Incidence of Urethrocuteanous Fistula after Primary Hypospadias Repair: A Meta-Analysis Study

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ABSTRACT

Background: Hypospadias affects approximately one in every 200–300 male live births. The most frequent complication after hypospadias repair is urethrocutaneous fistula, even in experienced hands.

Purpose: To provide an updated meta-analysis of the global incidence of urethrocutaneous fistula after primary hypospadias repair using different techniques.

Methods: The authors searched PubMed, Scopus, Web of Science [WOS], Cochrane, Embase, Medline, and Google Scholar from January 2016 to January 2022 using relevant keywords. The reference lists of full-text articles identified through the search were also checked to identify any potentially eligible studies. This study screened 110 studies, of which 15 fulfilled the eligibility criteria for inclusion in the final meta-analysis.

Results: A total of 2040 cases mentioned 287 ure throcutaneous fistula events, with a percentage of 14.068% [ranging from 11.012 to 18.05], significant heterogeneity [p-value <0.0001], and an I2 of 75.72% [inconsistency] with a 95% CI for I2 of 59.95 – 85.28. To our knowledge, this is the highest reported incidence of urethrocuteanous fistula after primary hypospadias repair compared to previous studies.

Conclusion: Urethrocutaneous fistula is the most frustrating complication after hypospadias repair; therefore, this meta-analysis review was designed to provide a pooled estimate of the updated and near-accurate incidence of urethra-cutaneous fistula after primary repair. These study findings could be important for surgeons and health personnel to consider during the preoperative period.

Keywords: Urethrocuteanous Fistula; Complications; Hypospadias; Primary Repair; Single-Stage; Urethroplasty.
INTRODUCTION

The urogenital tract is one of the body systems most frequently affected by congenital abnormalities. Hypospadias is also known to represent one of the most common urogenital congenital anomalies, affecting approximately one in every 200–300 male live births [1].

There is no doubt that a comprehensive text is needed to provide guidance for the best management of hypospadias with the least complicated outcomes [2]. Worldwide literature demonstrates wide discrepancy between published complication rates for different repair types and a poor evidence base for the current clinical management of hypospadias [3].

Urethrocutaneous fistula [UCF] is the most frustrating morbidity associated with hypospadias repair, with an incidence ranging from zero to over 35%. The average incidence is approximately 7.5%, but this percentage varies according to the surgeon's experience and the technique used during the operation [4].

In comparison with a 2015 published meta-analysis by Hardwicke et al. [4], this study aims to update information about the actual incidence of urethrocutaneous fistula after primary hypospadias repair using single-stage procedures, in order to provide updated guidance for the proper management of hypospadias repair.

MATERIALS AND METHODS

In this review, we followed the PRISMA statement guideline during this systematic review and meta-analysis preparation and performed all steps according to the Cochrane Handbook of Systematic Reviews of Intervention [5].

Search strategy and study selection: Authors searched PubMed, Scopus, Web of Science [WOS], Cochrane, Embase, Medline, and Google Scholar from January 2016 to January 2022 relevant keywords. The review's reference lists of full-text articles were checked to identify any potentially eligible studies. The included studies were manually screened to select other relevant studies.

Eligibility criteria and study selection: Authors included studies that followed these criteria: [1] Interventional and observational studies including clinical trials, cohort, and case-control. [2] All published studies in patients who underwent primary hypospadias repair. The exclusion criteria were as follows: [1] Published conference abstracts, letters, comments, editorials, practice guidelines, book, or book chapters. [2] Patients undergoing revision surgery were also excluded due to reported high fistula incidence that may affect the overall results. [3] Studies written in a language other than English, and finally, we excluded the duplicated articles by the same author unless those with longer follow-up studies. All published articles were screened with no restrictions for data search. Titles and abstracts were done in two parts, followed by full-text screening. Reference lists of the included studies were manually screened to find any other eligible studies that may be omitted from previous steps.

Quality assessment: The assessment of quality and risk of bias of the analyzed studies was performed using the Agency for Health Care Research and Quality [AHRQ] checklist. This list has 21 evaluation criteria, one item is scored as 1 if included in the article and 0 if it is not. A score of 8 or higher indicates a high-quality study.

Statistical Analysis: This meta-analysis was conducted by using Open Meta-Analyzer [OMA] [Computer program] [Version 5.4. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014]. Regarding the study outcomes, a risk ratio [RR] with a 95% confidence interval [CI] was used for dichotomous variables. Cochrane's P values and I2 were tested to examine heterogeneity among the studies. High heterogeneity most likely existed due to clinical and methodological factors, so the random effect model was adopted in this meta-analysis even though I2 was small. Funnel plots and the Egger regression test could not be performed due to the limited number of included studies.

RESULTS

A search for “hypospadias, primary repair, single stage repair” provided 110 studies, of which 17 were relevant to this study. A total of 110 abstracts were screened, of which 15 studies met the eligibility criteria. After collecting the information from the full-text articles, all 15 studies fulfilled the criteria to be included in the final meta-analysis.
Figure [1]: PRISMA flow diagram of the literature search results

Meta-analysis

Urethrocutaneous fistula

15 studies with a total of 2040 cases mentioned 287 urethrocutaneous fistula events with a percentage of 14.068% [ranging from 11.012 to 18.05] with significant heterogeneity and p-value <0.0001, I² [inconsistency] 75.72% and 95% CI for I² was 59.95 – 85.28

Table [1]: Meta-analysis of the urethrocutaneous fistula.

<table>
<thead>
<tr>
<th>Study</th>
<th>Total number</th>
<th>Event</th>
<th>Event rate [%]</th>
<th>95% CI of rate [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdelhalim et al. [10]</td>
<td>100</td>
<td>14</td>
<td>14.000</td>
<td>7.871 – 22.373</td>
</tr>
<tr>
<td>Daboos et al. [12]</td>
<td>80</td>
<td>4</td>
<td>5.000</td>
<td>1.379 – 12.310</td>
</tr>
<tr>
<td>Chalapathi et al. [15]</td>
<td>75</td>
<td>7</td>
<td>9.333</td>
<td>3.835 – 18.289</td>
</tr>
<tr>
<td>Chou et al. [16]</td>
<td>150</td>
<td>6</td>
<td>4.000</td>
<td>1.482 – 8.503</td>
</tr>
<tr>
<td>Krull et al. [17]</td>
<td>84</td>
<td>15</td>
<td>17.857</td>
<td>10.353 – 27.737</td>
</tr>
<tr>
<td>González et al. [18]</td>
<td>43</td>
<td>8</td>
<td>18.605</td>
<td>8.391 – 33.401</td>
</tr>
<tr>
<td><strong>Total [fixed effects]</strong></td>
<td><strong>2040</strong></td>
<td><strong>287</strong></td>
<td><strong>14.068</strong></td>
<td><strong>12.526 – 16.008</strong></td>
</tr>
<tr>
<td><strong>Total [random effects]</strong></td>
<td><strong>2040</strong></td>
<td><strong>287</strong></td>
<td><strong>14.068</strong></td>
<td><strong>11.002 – 18.015</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity

| Q      | 57.6648 |
| DF     | 14      |
| Significance level | P<0.0001* |
| I² [inconsistency] | 75.72% |
| 95% CI for I² | 59.95 – 85.28 |

Q: Total variance for heterogeneity; I²: Observed variance for heterogeneity; CI: Confidence interval [LL: Lower limit; UL: Upper Limit]
DISCUSSION

The main goal for hypospadias repair is to achieve both cosmetic and functional abnormalities. There are multiple surgical options and several proposed algorithms to guide urethroplasty decision-making [22]. Complications are common after hypospadias repair, ranging from fistulae to complete loss of the neourethra, requiring total reconstruction. The most frequent complications...
after hypo-spadias repair are urethrocutaneous fistulae and meatal stenosis, even in experienced hands [23].

Many Factors favoring the development of urethrocutaneous fistula were mentioned in the literature, the most important factors were meatal stenosis, Urethral stricture, Inadequate waterproofing, Use of improper sutures, needles, and suturing technique, Tension at suture line, and poor tissue handling and infection [24].

In this study, a total of 2040 patients were included in the selected studies. Although the year of publication was limited to 01/01/2016 onwards, retrospective and prospective studies reported on patient cohorts undergoing primary hypospadias repair between 2010 and 2016 were added. The age at which primary hypospadias repair was performed was reported in 15 studies varying greatly from 11 months to 62 months with a mean of 31.64 months. The study reported a mean follow-up of 34 months ranging from 6 to 112 months.

The most common operations for distal done were different types of the preputial flap [1105], TIP and its modifications [635], Duckett repair [133], MAGPI [83], Mathieu [16], Koyanagi [10], Thiersch–Dupla [9], other procedures [49].

The meatal position was reported in all studies and was anterior or distal [glanular/subcoronal/distal shaft] in 48.1%, middle [mid shaft] in 5.3%, and posterior or proximal [proximal shaft/ penoscrotal/scrotal/perineal] in 46.6% of cases.

Due to the high variability of surgical procedures and management protocols reported, no valid comparisons can be made or conclusions drawn about the optimum surgical technique or management.

The most commonly reported complication was urethrocutaneous fistula with 287 reported events with a percentage of 14.068% [ranging from 11.002 to 18.015] with significant heterogeneity and p-value <0.0001, I2 [inconsistency] 75.72% and 95% CI for I2 was 59.95 – 85.28.

A Similar meta-analysis Study was conducted by Hardwicke et al [4]. Pooled estimates of the proportions of complications following single staged hypospadias repair. The overall incidence was reported as the post-operative fistula was 7.5% [95% CI: 5.8 - 9.4]; urethral stricture or meatal stenosis 4.4% [95% CI: 3.1 – 5.8] and wound or glandular dehiscence 2.1% [95% CI: 1.3 – 3.1].

The pooled proportion of fistulae from European studies was 8.9% [95% CI: 5.2 – 13.3]; from African studies was 6.5% [95% CI: 3.4 – 10.6] and from Asian studies was 8.0% [95% CI: 6.3 – 9.9] [4]. In our study the pooled proportion of fistulae from European studies was 15.02%; from African studies was 10.0% and from Asian studies was 13.90% [Figure 3].

Figure [3]: Pooled proportion of fistulae upon the continent
Urethrocutaneous fistulae can present many years after the original hypospadias repair. The majority are diagnosed within the first year after surgery, and the median time to fistula presentation is 8.5 months with a range of less than one month to 13.9 years post-hypospadias surgery. Rates of fistulae are probably underreported due to short follow-ups, but more importantly, due to patients transferring to other surgeons for fistula repair [28].

Ceccarelli et al. conducted a study for the best surgical technique for distal hypospadias, they concluded that MAGPI [Meatal Advancement and Glandoplasty Procedure Incorporated] procedure, the TIP [Tubularized Incised Plate] urethroplasty with or without the Retik variation, and the Duckett technique were the 4 surgical techniques used for repair, where MAGPI was performed in 40 boys [21.3%], the TIP in 125 boys [67.4%]. Out of the whole population, 46 boys [24.6%] presented with at least one complication following their initial repair, with a median elapsed time of 11.5 months [range 6.5–22.5]. Surgical complications included: 19 fistulas [10.2%], 15 stenosis [8%], 6 dehiscence [3.2%], and 6 other or mixed complications [3.2%] [41].

These results were similar to Wilkinson et al. systematic literature review of mid-penile repairs in children using TIP and Mathieu since 1990 which detailed nearly similar UCF and meatal stenosis rates. TIP cases showed a mean fistula rate of 5.9%, with a range from 0 to 16%, and the mean meatal stenosis rate was 2.1%, ranging from 0 to 17%. On the contrary, Mathieu repaired cases showed a mean fistula rate of 6.7%, ranging from 0 to 9%, the mean meatal stenosis rate was 3.6%, extending from 0 to 6%, and the glandular dehiscence rate represented 1%, ranging from 0 to 8% [3].

A multicentric study at the Department of Urology, Mansoura, Egypt; Eberhard-Karls University, Germany; and University Putra Malaysia, Selangor, Malaysia; conducted that among 4034 patients in whom dartous flap was used to cover the neourethra, fistula occurred in 170 [4.2%]. Of the 3932 cases of distal hypospadias, the dartous flap was used as a single layer in 3077 patients [follow-up 1–87 months]. Among these, 156 [5.1%] developed a urethrocutaneous fistula. A significantly lower rate of fistula incidence was observed for double-layer dartous flap coverage in distal hypospadias. Fistula incidence was significantly higher among patients with proximal hypospadias [meatus proximal to the midshaft up to the penoscrotal junction]; nine of 102 patients developed fistulas [8.8% vs 5.1% for single-layer DF in distal hypospadias; p = 0.01] [26].

A retrospective study for the Complications of proximal hypospadias repair with transverse preputial island flap urethroplasty showed a total of 320 patients, with a mean follow-up of 40.2 months [range: 1–156 months]. Complications were encountered in 125 patients [39.1%], including fistulas in 53 [16.6%]. The mean timing of presentation with a complication was 15.8 months [median: 1.7, range: 1–145], of which 79.2% were early complications and 20.8% were late complications. These results indicate that transverse preputial island flap urethroplasty still has a high incidence of complications, even when performed by highly experienced physicians [14].

In a recent retrospective study conducted in the urology department at El Azhar University Hospital, Department of Urology discussing urethrocutaneous Fistula After Hypospadias Repair in children with a total of 316 cases who underwent hypospadias surgery between February 2015 and December 2020, 246 children followed up on for more than 6 months in this report and results revealed that 49 children out of 246 developed urethrocutaneous fistulae [19.8%, 49/246] [27].

This was similar to the extracted results from El Azhar University Hospital, Department of Plastic Surgery in the past 5 years span, 68 cases of hypospadias were done of which 54 of them were distal or mid penile, both repaired on one stage, 47 by Tip repair and its modifications, 5 by MAGPI technique, and 2 by Mathieu Technique, the study showed 7 cases with fistula after primary repair [12.9%].

A metanalysis study for the complications of hypospadias repair conducted at Ain Shams University concluded that in terms of urethral fistula, the incidence of fistula following repair of mid-penile hypospadias after TIP technique was 10.3%, after the Mathieu technique was 4.3%, after Modified Koyanagi technique was 13.7%, after Preputial Island flap technique was 2.6%, and after Lateral based flap technique was 4.8%. Thus, fistula is less common after the Preputial Island flap technique and Mathieu technique; while it was more common with the Modified Koyanagi technique [28].
In another study conducted at El Kasr Alainy Hospitals [Abo El Resh] for children with distal to mid-penile hypospadias repaired using Dorsal Inlay Graft Urethroplasty [DIGU]. The urethra-cutaneous fistula was detected in [10%] of cases. The fistulae were small and without meatal stenosis. Fistulae were repaired 6 months later by simple closure. Meatal stricture: [5%] patients with meatal stenosis; both responded to regular dilatation. Meatal retraction: [5%] patients with meatal recession. Failure: [5%] Patients with dehiscence “disrupted urethroplasty” both of them operated after 6 Months [29].

Conclusion

Patients undergoing hypospadias repair come from a heterogeneous cohort, with a wide range of variables. As such, strong recommendations have been difficult to make for the overall management of hypospadias and its outcomes, with most reporting studies being small-scale with subtle refinements to previously published techniques. To combat this problem, this literature review was designed to give a pooled estimate of the most commonly reported outcomes, for the most commonly performed surgical procedures, intending to produce a general estimation of urethrocuteaneous fistula incidence, we found that the incidence of fistula following repair was 14.068% [ranging from 11.012 to 18.05] with significant heterogeneity and p-value <0.0001. The limitations of this study included other factors that affected urethra-cutaneous fistula formation such as long-term outcomes including sexual function, urine stream, psychological assessment, and chordee that have not been approached in this review.

Compliance with ethical standards

Ethical approval: Considering the nature of this study, ethical approval was not required.

Human and animal rights: This study is a systematic review with meta-analysis of outcomes which does not include research directly involving human or animal participation.

Informed consent: Considering the nature of this study, informed consent was not required.

REFERENCES


