

ORIGINAL RESEARCH

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# Significance of inflammatory biomarkers and urethral histology in patients with urethral stricture disease in relation to treatment outcome—a single centre prospective study in the north-eastern part of India

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## Abstract

**Background:** Inflammation plays a very important role in defining the urethral stricture. Inflammatory biomarkers may play an important role in predicting the underlying pathophysiology as well as outcome of surgery. Histology of urethral strictures along with histology of urethra proximal and distal to stricture segment may have a role in predicting the outcome of the surgery. The literature discussing this aspect is rare; thus, this novel study aimed to find out the role of inflammatory biomarkers and urethral histology in predicting the outcome of surgery in urethral stricture disease.

**Methods:** This prospective study had 105 patients with age more than 15 years with urethral stricture. Baseline characteristics, routine blood tests including inflammatory blood markers (CRP, ESR, HbA1C, fasting insulin, serum ferritin, etc.) were recorded. They underwent various types of surgery, and first biopsy was taken from stricture segment and second biopsy from proximal to stricture segment and third biopsy from distal to stricture segment and evaluated for the presence of features of lichen sclerosus and inflammation. Primary endpoint was to diagnose the role of inflammatory biomarkers and histology of stricture in stricture recurrence.

**Results:** Their mean age was  $43.3 \pm 13.46$  years. Mean CRP of  $11.54 \pm 3.64$  in patients with failure and  $9.59 \pm 2.77$  in patients with successful outcome ( $p$  0.025). Other inflammatory biomarkers like HbA1C, fasting insulin, ESR, serum ferritin, NLR had no significant correlation with the outcome. The presence of features of lichen sclerosus like hyperkeratosis and severe inflammation in stricture segment predicted higher likelihood of failure. Histology of proximal and distal segment of urethral stricture had no significant relationship in predicting outcome. Staged urethroplasty with buccal mucosal graft outperformed single-stage urethroplasty in biopsy-proven LS strictures.

**Conclusions:** The present study found a negative impact of increased CRP and the presence of features of lichen sclerosus in urethral histology with the outcome of urethral stricture disease. Thus, our study confirms that inflammatory biomarkers (CRP) and histology of stricture segment play a significant role predicting the outcome of surgery.

**Keywords:** Inflammatory biomarkers, Histology of stricture, Neutrophil-to-lymphocyte ratio, Staged urethroplasty

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## 1 Background

Urethral stricture is relatively common in men with an associated prevalence of 229–627 per 100,000 males, or 0.6% of the risk population [1].

Aetiology of anterior urethral strictures is iatrogenic in 33%, idiopathic in 33% and, to a lesser extent, trauma in 19% and inflammation in 15% [2]. The choice of surgery for urethral stricture is based on multiple factors which include its location, length, aetiology, and availability of desirable graft or flap. Substitution urethroplasty is the mainstay of treatment for penile and panurethral strictures [3–5].

Lichen sclerosus et atrophicus (LS) affects urethra and causes complex strictures. It appears to develop more commonly in those suffering from systemic inflammatory conditions (e.g. metabolic syndrome) [6]. The histopathology of these strictures shows chronic inflammation.

In non-LS strictures, inflammation is also being recognized as a component [7, 8].

Inflammation plays a very important role in defining the urethral stricture. Inflammatory biomarkers may play an important role in predicting the underlying pathophysiology. So biomarkers like erythrocyte sedimentation rate (ESR), fasting insulin, glycosylated haemoglobin (HbA1C), C-reactive protein (CRP), serum ferritin, and neutrophil-to-lymphocyte ratio (NLR) which are associated with the inflammatory state have been investigated to relate with the outcome and severity of urethral strictures and correlate with urethral stricture with histology [9–19].

C-reactive protein exhibits elevated expression during inflammatory conditions such as rheumatoid arthritis, some cardiovascular diseases, and infection [9, 10]. As an acute-phase protein, the plasma concentration of CRP deviates by at least 25% during inflammatory disorders [9].

Glycated haemoglobin (HbA1c) is associated with inflammation being independent of blood glucose concentration and obesity in nondiabetic patients [12].

It is well established in adults that obesity is related to hyperinsulinemia and insulin resistance, both of which are well related to inflammatory state. Thus, fasting insulin can also be used as a marker of inflammatory state [13, 14].

There is a positive correlation between ferritin and CRP, signifying an underlying low-grade inflammation, leading to subsequent iron deficiency, most probably, because of inflammation-mediated iron sequestration in the reticuloendothelial system [16, 17].

High levels of ferritin are positively correlated with the risk of metabolic syndrome and obesity [16, 17].

ESR has been used as one of the markers of inflammation and has been found to be elevated in urethral

strictures [18, 19]. The neutrophil-to-lymphocyte ratio (NLR) is used to determine the prognosis of an inflammatory reaction and is a component of routine blood count analyses performed [20, 21].

This study examined the association of histology of urethral strictures and urethral segment proximal and distal to stricture and inflammatory biomarkers with the final outcome. It also compared different types of surgical techniques and their outcome.

## 2 Methods

The study was conducted from January 2019 to December 2020 at our institute. A total of 117 patients were included in the study but only 105 patients could be followed up, which were finally analysed as 12 patients were lost to follow up.

All patients (>15 years of age) had urethral stricture diagnosed by physical examination, uroflowmetry, RGU (retrograde urethrogram), MCU (micturating cystourethrogram) and on table urethroscopy.

Patients with comorbid conditions like diabetes mellitus, untreated urinary tract infections, skin lesions like psoriasis, recurrent urethral strictures and malignancy and patients who are unfit for general or spinal anaesthesia or refuse to participate in this study were excluded.

Their presenting complaints and past history were duly noted, and American Urological Association Symptom Score (AUASS) was calculated. Patients underwent physical examination of oral cavity, abdomen, genitalia and rectum. Preoperative anaesthetic assessment and clearance for surgery were taken.

The extent and diagnosis of urethral stricture were done by RGU (retrograde urethrogram), MCU (micturating cystourethrogram) and on table urethroscopy. Ultrasound of Kidney, Ureter, and Bladder (USG(KUB)) was done to see the status of upper urinary tract and bladder.

Markers of inflammations like erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), glycosylated haemoglobin (HbA1C), fasting insulin, serum ferritin and neutrophil-to-lymphocyte ratio (NLR) were obtained.

Types of surgical technique included single-stage buccal mucosal graft (BMG) urethroplasty -BMG urethroplasty (Kulkarni's technique) (BMGK), ventral onlay BMG urethroplasty (BMGVO), Asopa's dorsal inlay BMG urethroplasty (DIA), end to end anastomotic urethroplasty (EEA), Orandi's flap (OF) and staged urethroplasty (Johanson stage1 urethroplasty and dorsal inlay buccal mucosa graft urethroplasty in second stage) (JS). All the patients were operated by single surgeon, and histopathology was examined by the single pathologist.

Biopsies (total number –3) were taken from urethral stricture and urethra proximal and distal to stricture of each patient. These were examined to look for the

presence of features of lichen sclerosus et atrophicus which include 1) hyperkeratosis, 2) epithelial thinning or thickening, 3) basal cell layer degeneration, 4) dermal collagen homogenization, or 5) lichenoid lymphocytic or plasmacytic infiltrate. Features of inflammation were also seen in segments of urethra proximal and distal to stricture, and they were classified into no inflammation, mild, moderate, and severe degree of inflammation. The pathologist classified the severity of the inflammation as none, mild, moderate, or severe based on a grading system which is used in the literature associated with benign prostatic hyperplasia. These findings were correlated with the final outcome.

Complications during intraoperative and postoperative period were noted at wound site (both-site of urethroplasty and donor site if any) and classified using Clavien–Dindo system.

Patients were discharged with per urethral catheter (PUC) and supra pubic catheter (SPC) if any. PUC was removed after 4 weeks, and SPC was clamped. After successful voiding, SPC was also removed after 5 days.

Patients were followed up at 3 months, 6 months and 9 months after surgery with Uroflowmetry, AUASS and RGU, and urethroscopy if needed. Uroflow rate of more than or equal to 15 ml/s was taken as successful, and any subsequent procedure on urethra was considered unsuccessful.

## 2.1 Statistical analysis

Chi-square test was used to evaluate association between categorical variables. Data were checked for normality using Kolmogorov–Smirnov and Shapiro–Wilk test. Independent T test and ANOVA are used depending on fulfilment of normality assumption for continuous variables. A p value less than 0.05 was considered as statistically significant at 5% level of significance. All data were analyzed using SPSS version 21.

## 3 Results

The demographic characteristics of the patients in terms of age, body mass index, smokers, tobacco chewers, betel nut chewers along with history of any previous procedure such as circumcision, per urethral catheter insertion (PUC), HoLEP (holmium laser enucleation of prostate), ThULEP (thulium laser enucleation of prostate) were analysed (Table 1).

Their mean age was  $43.3 \pm 13.46$  years, and body mass index (BMI) was  $24.8 \pm 2.63$ . There were smokers (total- 17(16.2%), tobacco chewers (total- 6 (5.7%) and betel nut chewers (total- 9(8.6%)). Eleven patients gave history of previous procedure which included circumcision (six patients), HoLEP (one patient), ThULEP (two patients) and PUC insertion (two patients). Classification

of patients based on location of urethral stricture showed penile urethral stricture (10 patients), bulbar urethral stricture (40 patients) and panurethral stricture (55 patients). There were 19 patients with stricture length of more than 8 cm, 65 patients with stricture length of 5 to 8 cm and 21 patients with stricture length of 2 to 5 cm.

As per EAU classification of urethral stricture according to degree of urethral narrowing, all patients had high degree of urethral narrowing and almost equally divided in category 4 and 5 (Table 1).

Mean CRP of  $11.54 \pm 3.64$  in patients with failure and  $9.59 \pm 2.77$  in patients with successful outcome (Table 2). The **p value was 0.025** which meant CRP correlated significantly in those with adverse outcome. So increased CRP was associated with poorer outcome.

HbA1C values were within normal range in 91 patients (86.7%) and 14 patients (13.3%) had elevated values (Table 2). However, elevated values of HbA1C were not significantly associated with an adverse outcome (p value—0.11).

All patients had fasting insulin within the normal range (upto 25mIU/ml) (Table 2). Thus, it was inferred that fasting insulin level could not predict about the outcome of the surgery.

Mean value of serum ferritin (normal value- 11—306.8 ng/ml) of  $70.52 \pm 22.73$  in patients with failure and  $61.12 \pm 30.24$  in patients with successful outcome (Table 2). Their p value was 0.28 which was insignificant, and thus, there was no significant association with the outcome.

ESR (normal values upto 9 mm/hr) was elevated in both the groups-  $15.4 \pm 2.4$  in successful patients and  $15.8 \pm 2.7$  in unsuccessful patients (Table 2) but had no significant correlation with the outcome as p value was 0.53 showing that ESR did not correlate significantly with the outcome of urethroplasty.

Mean value of neutrophil-to-lymphocyte ratio (NLR) (normal values→1–3) was  $2.21 \pm 0.35$  in patients with failure and  $2.42 \pm 0.47$  with successful outcome. It could not predict the outcome as it was not significantly correlated (p value- 0.11) (Table 2).

LS was histologically established in thirty-seven patients, and the presence of various features was also evaluated. Hyperkeratosis was seen in 23 patients (62.2%) with LS and not seen in 14 (37.8%) patients with LS. Epidermal thinning was seen in 2 (5.4%) patients with LS and not seen in 35(94.6%) patients with LS. Dermal collagen homogenisation was seen in 9 (24.3%) patients with LS. Lichenoid lymphocytic infiltrate was seen in 13 (35.1%) patients with LS.

Table 2 shows that there were ten patients out of 37 patients diagnosed with LS who had adverse outcome. *Hyperkeratosis showed significant correlation with the*

**Table 1** Demographic variables and data related to various aspects of study

Patient Characteristics	N = 105 (number of patients)		
Age, mean ± SD (Standard Deviation) (years)	43.3 ± 13.46		
Body mass index, mean ± SD (kg/m2)	24.8 ± 2.63		
Smokers	17(16.2%)		
Tobacco Chewers	6(5.7%)		
Betel Nut Chewers	9 (8.6%)		
<i>History of previous procedure</i>			
Circumcision	6 (5.7%)		
HoLEP (Holmium laser enucleation of prostate)	1 (0.9%)		
ThULEP (Thulium laser enucleation of prostate)	2 (1.9%)		
PUC (Per urethral catheter) Insertion	2 (1.9%)		
<i>Classification based on aetiology of strictures</i>			
Iatrogenic	5 (4.8%)		
Idiopathic	39 (37.1%)		
LS (Biopsy proven)	37(35.2%)		
Traumatic	24(22.9%)		
<i>Classification of stricture on location</i>			
Penile	10 (9.52%)		
Bulbar	40 (38.09%)		
Panurethral	55 (52.38%)		
<i>Classification of stricture on length</i>			
2–5 cm	21(20%)		
5–8 cm	65 (61.90%)		
> 8 cm	19 (18.09%)		
<i>EAU classification of stricture on degree of urethral narrowing</i>			
Category	Total No. of Patients	No. of successful Patients	No. of unsuccessful patients
0	0	0	0
1	0	0	0
2	0	0	0
3	3	3 (100%)	0
4	52	45 (86.5%)	7(13.5%)
5	50	44 (88%)	6(12%)
<i>Complications of urethroplasty</i>			
Wound hematoma	2 (1.9%)		
Wound infection	14 (13.3%)		
Buccal mucosal graft necrosis	1(0.9%)		
Catheter displacement	3 (2.9%)		
BMG donor site bleeding	2 (1.9%)		
<i>AUASS SCORE</i>			
Pre-operatively	24.71 ± 3.37		
At 3 months	2.50 ± 1.28		
At 6 months	3.97 ± 1.85		
At 9 months	5.27 ± 3.54		

outcome (failure of surgery) ( $p$  value- 0.001). Epidermal thinning was seen in two patients (both had successful outcome). Epidermal thinning did not show any significant correlation with the outcome ( $p$  value—0.08).

Dermal collagen homogenisation was seen in nine patients. Dermal collagen homogenisation showed significant correlation with the outcome of surgery (failure) ( $p$  value—0.02). Lichenoid lymphocyte infiltration

was seen in thirteen patients. *Lichenoid lymphocyte infiltration* showed significant correlation with the outcome (failure) ( $p$  value—0.003).

From Table 2, patients showing mild inflammation in histopathology of stricture segment had no failure in urethroplasty. Six patients with moderate inflammation in stricture segment had failure in urethroplasty and in sixty-six patients with moderate inflammation had successful outcome. Cases with severe inflammation were present in seven unsuccessful cases and in fifteen

successful cases with  $p$  value of 0.02 showing significant relationship with the outcome (failure) of surgery.

Table 3 shows there were nine patients showing mild inflammation, those with moderate inflammation (seen in 14 cases) in urethral biopsy proximal to stricture had 3(21.40%) failed cases and 11 (78.60%) successful cases. Those with severe inflammation were seen in 1 (50%) failed case and 1 (50%) successful case. No inflammation was seen in 80 patients. It did not show any significant correlation with the outcome of surgery.

**Table 2** Correlation of markers/ histologic features with outcome in study population

Characteristic/marker	Patients with successful outcome (values/number)	Patients with unsuccessful outcome (values/number)	$p$ value
<b>CRP</b> (Mean $\pm$ SD)	9.59 $\pm$ 2.77	11.54 $\pm$ 3.64	<b>0.025</b>
HbA1c (Mean $\pm$ SD)	5.52 $\pm$ 0.56	5.78 $\pm$ 0.36	0.11
Fasting insulin (Mean $\pm$ SD)	5.01 $\pm$ 1.99	4.88 $\pm$ 1.79	0.82
Serum ferritin (Mean $\pm$ SD)	61.12 $\pm$ 30.24	70.52 $\pm$ 22.73	0.28
ESR (Mean $\pm$ SD)	15.4 $\pm$ 2.4	15.8 $\pm$ 2.7	0.53
N:L ratio (Mean $\pm$ SD)	2.4 $\pm$ 0.47	2.21 $\pm$ 0.35	0.11
<b>Feature of lichen sclerosis</b>			
1. <b>Hyperkeratosis</b>	17	6	<b>0.001</b>
2. Epidermal thinning	2	0	0.08
3. <b>Dermal collagen homogenisation</b>	7	2	<b>0.02</b>
4. <b>Lichenoid lymphocyte infiltration</b>	11	2	<b>0.003</b>
5. <b>Severity of inflammation</b>			
Mild	11	0	
Moderate	66	6	
<b>Severe</b>	15	7	<b>0.017</b>

**Table 3** Correlation of degrees of inflammation (mild/ moderate/severe) in urethral biopsy of proximal segment with outcome in the study population

Proximal to stricture	Patients with unsuccessful outcome (< 15 ml/s)	Patients with successful outcome ( $\geq$ 15 ml/s)	Total
Mild	0 (0%)	9 (100%)	9 (100.0%)
Moderate	3 (21.4%)	11 (78.6%)	14 (100.0%)
Severe	1 (50.0%)	1 (50.0%)	2 (100.0%)
Not Seen	9(11.25%)	71(88.75%)	80(100%)
Total	13 (12.4%)	92 (87.6%)	105 (100.0%)

**Table 4** Correlation of degrees of inflammation (mild/moderate / severe) in urethral biopsy of distal segment with outcome in study population

Distal to stricture	Patients with unsuccessful outcome (< 15 ml/s)	Patients with successful outcome ( $\geq$ 15 ml/s)	Total
Mild inflammation	0	2	2
Moderate inflammation	0	3	3
Severe inflammation	1	0	1
Not Seen	12	87	99
Total	13	92	105

**Table 5** Correlation of LS with length of stricture

Stricture length	Number of patients with LS		Total	p value
	YES	NO		
2–5 cm	2 (9.5%)	19 (90.5%)	21 (100%)	< 0.001
5–8 cm	20 (30.7%)	45 (69.3%)	65 (100%)	
> 8 cm	15 (78.9%)	4 (21.1%)	19 (100%)	
Total	37 (35.2%)	77 (64.8%)	105 (100%)	

**Table 6** Success rates of different types of surgery performed for urethral stricture in the study population

Type of surgery	Number of patients		Total
	Unsuccessful outcome	Successful outcome	
BMGK	5(17.8%)	23(82.2%)	28 (26.7%)
BMGVO	1(14.3)	6(85.71%)	7(6.7%)
DIA	1(11.2%)	8(88.8%)	9(8.6%)
EEA	2(8.4%)	22(91.6%)	24(22.9%)
JS	3(11.1%)	24(88.9%)	27(25.7%)
OF	1(10%)	9(90%)	10(9.5%)
Total	13(12.4%)	92(87.6%)	105(100%)

Table 4 shows those with mild inflammation present in two urethral biopsy—distal to stricture (both successful), moderate inflammation (seen in 3) in urethral biopsy—distal to stricture had 3 successful cases. Those with severe inflammation were seen in one patient (failed). But there was no significant correlation with the outcome.

In strictures of length (2–5 cm), LS was present in two patients (9.5%), urethral stricture of 5–8 cm, it was present in twenty patients (30.7%), and in more than 8 cm, it was present in 78.9% (Table 5). The *p* value is <0.001 which is significant and shows LS presents with pan urethral strictures or strictures of longer length.

In our study (Table 1), we found that the most common cause of stricture was idiopathic (39%) followed by lichen sclerosus (35.2%), trauma (21.9%), iatrogenic (4.8%).

Table 6 shows success rate of buccal mucosa graft urethroplasty (Kulkarni's technique) in 82.2%, ventral onlay buccal mucosa graft urethroplasty in 85.7%, dorsal inlay buccal mucosa graft urethroplasty in 88.8%, staged urethroplasty (Johanson stage1 urethroplasty with dorsal inlay buccal mucosa graft urethroplasty in second stage) in 88.8%, end to end anastomotic urethroplasty in 91.6% and Orandi's flap in 90%.

In biopsy-proven LS, staged urethroplasty (out of nineteen patients, sixteen were successful and three were failure) had a success rate of 84.2% and single-stage buccal mucosa urethroplasty (out of eighteen patients, eleven

were successful and seven were failure) had a success rate of 61.1%. 91.6% of traumatic and 90% of iatrogenic strictures had successful outcome (*p* value- 0.33).

The mean value of American Urological Association Symptom Score (AUASS) in patients prior to surgery was  $24.71 \pm 3.37$ , while postoperatively at 3 months, it was  $2.50 \pm 1.28$  at 6 months, it was  $3.97 \pm 1.85$  and at 9 months, it was  $5.27 \pm 3.54$ . The *p* value was <0.001 which was highly statistically significant.

Mean of duration of stay was about 5.50 days in BMG urethroplasty of Kulkarni Technique, 5.14 days in ventral onlay type of BMG urethroplasty, 5.67 days in Asopa's technique of BMG urethroplasty, 5.08 days in end to end anastomotic urethroplasty, staged urethroplasty ( first stage- 4.2 days and second stage- 5.1 days), and 5.5 days in Orandi's flap urethroplasty. In staged urethroplasty, duration of stay is much longer than single-stage urethroplasty as patient required two surgeries.

This study (Table 2) showed 1.9% of patients developed wound hematoma, 13.3% had wound infection, 0.9% of patient had graft necrosis, 2.9% of patients had catheter displacement, and 1.9% of patients had bleeding at buccal mucosa graft donor site which required reintervention.

#### 4 Discussion

Barbagli et al. [22] found those with habit of chewing areca nut/betel nut/tobacco chewing not to be ideal candidate for buccal mucosa harvesting. This has a clinical correlation as buccal mucosa graft may not have an optimal function as required.

We postulate that *increased CRP in nondiabetic patients can be used as a marker for increased risk of recurrence of urethral stricture as evidenced from our study* and supported by the findings of Sauver et al. [23] where they found an association between raised CRP levels and increased lower urinary tract symptoms.

We hypothesize that HbA1c cannot be used as a biomarker to predict recurrence in patients with urethral stricture. In contrast to our finding, Liu et al. [12] found HbA1c to be a marker of risk associated with inflammation. This contrast may be a due to our sample size being smaller and our exclusion of diabetic patients from our study.

We postulate that fasting insulin cannot be used as a marker for predicting outcome in patients with urethral stricture. This was in contrast to findings of Singh et al. [13] and Thomas et al. [14] who suggested fasting insulin as a marker of inflammation in obese patients.

No significant association could be found between serum ferritin and outcome of surgical management of urethral stricture, whereas Gillum et al. [16] reported serum ferritin as a marker of inflammation in obese men.



We propose that ESR though a marker of inflammation cannot be used for prediction of outcome in patients with urethral stricture as opposed to findings of Tambo et al. [18]. To confirm or contradict our findings, further studies with larger sample size are required.

However, in contrast to findings of Venugopalan et al. [24], N:L ratio failed to predict the outcome. This may be due to lower size sample and difference in characteristics of patients.

Those with lichen sclerosus (LS) have a higher chance of recurrence of stricture and staged buccal mucosa urethroplasty is a better option than the single-stage urethroplasty. Our findings were in accordance with the study of Belsante et al. [25] and Barbagli et al. [26] as lichen sclerosus is a progressive disease and tends to recur and cause failure.

We found LS is associated with panurethral strictures, this represented the fact that pan urethral strictures are common in patients with LS changes as corroborated by studies of Barbagli et al. [26].

On histological examination of urethral stricture, it was found that LS was present in 35.2% of patients. The presence of hyperkeratosis in urethral mucosa was highly indicative of LS as also supported by the study of Grimes et al. [7].

Our findings are similar to a study by Liu and colleagues [27] in which pathologic re-review of strictures of bulbar urethra identified two or more features characteristic of LS in 44% of patients. Urethral strictures with biopsy-proven LS were found to have a higher failure rate, and staged BMG urethroplasty was found to be better than single-stage BMG urethroplasty.

The presence of severe inflammation in stricture segment was related to adverse outcome, whereas mild to moderate inflammation did not have an bearing on outcome. Biopsy from proximal and distal segment of urethra showing absence of moderate to severe inflammation had a clinical correlation with better outcome but could not be proved statistically. These findings of ours get strengthened by findings of Ekerhult et al. [28]. They stated that histological findings of sclerosis in the resected urethral stricture specimen indicate a significantly higher risk for restriction after urethroplasty surgery.

EEA urethroplasty showed very good results in traumatic stricture with length upto 2 cm with similar results shown by Micheli et al. [29]. Orandi's flap urethroplasty had a success rate of 90% similar to results shown by Goel et al. [30]. Asopa's DIA showed similar results as shown by Aldaqadossi et al. [31]. Asopa technique preserves the blood supply to the urethral plate as the urethral plate

is not dissected off so it may be used in long urethral strictures.

Ventral onlay BMG urethroplasty has been found to be useful in bulbar strictures with success rates comparable to Wessells [32].

Patients had a remarkable reduction in AUASS score post urethroplasty, and duration of stay was found to be longer in staged urethroplasty.

## 5 Conclusions

With advancement in modern medicine, it has become imperative to find the markers which may reflect on the undergoing pathophysiology of the urethral stricture



(A) LS CHANGES SEEN ON GLANS PENIS



(B) POST CIRCUMCISION STATUS

**Fig. 1** a LS (lichen sclerosus) changes seen on glans penis, b post-circumcision status



**PANURETHRAL STRICTURE ON RGU**

**Fig. 2** RGU (retrograde urethrogram) showing panurethral stricture

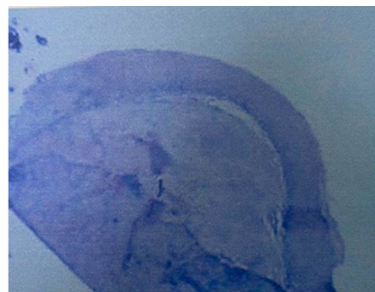


**ASOPA'S TECHNIQUE FOR SECOND STAGE  
JOHANSON'S URETHROPLASTY**

**Fig. 3** Intraoperative picture- dorsal inlay BMG urethroplasty (similar to Asopas Technique) in second stage

disease and can predict the outcome of surgery on follow-up. Our study is a step towards it (Figs. 1, 2, 3, and 4).

Clinically detected lichen sclerosus et atrophicus proven by histopathology of stricture segment showed increased risk of failure and recurrence in urethral stricture patients post-surgery. CRP is the only inflammatory marker which showed a high risk of failure when correlated with the outcome of treatment of urethral stricture. Findings suggestive of severe degree of inflammation in biopsy of urethral stricture had higher degree of failure.



**HYPERKERATOSIS SEEN IN URETHRAL STRICTURE  
SEGMENT**

**Fig. 4** Microphotograph of stricture segment showing hyperkeratosis

Due to lower sample size and short duration of follow-up, long-term multi-institutional studies are required for validation of the findings of this study.

#### Abbreviations

LS: Lichen sclerosus et atrophicus; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; HbA1C: Glycosylated haemoglobin; NLR: Neutrophil-to-lymphocyte ratio; AUASS: American Urological Association Symptom Score; BMG: Buccal mucosal graft; BMGK: BMG urethroplasty (Kulkarni's technique); DIA: Asopa's dorsal inlay BMG urethroplasty.

#### Authors' contributions

PKB contributed to the concept and design of the study. NS and MP contributed to the acquisition of data. SKB, DS, and RTP participated in data analysis and interpretation of data. PKB and NS were involved in drafting the manuscript and critical revision. All authors critically reviewed the manuscript and provided approval on the final draft being submitted, and take complete responsibility for data accuracy. All authors met the International Committee of Medical Journal Editors (ICMJE) authorship criteria and all those who met the ICMJE authorship criteria are listed as authors. All authors read and approved the final manuscript.

#### Funding

No funding was obtained for this study. (Not applicable).

#### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

Institutional Ethical Committee approval was taken prior to the commencement of study (IEC approval number: MC/190/2007/Pt-11/Jun-2019/29). This study was conducted in accordance with the Declaration of Helsinki. Written and informed consent was taken from all patients.

##### Competing interests

The authors declare that they have no competing interests.

##### Consent for publication

Taken from patients on an institutional consent form (available on request).

Received: 7 August 2021 Accepted: 17 October 2021

Published online: 15 January 2022



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