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Review Article

Hypospadias: A Comprehensive Review of Etiology, Classification, Diagnosis, and Management

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In boys, hypopadias is a congenital anomaly that affects 0.2 to 4.1 out of every 1000 live births and is distinguished by an improper position of the urethral opening. It is caused by faulty fusion of the urethral folds during pregnancy, which can lead to other issues such as urinary difficulties and penile curvature. The various types of hypopadias include glanular, coronal, subcoronal, midshaft, penoscrotal, scrotal/perineal, distal, proximal, and hypospadias cripple, which vary in severity depending on where the meatus is located. Effective therapy typically includes surgical correction to address functional and cosmetic concerns; the diagnosis is often made prior to birth. The disorder has a complex etiology that includes genetic and environmental factors, with an incidence rate of approximately 1 in 250 males. To avoid the condition's consequences, early detection and treatment are critical. Boys with hypopadias, a common congenital disorder, have an improperly positioned urethral entry, incomplete foreskin development, and a bent penile. It is caused by aberrant urethral and penile development in the fetus, particularly between weeks 8 and 14. Hypospadias is categorized into three types based on the position of the urethral openings: anterior, middle, and posterior. The sickness can be caused by a variety of factors, including hormonal and hereditary. Unusual urine streams and curvature are clinical signs that may indicate long-term problems. Clinical diagnosis is typically associated with other problems. Surgical correction is required to ensure functional and cosmetic normality, and is typically performed within 6 to 18 months. With proper administration, this treatment produces good results. Hypopadias requires multidisciplinary treatment as well as regular monitoring.

Keywords: Hypospadias, Congenital anomaly, Male genital defect, Androgen deficiency, Fetal urethral fold fusion defect, Chordee, Crooked penis.

INTRODUCTION

Hypospadias is a congenital abnormality of the male external genitalia characterized by abnormal urethral fold development and ventral foreskin position, resulting in a misplaced urethral opening. It is caused by insufficient fusion of the embryologic urethral folds during pregnancy and affects 0.2 to 4.1 out of every 1000 live semen drainage are impacted by hypopadias, a congenital disorder where the urethra opens on the underside of the penis rather than at the tip. It is widespread, usually treatable, and frequently necessitates surgery to create a functional penis without interfering with fertility or urine. A crooked penis and undeveloped neonates. Penile curvature (chordee) and other genitourinary anomalies may coexist with the disease. The proper therapy of hypopadias requires an interdisciplinary approach as well as additional research to improve assessment and treatment techniques. (1,2,3) Urine and foreskin are possible symptoms. Due to the urethral tube's improper closure during fetal development, which causes the meatus to appear anywhere along the penis or below, the diagnosis typically happens soon after birth. (4)

Epidemiology:

Hypopadias is the alternate most common anomaly in the manly reproductive system, affecting roughly 1 of boys at birth. It occurs in one in every 250 males. Although frequence estimates vary by country, milder cases may regard for as important as 4. Only

cryptorchidism is more frequent among manly natural deformations, and it substantially affects the penis. Data variation in public registries makes accurate assessment of prevalence and indigenous circumstances delicate; the United States claims a frequence of roughly 0.4, whereas Denmark estimates between 0.5 and 0.8.A South American study estimated a global frequence of 11.3 per 10,000 babies (lower than 0.1). (6,7)

Types of Hypospadias

Healthcare provides classify the type of hypospadias by where the urethra opens

- Glanular
- Coronal
- Subcoronal
- Midshaft
- Penoscrotal /Scrotal
- Perineal
- Distal
- Proximal
- Hypospadias Cripple

The diagram below shows the various types of hypospadias according to the position of the urethra.

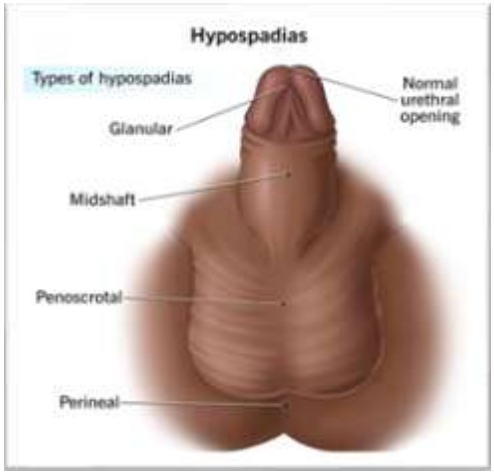

Fig.1.This illustration shows the categorization of hypospadias according to the position of the urethral opening, which varies from glanular to perineal types.

This diagram depicts the anatomical features of the penis and perineal area, emphasizing important structures and the various positions of hypospadias.

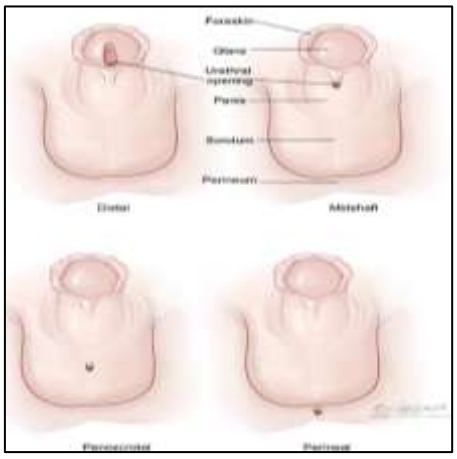

Fig.2. The illustration categorizes the different forms of hypospadias according to the position of the urethral opening: distal, midshaft, penoscrotal, and perineal.

A table describing the bracket, clinical symptoms, and inflexibility of hypospadias according to the anatomical position of the urethral meatus.

Table 1: This table provides a quick summary of the many kinds of hypospadias to help with clinical evaluation and care planning.

Type	Associated Features	Meatus Location	Source(S)
Glamular	Usually mild, minimal curvature	Near the tip of the penis	7,9,10,20
Coronal	Mild, little or no chordee	Coronal sulcus (just below)	7,9,10
Subcoronal	Often mild –moderate	Below the coronal sulcus	7,9,10
Midshaft	Variables curvature	Halfway down the shaft	1,7,9,10
Penoscrotal	More severe	Where the penis meets the scrotum	4,7,9,10
Scrotal/Perineal	Most severe	Below the scrotum	7,8,9,10
Distal	70-75% cases less severe	Granular, coronal, subcoronal	7,9,20
Proximal	25-30% more complex	Midshaft, penoscrotal	1,7,9,20
Hypospadias Cripple	Complex variable complications	Failed	9

Hypospadias Types and Features The inflexibility of the disease varies, with characteristics ranging from minor curve to major issues, impacting opinion and remedy. About 25- 30 of cases are proximal (Midshaft, Penoscrotal, Scrotal), whereas the remaining 70- 75 are distal (Glanular, Coronal, Subcoronal). Hypospadias Cripple" is a order for difficulties caused by unprofitable repairs. Hypospadias, a common natural condition in boys and men, is distinguished by an abnormal position of the urethral opening on the penis. It's constantly diagnosed at birth and has long- term goods on sexual and urinary function, as well as tone- regard. Cases, parents, and healthcare providers must be apprehensive of the symptoms, types, causes, and treatment options for this complaint (5).

Pathophysiology:

The major cause of hypospadias is insufficient or faulty urethral closure during embryogenesis, particularly between 8 and 20 weeks of pregnancy. Primordial genitalia develop during the initial hormone-independent phase of external genital development, which lasts five to eight weeks. In males, testicular differentiation triggers a hormone-dependent phase. Testosterone promotes the development of the urethral groove, which eventually leads to the urethra as the urethral folds unite, as well as the elongation of the genital tubercles. Testosterone promotes the development of the urethral groove, which eventually leads to the urethra as the urethral folds unite, as well as the elongation of the genital tubercles. Genetic anomalies in signaling pathways can cause malformations such as hypospadias and chordee. Only cryptorchidism is more frequent among male congenital malformations, and it mostly affects the penis. Data variation in national registries makes accurate assessment of incidence and regional occurrences difficult; the United States claims a prevalence of approximately 0.4%, whereas Denmark estimates between 0.5% and 0.8%. A South American study estimated a global frequency of 11.3 per 10,000 babies (less than 0.1%). Please see the photo below. (8)(9) Clinical photograph showcasing an external genital examination that points out an atypical location of the urethral opening.

Fig.3.This image illustrates a case of hypospadias, in which the urethral opening is situated on the underside of the penis rather than at the tip.

This figure showcases the surgical guidelines and the ordered stages of the process involved. This figure depicts the progressive pathophysiological processes that contribute to the formation of hypospadias during the differentiation of the fetal genitalia.

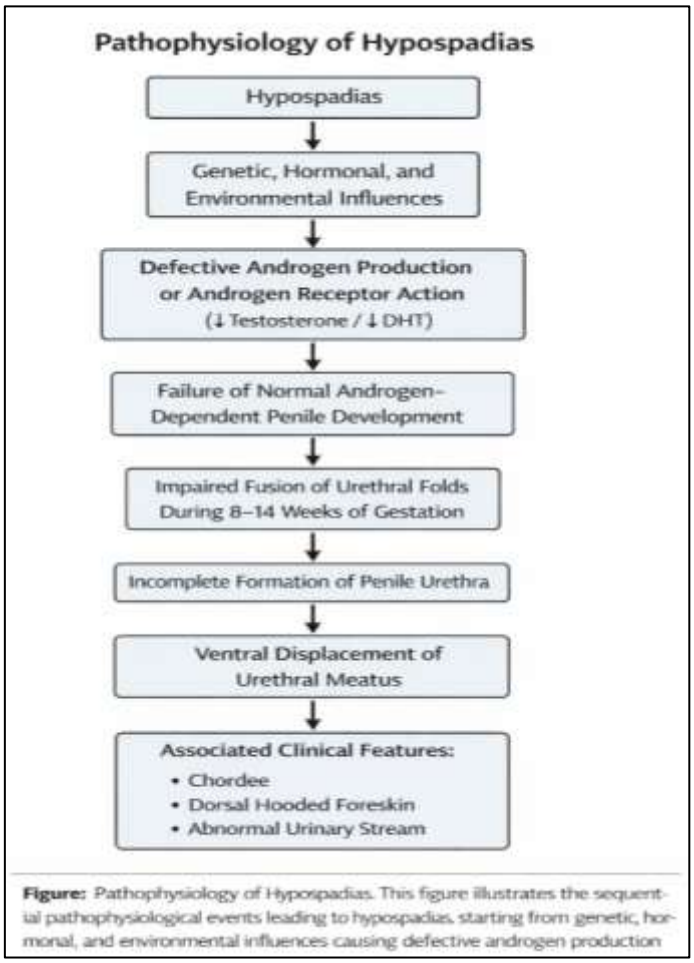

Fig.4. The illustration outlines the series of genetic, hormonal, and developmental processes that contribute to faulty urethral development and the ventral misplacement of the urethral opening in hypospadias.

Etiology:

Hypospadias, a natural condition with an abnormal urethral meatus placement, is allowed to be caused by

a combination of inheritable, endocrine, and environmental factors. Increased frequence in monozygotic halves and domestic clustering point to a inheritable predilection, with polygenic heritage most probably. Endocrine considerations include receptor insensitivity or androgen insufficiency, and affected individualities have been proven to have issues with testosterone conflation, which is generally caused by 5- nascence reductase mutations. Endocrine disruptors and aged maters are two exemplifications of environmental factors that are regarded to be significant contributors. The complaint is classified as anterior (generally subcoronal), middle, or posterior, depending on where the urethra is located. Recent exploration decreasingly suggests a two- megahit etiology involving both inheritable and environmental factors (10)

Symptoms

The urethral meatus is inaptly deposited on the underpart of the penis rather than the tip, which is the primary symptom of hypopadias. Other symptoms include chordee (downcast wind of the penis), undescended testicles, underdeveloped foreskin, and difficulty peeing. Identification is generally done during postpartum routine checks. To avoid issues, early discovery and treatment are critical. Common signs include irregular pee scattering, terminal dribbling, ornamental enterprises, and, in extreme cases, sexual difficulties. A timely medical scan is essential for effective treatment. (11,12)

Risk Factors

Although the cause of hypospadias is constantly unknown, the following effects could be

Family background

Babies who have a family history of hypospadias are more prone to experience this problem.

Genetics.

Certain gene mutations may intrude with the hormones that support the development of the mainly genitalia. Mama is over 35 times of age. According to certain exploration, there may be an increased chance of hypospadias in manly babe born to mothers aged than 35. Exposure to particulate adulterants when pregnant. There's some substantiation that suggests there may be a link between hypospadias and a mama 's exposure to particular hormones or substances, similar as artificial adulterants or fungicides, but fresh studies are demanded to confirm this. (20)

Diagnosis:

Hypopadias is defined by three penile anatomical abnormalities: an incorrect ventral opening of the urethral orifice, ventral curvature, and poor foreskin distribution with a deficient hooded foreskin. Variations include hypospadias sans hypospadias (ventral curvature with regular meatus) and megameatus intact prepuce (MIP, coronal meatus next to open glans). Endocrinological studies are essential in cases of undescended testis due to potential sex development issues, particularly in proximal or complex hypospadias. Diagnostic tests, such as ultrasonography and endoscopy, are used to diagnose nephro-urological abnormalities and urethral malformations. Clinical diagnosis is usually made at birth after evaluating the urethral meatus and potentially using imaging studies to identify abnormalities. Hormonal and genetic studies may be required to diagnose related syndromes (14,15,16)

Evalution:

The three primary kinds of hypospadias are distal (60–70% frequent), midshaft, and proximal. The categorization of hypospadias has changed throughout time. Glandular and sub-coronal distal hypospadias are also referred to as anterior or minor. While proximal hypospadias is classified as peno-scrotal, scrotal, or perineal, midshaft hypospadias is referred to as penile and includes other classifications. Urinary function is usually unaffected by mild hypospadias, but severe types may have narrower meatus and changed urine angles, which could result in problems including painful erections and infertility. Hypospadias can coexist with other genito-urinary abnormalities, including cryptorchidism and inguinal hernias in proximal cases, even though they are frequently isolated. Additionally, it is associated with about 200 disorders, such as CHARGE syndrome, Wolff-Hirschhorn, Smith-Lemli-Opitz, Denys-Drash, and WAGR (17,18,19)

Treatment:

Patients with hypospadias should be surgically examined within the first few weeks of life. Circumcision is not recommended if a penile abnormality exists, as the foreskin may be required for surgical repair. Proximal hypospadias is frequently associated with other genito-urinary disorders and may necessitate karyotype testing if cryptorchidism is discovered. Midshaft and distal hypospadias require surgical assessment without additional imaging. For proximal hypospadias, surgery is normally conducted in two stages with the goal of correcting curvature and producing cosmetic benefits. Testosterone can be given before surgery to enhance penile growth, but there are no set guidelines (20). Early intervention, ideally between 6 and 18 months, is critical to reducing psychological stress and the negative consequences of delayed repairs. The majority of hypospadias instances require outpatient surgery between the ages of 6 and 12 months, however lesser cases may not require intervention. Surgical methods may include urethra repair and temporary catheter implantation for recovery. Most hypospadias cases require outpatient surgery between 6 to 12 months of age, while minor cases may not need intervention. Surgical procedures may include urethra reconstruction and temporary catheter placement for healing. Children treated for hypopadias between the ages of 6 and 18 months recover faster and have fewer surgical complications. Early surgery enhances emotional development because children under the age of three rarely recall their procedure. The therapy is a sort of reconstructive plastic surgery that seeks to replace a missing urethra while also correcting its curvature. In addition to eliminating visual faults and boosting psychosocial adaptation, the surgery ensures that the external urethral opening is properly positioned for appropriate urine flow. Boys may benefit from psychotherapy to aid in their integration into society. [21]

Principals of Hypospadias Surgery:

- **Orthopedic surgery:** Following an artificial erection of the penis during surgery, penile curvature is assessed and managed. The Nesbit method is typically used to rectify the penis's curvature. Grafting the tunica albuginea can help straighten the penis in severe situations. Rarely is the chordee resected, and urethral plate conservation is required for tubularized incised plate (TIP) urethroplasty.

- **Urethroplasty:** The rebuilding of the absent distal urethra is known as urethroplasty. The surgical methods listed below vary mainly in urethroplasty: flap application, urethral plate incision, and free oral mucosa transplants.

- **Neourethral coverage:** The neourethra is protected from fistula formation by a second layer of tissue. Preputial, penile, or scrotal skin are frequently used to raise a pedicled subcutaneous (dartos) flap

- **Meatoplasty and glanuloplasty**: These procedures involve reconstructing the glans and meatus to create a meatus with a vertical slit at the tip of the penis

- **Skin closure**: A variety of methods, including as penile skin transfer, are used to cover the penile shaft with skin.

- **Meatal advancement and glanuloplasty:** is referred to as MAGPI Hypospadias Operation (Duckett, 1981b). Only modest distal hypopadias (cosmetic indication) can be treated with the MAGPI procedure. See chapter Urologic Surgery/MAGPI-method for hypospadias repair for technique and problems.

- **Urethroplasty using tubularized incised plate (TIP):** For distal to proximal penile hypopadias, TIP urethroplasty is a method for tubularizing the urethral plate (Snodgrass, 1994). The glans and meatus have good esthetic results, and the TIP urethroplasty is thought to be technically straightforward with a low rate of complications. Additionally, re-operation with a maintained urethral plate can benefit from TIP urethroplasty. Instead of being removed, the urethral plate is deeply and longitudinally cut. The urethral plate is sealed around a catheter following mobilization and tubularization. For more information, check the section on urologic surgery and tubularized incised plate (TIP) urethroplasty.

- **Repairing Mathieu Hypospadias**: For distal penile hypospadias, the Mathieu hypospadias repair is a good choice (Mathieu, 1932). The urethral plate is covered by raising and flipping a rectangle of skin over the proximal urethra. There is a variation of the original method with a V-incision of the flap (MAVIS = Mathieu and V incision sutured) to prevent a horizontal meatus. Unfavorable meatal cosmetics, skin flap necrosis with fistula, or urethral meatus stricture are the most frequent consequences. For more information, visit the section on Mathieu hypospadias repair and urologic surgery
- **For distal penile hypospadias:** For distal to mid-penile hypospadias, a pedicled preputial flap (island) is used to repair the missing urethra (Duckett, 1981b). To cover the preserved urethral plate, the flap is twisted around the penis and applied using an only technique. Following urethral plate resection, a tubular island flap is feasible. For more information, visit section Urologic Surgery (22)

This diagram showcases the surgical techniques and step-by-step procedures used in the repair of hypospadias.

Fig.5. The illustration depicts the pre-surgery condition, the surgical reconstruction of the urethra, and the postoperative results after hypospadias correction.

Tubularized incised plate urethroplasty:

1+2) Deep incisions between the urethral plate and glans wings, as well as a circumferential incision and degloving of the penile shaft
2+3) The urethral plate is deeply cut
4) Closure of the neourethra
5) Using a second layer of well-vascularized tissue from the preputium to cover the neourethra
6) Wound closure and glanuloplasty.

This illustration demonstrates the methodical surgical approach utilized in the initial phase of hypospadias correction.

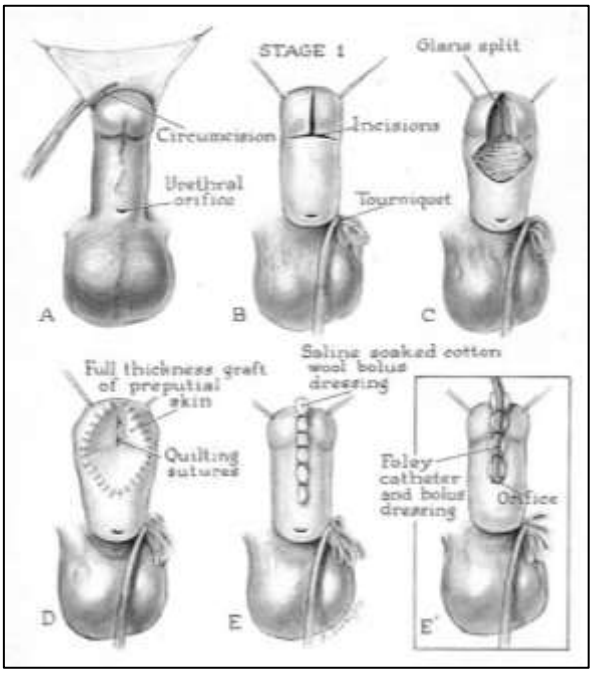

Fig.6. The diagram shows the progressive surgical steps comprising glans incision, graft application, suturing, and bandaging throughout the staged hypospadias repair process.

Mathieu hypospadias form

1) Circumferential gash with sparing of a parameatal skin delirium
2) The skin delirium is flipped distally to cover the urethral plate
3) Coverage of the neourethra using a alternate subcaste of well- vascularized towel from the preputium
4) Glanuloplasty and crack check

Prevention:

Hypopadias affects around one in every 250 newborn males, a common birth disorder whose prevalence is said to have risen in the last three decades. The syndrome is defined by varying degrees of penile curvature and an abnormal urethral opening in the penis. Although the precise origin of hypospadias remains unknown, endocrine disruptors and environmental factors are suspected to play a role. Animal studies have shown that certain estrogens, pesticides, antihistamines, and flame retardants can produce hypospadias at physiological amounts. Genetic investigations that reveal multiple markers associated with an increased incidence of hypospadias point to a combination of genetic susceptibility and environmental exposure during critical stages of urethral development. We plan to identify patients who are genetically predisposed to hypospadias in order to prevent it. In particular, this group should take every precaution to prevent maternal exposure to endocrine disruptors during the first trimester of pregnancy, which can result in hypospadias. (23)

CONCLUSION:

Hypospadias is a prevalent and medically significant congenital condition affecting the male external genitalia, noted for the abnormal location of the urethral opening, curvature of the penis towards the ventral side, and the incomplete formation of the foreskin. Occurring in about 1 in every 250 male births globally, it is a significant issue in the fields of pediatric urology and pediatric surgery. While this condition is typically identified at birth, its effects can persist beyond infancy, possibly influencing urinary function, sexual health, fertility, and psychosocial well-being in the long run if not addressed.The causes of hypospadias are intricate and involve multiple factors, including genetic factors, hormonal imbalances, and environmental effects. During the critical period of fetal genital development, especially between 8 and 14 weeks of pregnancy, disruptions in the production or functioning of androgens are pivotal in the failure of urethral folds to fuse and in the

abnormal development of the penis. Growing evidence indicates that endocrine-disrupting chemicals and the age of the mother being advanced are modifiable risk factors, underscoring the importance of preventive measures during the early stages of pregnancy. Hypospadias clinically manifests with varying degrees of severity, from mild distal types to more severe proximal forms that frequently coincide with additional genitourinary abnormalities. Proper classification based on the anatomical location of the urethral opening is crucial for effective management and surgical preparation. Timely diagnosis, thorough assessment, and recognition of accompanying anomalies are essential aspects of treatment, especially in complicated or proximal instances where evaluations of endocrine and genetic factors may be necessary. Surgical correction continues to be the primary approach to treatment, focusing on achieving both functional and aesthetic normalization of the penis. Developments in surgical methods, including tubularized incised plate urethroplasty, MAGPI, and flap-based repairs, have greatly enhanced results with minimal complication rates when conducted at the ideal age of 6 to 18 months. Timely intervention not only increases the likelihood of surgical success but also reduces psychological distress and aids in healthy emotional development. In summary, addressing hypospadias necessitates a collaborative effort from pediatricians, urologists, endocrinologists, and surgeons to achieve the best results. Ongoing investigation into its causes, prevention, and long-term effects is crucial for enhancing diagnostic approaches, advancing surgical methods, and minimizing the impact of the condition. With prompt identification, suitable surgical intervention, and consistent follow-up, the outlook for boys with hypospadias is very promising, enabling them to live healthy and fulfilling lives.

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