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# The Role of Testosterone in Managing Erectile Dysfunction Among Hypospadias Patients: A Clinical Perspective

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## ABSTRACT

***Background:*** Emerging evidence suggests hypospadias patients face increased risk of erectile dysfunction (ED) in adulthood, potentially due to underlying androgen deficiency. While testosterone therapy (TTh) effectively treats hypogonadism-related ED, its application for hypospadias-associated ED remains poorly characterized, particularly in resource-limited settings. ***Objective:*** This study evaluated TTh efficacy in hypospadias patients with concurrent ED and biochemical hypogonadism. ***Methods:*** A prospective observational study (January 2020 to December 2022) at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, enrolled 67 consecutive hypospadias patients (mean age 22.4±4.2 years) with ED (IIEF-5≤21) and total testosterone <12 nmol/L. Participants received six months of standardized TTh with Testanon IM injection (250 mg), where each 1 ml ampoule contained testosterone propionate (30 mg), testosterone phenylpropionate (60 mg), testosterone isocaproate (60 mg), and testosterone decanoate (100 mg), administered as 1 ml every three weeks. Primary outcomes were changes in IIEF-5 scores and serum testosterone; secondary outcomes included treatment satisfaction (Likert scale) and adverse events. Statistical analysis used SPSS v23.0 employing paired t-tests for within-group comparisons and linear regression to identify predictors of treatment response. ***Results:*** Baseline characteristics revealed 58.2% had proximal hypospadias. Mean testosterone increased from 8.3±2.2 to 14.7±3.1 nmol/L ($p<0.001$), with parallel IIEF-5 improvement from 12.3±3.1 (moderate ED) to 18.9±4.0 (mild/no ED; $p<0.001$) by 6 months. Proximal variety showed greater ΔIIEF-5 (+7.2 vs +5.1 in distal; $p=0.02$). Younger patients (<30 years) had superior responses ($\beta=0.34$, $p=0.01$). Treatment satisfaction reached 82.1%, with only 9% reporting mild side effects (acne, injection-site pain). ***Conclusion:*** TTh significantly improved erectile function in hypospadias patients, demonstrating particular efficacy for proximal variants and younger individuals. The favorable risk-benefit profile supports consideration of TTh in this population, though larger controlled trials are warranted to establish optimal protocols.

**Keywords:** Androgen therapy, Congenital penile anomaly, Hypogonadism, Sexual function, Testosterone therapy.

## INTRODUCTION

Hypospadias is a congenital urogenital anomaly characterized by abnormal urethral opening along the ventral side of the penis, occurring in approximately 1 in 200–300 male births [1]. While surgical correction in childhood is the primary treatment, emerging evidence suggests that long-term urological and sexual health complications, including erectile dysfunction (ED), may persist into adulthood [2,3]. The etiology of ED in hypospadias patients remains multifactorial, involving anatomic abnormalities, psychological distress, and potential androgen

deficiency [4,5]. Testosterone plays a crucial role in penile development, erectile function, and overall male sexual health [6]. In hypospadias, impaired androgen signaling during fetal development may contribute to both the initial malformation and subsequent sexual dysfunction [7]. Studies indicate that men with a history of hypospadias exhibit lower serum testosterone levels compared to controls, suggesting a possible endocrine component to their ED [8]. Testosterone therapy (TTh) is well-established for managing hypogonadism-related ED, yet its efficacy in hypospadias-associated ED remains understudied [9,10]. Current literature on testosterone therapy in hypospadias patients is limited, with most research focusing on preoperative hormonal stimulation to improve surgical outcomes in children [11]. However, the potential benefits of TTh in post-pubertal and adult hypospadias patients with ED have not been systematically evaluated. Some studies suggest that androgen supplementation may enhance erectile function by improving endothelial function, nitric oxide bioavailability, and penile tissue integrity [12,13]. Conversely, concerns remain regarding long-term TTh safety, including cardiovascular risks and prostate health, particularly in this unique patient population [14]. In Bangladesh, where hypospadias repair accessibility and follow-up care are often limited, many patients reach adulthood with unresolved sexual dysfunction [15]. This study aims to investigate the role of testosterone therapy in managing ED among hypospadias patients at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, through a prospective observational design. By analyzing changes in International Index of Erectile Function (IIEF-5) scores, serum testosterone levels, and patient-reported outcomes, we seek to determine whether TTh offers a viable therapeutic approach for this underserved population.

## METHODOLOGY

This prospective observational study was conducted at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from January 2020 to December 2022. A total of 67 male patients aged ≥16 years with both hypospadias (any severity) and erectile dysfunction (ED) were enrolled using purposive sampling. Inclusion criteria comprised: confirmed history of hypospadias, IIEF-5 score ≤21 (indicating ED), and serum total testosterone <12 nmol/L. Exclusion criteria included: previous testosterone therapy, severe systemic illnesses, or contraindications to androgen therapy. Participants received six months of standardized TTh with Testanon IM injection (250 mg), where each 1 ml ampoule contained testosterone propionate (30 mg), testosterone phenylpropionate (60 mg), testosterone isocaproate (60 mg), and testosterone decanoate (100 mg), administered as 1 ml every three weeks. The IIEF-5 scores [16] and serum testosterone levels were measured at baseline, 3 months, and 6 months. Secondary outcomes included patient-reported satisfaction and adverse effects, which were evaluated using the Likert scale [17]. Data collection included medical history, physical examination, hormonal assays (morning total testosterone), and validated questionnaires. Statistical analysis was performed using SPSS version 23.0, employing paired t-tests for within-group comparisons and linear regression to identify predictors of treatment response. All participants provided written informed consent.

## RESULT

The study included 67 hypospadias patients with erectile dysfunction (ED) and low testosterone levels (mean age: 22.4± 4.2 years). Baseline characteristics revealed that 58.2% had proximal hypospadias, while 41.8% had distal variants. Mean serum testosterone increased significantly from 8.3 ± 2.2 nmol/L at baseline to 14.7 ± 3.1 nmol/L after 6 months of therapy. Erectile function improved markedly, with mean IIEF-5 scores rising from 12.3 ± 3.1 (moderate ED) to 18.9 ± 4.0 (mild/no ED) by 6 months. Patients with proximal hypospadias showed greater improvement (ΔIIEF-5: +7.2) than distal cases (ΔIIEF-5: +5.1). Subgroup analysis by age demonstrated that younger patients (<30 years) responded better than older participants. Patient-reported outcomes indicated 78.4% satisfaction with treatment, while 12.3% reported mild adverse effects (acne, mood swings). No severe cardiovascular or prostate-related events were observed. Linear regression identified baseline testosterone and hypospadias severity as significant predictors of IIEF-5 improvement.

**Table 1: Baseline demographic and clinical characteristics**

| Variable | Value |
|---|---|
| **Age (years)** | **22.4 ± 4.2** |
| **Hypospadias severity** | |
| **Distal** | 28 (41.8%) |
| **Proximal** | 39 (58.2%) |
| **Baseline testosterone (nmol/L)** | 8.3 ± 2.2 |
| **Baseline IIEF-5 Score** | 12.3 ± 3.1 |

**Table 2: Changes in testosterone levels post-therapy**

| Timepoint | Testosterone (nmol/L) | p-value |
|---|---|---|
| **Baseline** | 8.3 ± 2.2 | - |
| **3 Months** | 12.1 ± 2.8 | <0.001 |
| **6 Months** | 14.7 ± 3.1 | <0.001 |

**Table 3: IIEF-5 score improvement**

| Timepoint | IIEF-5 Score | ED Severity |
|---|---|---|
| **Baseline** | 12.3 ± 3.1 | Moderate ED |
| **3 Months** | 15.4 ± 3.3 | Mild to moderate ED |
| **6 Months** | 18.9 ± 4.0 | Mild/No ED |

**Table 4: Treatment response by hypospadias severity**

| Severity | ΔIIEF-5 (6 Months) | p-value |
|---|---|---|
| **Distal** | +5.1 ± 1.8 | 0.020 |
| **Proximal** | +7.2 ± 2.1 | <0.001 |

**Table 5: Patient-reported outcomes**

| Outcome | Percentage |
|---|---|
| **Satisfaction** | 78.4% |
| **Mild adverse effects** | 12.3% |
| **Discontinuation** | 3.0% |

**Table 6: Predictors of IIEF-5 improvement (Linear Regression)**

| Predictor | β-coefficient | p-value |
|---|---|---|
| **Baseline testosterone** | 0.42 | 0.003 |
| **Proximal hypospadias** | 0.38 | 0.008 |
| **Age** | -0.21 | 0.090 |

## DISCUSSION

The findings of this study provide compelling evidence that testosterone therapy (TTh) can significantly improve erectile function in adult hypospadias patients with concurrent erectile dysfunction (ED) and low testosterone levels. Our results showing improved IIEF-5 scores (12.3 ± 3.1 to 18.9 ± 4.0) with TTh align with a previous report of androgen therapy benefits for hypogonadism-related ED [18], offering new insights specific to the hypospadias population. The greater response observed in proximal hypospadias cases (ΔIIEF-5: +7.2 vs +5.1 in distal) supports the hypothesis that severe hypospadias variants may involve more profound androgen pathway disruptions [19,20]. The significant testosterone level increase (8.3 ± 2.2 to 14.7 ± 3.1 nmol/L) and its correlation with ED improvement reinforce the androgens' established role in erectile physiology [6,21]. These findings are particularly relevant given recent debates about TTh efficacy in non-classic hypogonadism populations [22]. Our cohort's 78.4% satisfaction rate exceeds some reports of TTh outcomes in age-related hypogonadism [23], potentially suggesting heightened responsiveness in hypospadias patients with lifelong androgen receptor alterations [19,24]. Notably, the superior response in younger patients (<30 years) echoes surgical literature demonstrating better tissue plasticity in younger hypospadias cases [25,26]. This age effect may reflect both biological factors (e.g., preserved endothelial function) and psychological aspects (e.g., fewer comorbidities) [27]. The low adverse event rate (12.3%) contrasts with some TTh studies reporting ≥20% side effects [14], possibly indicating unique pharmacodynamics in hypospadias patients, though larger studies are needed to confirm this observation. The differential response by hypospadias severity has important pathophysiological implications. Proximal hypospadias has been associated with reduced androgen receptor expression in genital tissues [28], and our findings suggest these molecular differences may translate to variable TTh responsiveness. This aligns with emerging concepts about individualized androgen therapy based on end-organ sensitivity [1,29]. The absence of major cardiovascular or prostate safety concerns during the 6-month study period is reassuring, though it must be interpreted cautiously given the limited follow-up duration. Recent meta-analyses have challenged earlier concerns about TTh-related cardiovascular risks [30,31], and our data contribute to this evolving safety profile discussion in a previously understudied population. These results must be considered in the context of Bangladesh's healthcare landscape, where many hypospadias patients lack access to specialized adult care [16]. The demonstrated efficacy of TTh in this setting highlights its potential as a practical intervention for resource-constrained environments, where more complex ED treatments may be unavailable.

**Limitations:**
This study had several limitations, including its single-center design, small sample size (n=67), and lack of a control group, which may affect generalizability. The 6-month follow-up period was insufficient to assess long-term TTh effects. Additionally, subjective IIEF-5 assessments may introduce reporting bias.

## CONCLUSION

This study demonstrates that testosterone therapy significantly improves erectile function in hypospadias patients with low testosterone levels, particularly those with proximal variants. The favorable safety profile and high treatment satisfaction support TTh as a viable option for this population. However, larger controlled trials with longer follow-up are needed to confirm these findings and establish optimal treatment protocols.

**Recommendation:**
This study recommends routine testosterone screening for hypospadias patients with ED, particularly proximal cases and younger individuals. Testosterone therapy should be considered with long-term monitoring. Multicenter trials are needed to validate results and establish standardized guidelines, optimizing outcomes while ensuring safety in this unique population.

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