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The analysis of paternity and long-term sexual outcomes in adult hypospadias patients after urethroplasty: a systematic review and meta-analysis

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ABSTRACT

Background: Hypospadias patients need to undergo surgical management during childhood to enable a satisfactory quality of life, including sexual function in adulthood. While previous clinical trials have predominantly focused on urinary functional outcomes, recent investigations have expanded to examine sexual and reproductive consequences. Thus, this study aims to evaluate the postoperative clinical outcome and paternity in adult hypospadias patients after urethroplasty for hypospadias repair in childhood.

Method: A systematic literature search of electronic databases was performed based on PRISMA statements. The databases searched included PubMed, EbscoHost, Scopus, and Cochrane Library. Included studies are clinical trials that evaluate adult patients with hypospadias repair during childhood with various urethroplasty interventions, comparing postoperative clinical and sexual function, specifically paternity. All studies were evaluated based on the Newcastle-Ottawa scale and synthesized quantitatively with Review Manager 5.3.

Result: Among 185 studies in the initial search, only four cohort studies are eligible in this review, representing the analysis of 567 adult patients across the globe. Our analysis using a fixed-effect model revealed no statistically significant odds ratio 0.85 [95%CI: 0.55–1.31, p=0.78, I2=90%].

Conclusion: Urethroplasty in adults with repaired hypospadias showed no differences in paternity and sexual outcomes.

Keywords: *hypospadias, paternity, sexual function, surgery, urethroplasty*.
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INTRODUCTION

Hypospadias is one of the most frequent congenital urogenital disorders, affecting about 0.2% of male neonates globally.[1] Numerous environmental and genetic factors have been linked to interfering with the urethral plate's normal hormonal maturation, while the exact cause is still mostly unclear.[1,2] The primary short-term objective of hypopadias surgery is to achieve a penile morphology as near to normal anatomy as possible through structural correction. Surgical treatment is typically advised between 6 and 18 months of age.[1-3]

Surgical management, generally performed in early life, seeks to promote the proper functioning of urinary mechanisms and lay the groundwork for effective sexual performance in later life.[3] The aims of such interventions include ensuring adequate urinary flow dynamics, uncomplicated erectile function, and normal ejaculatory performance, as well as addressing aesthetic factors such as suitable meatal location, foreskin restoration, and symmetrical scrotum formation.[4] Nonetheless, extensive longitudinal research investigating the diverse effects of surgical correction on outcomes in adulthood is still limited. Research indicates that hypospadias may affect genital development during puberty and may have an effect on adult penile function, even with early surgical correction.[5,6]

While previous clinical trials have predominantly focused on urinary functional outcomes, recent investigations have expanded to examine sexual and reproductive consequences.[7,8] Understanding these long-term implications is crucial for establishing appropriate follow-up protocols and management strategies. Although several comparative studies have examined sexual function between hypospadias patients and control populations, with particular attention to compromised sexual psychology and penile development in proximal cases, these investigations have predominantly emphasized body image concerns.[9]

Consequently, critical questions regarding the capacity for satisfactory sexual function and successful establishment of reproductive relationships remain inadequately addressed, leaving significant knowledge gaps in our understanding of long-term outcomes for both patients and their families. This review examines current

available evidence of the long term impact on paternity in adults diagnosed with hypospadias after certain urethroplasty techniques to specifically address the extended sexual and fertility outcomes following hypospadias repair.

METHOD

Search Strategy

Literature search was carried out based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements across databases such as PubMed, EbscoHost, the Cochrane Library, and Scopus.[10] Authors used a blend of MeSH terms and keywords for a thorough search. Keywords may include "Hypospadia," "Postoperative Urethroplasty," "Paternity," "Sexual Function," and related synonyms.

Study Selection

This study included the following criteria that must be met for inclusion: articles in English published from the inception of the databases to January 2025, focusing on long term postoperative outcomes in adult patients with hypospadia repair during childhood with various urethroplasty techniques by evaluating the paternity and sexual functions of long term postoperative outcomes. Paternity rate was defined as the age at which the patients who had offspring had married, while sexual functions were defined as experiences in sexual intercourse and ejaculation, evaluated using validated questionnaires such as the International Prostate Symptom Score (IPSS), the International Index of Erectile Function (IIEF-15). Both were the primary outcomes of this study since they are highly associated with the long-term outcomes in adult hypospadias after urethroplasty. The studies were excluded if they were not published in English, solely focused on animal models or in vitro experiments, studies about adult primary hypospadias repair, patients with sex development disorders, two with mixed gonadal dysgenesis, and one with XX male, irretrievable full text, and studies that did not fulfill the methodological quality based on Scopus or Sinta indexes. Subsequently, all relevant articles were organized using Mendeley Reference Manager, which was employed to eliminate duplicate records both automatically and manually. The final collection of articles was then exported to Microsoft Excel for screening based on title and abstract, followed by a meticulous examination of the full texts. During the selection procedure, any disputes were settled by discussion and agreement.

Data Extraction

Authors extracted data from the literature by recording, including publication year, study design, participant demographics, detailed descriptions of the urethroplasty, and the outcomes of paternity and sexual functions. Extraction will be conducted independently by the research team, ensuring consistency and accuracy in the data collated. In cases where disagreements arose during the screening or data extraction process, the authors resolved them through mutual discussion. A third independent author served as an arbitrator and made the final decision if a consensus could not be reached.

Assessment of Risk of Bias

Authors independently evaluated the quality of the research papers using distinct tools, the Newcastle-Ottawa scale (NOS) for observational studies.[11] The NOS employs three criteria to assess observational studies: sample selection, study comparability, and study result, encompassing eight items with scores ranging from 0 to 9. Scores within 0-3, 4-6, and 7-9 correspond to studies of poor, moderate, and high-quality, respectively. In case of any disagreements between the two authors during the assessment process, they were resolved through consensus.

Statistical Analysis

Review Manager 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used to conduct the statistical analysis. Using dichotomous outcomes, the event parameter was evaluated. The Q or I^2 test was used to calculate the degree of trial heterogeneity. When there was evidence of considerable trial heterogeneity (P0.10 and/or I^2>50%), a random-effects model was applied.

RESULTS

Initial search found 185 potential articles; after excluding duplicates, there are 155 unique articles. Following that, 75 records had a relevant title and abstract, and only 20 of them are available for full-text access. After screening based on eligibility criteria and exclusive criteria, 4 records are eligible for quantitative and qualitative synthesize in this study. These studies are cohort studies with 4 cohorts recruiting 567 adult patients with a history of hypospadias repair during childhood across the globe. Figure 1 presents the comprehensive literature search strategy and screening process. Table 1 shows the characteristics of the included studies. All the included studies are high-quality articles based on the NOS score (Table 2), representing the robust methodology and results for each study.

Two cohort studies were analyzed to assess the odds ratio between adult post-repaired hypospadias and healthy control groups' evaluation of paternity events. Our analysis using a fixed-effect model revealed no statistically significant difference with an odds ratio of 0.85 [95%CI: 0.55 – 1.31, p= 0.78, I2=90%] as seen in Figure 2.

DISCUSSION

Our findings suggest that hypospadias surgical intervention generally preserves sexual function while achieving satisfactory psychosexual outcomes and paternity rates similar to health controls. However, ejaculatory complications remain a significant challenge, particularly in proximal cases requiring extensive reconstruction. However, long-term sexual outcome studies following hypospadias surgical intervention present significant methodological challenges in clinical research.

The major limitations include patient drop-out over the long period needed for sexual maturation, problems in finding participants, and the reluctance of some to participate in sexuality-focused studies.[12-15] There is some evidence that participants with hypospadias may overreport their sexual function, while those who refuse participation might represent a group particularly dissatisfied with their results.

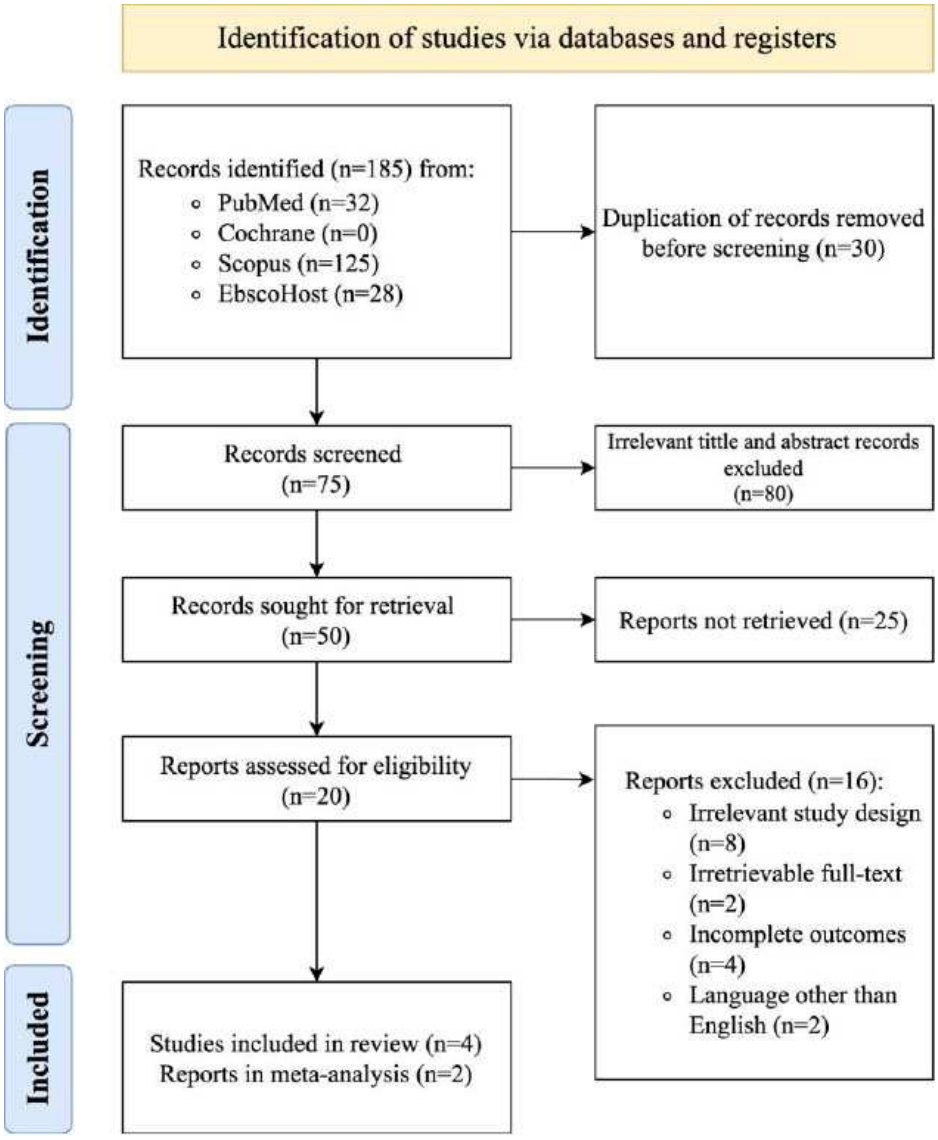

Figure 1. PRISMA Flow Chart.

There was considerable reluctance to discuss problems of penile abnormalities in those with proximal hypospadias.[12-15] Assessment of the benefits of surgery may be usefully augmented by comparison with age-matched, untreated hypospadias control groups, but these are extremely hard to find.

Sexual desire and behavior did not significantly differ between the surgery and control groups. According to these findings, sexual function is typically preserved following surgical repair of hypopadias, which is in line with findings from other studies.[4] In the meantime, a long-standing theory contends that long-term psychosexual development may be negatively impacted by surgically correcting hypospadias.[16] Commonly reported psychosexual sequelae include a reluctance to seek sexual experiences, a desire to conceal genitalia in public situations, feelings of shame during sexual intercourse, and incidents of teasing by peers. These issues are generally more pronounced in patients with proximal hypospadias compared to those with distal forms. In contrast, most studies have shown that surgical repair of hypospadias during childhood has no adverse effects on psychosexual function in adulthood. Parameters such as sexual inhibition, sexual intercourse frequency, masturbation, and sexual partners have been reported to be similar to those of control groups.[12-15]

Ejaculatory problems following hypospadias repair are difficult to evaluate due to the lack of standardized assessment tools. Consequently, it is often impossible to compare studies dealing with ejaculation problems, a task made even more difficult by the fact that hypospadias classifications are heterogeneous and that countless surgical techniques have been used for their repair. Nevertheless, it appears that ejaculation-related problems significantly impact the long-term sexual functioning of most patients. Reported problems with ejaculation include anejaculation, milking of the ejaculate, dribbling, spraying of the ejaculate, delayed ejaculation, painful ejaculation, retrograde ejaculation, and premature ejaculation.[4,14,15]

Testicular dysfunction may be linked to hypospadias. The disability is thought to be associated with testicular dysgenesis syndrome, and men who have hypospadias may become infertile or subfertile. Parental subfertility is an established factor in the etiology of hypospadias, but the true fertility potential of patients with hypospadias is poorly characterized.[4] Population-based studies have reliably reported that men with hypospadias have reduced paternity rates. Skarin et al. reported a reduced paternity rate in this group.[16] The study found an increased likelihood of these men using assisted reproductive technologies, regardless of the severity of the hypospadias or the presence of cryptorchidism, with the greatest association in proximal cases.[16] According to Schneuer et al., men with hypopadias had a 21% lower paternity rate than those without the condition (19.2% vs. 31.2%).[17] Additionally, paternity rates among hypospadias patients tended to decline as the severity of the condition increased (midshaft and proximal versus glandular instances).[13,15,17] Supporting these findings, a Danish registry study showed lower successful paternity rates among men with hypospadias repair, where only 24% of 1,083 men were registered as fathers compared with 29.4 % of age-matched native Danish men.[18] Whether these reduced paternity rates arise from impaired semen quality or functional factors remains to be elucidated and awaits further study.

The present study acknowledges certain limitations to our findings due to methodological constraints that

Table 1. Summary of study results

Authors	Location	Number of analyzed patients (n)	Comparison groups (n)	Mean age at first operation in years (SD/ range)	Classification of hypospadia	Type of repair	Sexual functioning/ satisfaction	Paternity
Kiss et al.; 2011[12]	Hungary	167 (104 vs 63)	Age-matched healthy men (n=63)	4.5 (3–7)	-Midshaft -Proximal	Denis Browne procedure	- Satisfaction: yes; 92% vs 84%, *P* = 0.15 (NS) - Sexual satisfactions scale (0–10): 9 (7.5–10) vs 8 (6–9) *P* = 0.007 - Masturbation; yes 58% vs 75% *P* =0.33 (NS) - Satisfaction scale (0–10): 6 (4–8) vs 8 (7–9) *P*<0.0001	Has a child? Hypospadias: 33% (34/104) vs control: 38% (24/63), *P* =0.92 (NS)
Kanematsu et al.; 2016[13]	Japan	108	Healthy survey control (n=108)	4.7 (2–17)	-Glandular & penile (n=57) -Proximal (n=36) -Unknown (n=15)	Two-stage repair: inverted preputial flap & Johansson technique	- IIEF-5 Q1 only (for intercourse): 3 (1–5) - The final rate of successful achievement of intercourse in patients with proximal-type hypospadias was also lower compared with those who had milder-type disease (100% vs 72%)	- Rate of paternity was associated with the absence of additional surgery after undergoing the repair (*P*=0.013) - Paternity: 31/108 vs 40/108
Rynja et al.; 2018[14]	Netherland	202 (12 vs 42 vs 148)	-Distal hypospadias (n = 42) -Control group of male medical students (n = 148)	1.3 (1.1–2.7) vs 1.3 (0.9–3.4) (NS)	-Primary proximal hypospadias (n=12) -Distal hypospadias (n=42)	Transverse preputial island tube	IIEF-15: - Erectile function 28.5 vs 29.0 vs 29.0 (NS) - Intercourse satisfaction 10.0 vs 12.5 vs 11.0 (NS) - Orgasmic function 7.5 vs 10.0 vs 10.0 (*P*<0.05, both) Ejaculation problems: proximal vs distal, dripping/ manual 4/9 vs 4/38, *P* < 0.05	Paternity: 4/12 vs 33/42, *P*<0.01
Kanematsu et al.; 2019[15]	Japan	90 (12 vs 78)	-reoperated for non-obstructive cause & no reoperation (n=78) -control group of male medical students (n = 148)	4.3 ± 2.9	-Glandular & penile (n=44) -Proximal (n=34) -Unknown (n=12)	Two-stage repair: inverted preputial flap & Johansson technique	- IIEF-5 Q1: 3.3 ± 0.9 vs 3.3 ± 1.0, *P*=1 - The sexual intercourse rate was statistically equivalent between the study group and the study controls (*P*=0.76) - Weak or incomplete ejaculation in the urethral obstruction group vs the control group (66.7% vs. 15.6%, *P* = 0.0017).	Paternity was absent in the patients who were reoperated for obstructive complications (0/12) of the urethra vs healthy control 31/78, *P*=0.2

Abbreviations: n: number, NS: not significant, IIEF-15: (5–75 points) international index of erectile function, *P*: p-value, SD: standard deviation, N/A: not available

Table 2. **Newcastle-Ottawa Scale (NOS) quality assessment of the selected articles**

Reference	Selection (max 4 stars)	Comparability (max 2 stars)	Exposure (max 3 stars)	Total	Interpretation
Kiss et al.; 2010[12]	★★★	★★	★★★	8	Good
Kanematsu et al.; 2016[13]	★★★	★★	★★★	8	Good
Rynja et al.; 2018[14]	★★★	★★	★★★	8	Good
Kanematsu et al.; 2019[15]	★★★	★	★★★	7	Good

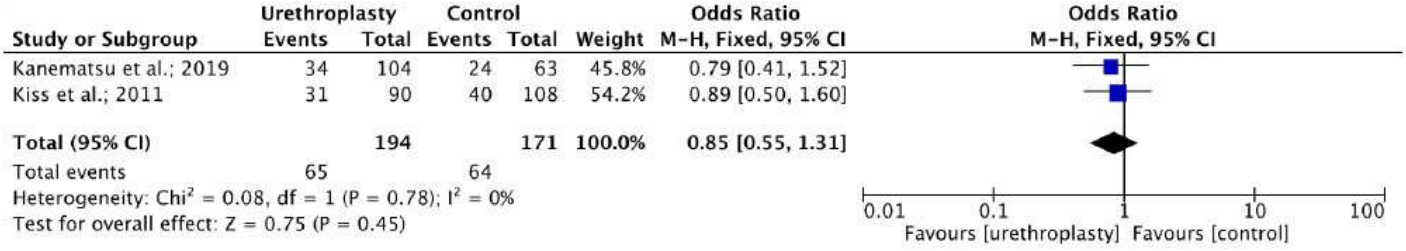

Figure 2. Fixed-effect modeled forest plot for evaluation paternity between adult post-repaired hypospadias and healthy control groups.

warrant consideration. Firstly, selection bias may have been introduced because observational studies constituted the majority of the papers in our systematic review, using exploration of the past two decades of medical records. Secondly, patient attrition during extended follow-up periods leads to difficulties in maintaining long-term contact with study participants. Thirdly, potential response bias in self-reported outcomes, as the studies relied on questionnaires. This limitation may raise concern for the possible idealization of sexual performance in respondent data. Lastly, limited availability of age-matched non-surgical control groups as comparators.

CONCLUSION

In conclusion, analysis of the available evidence implies that urethroplasty in adults with repaired hypospadias showed no differences in paternity and sexual outcomes. While current evidence supports the efficacy of surgical intervention in preserving sexual function, further research is needed, particularly focusing on long-term outcomes and objective assessment measures. Future studies would benefit from improved methodological approaches to address current limitations in data collection and analysis.

DISCLOSURE

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Ethical Clearance

Ethical clearance was not required since this was a systematic review.

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Conflict of Interest

None.

Author Contribution

TMSU is involved in concepting, designing, conducting, and supervising the study; also writing and preparing the manuscript. LOA was involved in designing and conducting the study, as well as writing and preparing the manuscript. All authors had agreed to this final version of the manuscript to be submitted to this journal.

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