faculty of Medicine, University of Indonesia, Jakarta, [4]Biomedical Science Department, Faculty of Medicine, Airlangga University, Surabaya, Indonesia

Abstract: Bladder exstrophy is a rare congenital condition of the pelvis, bladder, and lower abdomen that opens the bladder against the abdominal wall, produces aberrant growth, short penis, upward curvature during erection, wide penis, and undescended testes. Exstrophy affects 1/30,000 newborns. The bladder opens against the abdominal wall in bladder exstrophy, a rare genitourinary condition. This study is vital to provide appropriate therapy choices as a basis to improve patient outcomes. This study may explain bladder exstrophy and provide treatment. Epispadias, secretory placenta, cloacal exstrophy, and other embryonic abnormalities comprise the exstrophy-spades complex. The mesenchymal layer does not migrate from the ectoderm and endoderm layers in the first trimester, affecting the cloacal membrane. Embryological problems define the exstrophy-aspidistra complex, which resembles epimedium, classic bladder, cloacal exstrophy, and other diseases. Urogenital ventral body wall anomalies expose the bladder mucosa, causing bladder exstrophy. Genetic mutations in the Hedgehog cascade pathway, Wnt signal, FGF, BMP4, Alx4, Gli3, and ISL1 cause ventral body wall closure and urinary bladder failure. External factors such as high maternal age, smoking moms, and high maternal body mass index have also been associated to bladder exstrophy. Valproic acid increases bladder exstrophy risk; chemicals and pollutants during pregnancy may increase bladder exstrophy risk. Bladder exstrophy has no identified cause despite these risk factors. Exstrophy reconstruction seals the bladder, improves bowel function, reconstructs the vaginal region, and restores urination.

Key words: Congenital abnormalities, Bladder exstrophy, Fetal anomalies, Urogenital system, Reproductive health

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Introduction

Bladder exstrophy or bladder exstrophy is a type of disorder of the genitourinary system, which is characterized by the opening of the bladder against the abdominal wall. The bladder is open, with urine passing through an open, roofless (suprapubic) space in the abdominal area, the bladder mucosa is stretched, attached to the skin of the abdomen, and the ball splits the pubic bone. This problem usually occurs with epispadias, the bladder sphincter is often not well developed [1].

Abnormalities with bladder exstrophy include a short

Corresponding author:
Ria Margiana
Department of Anatomy, Faculty of Medicine, University of Indonesia, Jakarta 10430, Indonesia
E-mail: ria.margiana11@gmail.com
Zakiyatul Faizah
Biomedical Science Department, Faculty of Medicine, Airlangga University, Surabaya 60132, Indonesia
E-mail: zakiyatul-f@fk.unair.ac.id

*These authors contributed equally to this work.

penis (forebore 50% shorter than normal control), upward curvature during erection (cord-dependent), wide penis (30% wider than normal control), undescended testes caused by abnormal growth. In a flat scrotum, an inguinal hernia occurs because the inguinal canal is not properly formed, and the separation of the symphysis pubis causes external rotation of the hip and sacroiliac joints so that children have a gait that gradually decreases with age [2].

Cases of exstrophy are rare, but they occur in approximately 1 in 30,000 births. Therefore, the clinician should consider this information as a congenital abnormality of the lower urinary tract. The prognosis for this problem is good if treated promptly from the first diagnosis, appropriate referrals involve multiple disciplines including urological surgery, and subspecialties of urology and endocrinology, including pediatricians and neurologists. Multidisciplinary support to prevent the risk of kidney failure in youth, pregnancy, sexual dysfunction in the elderly, and blood gland disorders (cryptorchidism) that often follow bladder infections. This problem causes psychological losses for the family because the length of stay in the hospital, and minimum care costs until the child reaches adulthood are separate problems that need to be addressed [3]. Therefore, it is hoped that this information can add a brief scientific insight that is useful for doctors who are interested in the field of andrology, urology, reproductive system diseases, and endocrine science.

Bladder exstrophy is a disorder in which the bladder opens against the abdominal wall that occurs in newborns. This problem results from failure of the abdominal wall after infra-umbilical closure, which usually occurs in the second to third trimesters. These disorders increase the risk of urinary incontinence, infections, intermittent catheter use, vesicoureteral reflux, and cosmetic problems such as a bifida clitoris. The disease is often accompanied by epispadias, and the bladder sphincter is often absent. In girls, bladder exstrophy is usually accompanied by the presence of a detached clitoris and labia when the nipple opening is enlarged and stenotic. Because the abdominal wall is limited to bladder exstrophy, all patients with bladder exstrophy will undergo uterine circumcision until anterior closure.

This information is so scarce that the ratio of chances of finding a case is about 1:30,000 births. The bladder exstrophy involves multiple fields of study, such as urology, pediatrics, endocrinology, and surgery, as depicted in Fig. 1. This is to prevent problems such as infertility, risk of kidney failure, and erectile dysfunction in the elderly. The side ef-

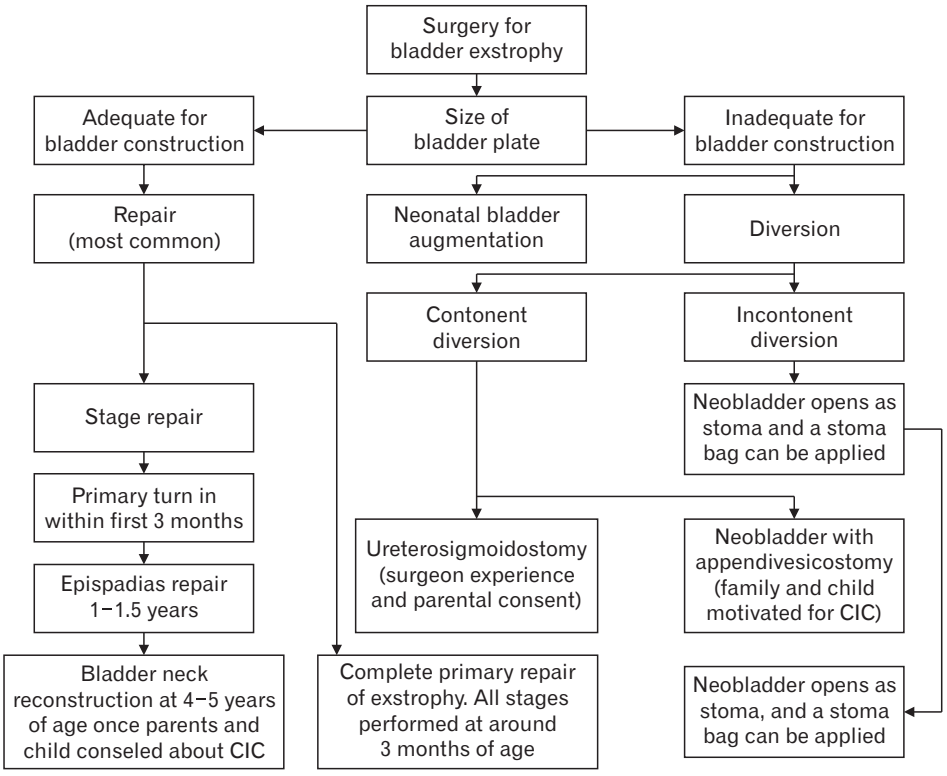

Fig. 1. Course and variation of bladder exstrophy cases. CIC, clean intermittent catheterization.

fects of bladder exstrophy are generally good, depending on early diagnosis and appropriate treatment. So it is expected for doctors that this information can add good information for doctors [4].

This research investigates the characteristics that increase a person's likelihood of developing bladder exstrophy, a very uncommon genitourinary condition in which the bladder opens against the abdominal wall. Because we need to understand the genesis and risk factors of this condition in order to develop suitable therapy options and enhance patient outcomes, this study is extremely important. The utilization of survey research in this study to investigate risk factors and illness outcomes in embryological abnormalities such as epispadias, secretory placenta, cloacal exstrophy, and others is a novel approach that was taken by the researchers.

Review

Risk factors that are thought to increase the likelihood of developing bladder exstrophy

Bladder exstrophy is a sort of congenital anomaly that affects the urinary tract, pelvic bones, and abdominal wall below the pelvis. This version of the condition is extremely rare. The following are some of the factors that are thought to increase the likelihood of developing bladder exstrophy:

1. As a result of the involvement of genetic variables, it is widely accepted that bladder exstrophy has a genetic basis at least in some cases. If a member of your family already suffers from bladder exstrophy, there is a higher likelihood that you will also pass the condition on to one of your children [5].

2. Age of the mother: Pregnant women who are over the age of 35 at the time of their pregnancy have an increased probability of having a kid who is affected by bladder exstrophy. Other risk factors include having a sibling who has bladder exstrophy and having a child who has a family history of bladder exstrophy [5].

3. The medical ailment known as bladder exstrophy is far more common in males than it is in females [6].

4. Tobacco use: Pregnant women who smoke have a greatly increased risk of having a child who is affected by bladder exstrophy. This risk is mostly attributed to the fact that bladder exstrophy is an inherited condition [5].

5. Medications: There is a correlation between the use of some medications, such as valproic acid, and an increased risk of bladder exstrophy. This is something that is especially true for women [7].

6. Environmental factors: There is some speculation that being exposed to certain chemicals and pollutants in the environment during pregnancy may increase the likelihood of developing bladder exstrophy [6].

Even though these risk factors have been identified, the particular etiology of bladder exstrophy is not yet fully understood despite this. Remembering this is essential, so keep that in mind.

These embryological diseases are classified as exstrophy-spades complex, which includes embryonic defects such as epispadias, secreted placenta, cloacal exstrophy, and many other changes. This defect occurs in the first trimester when the primitive cloaca separates into the urogenital sinus and hindgut, which coincides with the maturation of the abdominal wall, when the mesenchymal layer does not migrate from the ectoderm and endoderm layers, affecting the cloacal membrane because unstable (broken), a layer of mucus accumulates on the skin. Premature rupture occurs before caudal mesodermal translocation as a result of various infra-umbilical anomalies [8]. Abnormalities with the development of the pelvic bones are quite different between the symphysis pubis and the outer part of the femur [9]. The incidence is 1 in 30,000 births, diagnosed at birth because it looks directly in the abdominal area. Mostly, men, the ratio of cases between men and women is 2:1 [10]. The chance of this happening to the next child is 1 in 100 or 1 in 70 if the parents have the same history. Risk factors and etiology are unclear and are not historical [11].

Bladder exstrophy is classified according to its embryological abnormalities such as exstrophy-aspidistra complex, which resembles epimedium, classic bladder, cloacal exstrophy, and many other disorders. The disorder begins to appear in the first trimester when the cloaca long separates into the urogenital nose and hindgut when the abdominal wall matures. If the mesenchyme fails or is unable to undergo endodermal and ectodermal processes, this results in cloacal rupture or instability. Premature rupture of the cloacal membrane before caudal translocation causes a variety of infra-umbilical abnormalities. Most of these abnormalities are accompanied by developmental failures of the pelvic bones such as separation of the symphysis pubis and external rotation of the femur [12].

Bladder exstrophy is easy to diagnose because you can determine it directly by viewing the bladder at birth. The cause of this disease is still unclear and there is no history. Cases of bladder exstrophy in boys are more common in girls with a ratio of 2:1 [13].

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a. Classic bladder exstrophy:

This disorder occurs on the abdominal wall along with the bladder, and in the lower abdomen, the distance between the anus and the umbilical cord is reduced and an inguinal hernia is often seen because of the wide inguinal ring. Often in these situations, the bacteria in the genital area are usually normal [3].

b. Epispadias:

This disorder is often seen in the short and wide phallus, flat and open glands, and dorsal spermatogonia found in the urethra and oral anus. Usually, the pubic symphysis is wide and the abdominal muscles are distinct.

c. Extrophic cloacal:

This disorder is usually found in the anterior part of the bladder and is divided into 2 parts and is usually associated with abnormalities in the omphalocele. This condition is also often associated with heart failure, and kidney and intestinal problems. Other abnormalities such as hydrocephalus and myelomeningocele are also common in these cases.

d. Variants-extrophy variants:

This problem is divided into two types, namely supravesical fissure and patent urachus [3]. Whereas in the supravital fissure the bladder is usually found near the normal umbilicus and external genitalia, in the patent urachus it is an abnormality of the musculoskeletal system that opens to the umbilicus, while the superior vesical fissure usually appears infra umbilical.

The surgical management of exstrophy is known as reconstruction which aims to close the bladder, improve bowel function, reconstruct the genital area, and finally restore urination. There are three levels of this arrangement. The goal of Phase I is to protect the upper urinary tract and help growth in the later phase which is usually done shortly after the baby is born. The bladder must be closed within 72 hours after birth. If it is too late, an osteotomy should be performed to insert the bladder into the pelvic ring. Phase II aims to improve the structure of the genital area and encourage bladder growth to increase resistance to radiation. This stage usually occurs when the child is 1 year old. Stage III is usually completed by the time the child is 4 years old. The goal is to build peace and increase self-confidence. At this stage, bladder neck reconstruction is performed to void and treat vesicoureteral reflux [14].

Supravesical fissure, a variant of extrophic bladder

Supravesical Fissure, Variant of the Extrophic Bladder in Fig. 2 had a supravesical fissure which is a rare variant of exstrophy bladder. Where usually in the exstrophy bladder there are also abnormalities in the genital organs while in the supravesical fissure, the genital organs are normal which matches the patient's appearance. A surgical procedure should be performed in extrophic bladder with supravesical fissure, namely functional reconstructive surgery, which consists of 3 stages, namely stage I aims at reconstruction of the bladder must be carried out within the first 72 hours because this time is the right time for flexibility of the pelvic ring.

Diagnosis of a patient with supra vesical fissure

As a variant of extrophic bladder in the unborn child is still in the womb, examination for indications of this anomaly can be done, specifically using ultrasonography (USG). A physical examination can also be used to diagnose the condition after the infant is born. Before the newborn leaves the hospital, bladder exstrophy repair treatments are typically carried out. Urine tests, blood tests, X-rays, and ultrasounds are performed in advance of surgery if necessary [15].

Morphology and etiology of bladder exstrophy

Bladder exstrophy is the rare congenital defect of the genitourinary tract. It is characterized by the complete or partial disappearance of the bladder wall and the anterior abdominal wall. This condition is characterized by exposed

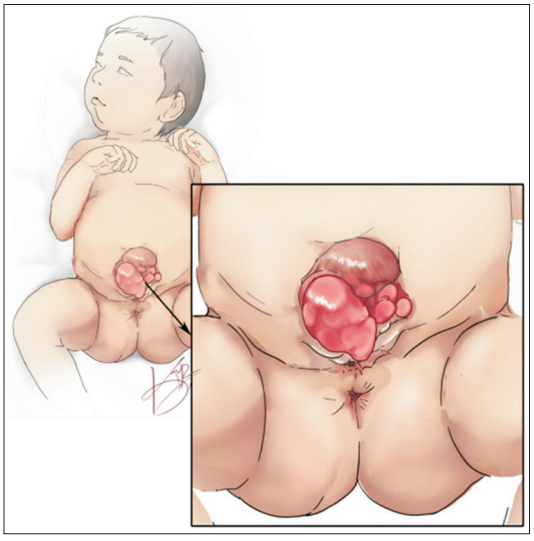

Fig. 2. Supravesical fissure, a variant of extrophic bladder.

mucosa of the bladder and is frequently accompanied by epispadias, a deformity affecting either the penis or clitoris in females. Patients with bladder exstrophy have an enlarged and depressed pelvis, a diastasis in the pubic region, and the absence of the anterior bladder wall and abdominal wall. These are the condition's morphological characteristics [7].

Other congenital urinary tract abnormalities, such as posterior urethral valves, urethral atresia, ureteropelvic junction obstruction, and vesicoureteral reflux, should be considered in the differential diagnosis of bladder exstrophy. In addition, additional potential causes of abdominal wall abnormalities, such as omphalocele and gastroschisis, should be considered during differential diagnosis [7].

Some of the signs of bladder exstrophy include a turned-up bladder that protrudes from the body. The urinary system, as well as the digestive and reproductive systems, are frequently affected by bladder exstrophy. Damage can occur to the pelvic bones, bladder, genitalia, end of the large intestine, and the open end of the anus. Vesicoureteral reflux may also occur in children with this condition. Because of this, urine exits the bladder and returns through the tubes leading to the kidneys.

It is unclear what specifically causes bladder exstrophy. Several studies, however, reveal a connection between families, indicating that history matters. When a child has bladder exstrophy, the bladder is born protruding from the abdominal wall. To confirm the diagnosis of bladder exstrophy and rule out any other issues, the doctor will utilize an MRI or X-ray. On a prenatal ultrasound or MRI of the fetus, the bladder can occasionally be seen by the doctor. The bladder is unable to empty because the pubic bone must be separated (the bone that forms the abdomen). The genital area is smaller than usual. More than usual, the vagina is joined to the stomach [16].

Due to the absence of knowledge about the causes and risk factors of bladder exstrophy in patients, the authors hypothesized that a genetic mutation has arisen in the fetus during gestation. The hypothesis on genetic mutations can be seen in the Table 1 [17, 18].

Treatment of bladder exstrophy

The treatment's primary objectives are:

- Including the pelvis, bladder, and rear of the urethra.
- Restoring sperm's typical form and function in either boys' or girls' other sex organs.
- Rebuild the bladder to enable extended pee storage without endangering the kidneys.

Reconstruction that is done gradually is one of the therapeutic methods. The procedure, which will take place throughout the infant's first year, includes the treatment. The initial stage of the reconstruction is really helpful. It is frequently necessary to perform additional surgery to restore the child's ability to urinate and/or to repair external organs [15].

Conclusion

An extremely uncommon form of congenital abnormality, bladder exstrophy affects the urinary tract, pelvic bones, and abdominal wall below the pelvis. Several of the following

Table 1. Gene mutation caused classic bladder exstrophy

Type of mutation/genotype	BEEC type and associated anomalies	References
Shh and FGF 8	CBE	[17]
	Developmental disorders of the genital tubercle	
	Absent cloacal membrane	
	A cloacal membrane is formed but directed caudally	
BMP	CBE	[18]
	Deformity or failure of the body wall closure	
Alx 4	CBE	[17]
	Defects affecting developmental processes in the formation of the ventral body wall	
	External genital organs, such as phenotypic abnormalities of the bladder with epispadias concomitant with defects of the upper genital tubercle	
Gli 3	CBE	[17]
	Damage to the body wall covering	
ISL 1	CBE	[18]

BEEC, bladder-exstrophy-epispadias complex; CBE, classic bladder exstrophy.

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are considered to be risk factors for bladder exstrophy: Bladder exstrophy is assumed to have a hereditary component due to the fact that genetic factors are involved. There is an increased chance of having a child affected by bladder exstrophy if a member of your family already has the ailment; Age of the mother: Pregnant women who are above the age of 35 at the time of their pregnancy have a greater chance of having a child who is affected by bladder exstrophy; The condition known as bladder exstrophy is more prevalent in males than in girls. Male sex; Tobacco use: Pregnant women who smoke have a significantly increased risk of having a child who is affected by bladder exstrophy; drugs: Certain drugs, such as valproic acid, have been linked to an increased incidence of bladder exstrophy. This is particularly true for women; Environmental factors: During pregnancy, being exposed to certain environmental chemicals and pollutants may raise the risk of bladder exstrophy. Despite the fact that these risk factors have been found, the specific etiology of bladder exstrophy is not completely understood. This is a crucial point to keep in mind.

ORCID

Ria Margiana: https://orcid.org/0000-0002-6747-0117
Widya Juwita: https://orcid.org/0000-0001-8454-0327
Khoirul Ima: https://orcid.org/0000-0001-5164-9334
Zakiyatul Faizah: https://orcid.org/0000-0003-0962-9123
Supardi Supardi: https://orcid.org/0000-0001-8497-3536

Author Contributions

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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