National Board of Examination Journal of Medical Sciences
Volume 1, Issue 8, August 2023, ISSN 2583-7524

National Board of Examination (NBE)
Journal of Medical Sciences

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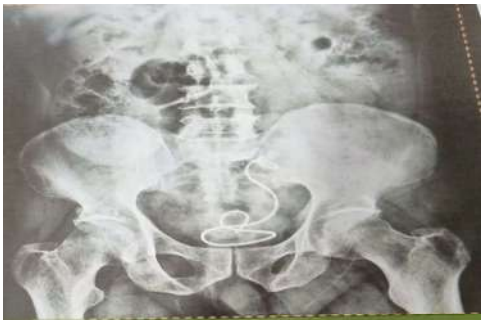
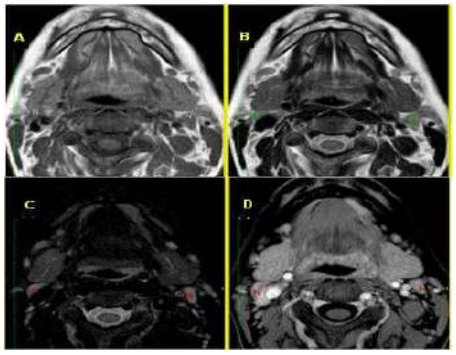
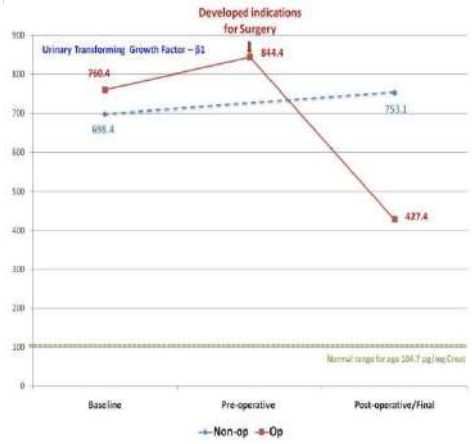


Xray KUB image of the patient showing the retained Double J stent in the left sided ectopic pelvic kidney



A uniformly enhancing mass lesion in MRI
A-T1W Axial
B- T2W Axial
C- STIR Axial
D- Contrast T1W Axial

A. & B. Ventral aspect of the penile shaft with multiple openings, puckered skin, empty left scrotum and right sided streak gonad
C. Three urinary streams while voiding



uTGF-β1 in children with pelvi-ureteric junction-type of hydronephrosis during follow up

NATIONAL BOARD OF EXAMINATIONS –
JOURNAL OF MEDICAL SCIENCES

Volume 1 • Issue 8 • August 2023

National Board of Examination - Journal of Medical Sciences

Volume 1, Issue 8, Pages 478–483, August 2023

DOI 10.61770/NBEJMS.2023.v01.i08.001

EDITORIAL

Universal Health Coverage (UHC) in India: Challenges and Strategies

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Accepted: 01-August-2023 / Published Online: 04-August-2023

The World Health Organization (WHO) has been actively advocating for Universal Health Coverage (UHC) for many years. UHC is a fundamental concept that envisions all individuals and communities have access to essential health services without facing financial hardship. The history of WHO's involvement in promoting UHC can be traced back to the Alma-Ata Declaration in 1978. During the International Conference on Primary Health Care held in Alma-Ata, Kazakhstan, WHO and UNICEF co-organized this landmark event. The declaration emphasized the importance of primary health care as the key to achieving Health for all by the year 2000. It recognized that access to essential health services is a fundamental human right and an integral part of economic and social development.

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However, despite the ambitious goal set by the Alma-Ata Declaration, Health for All by the year 2000 was not fully achieved. In response to the challenges faced, the global health community renewed its focus on UHC in the 21st century. In 2005, the World Health Assembly, the decision-making body of the WHO, adopted a resolution urging member states to work towards achieving UHC. This resolution marked an official commitment to the promotion of UHC as a central pillar of health system strengthening.

In 2010, the World Health Report "Health Systems Financing: The Path to Universal Coverage" was released, which provided further guidance on implementing UHC. The report outlined key principles and strategies for financing health systems in a way that would move countries closer to UHC. In 2012, the 65th World Health Assembly adopted another resolution on UHC, urging countries to take specific actions towards achieving it. The resolution highlighted the importance of

expanding access to quality health services, with a particular focus on vulnerable and marginalized populations.

The Sustainable Development Goals (SDGs), adopted by the United Nations in 2015, included UHC as one of the key targets (SDG 3.8). This further elevated the prominence of UHC on the global health agenda, as it became an integral part of the broader effort to improve health and well-being worldwide. Over the years, WHO has continued to provide technical support to countries in their efforts to design and implement UHC policies and programs. The organization works with governments, civil society organizations, and other stakeholders to advocate for equitable and accessible health systems.

National Status of UHC in India

Universal Health Coverage (UHC) has been a significant focus of the World Health Organization (WHO) in India. The concept of UHC aligns with India's commitment to providing accessible and affordable healthcare services to its population.

This can be better understood by the overview initiative taken by Govt. of India over the time in promoting UHC in India

National Health Policy of 1983

India's National Health Policy of 1983 recognized the goal of *"Health for All"* and emphasized the importance of primary healthcare and equitable distribution of healthcare resources. The WHO provided technical assistance in the development of this policy, supporting India's efforts to strengthen its healthcare system.

Alma-Ata Declaration and Primary Health Care

India was one of the signatories of the Alma-Ata Declaration in 1978, which underscored the significance of primary health care in achieving Health for All. The principles laid out in the declaration influenced India's approach to healthcare, with a focus on primary healthcare services and community-based health programs.

Health Sector Reforms

In the 1990s and early 2000s, India embarked on health sector reforms to improve healthcare delivery and access to services. The WHO provided technical support and expertise during this period to help the Indian government implement various health programs and initiatives.

National Rural Health Mission (NRHM)

Launched in 2005, the NRHM was a flagship program of the Indian government aimed at strengthening healthcare in rural areas. The program focused on maternal and child health, immunization, nutrition, and communicable diseases. The WHO collaborated with India in implementing NRHM and enhancing the quality of healthcare services.

Ayushman Bharat - Pradhan Mantri Jan Arogya Yojana (PM-JAY)

In 2018, India launched the Ayushman Bharat program, which comprises two components - the Health and Wellness Centers (HWCs) and PM-JAY. PM-JAY is the world's largest government-funded health insurance scheme, providing health coverage to over 500 million vulnerable individuals. WHO has been supporting the government in the implementation and scaling up of Ayushman Bharat.

COVID-19 Pandemic Response

During the COVID-19 pandemic, the WHO collaborated closely with the Indian government in managing and mitigating the impact of the pandemic. This included technical

assistance in areas like testing, treatment protocols, and vaccine distribution.

Throughout these initiatives and programs, the Govt. of India has played a significant role to achieving Universal Health Coverage. By providing technical expertise, policy guidance, and strategic support, the WHO has been instrumental in strengthening India's healthcare system and making healthcare services more accessible to its vast population.

The role of National Board of Examination in Medical Sciences (NBEMS)

The National Board of Examination (NBE) in India plays a crucial role in contributing to the achievement of Universal Health Coverage (UHC) goals in the country. As an autonomous body under the Ministry of Health and Family Welfare, Government of India, the NBE is responsible for conducting postgraduate medical examinations and accrediting medical institutions for various training programs. By taking following initiatives NBE contributes to India's UHC goals:

Ensuring Quality Healthcare Professionals

The NBE conducts postgraduate medical examinations, including Diplomate of National Board (DNB) and other specialty courses. By setting and maintaining high standards for medical education and training, the NBE ensures that qualified and skilled healthcare professionals are produced. Quality healthcare professionals are essential to delivering effective and safe healthcare services, which is a critical component of achieving UHC.

Expanding the Healthcare Workforce

The NBE's accreditation of medical institutions for postgraduate training programs helps in expanding the healthcare workforce in the country. More qualified specialists and super-specialists are trained through NBE-accredited institutions, leading to an increased pool of healthcare providers across various regions of India. This, in turn, helps in addressing the shortage of healthcare professionals and improving access to healthcare services, a key aspect of UHC.

Addressing Regional Disparities

The NBE's focus on accrediting medical institutions in different parts of the country helps in addressing regional disparities in healthcare access. By promoting the establishment of accredited institutions in underserved areas, the NBE contributes to the equitable distribution of healthcare resources, which is an essential component of UHC.

Promoting Specialized Care

NBE's role in conducting examinations and training programs for various medical specialties and super-specialties helps in promoting specialized healthcare services. As UHC aims to provide a comprehensive range of essential health services, including specialized care, the NBE's focus on postgraduate medical education and training aligns with this goal.

Strengthening Health Systems

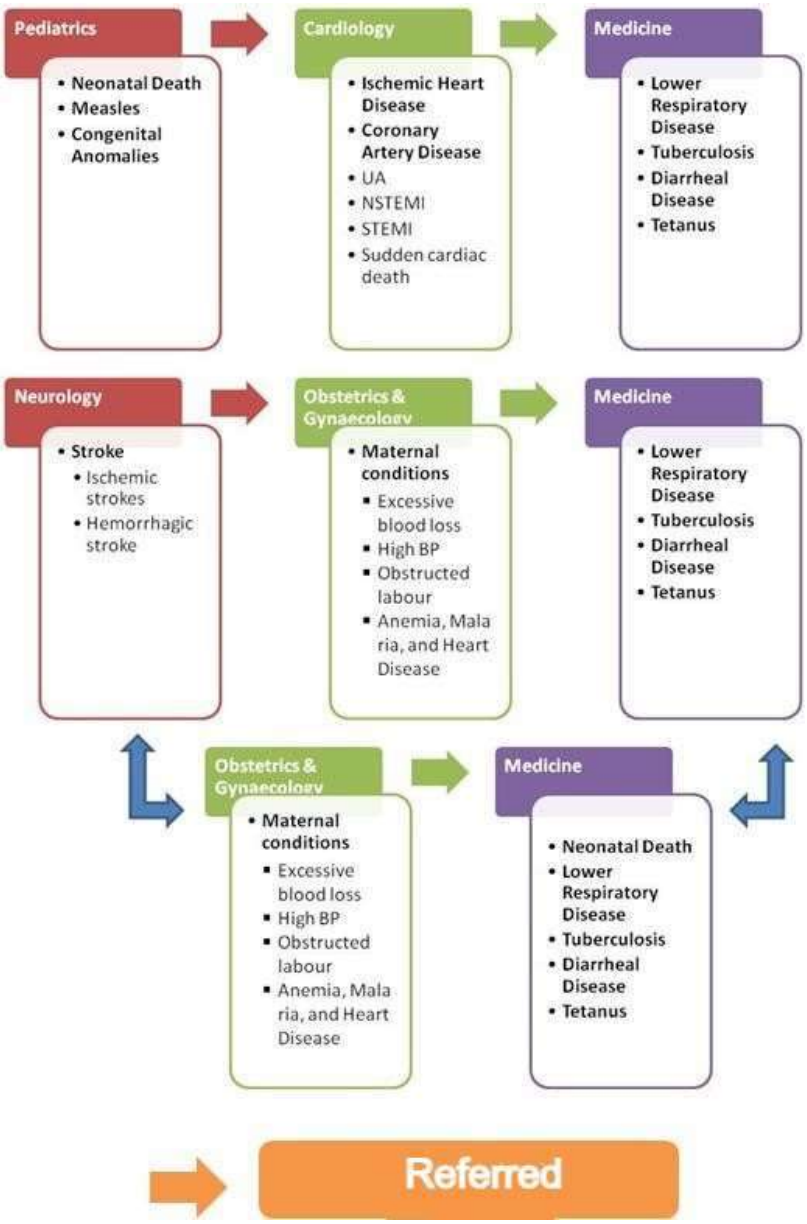
Through its accreditation process and examination standards, the NBE contributes to the strengthening of India's health systems. By ensuring that medical institutions meet certain quality criteria and standards, the NBE supports the development of robust healthcare systems capable of delivering quality services to all citizens, regardless of their socio-economic status.

Supporting Skill Development

The NBE's focus on continuous medical education and training helps in the skill development of healthcare professionals. This is crucial for ensuring that the healthcare workforce remains up-to-date with the latest

medical advancements and can provide evidence-based and efficient healthcare services, which is essential for achieving UHC.

The National Board of Examination plays a vital role in enhancing the quality of healthcare education and training in India, expanding the healthcare workforce, addressing regional disparities, and strengthening health systems. These efforts contribute significantly to the country's progress towards achieving Universal Health Coverage and ensuring that all citizens have access to essential health services. The NBEMS proposed model to towards achieving UHC is depicted in Figure 1.



The patients requiring specialist such as Cardiologist, Neurologist and Nephrologists etc. will be referred to Tertiary Care Hospitals

Figure 1. Current and proposed model of evidence based health system to counter top 10 causes of deaths in India.

The crucial components for achieving UHC in India

The components outlined by Kumar et al. (2016) [1] for the Universal Health Coverage (UHC) model in India are indeed crucial for achieving equitable and comprehensive healthcare access for all citizens. These componentsare discussed briefly by Kumar et al. [1] as follows:

Focus on Outpatient Care

Providing financial coverage for outpatient care is essential for UHC. Many health issues can be effectively managed at the primary care level, reducing the burden on hospitals and tertiary care facilities. This approach promotes early detection and management of health conditions, leading to better health outcomes and cost savings in the long run.

Gatekeeping and Referral System

Implementing a structured referral system and gatekeeping for tertiary care facilities ensures that patients receive appropriate and timely care. It helps in optimizing resource utilization and ensures that patients receive care at the appropriate level of the healthcare system, with specialized care reserved for those who truly need it.

Geographical Coverage with Primary Care Teams

To achieve UHC, it is essential to establish primary care teams led by licensed physicians who can provide comprehensive healthcare services across all age groups, genders, and organ systems. This ensures that healthcare is accessible to people regardless of their location, addressing geographical disparities in access to healthcare.

Strengthening General Health System

Instead of focusing solely on vertical programs for specific diseases, investing in the overall strengthening of the health system is vital. This approach promotes a more comprehensive and integrated healthcare delivery system, addressing multiple health needs simultaneously.

Primary Care as the Foundation

Placing primary care at the core of the healthcare system is crucial. Primary care is often the first point of contact for patients, and well-functioning primary care services can effectively address a significant proportion of health issues, leading to improved health outcomes and cost-effectiveness.

Population-Based Targets and Incentives

Linking financial compensation and incentives to objective population-based targets can encourage healthcare providers to focus on preventive measures and population health outcomes. This approach aligns the incentives of healthcare providers with the overall health goals of the population.

High-Quality Clinical Governance

Ensuring high-quality clinical governance, regulation, safety, and adherence to quality benchmarks are essential for delivering effective and safe healthcare services. It helps maintain standards of care and enhances patient confidence in the healthcare system.

Personal-Centered Comprehensive Care

Providing personalized and comprehensive care in the community setting strengthens the doctor-patient relationship and enhances patient satisfaction. It promotes continuity of care and ensures that individuals receive the care they need within their community.

Establishment of a Central Authority

Having a central authority with a status comparable to other key regulatory bodies ensures effective oversight and governance of the healthcare system. This authority should have the mandate &be insulated from any interference which may jeopardize its independent functioning in the best interest of the public.

Conclusion

Universal Health Coverage (UHC) has been a significant focus of the World Health Organization (WHO) in India. The concept of UHC aligns with India's commitment to providing accessible and affordable healthcare services to its population. The NBEMS along with support of Govt. of India can play a crucial role in contributing to the achievement of Universal Health Coverage (UHC) goals in the country. The implementationof above mentionedcomponents will require collaborative efforts between the government, healthcare providers, civil society, and other stakeholders. By adopting this UHC model, India can make significant strides towards achieving universal and equitable healthcare access for all its citizens.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 484–496, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.002

ORIGINAL ARTICLE

Diagnostic significance of urinary transforming growth factor–β1 in the management of children with moderate to high grade pelvic-ureteric junction obstruction

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Accepted: 01-August-2023 / Published Online: 04-August-2023

Abstract

Objective: The aim of the present study is to evaluate the role of urinary transforming growth factor – β1 (uTGF-β1) in congenital unilateral pelvi-ureteric junction obstruction (PUJO) upto the point of developing conventional indications for surgery and after pyeloplasty with the aim to explore the development of targeted therapeutic strategies aimed at modulating its effects and attenuating renal fibrosis.

Methods: Sixty two children with unilateral pelvi-ureteric junction obstruction, consisting of 46 boys and 16 girls, with a mean age of 9.4 months forms the study group. Twenty three out of 62 (37.1%) developed indication for surgery after a mean follow-up of 24.2±3.7 months. The uTGF-β1 levels have been measured by ELISA at different points of intervals, i.e., before indications for surgery, at the development of indications for surgery and after surgical intervention and compared with children continued to follow-on without indications for surgery.

Results: In children, who were continued to be followed up without indications for surgery, 39 had a mean baseline uTGF-β1 levels of 698.4mg/pg/Cr. which increased to 753.1mg/pg/Cr. (p valuie <0.001) after a follow-up of 24.1 months). As the children developed indications for surgery and subsequently underwent surgical intervention (n = 23), the mean uTGF-β1 baseline levels of 760.4mg/pg/Cr. were increased to 844.4mg/pg.Cr. just before the point of surgical intervention.

Conclusion: Urinary TGF-β1, hold the promise as a potential tool in the diagnosis and follow-up of hydronephrosis. The current evidence suggests that raised uTGF-β1 levels can effectively identify hydronephrosis with early parenchymal injury.

Keywords: uTGF-β1, Pelvi-ureteric junction obstruction (PUJO), Transforming growth factor-β (TGF-β)

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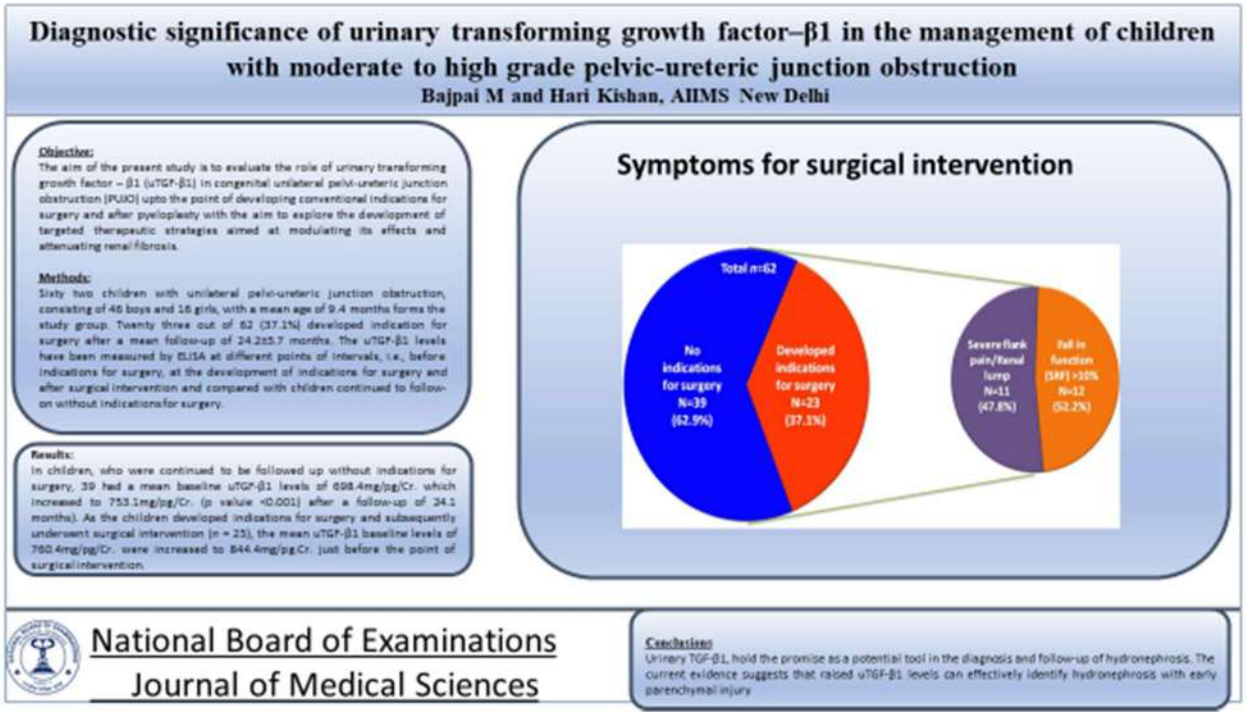
Graphical Abstract



Introduction

Transforming growth factor-β (TGF-β) has long been recognized as a key cytokine involved in the pathogenesis of renal inflammation and fibrosis [1]. The TGF-β superfamily encompasses a range of proteins, including TGF-βs, activins, inhibins, growth and differentiation factors (GDFs), bone morphogenetic proteins (BMPs), and glial-derived neurotrophic factors (GDNFs) Among the TGF-β isoforms found in mammals, there are three major forms: TGF-β1, TGF-β2, and TGF-β3 [2]. TGF-β1, in particular, has been extensively studied and is considered a profibrotic mediator in various kidney diseases [1]. Its role in promoting fibrosis is well established, as it can stimulate the production of extracellular matrix components, such as collagen, and inhibit the breakdown of existing extracellular matrix. This can lead to the accumulation of fibrotic tissue in the kidneys, impairing their normal function. The involvement of TGF-β1 in renal inflammation and fibrosis suggests that it may play a critical role in the progression of kidney diseases. Understanding the mechanisms by which TGF-β1 contributes to these processes can potentially lead to the development of targeted therapeutic strategies aimed at modulating its effects and attenuating renal fibrosis.

The challenges faced by urologists in managing fetal and postnatal hydronephrosis, particularly due to pelvi-ureteric junction obstruction (PUJO). It emphasizes the importance of accurate diagnostic tools to identify cases requiring surgical intervention and to assess renal function deterioration [3]. The current management criteria for PUJO rely on various diagnostic modalities, including serial ultrasonography, diuretic renogram, 99mTc dimercaptosuccinic acid (DMSA) scintigraphy, and excretory urography. The negative response to diuretic stimulation and renal function loss are indicators for surgical intervention i.e. pyeloplasty. The diuretic renogram, despite its invasiveness and use of ionizing radiation, is

commonly used for clinical evaluation of hydronephrosis. Moderate to severe grade hydronephrosis may lead to parenchymal function deterioration which will recovered or plateaued after pyeloplasty. Some patients experience continued renal function decline even after pyeloplasty. This unpredictable course of PUJO necessitates the availability of simple and accurate diagnostic tools to detect early renal function deterioration caused by obstruction before it becomes irreversible [4-6].

The pathophysiology of obstructive uropathy involves complex mechanisms that alter the expression of different growth factors. Growth factors play a role in renal wound healing processes. Urinary TGF-β1 has been associated with both normal and pathological conditions of the urinary tract, including vesicoureteral reflux and hydronephrosis. The aim of the present study is to evaluate the role of Urinary TGF-β1 in congenital PUJO before indications for surgery, at the development of indications for surgery and after pyeloplasty in operated group and to measure the levels of urinary TGF-β1 at the diagnosis and at the completion of study tenure in patients without indications for surgery. Additionally, we correlate this cytokine levels with other traditional markers such as DTPA, DMSA, glomerular filtration rate (GFR), grading of hydronephrosis as per society for foetus urology (SFU), serum creatinine (S.Cr.) and plasma renin activity (PRA) to get insights into the pathophysiology and management of PUJO.

Methodology

This prospective case-control study conducted at Department of Paediatric Surgery, All India Institute of Medical Sciences, New Delhi on patients registered in Wednesday Paediatric Urology Clinic from January 2015 to December 2019.

A total of 93 antenatal diagnosed hydronephrosis patients were initially assessed for inclusion in the study. However, 31 patients were excluded in which 14 cases were bilateral hydronephrosis, 10 had secondary vesico-ureteric reflux, 4 had multicystic kidney disease, 2 had horshoe kidney and one had poly cystic kidney disease. Therefore, the final sample population included 62 patients, consisting of 46 boys and 16 girls, with a mean age of 9.4 months (SD±5.0 months; range: 1 month to 18 months). These patients were matched with 10 controls. (Table 1). The study enrolled patients with unilateral PUJO only. The diagnosis of PUJO has been made on the basis of prenatal and postnatal ultrasonography findings, with the patients exhibiting normal renal function and receiving antibiotic prophylaxis. Twenty three out of 62 (37.1%) developed indication for surgery after a mean follow-up of 24.2±3.7 months (range 18 to 32 months). In 23 children developed indication for surgery 12 had a fall in SRF by >10% and 11 had severe flank pain or abdominal lump. This information outlines the characteristics of the study population, the inclusion criteria, and the initial presentation of the patients with PUJO.

As per the treatment protocol various imaging investigations have been performed to assess the patients with suspected or diagnosed ureteropelvic junction obstruction (PUJO). The inclusion criteria for imaging required ultrasonography showing moderate to gross dilatation of renal pelvis and calyces. The severity of hydronephrosis has been classified into grades III to IV, following the SFU classification [7]. The Tc-99m-DTPA plasma clearance by SPSM (true GFR) has been calculated as per the Russel's method: In this equation, the values of A and B are calculated using the variable T, which represents the sampling time in minutes. The calculations for A and B are as follows:

$A = -0.278T + 119.1 + 2450/T$ $B = 2.886T - 1222.9 - 16820/T$

Table 1. Demographic characteristics of the recruited children

1.	Number of patients	*n*=62
2.	Age [Mean±SD (Range)]	32.1±3.7 (1–84 months)
3.	Follow-up [Mean±SD (Range)	46.0±5.4 (36–61 months)
4.	Gender Male (%) Female (%)	 46 (74.2%) 16 (25.8%)
5.	Side of obstruction Right (%) Left (%)	 33 (56.5%) 27 (46.5%)
6.	Grade of hydronephrosis Gr. III (%) Gr. IV (%)	 21 (33.9%) 41 (66.1%)

The values of D and P should be provided in counts per minute (cpm), and T should be the sampling time in minutes (180 min in this case).

Blood samples were taken to assess the PRA levels and serum creatinine (Cr) values. PRA was measured by radioimmunoassay using a commercially available kit. (Normal PRA range according to the age —1–12 months = 4–8 ng/ml/hour; 1–3 years = 1–9 ng/ml/hour; 3–6 years = 1–5 ng/ml/hour. Cr was assessed by the kinetic enzymatic method at 6 monthly interval. The concentration of urinary TGF-β1 was measured using a commercially available quantitative sandwich enzyme-linked immunoassay (ELISA) kit. Standard curves were created, and the values obtained were expressed as pg/mL.

Healthy controls – Children with no renal pathology at the time of the enrollment of the patients who consented for the enrollment were considered healthy controls. The absence of renal pathology was confirmed by laboratory tests (renal function) and a renal ultrasonography. Urine samples from controls were collected by spontaneous voiding after completing the imaging tests and analyzed following the same procedures as in the case of the obstructive hydronephrosis group.

Statistical analysis - Data were analyzed with Statistic software package SPSS version 26 qualitative variables were expressed as percentages and quantitative variables as mean ± standard deviation. To compare two quantitative variables with normal distribution of data, a compare means student t-test analysis has been used and for operated group where measures are more than two a repeated measure ANOVA has been applied. $P < 0.05$ (CI 95%) was considered statistically significant. The protocol was approved by the Institute Ethics Committee at All India Institute of Medical Sciences, New Delhi 110029.

Results

Twenty three patients underwent Anderson-Hynes dismembered pyeloplasty, which was performed by a single surgeon (MB).

Histological findings confirmed the presence of obstruction in the obstructed segment of the PUJO patients. The typical pattern of PUJO, characterized by muscle hypertrophy/hyperplasia, collagen deposition, subepithelial fibrosis, and mild inflammatory infiltrate, was observed in 16 patients. Seven patients had an uncertain PUJO pattern, which was characterized by vascular congestion, edema, and mild inflammatory infiltrate with lymphocytes being predominant.

In patients with non-operative management (n=39) a consistent rising trend has been observed in the PRA and uTGF-β1 (p.value <0.001). (Table 2) In the postoperative follow-up, a significant decrease in urinary TGF-β1 and PRA values was observed. The control group consisted of 20 children (14 boys and 6 girls) without renal pathology at the time of preoperative evaluation. The mean age ± SD of the control group was 22.0±9.2 months (12-36 months). The mean uTGF-β1 concentration in the children with PUJO, as measured in the baseline urine samples, were significantly higher compared to the control group. The PUJO children had a mean concentration of 721.4pg/mg/Cr.±144.2, while the control group had a mean concentration of 113.5pg/mg/Cr. ± 16.6 ($p < 0.0001$).

In children, who were continued to follow-up without indications for surgery, 39 had a mean baseline uTGF-β1 levels of 698.4±159.2 which increased to 753.1±170.9 (p.valuie <0.001) after a follow-up of 24.1±3.93 (range 18-36 months). On the other hand, in children who developed indications for surgery and subsequently underwent surgical intervention (*n*=23), the mean uTGF-β1 levels at baseline were 760.4±105.5 which increased to 844.4±142.5 just before surgical intervention. This trend indicates that the children who are candidates for surgery have higher levels of uTGF-β1 at presentation as compared to those needing a period of observation (Table 2). After surgery, the mean uTGF-β1 concentration in the postoperative samples fell down significantly, as compared to the mean preoperative concentration. The postoperative mean concentration was 427.4±88.1, while the preoperative mean concentration was 844.4±142.9 ($p < 0.0001$). The uTGF-β1 levels are significantly associated with raised PRA in, both, the non-operated as well as the operated groups. This correlation was also not found to be significant with SRF & GFR. levels in the conservatively follow-on patients but significantly correlated with SRF and GFR in those who later developed indications for surgery. The uTGF-β1 levels did not show a correlation with creatinine levels in both the groups (Table 3).

A cut-off point for uTGF-β1 was determined as 104.7 pg/mg Cr., which was derived from the third quartile of uTGF-β1 levels measured in healthy controls. Patients with a uTGF-β1 level above 104.7 pg/mg Cr. had a 4.25-fold relative risk (RR) (95% confidence interval, 1.08-10.01) of having functional loss compared to patients with levels below 104.7 pg/mg Cr.. We have found that there was a linear correlation between the percentage of relative renal function loss and uTGF-β1 levels in patients with who developed indications for surgery. On the other hand, the study evaluated whether there was a linear correlation between the consistent rise in PRA and uTGF-β1 levels. The results showed no significant relationship between the serum creatinine and uTGF-β1.

Table 2. Changes in different parameters of upper tract damage between patients developed indication for pyeloplasty and patients without indications for surgical intervention.

Parameters	Patients with no indication for surgical intervention (*n*=39)	Patients developed indication and underwent pyeloplasty (*n*=23)
SRF		
Initial	43.7±2.9	43.4±3.3
Final	42.4±3.5	35.2±5.4
Df. with 95% CI*	1.4 (0.4, 2.3)	8.2 (6.5, 9.3)
P.value	0.007	0.001
GFR		
Initial	97.7±16.4	88.3±13.0
Final	95.4±11.6	69.7±12.3
Df. with 95% CI*	2.3 (-2.0, 6.7)	18.6 (14.3, 22.1)
P.value	0.285	0.001
S. Cr.		
Initial	0.7±0.2	0.7±0.3
Final	0.7±0.3	0.9±0.3
Df. with 95% CI*	-0.06 (-0.2, 0.04)	-0.1 (-0.3, 0.02)
P.value	0.256	0.082
PRA		
Initial	7.1±2.5	13.0±6.6
Final	11.2±4.7	17.5±7.1
Df. with 95% CI*	-3.1 (-4.4, -1.8)	-4.5 (-6.3, -2.8)
P.value	0.001	0.001
uTGF-β1		
Initial	698.4±159.2	760.4±105.5
Final	753±170.9	844.4±142.5
Df. with 95% CI*	54.6 (-76.9, -32.9)	-84.0 (-124.8, -43.2)
P.value	0.001	0.001

*Difference with 95% Confidence Interval (Lower and Upper)

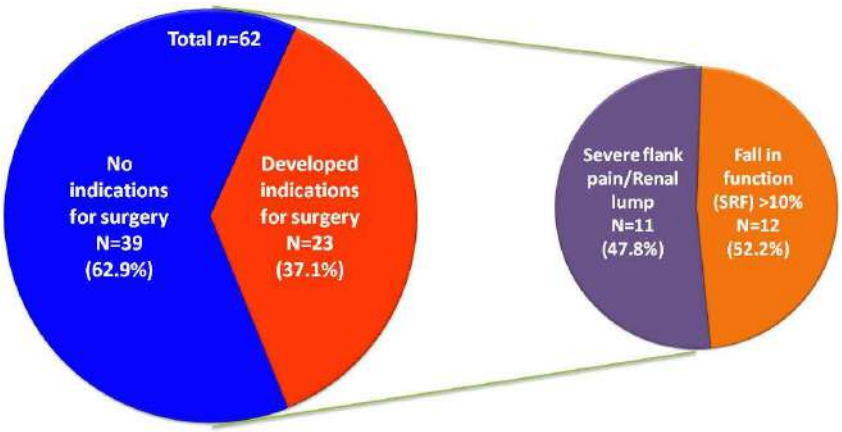


Figure 1. Symptoms for surgical intervention

Table 3. Impact of surgical intervention on renal function parameters including uTGF-β1 and PRA.

Mean±SD	**uTGF-β1**	**SRF**	**GFR**	**PRA**
A. Baseline	760.4±105.5	43.4±3.3	88.3±13.0	13.9±6.6
B. Pre-operative	844.4±142.5	35.2±5.4	69.7±12.3	17.5±7.1
C. Post operative	427.4±88.0	40.9±6.6	86.7±7.5	4.7±1.3
A–B Df*	-84.0 (124.8, -43.2)	8.2 (6.5, 9.3)	18.6 (14.3, 22.1)	-4.5 (-6.3, -2.8)
P.Value	**<0.001**	**<0.001**	**<0.001**	**<0.001**
B–C Df*	417.0 (355.5, 478.6)	-5.7 (-7.5, -3.9)	-17.4 (-23.3, -11.6)	12.8 (9.8, 15.9)
P.Value	**<0.001**	**<0.001**	**<0.001**	**<0.001**

* Df = Difference 95%CI (Lower, Upper)

Correlation between PRA and uTGF-β1

In our previous studies, specifically focused on PRA as an early prognostic marker of renal damage, we have reported that kidneys with higher levels of PRA have an increased probability to functional loss in children with hydronephrosis. The same applies for uTGF-β1 [9-11]. In another study, we have shown, that, patients followed nonoperatively had an increase in plasma renin activity (PRA), decrease in split renal function and glomerular filtration rate (GFR) as compared to controls. However, these changes were more significant in the group of patients who underwent pyeloplasty, during the pre-operative follow-up [12].

Specifically, in the operated group, mean PRA increased by 64.7% between the initial measurement (15.9 ng/ml) and the immediate preoperative measurement (26.2 ng/ml). Following surgery, PRA levels fell in all & returned to normal in the majority. On the other hand, in the nonoperatively followed patients, PRA continued to rise throughout the follow-up period. These findings suggest, that, raised PRA is reflective of obstructive stress in the tubulo-interstitial compartment which is present even in children followed non-operatively. In the present study, uTGF-β1 also reflected the same impact. However, all patients showed a significant decrease by 49.4% in uTGF-β1 (from 844.4 to 427.4 pg/mg Cr.) levels after surgical intervention but plateaued at higher levels with none reaching the normal range as compared to the controls (Figures 2 and 3).

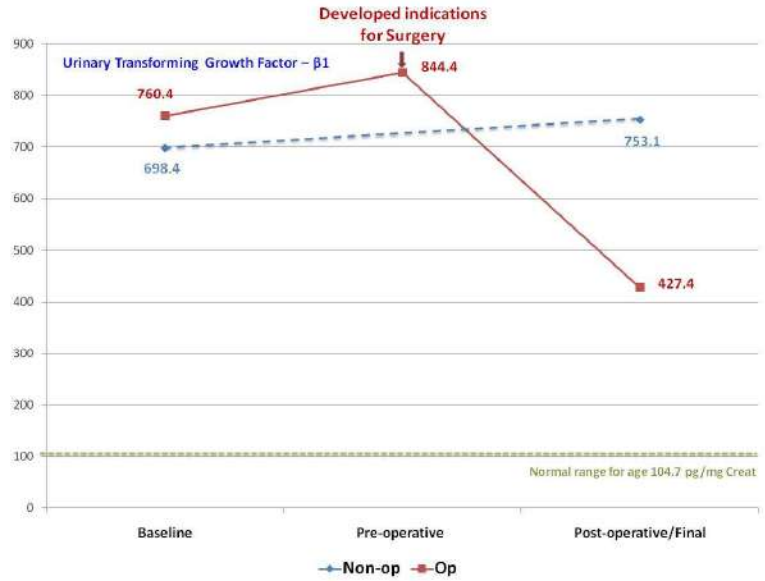


Figure 2. Outcome of uTGF-β1 in children with and without indications for surgery (baseline and final for non-operated group and baseline, pre-operative and post operative in children who underwent surgical intervention)

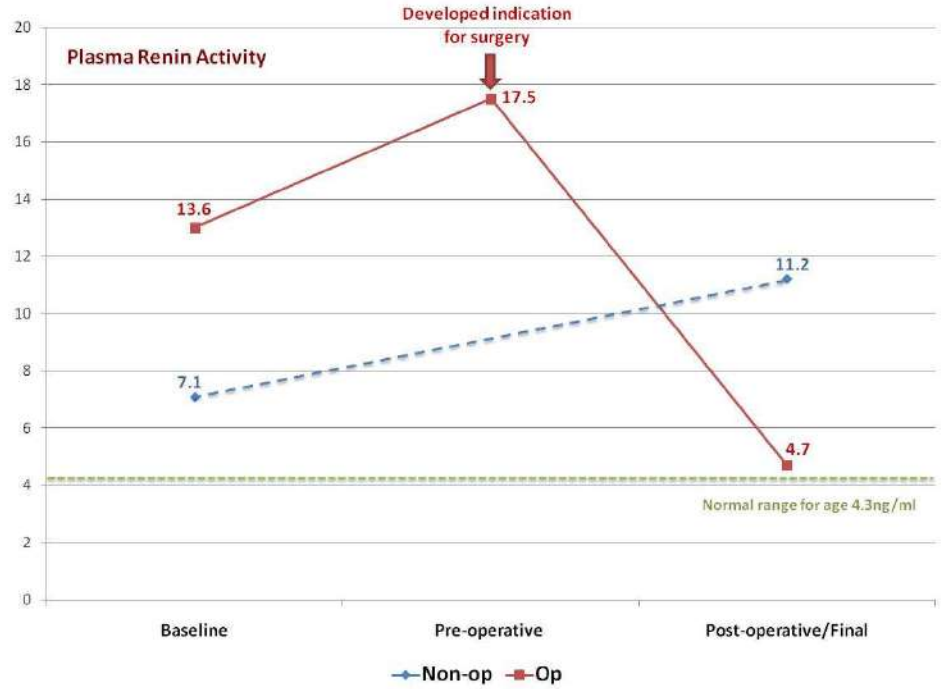


Figure 3. Outcome of PRA in children with and without indications for surgery (baseline and final for non-operated group and baseline, pre-operative and post operative in children who underwent surgical intervention)

Discussion

In cases of hydronephrosis, renal ultrasonography plays an important role in determining the characteristics of the condition, such as the appearance of the renal parenchyma, the diameter of the renal pelvis, and the status of the calyces. These factors help in determining the grade of hydronephrosis. However, it is important to note that the current markers of renal function detect obstruction significantly later in the natural history. There is no controversy, that, once obstruction is diagnosed surgery is the only treatment. However, search for the discriminatory factor which could distinguish between obstructed cases requiring surgery from those who would not has eluded the urologists for almost 4 decades. As a result, serial ultrasound studies are being performed over a period of time to assess any changes or progression of the condition [13]. Currently, diuretic renography is commonly used for the diagnosis of hydronephrosis, and it is preferred over excretory urography due to its lower radiation exposure and lack of nephrotoxicity. However, there are limitations to its diagnostic accuracy, particularly in cases of partial excretory response. Various factors, such as renal maturity, patient hydration, distensibility and volume of the collecting system, and the presence of a bladder catheter, can influence the results of the diuretic renogram [14].

Given the limitations and variability in the diagnostic tools for hydronephrosis [15], there is a need to detect renal injury at an early stage and have effective diagnostic and follow-up tools that are easy to use, reproducible, reliable, and minimally invasive, especially in pediatric populations. In recent years, there have been significant advances in understanding the pathophysiology of obstructive uropathy, particularly the role of pro-inflammatory components. These advances may contribute to the development of improved diagnostic and monitoring approaches for hydronephrosis [16]. Obstruction of the upper urinary tract triggers a series of molecular and histological events. One of the key pathways involved is the renin-angiotensin system, which becomes activated in response to the obstruction. This activation leads to the expression of profibrotic cytokines and transcription factors, including tumor necrosis factor-α (TNF-α), nuclear factor-κB (NF-κB), and transforming growth factor-β1 (TGF-β1) [17].

uTGF-β1, in particular, plays a significant role in the pathogenesis of renal fibrosis in cases of congenital hydronephrosis. Studies have shown that TGF-β1 protein and gene expression are predominantly localized in the proximal tubular cells of the kidney affected by hydronephrosis. It is believed that the process of epithelial-to-mesenchymal transition (EMT) is a major contributing factor to the development of renal fibrosis in congenital hydronephrosis. EMT refers to the transformation of epithelial cells into mesenchymal cells, which possess migratory and invasive properties. This transition is associated with the loss of cell-cell adhesion molecules and acquisition of mesenchymal markers. In the context of hydronephrosis, EMT contributes to renal fibrosis, leading to structural changes and functional impairment of the affected kidney [18]. TGF-β1 is a cytokine with a molecular weight of 25 kDa and is composed of two subunits connected by a disulfide bond. It is initially synthesized as an inactive prohormone. The active form of TGF-β1 binds to the type-II TGF-β receptor, leading to the activation and phosphorylation of the type-I TGF-β receptor. The activated type-I receptor, along with the TGF-β transcription-regulating complex, then translocates into the nucleus, where it exerts the effects of TGF-β1 [19].

The primary function of TGF-β1 is the regulation of extracellular matrix deposition and fibrinogenesis. It stimulates the proliferation of fibroblasts and induces the production of

collagen, proteoglycans, laminin, and fibronectin. TGF-β1 also inhibits collagenase, which is an enzyme that breaks down collagen. Furthermore, TGF-β1 inhibits fibrinolysis by promoting the production of plasminogen and its conversion to plasmin. It decreases the activity of metalloproteinases, which are enzymes involved in matrix degradation, and stimulates the production of protein receptors that attract macrophages. These activities of TGF-β1 contribute to fibrosis and the loss of renal function. In various urological and non-urological conditions, including vesicoureteral reflux and hydronephrosis, TGF-β1 can be excreted in the urine [20]. In another study, the concentration of TGF-β1 in bladder urine of patients with obstructive hydronephrosis was nearly three times higher than that in controls without renal pathology. Additionally, TGF-β1 levels in renal pelvic urine were found to be higher than in bladder urine [21].

These findings are consistent with previous studies conducted by Palmer et al. [22], Furness et al., [21] and El-Sherbiny et al. [23].

In terms of the correlation between preoperative radiographic studies and urinary TGF-β1, a correlation has been found between the percentage of relative renal function loss on DMSA scintigraphy and the level of intraoperative TGF-β1 [24]. However, no such correlation was found when comparing TGF-β1 with preoperative bladder urine, likely due to the dilution of TGF-β1 by urine from the contralateral kidney [25].

No difference has been found in urinary TGF-β1 levels, postoperatively, between patients with or without renal scars [26].

The study by Taha et *al*. demonstrated a significant increase in TGF-β1 values at one month post pyeloplasty, followed by a gradual decrease to significantly low levels one year postoperatively. The authors observed a significant decrease in bladder urinary TGF-β1 levels at three and five months after surgery, approaching values similar to those of controls without renal pathology. Additionally, there was a simultaneous decrease of almost 60% in hydronephrosis compared to preoperative values. These findings suggest that urinary TGF-β1 is not only useful for the diagnosis of upper urinary tract obstruction but could also serves as a reliable biomarker for monitoring the progression of the disease, comparable to traditional markers. It is believed, that, a longer follow-up would not yield different results in terms of TGF-β1 concentration, although further decreases in renal pelvic diameter may be expected over time [27].

Our study involved two groups of children: one group continued to be followed up without indications for surgery, and the other group developed indications and underwent surgical intervention. In the group of children who continued to be followed up without surgery (n=39), the mean baseline levels of uTGF-β1 (transforming growth factor beta-1) were 698.4±159.2. After a follow-up period of 24.1±3.93 months (ranging from 18 to 36 months), the uTGF-β1 levels increased to 753.1±170.9 (p.value < 0.001). This suggests that in the absence of surgical intervention, there was an increase in uTGF-β1 levels over time. On the other hand, in the group of children who developed indications for surgery (n=23), (Fig. 1) the mean baseline uTGF-β1 levels at presentation were higher at 760.4±105.5. Immediately prior to surgery, the uTGF-β1 levels further increased to 844.4±142.5. Following surgical intervention, the postoperative mean uTGF-β1 concentration was significantly lower than the mean preoperative concentration. The postoperative concentration was 427.4±88.1, while the preoperative concentration was 844.4±142.9 (p < 0.0001). These observations imply, that, raised levels of uTGF-β1 above normal are indicative of obstructive stress which could be relieved only with pyeloplasty.

The study also found that uTGF-β1 levels were significantly associated with the protein-to-creatinine ratio (PRA) in both the non-operated and operated groups. However, uTGF-β1 levels did not show a significant correlation with serum creatinine (Cr) levels in either group. In the conservatively followed group, uTGF-β1 levels did not significantly correlate with the levels of serum creatinine (Cr), split renal function of the obstructed side and glomerular filtration rate (GFR). However, in the group that developed indications for surgery, uTGF-β1 levels significantly correlated with SRF and GFR, indicating a relationship between uTGF-β1 and renal function. Our study has also established a correlation between baseline to preoperative and preoperative to postoperative levels of plasma renin activity protein-to-creatinine ratio (PRA) and renal histopathological changes in unilateral pelviureteric junction obstruction (PUJO). This finding suggests that PRA levels can serve as an early indicator of renal injury in this condition. In our previous studies we have specifically highlighted the role of PRA as an early prognostic marker of renal injury. In our earlier studies, we have reported that kidneys with hydronephrosis & normal function on isotope renography but elevated PRA levels, if not operated early, are associated with risk of functional loss. These observations further underscore the predictive value of elevated PRA in the early identification of unilateral PUJO requiring surgery [8-10].

In the present study, uTGF-β1 (transforming growth factor beta-1) has been observed to play a similar role. The elevated levels of uTGF-β1 are indicative of renal injury and serve as a predictive factor in the early identification of cases needing surgery. No significant correlation was found between the chronological age of the patients and the levels of uTGF-β1 or the percentage of renal function loss. Our findings suggest that uTGF-β1 can be a valuable tool for diagnosing obstructive hydronephrosis.

Conclusion

Urinary TGF-β1, hold the promise as potential tools for the diagnosis and follow-up of hydronephrosis. The current evidence suggests that uTGF-β1 can effectively identify early parenchymal injury & serve as a maker of obstruction in in PUJO-type hydronephrosis. In the present study, it was also observed that plasma renin activity (PRA) progressively increased from the time of presentation to the time of surgery in children with ureteropelvic junction obstruction. Being an early player in the cascade of events following renin angiotensin system activation, PRA serves as an early marker of obstructive stress in the tubule-interstitial compartment. It is noteworthy that the levels of uTGF-β1 and PRA are altered prior to the changes in parameters of actual renal injury, such as split renal function and glomerular filtration rate (GFR). Thus, PRA can serve as an early indicator of renal dysfunction in the context of ureteropelvic junction obstruction. Following the surgical intervention (pyeloplasty), uTGF-β1 and PRA levels were reduced in all children. These findings highlight the early diagnostic, clinical utility of monitoring uTGF-β1 and PRA levels in antenatally diagnosed & postnatally confirmed, PUJO-Type hydronephrosis. By detecting changes in these markers early on, pediatric surgeons can intervene to prevent further renal injury and optimize patient outcomes.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest: The authors declare that they have no competing interests.

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National Board of Examination - Journal of Medical Sciences

Volume 1, Issue 8, Pages 497–505, August 2023

DOI 10.61770/NBEJMS.2023.v01.i08.003

ORIGINAL ARTICLE

Correlation of fasting lipid profile in non-diabetic CKD patients on conservative management

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Accepted: 23-June-2023 / Published Online: 04-August-2023

Abstract

Background- Chronic kidney disease is emerging as a major chronic disease worldwide. There is surge in incidence of CKD in developing countries that is likely to pose a major problem in both health and economic sector. Ultimately, ESRD occurs due to progressive and unrelenting loss of nephron function.

Aim- This study aims to investigate the potential correlation between fasting lipid profile and carotid intimal thickness in non-diabetic CKD patients who are undergoing conservative management.

Discussion- CKD comprises of a spectrum of disease processes which results in metabolic, excretory, and synthetic failure culminating into the buildup of non-protein nitrogenous compounds and presents with numerous clinical features.

Conclusion- The findings of this study indicate a significant correlation between fasting lipid profile in CKD patients who are non-diabetic and undergoing conservative management.

Keywords- CKD, Fasting lipid profile, Carotid intimal thickness, HDL, LDL, VLDL

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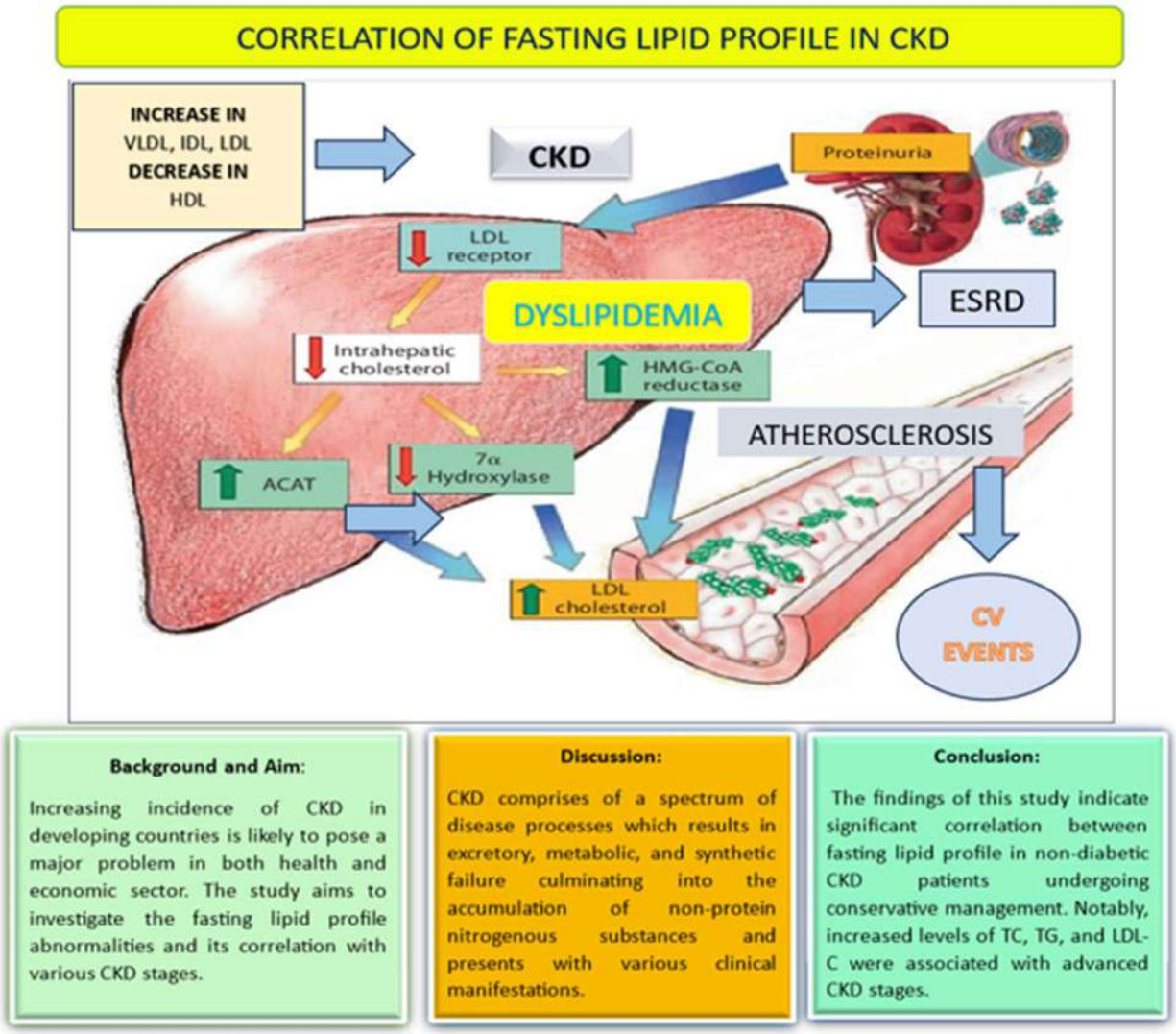
Graphical Abstract



Abbreviations-

CKD	:	Chronic Kidney Disease
ACAT	:	Acyl-Coenzyme A Cholesterol Acyltransferase
FGF-23	:	Fibroblast Growth Factor
GFR	:	Glomerular Filtration Rate
HMG CoA	:	Hydroxymethyl Glutaryl Coenzyme A
HDL	:	High Density Lipoprotein
ESRD	:	End Stage Renal Disease
LCAT	:	Lecithin Cholesterol Acyltransferase
TG	:	Triglycerides
LPL	:	Lipoprotein Lipase
LDL	:	Low Density Lipoprotein
VLDL	:	Very Low-Density Lipoprotein

Introduction

CKD is a globally recognized chronic condition that is rapidly increasing in prevalence, particularly in developing countries. This upward trend in CKD incidence presents significant challenges in both the healthcare and economic sectors. The etiology of CKD varies, with hypertension, diabetic nephropathy, glomerulonephritis, and nephrosclerosis being the most prevalent underlying causes. CKD is characterized by a decline in GFR and nephron population reduction on histology. The clinical course typically follows a progressive and relentless pattern, leading to ESRD with a complete loss of nephron function. ESRD, the final common pathway of various kidney injuries, manifests as renal bone disease, hypertension, anemia, nutritional impairment, neuropathy, reduced quality of life, and decreased life expectancy [1].

CKD Pathophysiology

CKD encompasses a diverse range of pathological processes that result in impaired excretory, metabolic, and synthetic functions, leading to the buildup of non-protein nitrogenous compounds and manifesting in various clinical features. The fundamental pathology of CKD is attributed to injury, inflammation, or hypertensive scarring, which ultimately leads to the loss of functional nephrons and progressive mechanisms resulting from long-term reduction in renal mass. This reduction is often due to increased glomerular capillary pressure and flow, leading to hyperfiltration and subsequent hypertrophy [2]. Moreover, it has been proposed that hyperfiltration and the reabsorption of proteins by the kidneys activate inflammatory responses mediated by vasoactive molecules such as cytokines and growth factors, ultimately leading to glomerular scarring [3]. Factors such as proteinuria, endothelial dysfunction, low-grade inflammation, dyslipidemia, and hypertension play prominent roles in CKD pathogenesis. Endothelial dysfunction, in particular, plays a pivotal role in initiating renal damage, leading to glomerulosclerosis and eventual renal failure [4].

CKD and dyslipidemia

In CKD, dyslipidemia acts as an independent risk factor contributing to disease progression. Several mechanisms are implicated in the development of kidney damage induced by lipid abnormalities. In renal failure, the concentration of lipoproteins may increase due to enhanced synthesis, reduced catabolism, or a combination of both processes. Among the lipid abnormalities commonly observed in CKD, hypertriglyceridemia and decreased HDL concentration are frequently noted [5].

In patients with CKD, there is an observable qualitative change in LDL particles. Specifically, there is a bigger proportion of highly atherogenic small density LDL (sdLDL). Certain modified LDL particles, such as Malondialdehyde-modified LDL and oxidized LDL (ox-LDL) have an affinity for binding to scavenger receptors on the surface of macrophages. This binding leads to cholesterol accumulation within macrophages, causing their evolution into foam cells within the vascular wall. Such processes contribute to the occurrence of atherosclerosis. Additionally, patients with

CKD exhibit significantly higher levels of lipoproteins, further correlating with an increased risk of atherogenesis and cardiovascular mortality [6].

Hypertriglyceridemia is commonly observed in patients with renal failure. One of the primary mechanisms contributing to this abnormality is the impaired activity of lipoprotein lipase, an enzyme involved in lipid metabolism. Additionally, various uremic toxins produced in renal failure directly inhibit the enzymes responsible for lipid metabolism [7].

In patients undergoing hemodialysis, triglyceride levels are typically elevated compared to those who are not undergoing dialysis. This elevation can be attributed to procedure of hemodialysis where heparin is used which have an inhibitory effect on lipoprotein lipase responsible for hydrolysis of TG's. Therefore, hypertriglyceridemia is considered an early characteristic of renal failure [8].

In CKD, there is a delay in the catabolism of VLDL leading to a rise in its concentration. Uremia is linked with depleted levels of apolipoprotein C-II and a decreased cholesterol content in high-density lipoprotein (HDL). Apo C-II is shifted from HDL to VLDL, and reduced levels of Apo C-II result in reduced metabolism of VLDL and triglycerides [9].

Multiple mechanisms contribute to the impaired reverse cholesterol transport resulting in reduction in cholesterol levels, which is often indicative Apolipoprotein AI (Apo AI), the activator of LCAT, is depleted in CKD due to downregulation of hepatic Apo AI genes.

As a result, the activity of LCAT, which is responsible for the esterification of cholesterol, is reduced, leading to faulty maturation of HDL. The function of LCAT constantly diminishes in CKD, resulting in lower levels of HDL [10].

CKD and Cardiovascular correlation

CKD is a significant predictor of atherosclerotic CVD and remains the leading cause of mortality and morbidity. The pathogenesis of atherosclerosis in CKD involves oxidative stress, where an imbalance between prooxidant and antioxidant systems contributes to an increased burden of atherosclerosis [11].

Increased levels of FGF-23, phosphate, anemia, and hyperparathyroidism, which are associated with CKD, play a substantial role in the development of occlusive coronary, cerebrovascular, and peripheral vascular diseases. Vascular remodeling is a characteristic feature of CKD, affecting both small and large arteries like aorta and coronary vessels. This remodeling is driven by medial calcification, which diminishes arterial compliance and leads to a rise in pulse pressure and systolic hypertension [12].

Consequently, this process causes aortic stiffness, left ventricular hypertrophy, and ultimately leading to myocardial infarction.

Methods

To achieve this objective, a cross-sectional study was conducted on a cohort of non-diabetic CKD patients receiving conservative management. The study involved measuring the fasting lipid profile

parameters, including total cholesterol, very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and low-density lipoprotein cholesterol (LDL-C). In early morning, a 12-hour fasting venous sample was collected in plain vial to measure the fasting lipid profile. The sample was allowed to clot and then centrifuged at 3000 RPM to separate the serum, which was subsequently sent for analysis. The lipid profile analysis was performed using the following principles:

1. Serum cholesterol was measured using the Triden method [13].
2. Serum HDL cholesterol was measured using the HDL-HDL Dimer Method [14].
3. Serum triglycerides were measured using the glycerophosphate oxidase method [15].
4. Serum LDL cholesterol was estimated using the Friedewald formula [16].
5. Serum VLDL cholesterol level equals to plasma triglyceride level divided by 5, representing the cholesterol-to-triglyceride ratio in VLDL particles.

Table 1. Distribution of laboratory parameters among study participants

Parameter	N	Mean	Standard Deviation	Minimum	Maximum
HB	90	8.18	2.26	3.40	15.20
TLC	90	9571.77	4849.22	1009.00	31400.00
PLT	90	227.94	102.93	60.00	542.00
B UREA	90	108.94	59.11	26.70	320.00
CREATININE	90	3.33	1.53	1.60	8.74
GFR	90	23.51	10.94	5.00	52.00
S ALBUMIN	90	2.99	.68	1.45	4.78
TOTAL CHOL	90	176.02	64.72	52.00	476.00
TG	90	178.06	69.02	50.87	405.90
HDL	90	39.31	12.67	17.00	102.00
LDL	90	101.32	53.43	11.80	388.40
VLDL	90	35.52	13.66	10.17	81.20
HbA1c	90	5.30	.34	4.20	5.80

Results

The study was conducted at GMSH-16 in Chandigarh and included 90 participants. The mean age of study participants was 54.01 ± 12.73 years, with the highest number of participants (31, 34.4%) falling in the age group of 51-60 years. The mean BMI of the study participants were 24.98 ± 3.38 kg/m². The mean systolic and diastolic blood pressure was 141.22 mmHg

and 83.76 mmHg respectively. The mean estimated glomerular filtration rate (GFR) was found to be 23.51 in the 90 cases.

In the present study, several parameters were evaluated, and it was observed that mean hemoglobin, GFR, and serum albumin levels were low, while serum creatinine and blood urea levels were high, as shown in Table 1.

The correlation between individual parameters of the lipid profile and the stage of chronic kidney disease is presented in Tables 2, 3, 4, 5, and 6.

Table 2. Correlation of Total Cholesterol with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
TOTAL CHOL	N	27	39	24	5.648	.005**
	Mean	151.63	172.53	209.13		
	SD	81.89	53.50	45.11		

Table 3. Correlation of Triglyceride level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
TG	N	27	39	24	3.948	.023*
	Mean	149.68	183.82	200.64		
	SD	58.73	68.87	71.86		

Table 4. Correlation of LDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
LDL	N	27	39	24	4.753	.011*
	Mean	84.56	96.73	127.64		
	SD	73.55	42.09	30.28		

Statistical analysis using Pearson's correlation coefficient was performed to assess the association between lipid profile parameters and CKD stages. The mean LDL ($p<0.011$), total cholesterol ($p<0.005$), VLDL ($p<0.022$), and triglyceride level ($p<0.023$) showed a significant increase as CKD stages progressed from 3 to 5. Additionally, the mean HDL cholesterol level decreased in stage 3 CKD patients.

Table 5. Correlation of VLDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
VLDL	N	27	39	24	4.013	.022*
	Mean	29.86	36.67	40.02		
	SD	11.68	13.74	13.98		

Table 6. Correlation of HDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
HDL	N	27	39	24	.467	.629
	Mean	37.98	38.98	41.35		
	SD	11.22	10.51	17.03		

Conclusion

This study's findings indicate a significant correlation between fasting lipid profile in non-diabetic CKD patients undergoing conservative management. Notably, increased levels of total cholesterol, triglycerides, and LDL-C were found to be linked with progression of CKD stages, while lower levels of HDL-C were also linked to with progression of CKD stages.

Future scope

The correlation between fasting lipid profile and carotid intimal thickness in non-diabetic CKD patients undergoing conservative management has emerged as an intriguing area of research. With the well-established link between lipid abnormalities and atherosclerosis progression, understanding the specific association between these two factors holds great potential for risk assessment, therapeutic strategies, and improved patient outcomes. Several promising avenues can be explored to expand our knowledge of this correlation:

- Conducting longitudinal studies will be crucial to establish a cause-and-effect relationship.
- Further investigation is warranted for prognostic value of fasting lipid profile and carotid intimal thickness allowing for more targeted interventions and improved management in non-diabetic CKD patients.
- Future research should focus on assessing the impact of lipid-lowering therapies, lifestyle modifications.
- Investigation of biomarkers of oxidative stress, inflammation, and endothelial dysfunction associated with carotid intimal thickness can contribute to a comprehensive understanding of the disease process.

These efforts will ultimately lead to improved patient outcomes and personalized care, effectively reducing the burden of cardiovascular disease in CKD patients.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 506–521, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.004

ORIGINAL ARTICLE

Standard MRI sequence for imaging and methods of calculation of depth of invasion in squamous cell cancers of Tongue

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Accepted: 29-July-2023 / Published Online: 04-August-2023

Abstract

Aim: To establish a standard MRI sequence for imaging of squamous cell cancers (SCC) of tongue and to evaluate various methods of calculation of depth of invasion in SCC of Tongue.

Background: Magnetic resonance imaging (MRI) is the best modality of imaging for tongue cancers. DOI is added to the staging of oral cavity squamous cell cancers by TNM AJCC Cancer Staging.

Materials and Methods: Visual rating: 1 - poor; 2 - acceptable; 3 - good; 4 – excellent, for the assessment of MRI sequences. Four protocols for the measurement of MRI derived DOI : axial reconstructed thickness, axial invasive portion, coronal invasive portion, and optimal method selection. Study design: Prospective study. Sample size: 50n.

Conclusion: This study shows that tongue masses are best evaluated on contrast enhanced scans, but STIR images in non-contrast studies provide near comparable results in delineation of the lesion. Maximum correlation was observed when the DOI was measured when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI.

Keywords: DOI, Tongue, Carcinoma, Tumour, MRI, depth

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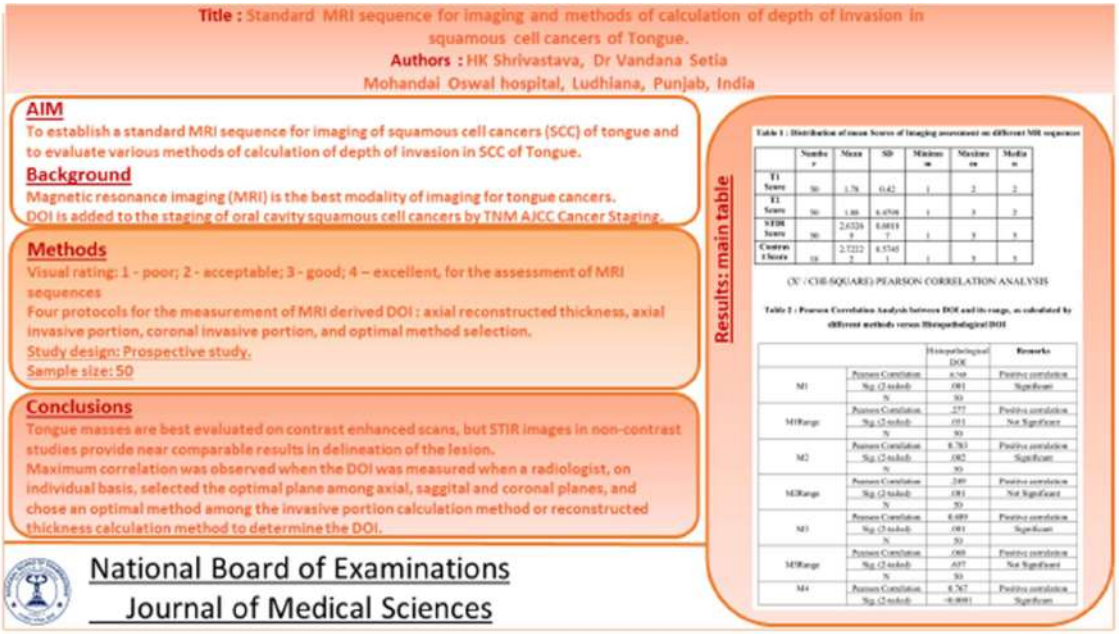
Graphical Abstract



Introduction

In the Indian subcontinent, oral cavity SCC are a major health problem. They are amongst the top three cancers in the country [1]. Risk increases with practices such as tobacco chewing, betel's quid, etc. prevalent in the low-income groups. Delay of detection of oral cancer among these individuals occurs from insufficient exposure to new diagnostic aid [2]. Oral precancerous lesions and pathologies like leukoplakia and submucous fibrosis can also transform to oral cancer [3].

The most common oral cavity site for squamous cell carcinoma (SCC) is tongue. Tongue SCC are one of the most aggressive tumors. Usual subsite of involvement is the lateral border of tongue involving the under surface [4]. Usual location of the tumors situated dorsally in the tongue is near the midline but are uncommon. Invasion of the floor of the mouth is more seen in tumors epi-centered in the anterior third of the oral tongue [5]. The musculature of the tongue as well as the lateral portions of the floor of mouth are usually infiltrated by the carcinomas involving middle-third of tongue. The posterior third lesions also infiltrate the musculature of the tongue and the floor of mouth but they may also involve mandible, base of tongue, anterior tonsillar pillar and glosso-tonsillar sulcus [6].

Surgery is mainstay of treatment of SCC tongue. Adjuvant treatment plan may consist of radiotherapy / concurrent chemo-radiotherapy which depends on various histopathological features like tumour size, lymph node positivity, depth of invasion (DOI) perineural invasion (PNI), resection margin status, etc. Carcinoma tongue patients may suffer from recurrence at primary tumor site or in the neck if not properly evaluated preoperatively [7].

Depth of invasion (DOI) is a characteristic that has been recently added to the staging of oral cavity squamous cell

cancers by the TNM AJCC Cancer Staging, Eighth Edition. DOI of tongue carcinoma is the perpendicular distance of the deepest point of tumor from the level of basement membrane of the nearest intact squamous mucosa.

Positive resection margin has a poor prognosis [8]. According to the NCCN guidelines, the tongue cancer resected margins should be ≥ 5mm [9]. Nearly 35% of patients present with metastatic lymphadenopathy [10]. Among these, submandibular and jugulodigastric nodes are the first echelon involved nodes. Bilateral lymph node involvement is seen in 5% of patients [11]. The overall occult metastatic rate in clinically N0 neck is approximately 30% [12].

Magnetic resonance imaging (MRI) has become the best modality of imaging in detection and evaluation of tongue cancers. The basis of this diagnostic technique relies on variation of hydrogen spin density, longitudinal relaxation time (T1), and transverse relaxation time (T2) of investigated tissues. High sensitivity and specificity can be achieved in lesion detection with contrast enhanced MRI, short tau inversion recovery (STIR) images (fat suppressed). While diagnosing a tongue lesion, T1 weighted (T1W) images provide fine anatomical details and fat suppressed enhanced scans provide good contrast between the normal portion of the tongue and the tumor [13].

MRI can accurately measure DOI and size of tumor, and can detect perineural invasion (PNI) and neck lymph nodes [14]. Some clinical studies that correlate the likelihood of cervical nodal metastasis with DOI have been performed. According to these studies, DOI is the single most important factor predicting the lymph node metastasis. While there have been various studies where MRI has been used to predict DOI in tongue SCC, most had some limitations like retrospective study design, small sample size, and exclusion of superficial lesions [15]. The rationale behind conducting the study is to compare and co-relate the accuracy of DOI in tongue squamous cell cancers on MRI and histopathology.

The current study was conducted in Radiology Department of a tertiary care hospital in northern part of India over a span of 1.5-year period between December 2020 and May 2022. Protocol of the study was pre-approved by the institutional ethics committee (IEC) before subjects were recruited; this is done in line with Second Declaration of Helsinki wherein the ethical principles for human investigation are laid. Before their enrollment in this study, from all patients, a written informed consent was obtained (IEC – IEC, Mohandai Oswal Hospital; IEC Approval Reference Number- IEC/MOH/2020-03; IEC Approval Date: 10/12/2020) (Figures 1 to 6).

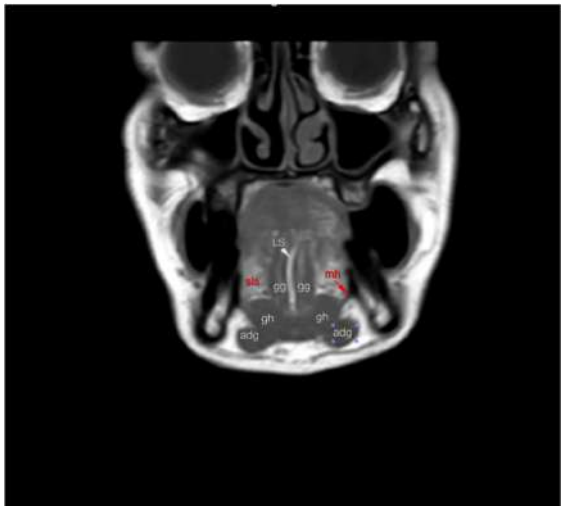


Figure 1. Anatomy: Coronal T1W MRI shows genioglossus (gg) muscles delineated as vertical pillar-like para-midline structures. The geniohyoid (gh) muscles appear subtly wider than and below the genioglossus muscles. The sublingual spaces (sls) and lingual septum (LS) show high signal intensity on T1W images. Mylohyoid (mh) separates oral cavity from the floor of mouth which contains the anterior belly of Digastric (Adg) muscles.

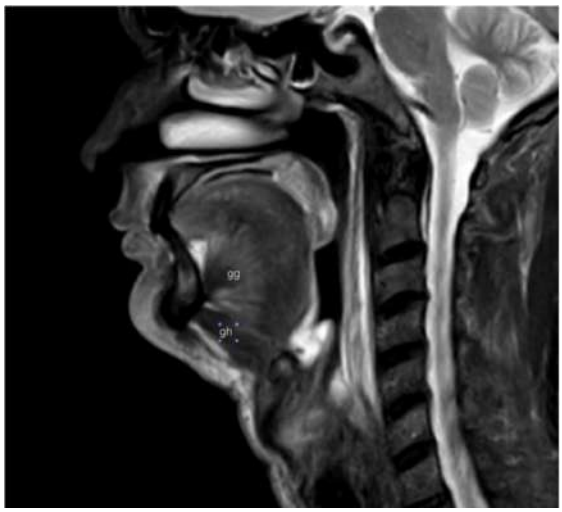


Figure 2 Anatomy: Sagittal T2-weighted MR image demonstrates dark-hypointense geniohyoid muscles (gh) from genial tubercle to hyoid and the fan-shaped genioglossus muscles (gg).

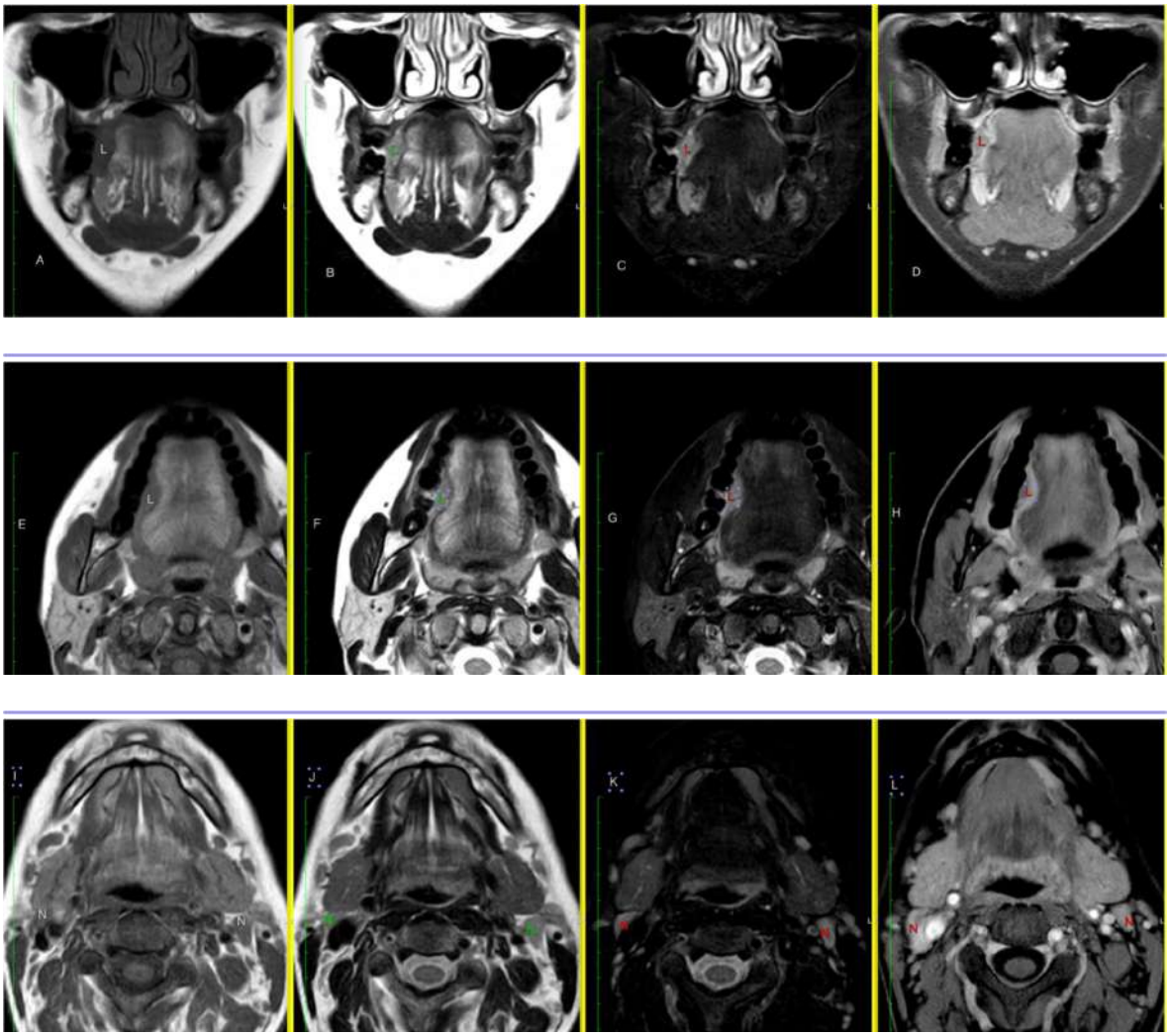


Figure 3. Pathology: **A** T1W Coronal **B** T2W Coronal **C** STIR Coronal **D**- Contrast T1W Coronal **E** T1W Axial **F** T2W Axial **G** STIR Axial **H** Contrast T1W Axial **I** T1W Axial **J** T2W Axial **K** STIR Axial **L** Contrast T1W Axial

A uniformly enhancing mass lesion (marked L in subsets A-H of figure 3), hyperintense on T2W sequence, is seen in the right anterolateral portion of tongue, beginning 2 cm posterior to the tip & extending over an AP span of 2 cm. Craniocaudally it measures 2 cm.
A mildly enlarged node(N) (10 mm in short axis) in the ipsilateral level II location & a mildly enlarged node(N) (12 mm in short axis) are seen in the contralateral (left) level II location.
The depth of invasion measured by MRI was 6.3mm by method 1, 6.2mm by method 2 and 4.8 mm by method 3. On histopathology it has a depth of invasion of 5 mm. 30 lymph nodes were evaluated, none was metastatic (0/30).

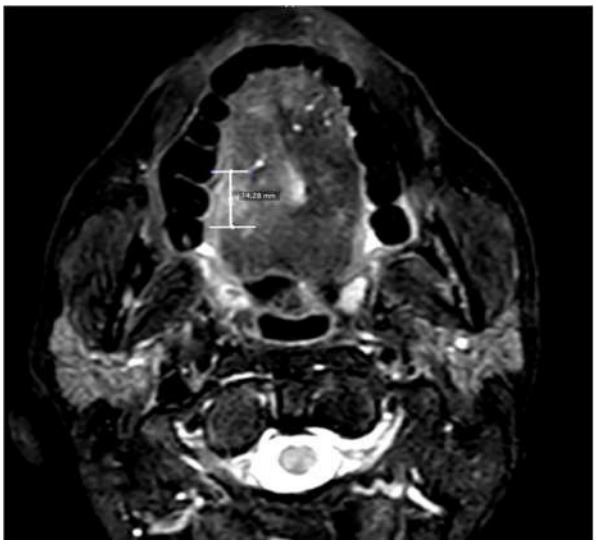


Figure 4. STIR Axial: Size in anteroposterior (AP) dimension: The length of a lengthiest vertical line separating two parallel horizontal lines drawn anteriorly and posteriorly along the tumor-mucosal junction.

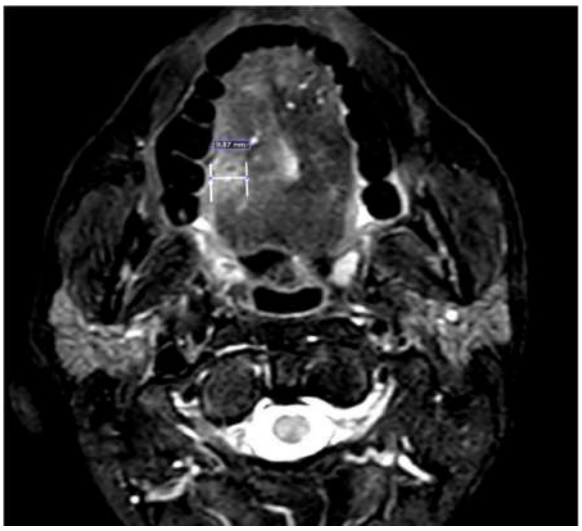


Figure 5. STIR Axial: Size in transverse (Tr) dimension. The length of a lengthiest horizontal line separating two parallel vertical lines drawn laterally from the lateral aspect of the tumor, and medially along the tumor-mucosal junction.

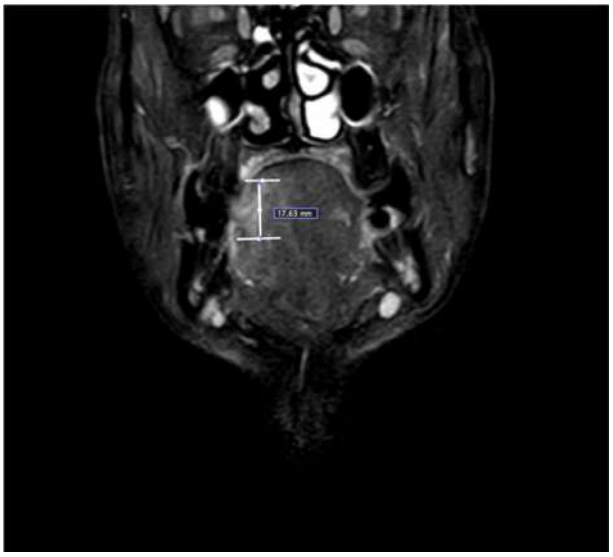


Figure 6. Contrast T1W Coronal: Size of the craniocaudal (CC) dimension: The length of a lengthiest horizontal line separating two parallel horizontal lines drawn superiorly from the superior aspect of the tumor, and inferiorly along the tumor-mucosal junction.

Aim

To establish a standard MRI sequence for imaging of squamous cell cancers (SCC) of tongue and to evaluate various methods of calculation of depth of invasion in SCC of Tongue.

Materials and Methods

Hypothesis: There is no difference between DOI calculated by MRI & histopathological report in SCC of tongue.

Study area: The study shall be conducted in the Department of Radio-diagnosis, Mohandai Oswal hospital, Ludhiana

Study design: It was a Prospective study.

Study duration: 1.5 year time period

Study population: This study was conducted on the patients of either sex eligible for the study during the study duration on the basis of clinical suspicion.

Sample size determination: Assumption of 90% power and 1% significance level (significant at 99% confidence level) was considered for calculating the sample size. In the reference study *(Correlation between clinical and MRI assessment of depth of invasion in oral tongue squamous cell carcinoma),* the correlation between measurements of DOI was 0.64 with a 95 % C.I. between 0.43 - 0.84 ($p < 0.001$). If we consider 99% accuracy and true relative error for experimental subjects is 10% along with 0.8 effect size, it was estimated that at least 30 experimental subjects needed for the study. Sample Size Formula = $N = [(Z\alpha+Z\beta)/C]2 + 3$ Where $C = 0.5 * \ln[(1+r)/(1-r)] = 0.758$ at $r=0.64$. The standard normal deviate for $\alpha = Z\alpha = 2.58$ The standard normal deviate for $\beta = Z\beta = 1.28$ $\alpha = 0.05$ (i.e. Confidence level = 95%) By 18 months, 50 patients were included in the study.

Inclusion criteria:

- History of no previous malignancies.

- A measurable tumor must be present on pretreatment MRI done within 1 month before surgery.
- Histo-pathological data on the surgical specimens should be available.
- No previous pre-operative chemo-therapy or radio-therapy.

Exclusion criteria:

- Allergic reaction to contrast agent
- Pre-existing nephrogenic systemic fibrosis
- Estimated Glomerular filtration rate less than 30 mL/min/1.73m^2
- Referral-in with a MRI scan that was already reviewed by the surgeon prior to the clinical exam and enrolment in the study
- Only CT imaging.
- Carcinoma in situ or a previous incisional or excisional biopsy
- Previous head and neck radiation or chemoradiation

Data collection methods:

Patients who had to undergo MRI for tongue cancer were included in this study. A 1.5-T imaging MRI (Phillips achieva or Phillips ambition) was used to undertake the MRI examinations. The imaging parameters were as follows: 4.6/2.2; flip angle - 10°; Field of view (FOV) - 34 × 34 cm; matrix - 320 × 320; section thickness - 2 mm; and acquisition time - 180 seconds. T1W, T2W, STIR and Contrast T1W sequences and some additional MRI sequences were obtained as per requirement. Gadotrast (gadoteric acid 279.32mg meglumine 97.60mg) (amount - 0.01 mmol/kg, rate -2 ml/s) was used for contrast imaging followed by saline flush (20ml, 2 ml/s). Dynamic contrast enhanced images were obtained at minutes one, two, and six after contrast material injection.

Image Interpretation:

Radiologist was blinded from the pathological information. He used a visual rating: 1 - poor; 2 - acceptable; 3 - good; 4 – excellent, for the assessment of MRI sequences in delineation of tumor. Adjustment of the grayscale, window width, and zoom factor were allowed for optimized interpretation of images.

Four protocols were utilized for the measurement of MRI derived DOI -

In method 1, the axial reconstructed thickness, the difference between (A) the distance between the lingual septum and the surface on the unaffected side and (B) the distance between the septum and the point of deepest invasion on a horizontal line is measured on axial images.

In method 2, the axial invasive portion, junctions of the tumor and the normal mucosa on both sides were connected by a reference line. The length of the line perpendicular to reference line connecting reference line with the deepest point of tumor invasion is measured on axial MRI while ignoring the protruding portion.

In method 3, the coronal invasive portion, the invasive portion was measured on coronal MRI just as method 2 while ignoring the protruding portion.

In method 4, optimal method selection, when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI, for example, coronal for dorsum of the tongue or axial plane for lateral edge (Figures 7 and 8).

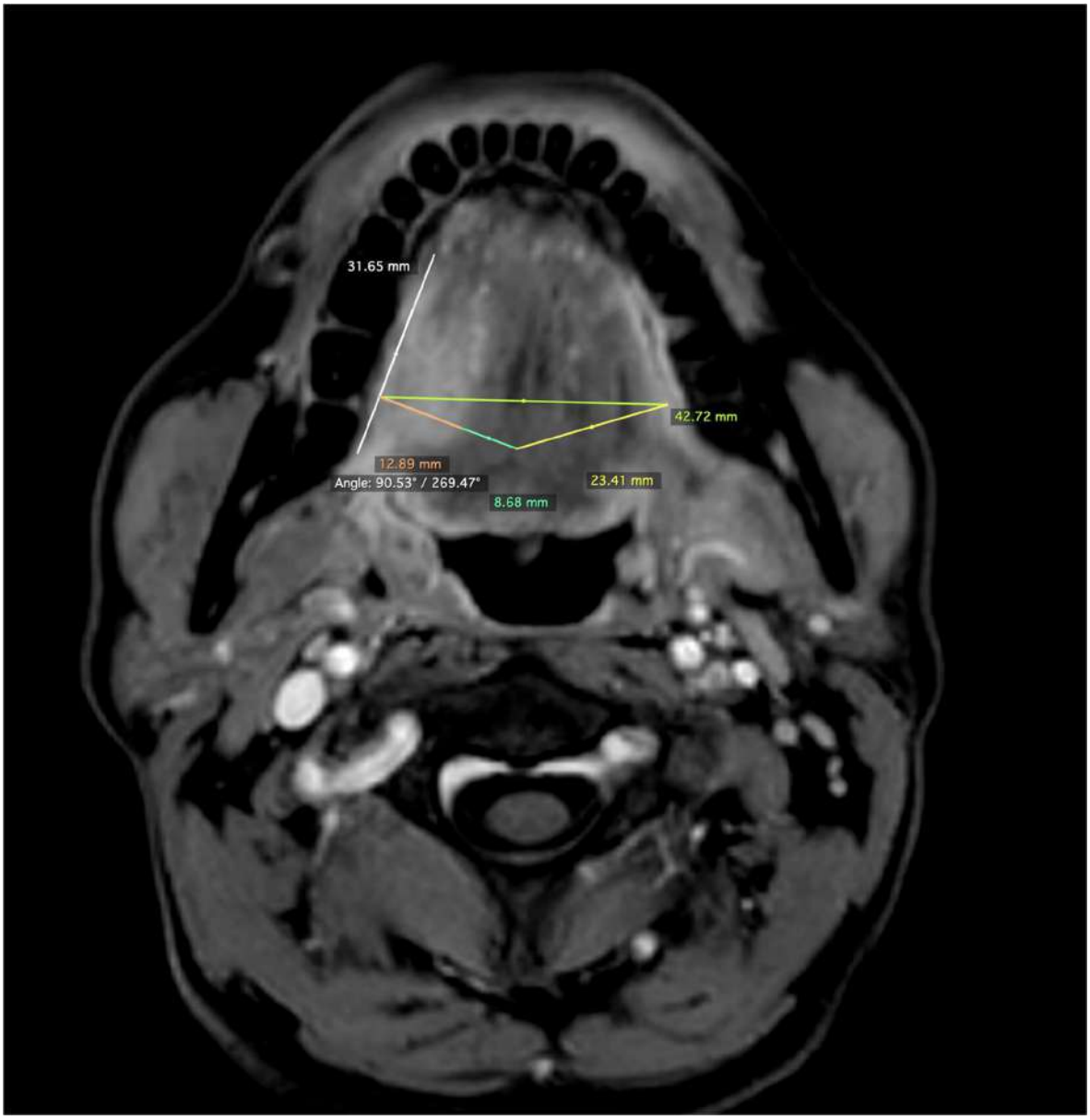


Figure 7. Depth of Invasion : Method-1 and Method-2: Axial T1 weighted with contrast enhancement image shows a tongue cancer radiological DOI measured 12.9 mm by method 1, 14.7 mm by method 2 (23.4-8.7).

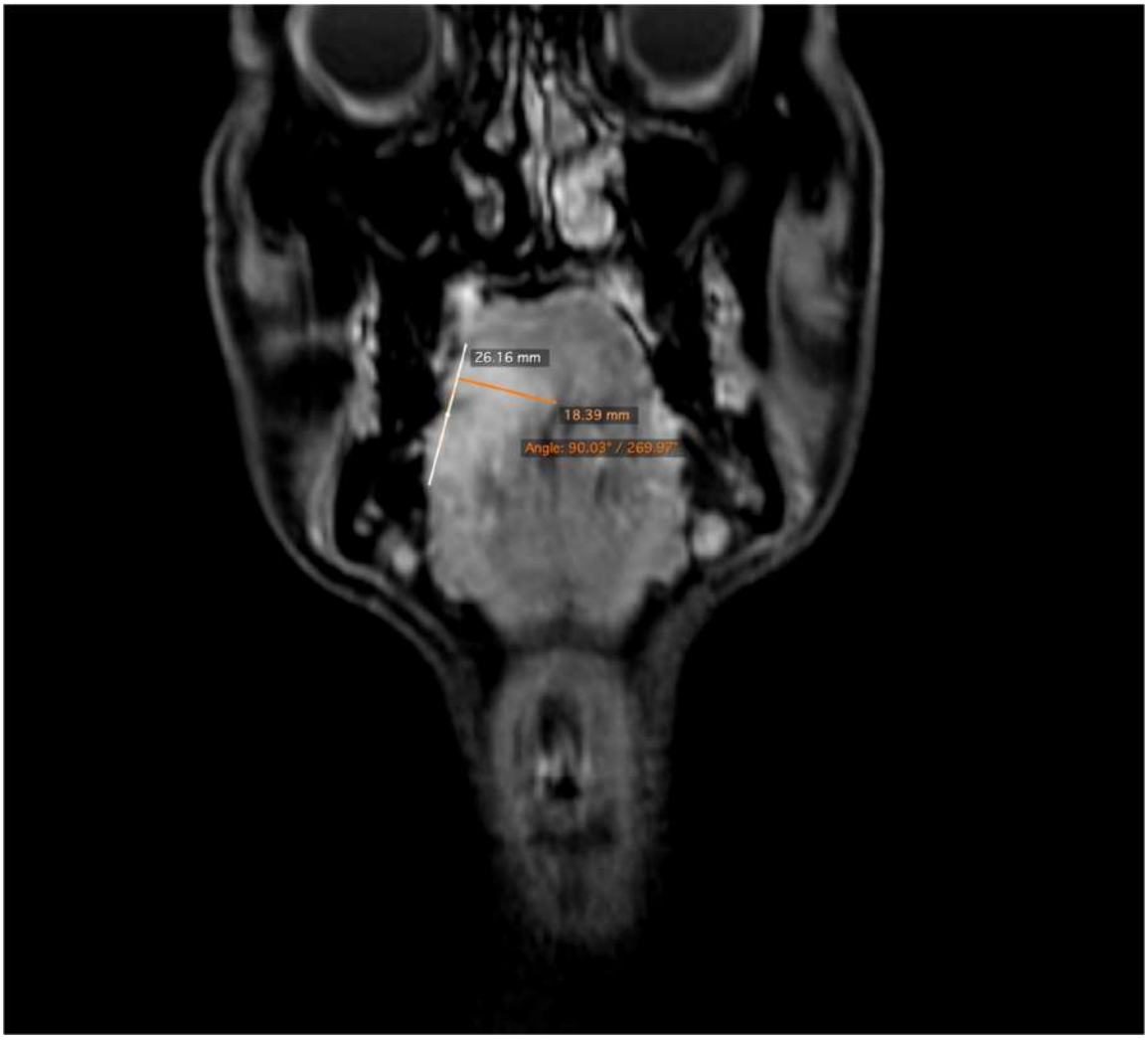


Figure 8. Depth of Invasion Method-3: Coronal T1 weighted with contrast enhancement image shows radiological DOI measured 18.3 mm by method 3.

Surgical Procedure and Histopathological Analyses

All patients had to undergo trans-oral surgical resection of tongue and selective lymph node dissection in the neck as primary treatment. The specimen were sent for histopathological analysis. Fixation was done in neutral buffered 10% formalin. Staining was done with hematoxylin and eosin. Slides were evaluated by an experienced pathologist blinded to the DOI evaluated on MRI. If the surgical margin were found to be negative on all slides, DOI was measured. It corresponded to the maximum distance between the basement membrane of the adjacent normal mucosa to the deepest point of invasion while ignoring the presence or absence of ulceration or protrusion.

Statistical assessment of output

The visual assessment of different MRI sequences was evaluated. Comparison between MRI derived DOI and histo-pathological DOI was done using Chi square tests and using Pearson correlation. Results were considered as significant only if the p-value was found to be less than or equal to 0.05.

Result & Analysis (Tables 1 and 2)

Table 1: Distribution of mean Scores of Imaging assessment on different MR sequences

	Number	Mean	SD	Minimum	Maximum	Median
T1 Score	50	1.78	0.42	1	2	2
T2 Score	50	1.88	0.4798	1	3	2
STIR Score	50	2.63265	0.60187	1	3	3
Contrast Score	18	2.72222	0.57451	1	3	3

(X^2 / chi-square) pearson correlation analysis

Table 2. Pearson Correlation Analysis between DOI and its range, as calculated by different methods versus Histopathological DOI

		Histopathological DOI	**Remarks**
M1	Pearson Correlation	0.749	Positive correlation
	Sig. (2-tailed)	.001	Significant
	N	50	
M1Range	Pearson Correlation	.277	Positive correlation
	Sig. (2-tailed)	.051	Not Significant
	N	50	
M2	Pearson Correlation	0.783	Positive correlation
	Sig. (2-tailed)	.002	Significant
	N	50	
M2Range	Pearson Correlation	.249	Positive correlation
	Sig. (2-tailed)	.081	Not Significant
	N	50	
M3	Pearson Correlation	0.689	Positive correlation
	Sig. (2-tailed)	.001	Significant
	N	50	
M3Range	Pearson Correlation	.068	Positive correlation
	Sig. (2-tailed)	.637	Not Significant
	N	50	
M4	Pearson Correlation	0.767	Positive correlation
	Sig. (2-tailed)	<0.0001	Significant
	N	50	
M4Range	Pearson Correlation	.304*	Positive correlation
	Sig. (2-tailed)	.032	Significant
	N	50	

M1

The value of Pearson Correlation Coefficient (r) was 0.749. The positive correlation was found between Histopathological DOI versus M1. The P-Value was .001. The result was statistically significant.

M2

The Pearson Correlation Coefficient value (r) was 0.783*. The positive correlation was found between Histopathological DOI versus M2. The P-Value was .002. The result was statistically significant.

M3

The Pearson Correlation Coefficient value (r) was 0.689. The positive correlation was found between Histopathological DOI versus M3. The P-Value was .001. The result was statistically significant.

M4

The Pearson Correlation Coefficient value (r) was 0.766. The positive correlation was found between Histopathological DOI versus MIV. The P-Value was <0.0001. The result was statistically significant (Figures 9 to 12).

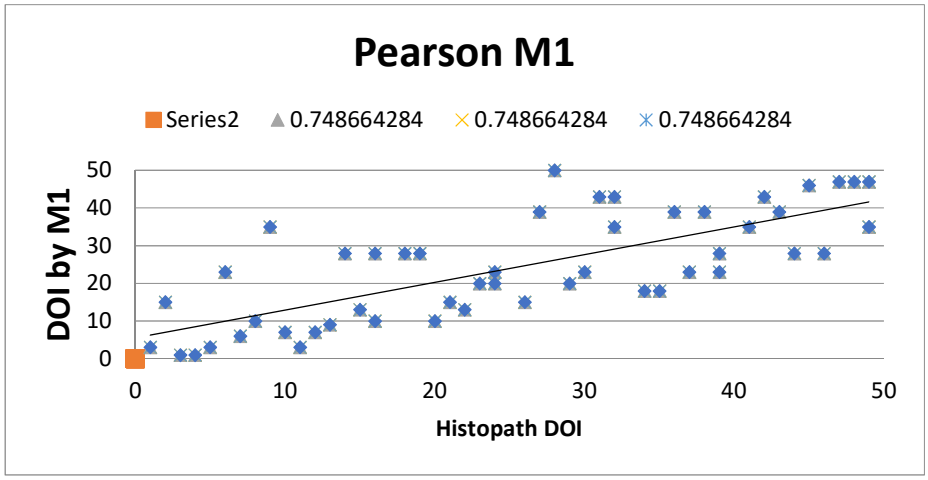


Figure 9. Intraclass correlation coefficient for DOI measured by M1 with histopathological DOI = 0.860887.

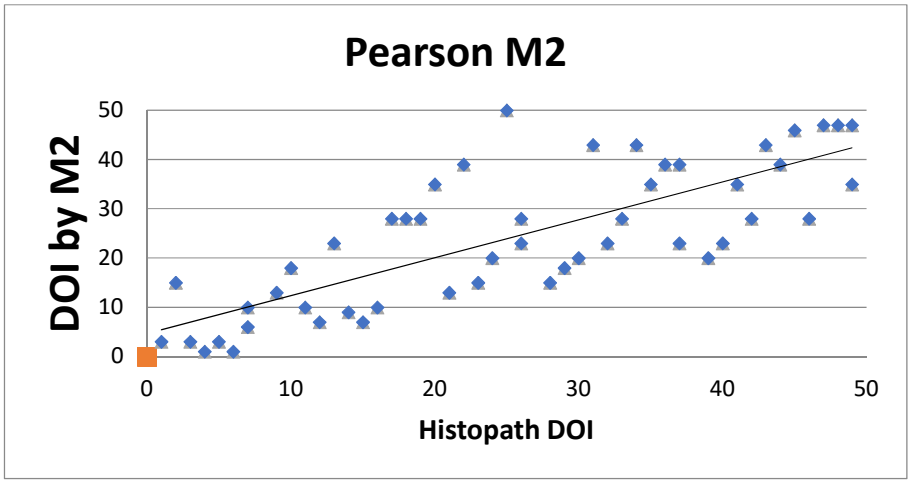


Figure 10. Intraclass correlation coefficient for DOI measured by M2 with histopathological DOI = 0.855315

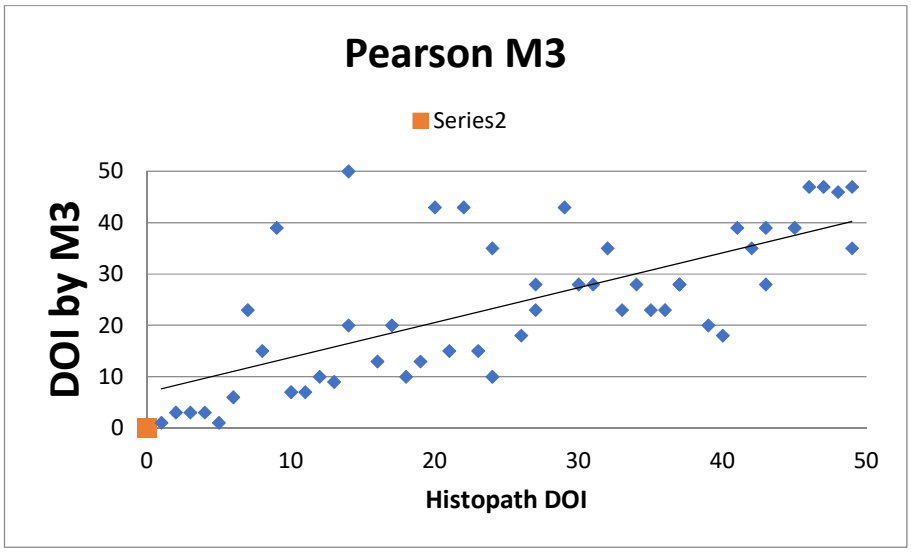


Figure 11. Intraclass correlation coefficient for DOI measured by M3 with histopathological DOI = 0.870972

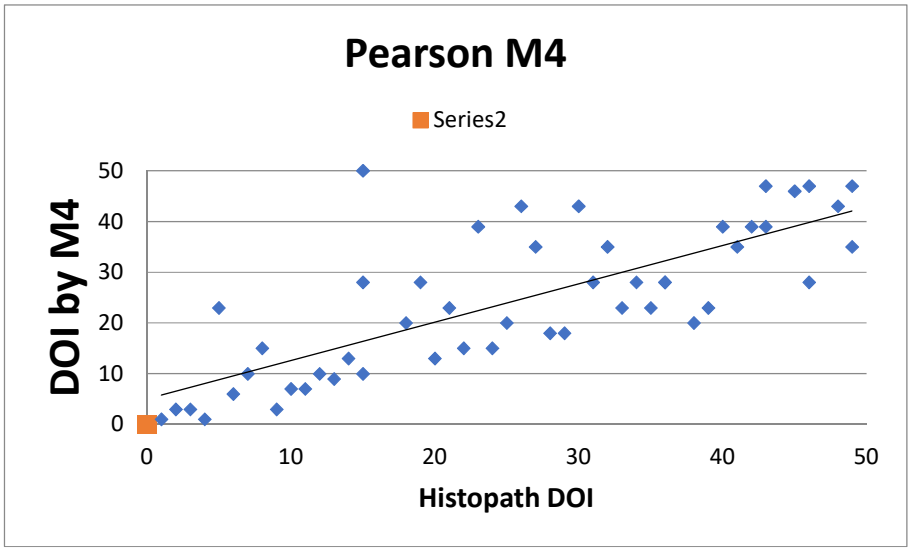


Figure 12. Intraclass correlation coefficient for DOI measured by M4 with histopathological DOI = 0.879721

Discussion

This study was a Prospective study which included a total of 50 patients and was conducted at Department of Radio-diagnosis, Mohandai Oswal hospital, Ludhiana.

To Establish a Standard MRI Sequence for Imaging of SCC of Tongue

In our study, for analysis of adequateness of MR sequence for optimal image visualization, the four-point visual scale detailed in the methodology of this thesis was used to delineate the tumour; the mean T1 Score was [1.7800± 0.42], the mean T2 Score was [1.8800± .4798], the mean STIR Score was [2.63265± 0.60187] and the mean Contrast enhanced Score was [2.72222 ± 0.57451]. Murakami et al. [16]

(2019) found that T2WI and fat suppressed CE-T1WI provided high mean scores, however, the MRI sequence for optimal evaluation of SCC of tongue had to be selected individually each patient. In our study, STIR images in non-contrast studies provide near comparable results to the contrast enhanced sequence in delineation of the lesion.

Determination of Best Method for Evaluation of DOI On MRI

In Bland Altman analysis in our study, Intraclass correlation coefficient (ICC) for histopathological DOI with DOI measured by M1 was 0.860887, by M2 was 0.855315, by M3 was 0.870972 and by M4 was 0.879721.

Our results are in concurrence with the study done by Murakami et al. [16] (2019) in which the correlation between MRI derived DOI and histo-pathological DOI were found to be good by when the radiologist selected the optimal method (ICC of 0.611). Method of determination of DOI on MRI cannot be standardized because the anatomical orientation of the tongue in 3-dimension is in a curvilinear fashion, so most lesions cannot be captured in the entirety in one plane; secondly there is extreme variability in the location of the lesion with respect to tongue margin in different planes; hence, the decision on the method to be used has to be taken on case to case basis by the radiologist.

Conclusion

MRI is now considered an essential component in the pre-treatment evaluation of SCC tongue. It provides precise information regarding the size and DOI to optimize treatment strategy.

This study shows that tongue masses are best evaluated on contrast enhanced scans, but STIR images in non-contrast studies provide near comparable results in delineation of the lesion, rendering contrast enhanced evaluation a modality reserved for problem solving circumstances due to its additional cost, invasive nature and the possibility of contrast reaction.

According to the study, maximum correlation was observed when a radiologist, on individual basis, selected the optimal plane among axial, saggital and coronal planes, and chose an optimal method among the invasive portion calculation method or reconstructed thickness calculation method to determine the DOI, for example, coronal for dorsum of the tongue or axial plane for lateral edge.

Limitations of the Study

Lacunae are present in my study in spite of my sincere efforts. The short falls include:

1. The study has been done in a single tertiary care hospital.
2. Hospital bias cannot be ruled out.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 522–532, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.005

ORIGINAL ARTICLE

Clinical profile of patients and various modes of management in acute colonic pseudo obstruction

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Accepted: 26-July-2023 / Published Online: 04-August-2023

Abstract

Aims & Objectives: To see the various modes of management in patients who diagnosed with Acute Colonic Pseudo obstruction (ACPO). The primary objective is to find out the clinical profile of patients of ACPO.

Material and Methods: This was an observational study which would require conservative mode Ryle's tube, flatus tube, electrolyte correction, colonoscopy. Intervention option like decompression tube or surgical management as per treatment algorithm, All the information required as per study proforma was collected over the first encounter. Follow up is not required. No additional cost burden on patient for this study.

Results: A total 23 patients were enrolled for study. Various modes according to the algorithm had been tried for management of ACPO. All patient had undergone X Ray Abdomen and/or CT scan. 4 out of 23 patients (17.4%) were on conservative measures, out of 2 patients were resolved and 2 died. Conservative measures included Nil by mouth, nasogastric decompression, rehydration, electrolyte correction and passage of flatus tube per rectum for 48 hours. One patient had been tried pharmacological therapy by injecting neostigmine but remained unsuccessful, rest had contraindications to pharmacological therapy. The other 19 patients failed to respond with conservative measures and thus they underwent interventional procedure (colonoscopy) which had not revealed any mechanical cause. Out of 19 patients,15 patients were benefited by placement of colonic decompression tube for 3 days. One patient treated with tube caecostomy. One patient had ceacal perforation for which Colectomy and ileostomy was done.

Conclusions: ACPO occurs in heterogenous group of patients, the exact aetiology and pathogenesis is not known. There should be high level of clinical suspicion. Once the diagnosis of ACPO has stablished and initial conservative management is unsuccessful, further measures are to be taken as per decisional algorithm. Colonoscopy and insertion of decompression tube leads the list of interventional procedure. In view of its high associated mortality, surgical intervention should only be a last recourse after failure of endoscopic procedures or when colonic perforation makes surgery unavoidable.

Keywords: ACPO (Acute colonic pseudo-obstruction), colonic decompression, tube caecostomy

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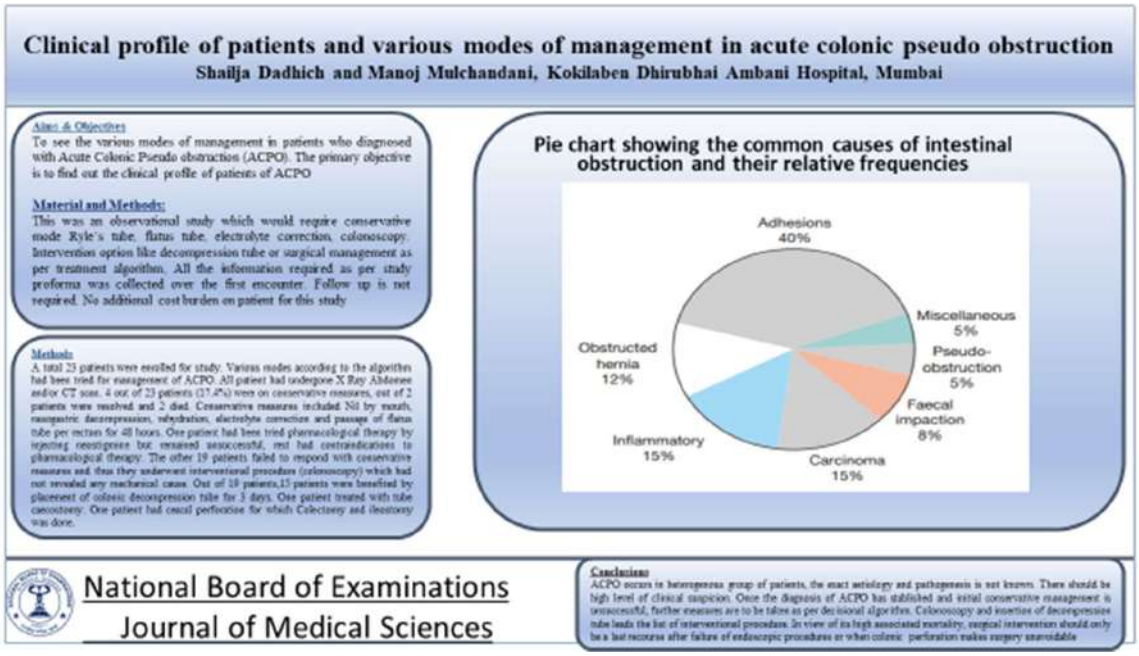
Graphical Abstract



Introduction

Acute colonic pseudo-obstruction (ACPO) or Ogilvie's syndrome (OS), consists of dilatation of all of the colon and rectum without intrinsic obstruction or extrinsic inflammatory process [1]. Wegener et al. [2] found ACPO has been associated with a diverse array of underlying conditions. It consists acute physiologic insults. The pathophysiology of ACPO is incomplete till now. The British surgeon Sir William Heneage Ogilvie [3] described unopposed parasympathetic activity following the disruption of the sympathetic supply by the cancer. Symptomatology consists of pain in abdomen, distension, nausea, and vomiting. Inability to pass flatus and stool are common but not frequently present. The clinician should suspect ACPO when no mechanical cause has found, in a patient who continues to have bowel dysfunction, including diarrhoea. Abdominal tenderness points towards ischemic bowel or perforation. It is a diagnosis of exclusion.. It is necessary to rule out mechanical obstruction. A patient who presents with symptoms of ACPO, multiple diagnostic modalities should be considered to diagnose. All Laboratory parameters are rarely diagnostic. Although correction of electrolyte may be helpful in the treatment. An elevated white blood cell count, lactate, or C-reactive protein may be a cause of more perforated bowel. An initial radiographic abdominal X Ray may help identify an obstruction and rule out anatomic cause of obstruction, such volvulus. A caecal diameter of 9 to 12 cm is suggestive of to cause impending perforation [4]. A typical radiographic finding of ACPO on CT scan is pan colonic dilation with no transition point [5]. The strategy of management for ACPO remains conservative in initial phase [6]. After ruling out a mechanical colonic obstruction, treatment begins with conservative medical therapy. It involves discontinuing oral intake, nasogastric tube decompression, correcting electrolyte, discontinuing opiates, correcting any fluid imbalance, cessation of any antimotility agents, and discontinuing oral intake, if possible, patient should be mobilized. In a stable, but

non-responders, the next step is to proceed with pharmacologic modality as neostigmine in a cardiac-monitored setting [7]. If pharmacologic therapy is unsuccessful for a patient, endoscopic colonic decompression together with the insertion of a large diameter soft catheter rectal tube is the next course of action. Alternatively, by inserting a lengthy catheter into the cecum while being guided by a fluoroscope, prolonged decompression can be accomplished. Surgical techniques may be required if conservative, medical, pharmaceutical, and endoscopic therapies fail to resolve ACPO. These include PEC or surgical caecostomy tube placement or subtotal colectomy. Of these operations, resection or exteriorization/caecostomy are the operations of preference when necessary since they have the highest success rate with the lowest morbidity [8].

The aim of the study was to see the various modes of management in patients who diagnosed with Acute Colonic Pseudo obstruction (ACPO). The primary objective is to find out the clinical profile of patients of ACPO. The secondary objectives were to understand diagnostic and treatment modalities of ACPO and to establish a clinical diagnostic criterion by segregating patients, clinical presentation, laboratory findings and radiological evidences in order to understand the pattern of distribution in Indian population more clearly.

Patient and Methods in Clinical Studies

The present study is an observational retro-prospective, single centre study conducted in the Department of General Surgery at Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute from June 2021 to June 2022. All patients who had diagnosed with ACPO were enrolled for the study. Patients with intestinal obstruction for that no cause had been found, admitted in ward, ICU, Stroke unit of Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute included after taking informed written consent. Institutional ethical and scientific committee clearance was obtained for conducting this study. Information was collected regarding comorbidities, previous surgical history and modality which resolved the acute condition.

Inclusion Criteria:

Patient age group 18 and above of either sex Male and female patients will be included who were hospitalized patient whose signs and symptoms shows intestinal obstruction for which no cause has been and voluntarily sign a consent form.

Exclusion Criteria:

Patient of intestinal obstruction whose mechanical cause has been found.

The patients who are diagnosed with ACPO would be selected for the study. They would be explained about the study in detail and then would be presented with the Informed consent form. Only those patients would be included in the study who consent for it. Once consent is obtained, information regarding the patient would be collected, including clinical history, examination, and relevant investigation reports (like blood investigations, other radio diagnostic scans and colonoscopy findings already done or advised by the consultant). All this information would be later compiled in tabular and chart form for analysis. This is an observational study which would require conservative mode, Ryle's tube, flatus tube, electrolyte correction, colonoscopy, decompression tube or surgical management as per treatment algorithm. All the information required as per the Study proforma is collected over the first encounter. Follow-

up is not required. No additional cost burden on a patient for this study.

Measurement of the outcome of interest:

This was an observational study which would require conservative mode Ryle's tube, flatus tube, electrolyte correction, colonoscopy. Intervention option like decompression tube or surgical management as per treatment algorithm, All the information required as per study proforma was collected over the first encounter. Follow up is not required. No additional cost burden on patient for this study.

Results and Analysis

A total 23 patients were enrolled for study. Various modes according to the algorithm had been tried for management of ACPO. All patient had undergone X-Ray Abdomen and/or CT scan. 4 out of 23 patients (17.4%) were on conservative measures, out of 2 patients were resolved and 2 died. Conservative measures included Nil by mouth, nasogastric decompression, rehydration, electrolyte correction and passage of flatus tube per rectum for 48 hours. One patient had been tried pharmacological therapy by injecting neostigmine but remained unsuccessful, rest had contraindications to pharmacological therapy. The other 19 patients failed to respond with conservative measures and thus they underwent interventional procedure (colonoscopy) which had not revealed any mechanical cause. Out of 19 patients, 15 patients were benefited by placement of colonic decompression tube for 3 days. One patient treated with tube caecostomy. One patient had ceacal perforation for which Colectomy and ileostomy was done (Figures 1 to 4).

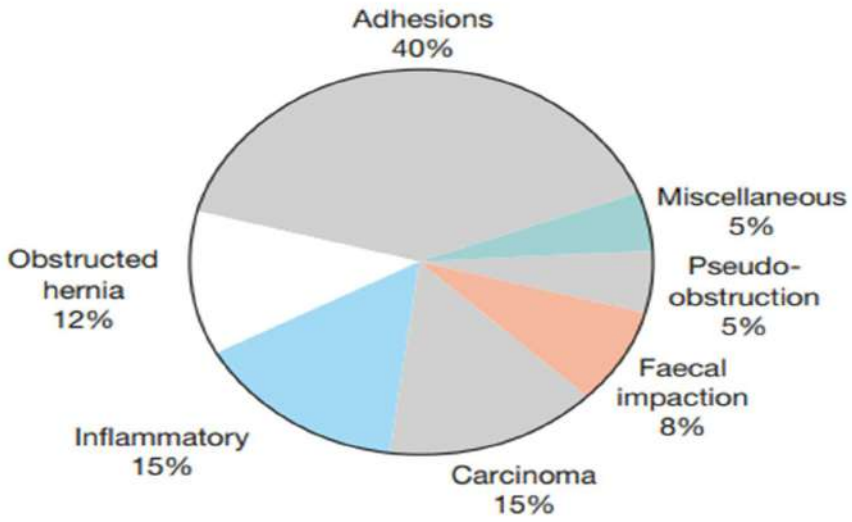


Figure 1. Pie chart showing the common causes of intestinal obstruction and their relative frequencies

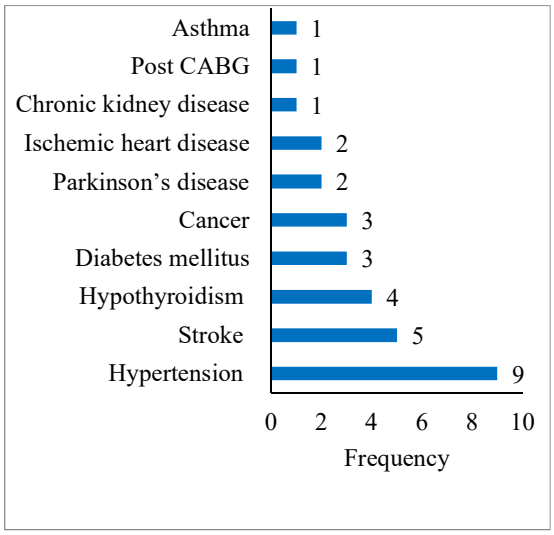


Figure 2. Distribution of patient underwent surgery and comorbidities

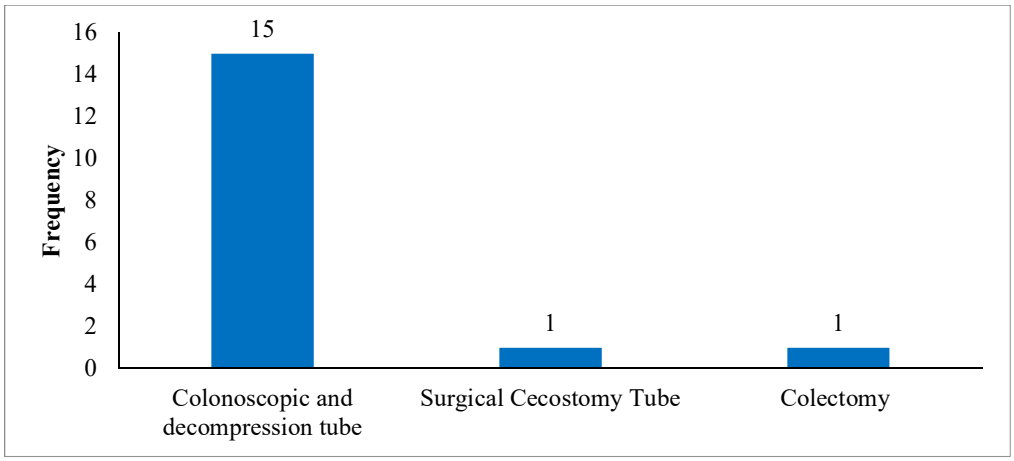


Figure 3. Distribution of surgical intervention in ACPO

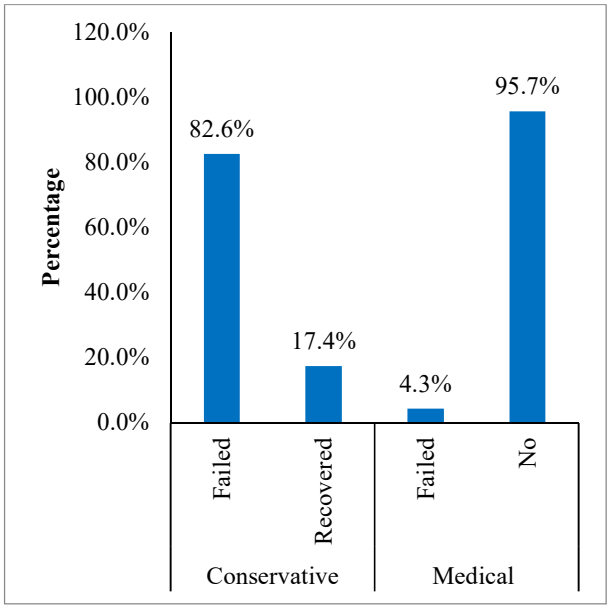


Figure 4. Failure rate of conservative and medical treatment in ACPO

Clinical Pictures (Figures 5 to 8)

Figure 5. Distended abdomen, tender with the presence of tympanic note

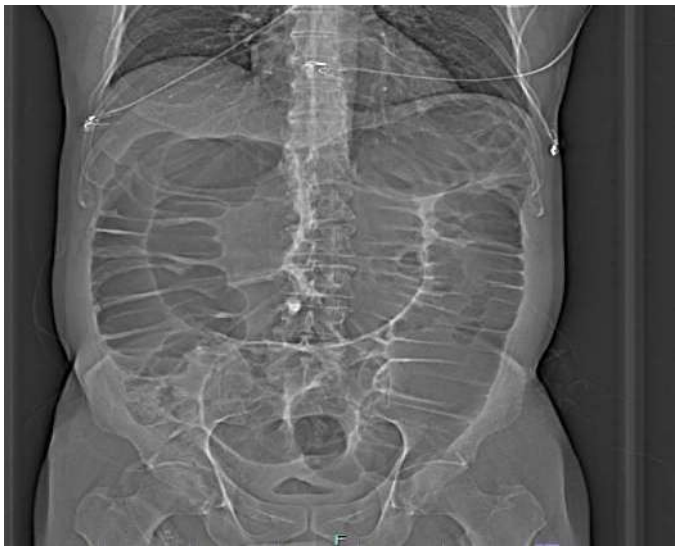


Figure 6. X-Ray Abdomen supine view shows massive colonic dilation

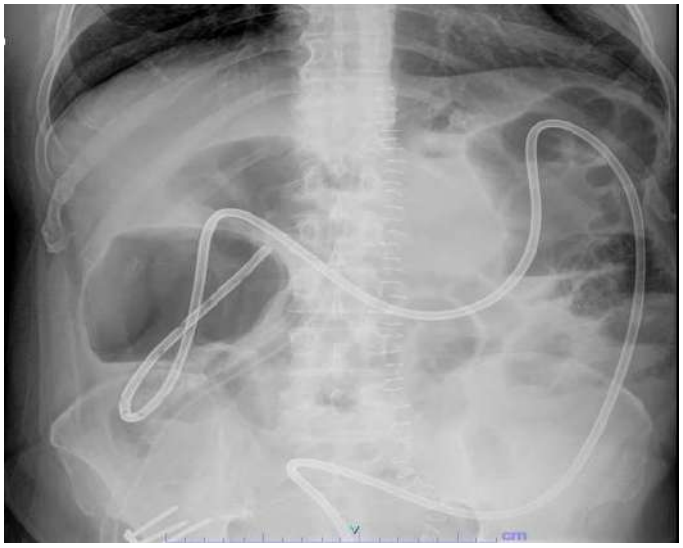


Figure 7. Decompression tube in situ

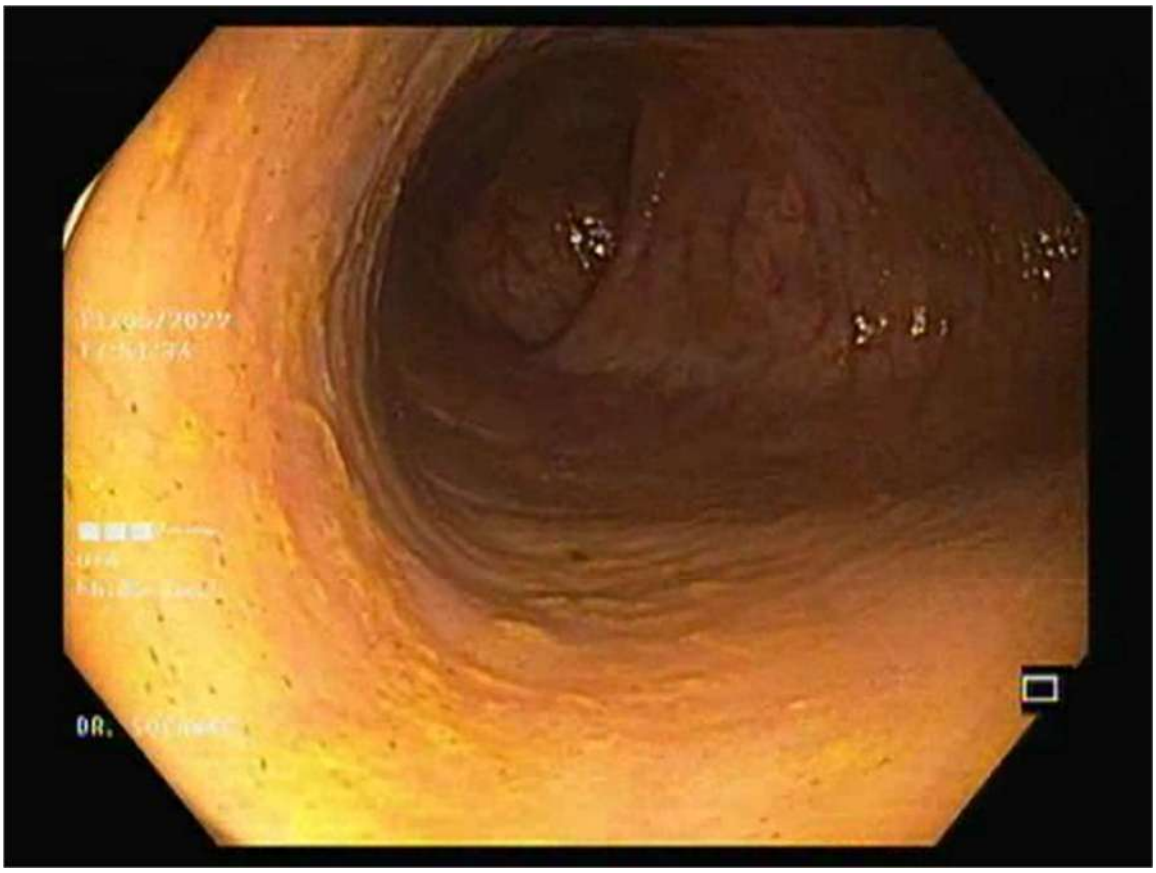


Figure-8. Grossly dilated colon

Discussion

This was a hospital based, retro-prospective, observational, single centre study to see clinical profile of patients and various mode of management in ACPO. Current literature on ACPO describes Intestinal pseudo-obstruction is a rare and heterogeneous syndrome caused by severe disorders of gastrointestinal motility.

A total 23 cases of ACPO enrolled in this study. Of these 17 patients were males and 6 were female indicating a male preponderance. This is similar to previous studies which suggest ACPO was diagnosed in 36 patients, 24 of whom were men. The mean age of presentation of patients was 67. It has wide range of age distribution from 37 to 88 years.

De Giorgio et. al. has studied that ACPO is a disease group difficult to diagnose due to occurrence in the elderly patient group with comorbidities and because it is not considered during differential diagnosis [5].

The most comorbidity observed in patients was hypertension as seen in 9 (39.1%) patients followed by hypothyroidism observed in 4 (17.4%) patients. 3 (13.0%) patients had diabetes mellitus and 2 (8.7%) each had suffered from stroke, Parkinson's disease (8.7 %), cancer (8.7 %) and ischemic heart disease (8.7%) One patient each had history of asthma (4.3 %), chronic kidney disease (4.3 %), post CABG (4.3 %)

Wegener et al. described in a In a study of 1,027 patients, postoperative circumstances (23%) and cardiopulmonary illnesses (17.5%), other systemic disorders (15%), and trauma (11%), were found to be the most frequently related factors with ACPO [2].

Out of the 23 patients, 9 (39.2%) had not undergone any surgery whereas 14 patients had undergone different types of surgery. 17.4% underwent craniotomy, Whereas Cardiac surgery (4.3%) hysterectomy (4.3%), Bariatric Surgery (4.3%), intestinal surgery (4.3%). Whereas 8.7% had prostate surgery, vertebroplasty each.

Vanek [12] had described epidemiology in 400 patients. 19% of instances followed spinal cord injury, pelvic surgery, or delivery. The following circumstances may also be linked to the emergence of ACPO: Other conditions include pharmacological reasons (opioids, antidepressants), transplantation, systemic infection (10%), acute cardiac events (10%), intensive care or volume resuscitation (9%), and orthopaedic treatments (pelvic fractures) (18%).

The most common clinical observation in patients was an increase in abdominal girth as seen in all 23 patients. (100%). Apart from increased abdominal girth, constipation was the most common clinical feature as seen in 20 patients (87%) whereas diarrhoea was observed in 3 (13%) patients. Bowel sounds and pain in abdomen was present in 12 (52.2 %) patients whereas vomiting was seen in 12 patients. (52.2 %)

Naseem Sunnoqrot reported hypokalaemia resulting from the symptoms of colonic pseudo-obstruction include frequent, watery diarrhoea with a high potassium and low sodium content. Instead of being caused by the obstruction of sodium reabsorption or chloride secretion, which are the two most frequent pathophysiologic processes of secretory diarrhoea, the diarrhoea is secretory and driven by potassium secretion [9].

Out of the 23 patients, 7 patients had low serum potassium levels of <3.5 mmol/L whereas 1 had slightly elevated levels of >5.1 mmol/L. Minimum potassium levels observed in patient was 2.6 mmol/L whereas maximum levels observed were 5.2 mmol/L. The mean serum potassium levels were 3.8 mmol/L.

Out of the 23 patients, 9 patients had low serum sodium levels of less than 136 mEq/L whereas rest 14 had normal serum sodium levels. Minimum sodium levels observed in patient was 122 mEq/L whereas maximum levels observed were 145 mEq/L. The mean serum sodium levels were 135.7 mEq/L.

Of the 23 patients, 2 had low WBC (<4000 cell/mL) whereas 9 had WBC in normal range whereas 12 had high WBC of >11000 cell/mL. Minimum WBC level was 2900 cells/mL whereas maximum WBC level was 24070 cells/mL. Mean WBC cell count was 11542 cells/mL.

All 23 patients had high CRP levels. Of the 23 patients, 2 had normal serum lactate levels (0.4 – 0.6 mmol/L) whereas 21 had high serum lactate levels (>0.6 mmol/L).

From the 23 patients, 14 had ceacal diameter between 3-8 cm whereas 9 had ceacal diameter of >8 cm. The minimum ceacal diameter in patients was 4 cm whereas maximum was 10.8 cm. The mean ceacal diameter was 7.3 cm.

Rondeau et al. reported 8 men were among the 12 patients (mean age: 80.2 years). They were all experiencing stomach ache. Seven patients had occlusive syndromes. Two of

the victims experienced septic shock. The cecum has an average diameter of 10 cm. For 9 cases, the entire colon was distended [10].

From the 23 patients, 2 had mid-transverse colon diameter of <5 cm, 10 had mid-transverse colon diameter of 5-6.5 cm and 11 had mid-transverse colon diameter of >6.5cm. The minimum Mid-transverse colon diameter was 4.7 cm and maximum Mid-transverse colon diameter was 12 cm. The mean Mid-transverse colon diameter was 7 cm.

Lee et al. noted on faecal gaseous distension of the transverse colon, faecal gaseous distension of the ascending colon, gaseous distended transverse colon, and gaseous small bowel loops were all visible on plain radiography. On CT scans, it was discovered that small bowel dilatation and pneumatosis intestinalis were present, as well as that faecal fluid had enlarged the ascending and transverse colon and faecal gas had enlarged the transverse and ascending colon [11].

Out of 23 patients, small bowel dilation was present in 8 patients whereas it was absent in 15 patients.

Form the 23 patients, 19 had undergone colonoscopy who failed to conservative measures. Decompression tube was placed in 16 patients out of 19 patients.

This cautious strategy has a success rate of up to 70% and an overall mortality rate of 14% [5].

Vanek and Al-Salti When necessary, tube cecostomy has been reported to have up to 100% success rates [12].

Conservative treatment failed in 19 patients and medical treatment failed in 1 patient. From the 23 patients, 15 underwent Colonoscopy and decompression tube, 1 underwent Surgical Cecostomy Tube and 1 underwent Colectomy.

Saunders et al. [5] the major causes of a high mortality rate could be attributed to ageing, coexisting illnesses, and the emergence of colonic necrosis and perforation. We had a mortality rate of 18%.

Magda et al. reported that ACPO related with a serious underlying condition and a low inpatient mortality at the moment [13]. In our study, out of 23 patients, 2patients did not survive whereas 21 recovered.

Conclusion

ACPO occurs in heterogenous group of patients, the exact aetiology and pathogenesis is not known. There should be high level of clinical suspicion. Once the diagnosis of ACPO has stablished and when initial cautious management fails, additional measures are to be taken as per decisional algorithm. Colonoscopy and insertion of decompression tube leads the list of interventional procedure. Surgery should only be used as a last resort following the failure of endoscopic techniques or when colonic perforation makes surgery necessary due to its high related mortality.

Statements and Declarations

Conflicts of interest – The authors have no competing interests to declare that are relevant to the content of this article

Funding – No funding was received for conducting this study

Ethics approval

Ethics committee approval was obtained from the Ethics Committee of Kokilaben

Dhirubhai Ambani Hospital, Mumbai Maharashtra. It was an observational study with all the procedures being performed as part of the routine care. A written informed consent was taken from all patients enrolled in the study.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 533–540, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.006

CASE REPORT

Forgotten DJ stent with calculus in a ectopic kidney: A rare case report

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Accepted: 21-July-2023 / Published Online: 04-August-2023

Abstract

Urologists commonly make use of ureteral double J stents in endourology. If a DJ stent is forgotten to be removed, then complications happen in the form of encrustations, infection, migration, renal dysfunction and hydronephrosis. Ectopic pelvic Kidney is a relatively rare congenital anomaly caused by lack of ascent of the kidney. We report a very rare case of forgotten DJ stent in an ectopic kidney in a 55 years old patient with diabetes mellitus with history of left sided open pyelolithotomy done 21 months back. Redo open surgery was done to remove DJ stent along with stone removal.

Keywords: Ectopic kidney, retained DJ stent, CAKUT, calculus

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Introduction

Congenital anomalies of the kidney and urinary tract commonly designated as CAKUT are rare abnormalities and they include a wide spectrum from abnormal numbers, shape and positional anomalies to fusion, and urinary tract anomalies. Ectopic pelvic kidney is a congenital abnormality caused by lack of ascent of the kidney. Ureteral double J (DJ) stenting after stone surgery is done routinely in such kidneys. To our knowledge forgotten DJ stent in ectopic pelvic kidney has been scarcely described in literature. Here we present a case of forgotten DJ stent post left sided open pyelolithotomy which was removed by open surgery.

Case report

A 59-year-old male presented to the outpatient department of a tertiary care centre with complaints of left sided lower abdominal pain. The pain was intermittent colicky in nature. The patient reports history of left sided open pyelolithotomy done for left sided large renal pelvic calculus in the left sided ectopic pelvic kidney with DJ stenting. The DJ stent was forgotten to be removed post-surgery and has been retained in the left kidney since last 18 months. Patient was further evaluated using Xray KUB (Kidney, ureter and urinary bladder) which revealed ectopic left pelvic kidney with retained DJ stent in situ (Figure 1).

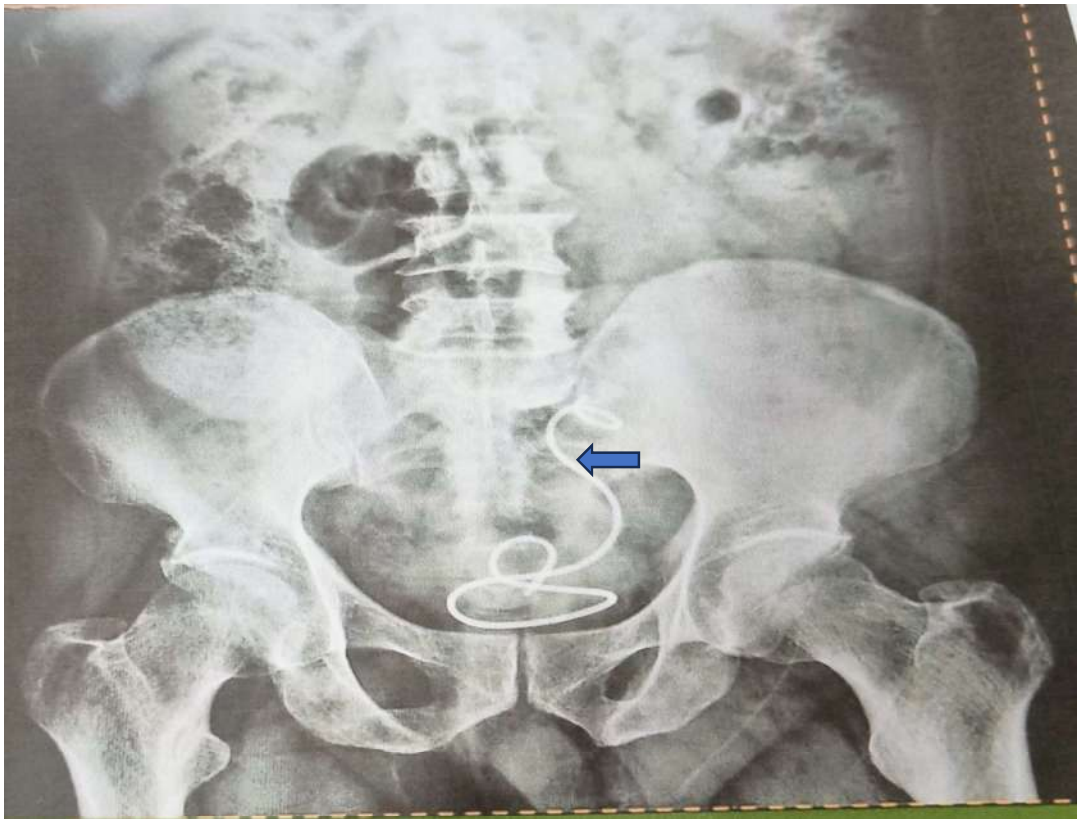

Figure 1. Xray KUB image of the patient showing the retained Double J stent in the left sided ectopic pelvic kidney.

Patient then underwent CT KUB (Computerised Tomography-Kidney ureter and Bladder) which revealed ectopic left sided kidney with retained DJ stent with encrustations all around along with 3.5 cm calculus with density of 500 Hounsefield units (HU) (Figure 2).

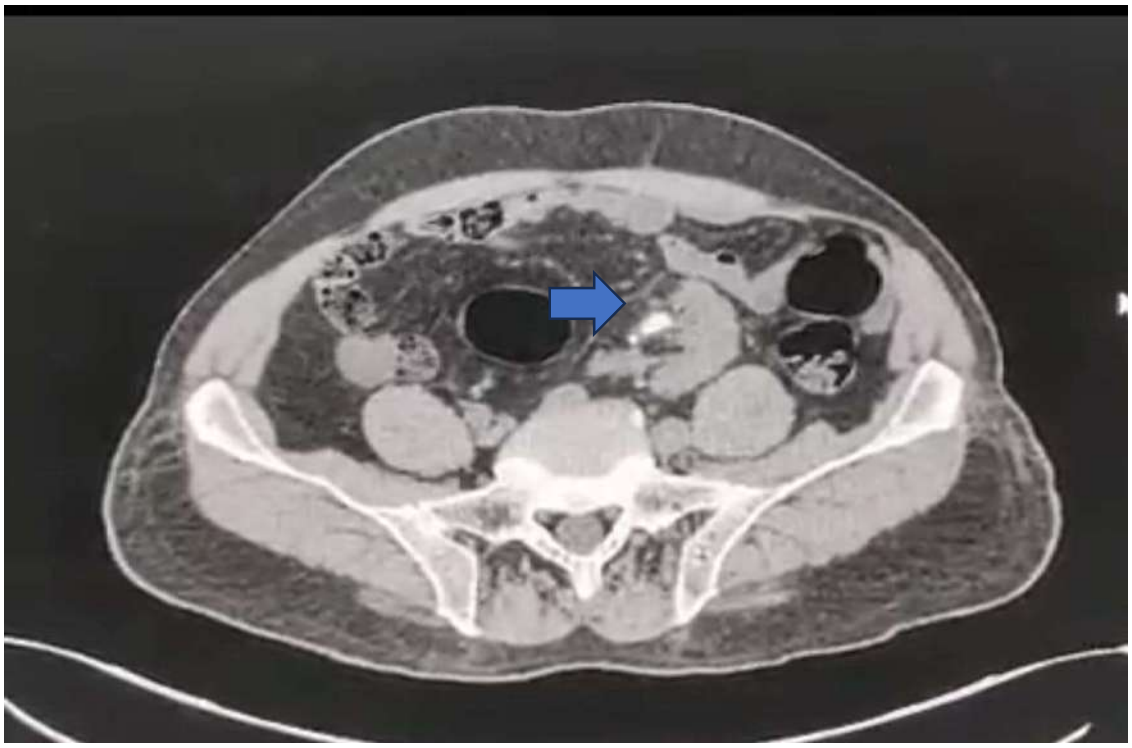

Figure 2. Plain CT-KUB image -axial section showing calculus in the left ectopic pelvic kidney.

In view of the large stone burden and the encrusted stent and the ectopic location of the left kidney, decision was made to go ahead with Left sided open pyelolithotomy with retrieval of the calculus and the DJ stent.

Preoperatively surface marking was done under fluoroscopic guidance to mark tge position of the stone in the left ectopic pelvic kidney (Figure 3).

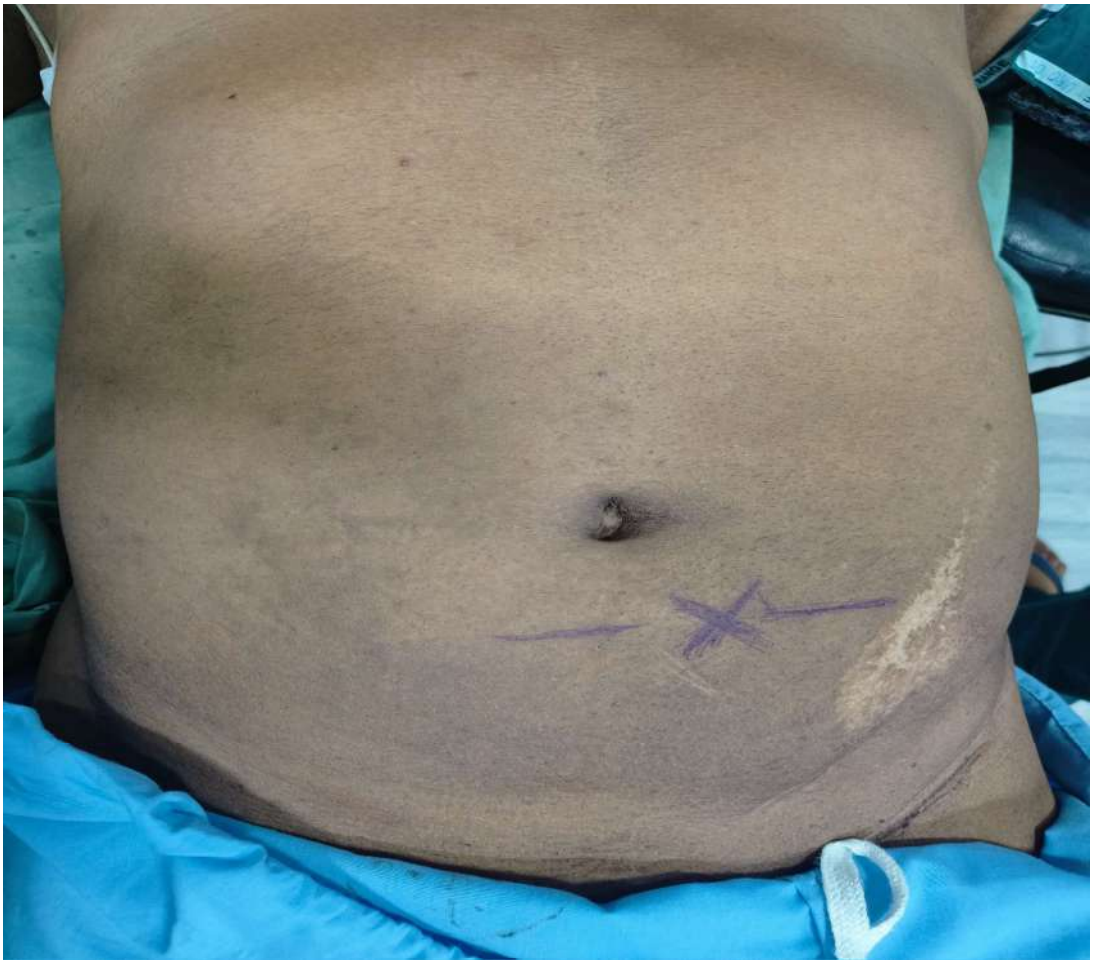

Figure 3. Clinical picture of the patient showing surface marking of the stone done on table before the commencement of the surgery done under fluoroscopic guidance.

Through a lower midline incision, patient was explored. The left ectopic pelvic kidney was carefully exposed after dissecting the bowel and the peritoneum cranially. Then through a longitudinal pyelolithotomy, the retained DJ stent with encrustations was carefully removed along with the calculus in the left renal pelvis followed by placement of new double J stent and closure of the pyelolithotomy using 3-0 PDS and placement of abdominal drain. (Figures 4, 5 and 6).

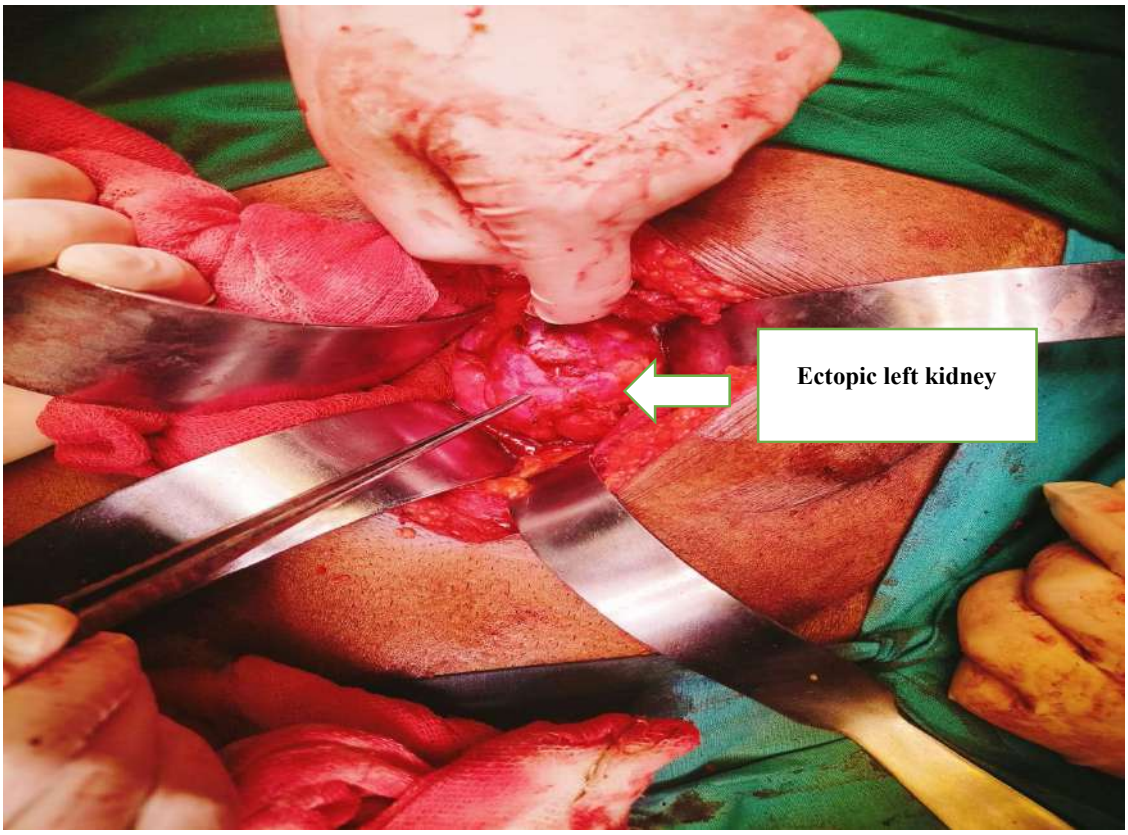

Figure 4. Intraoperative image showing the ectopic left pelvic kidney.

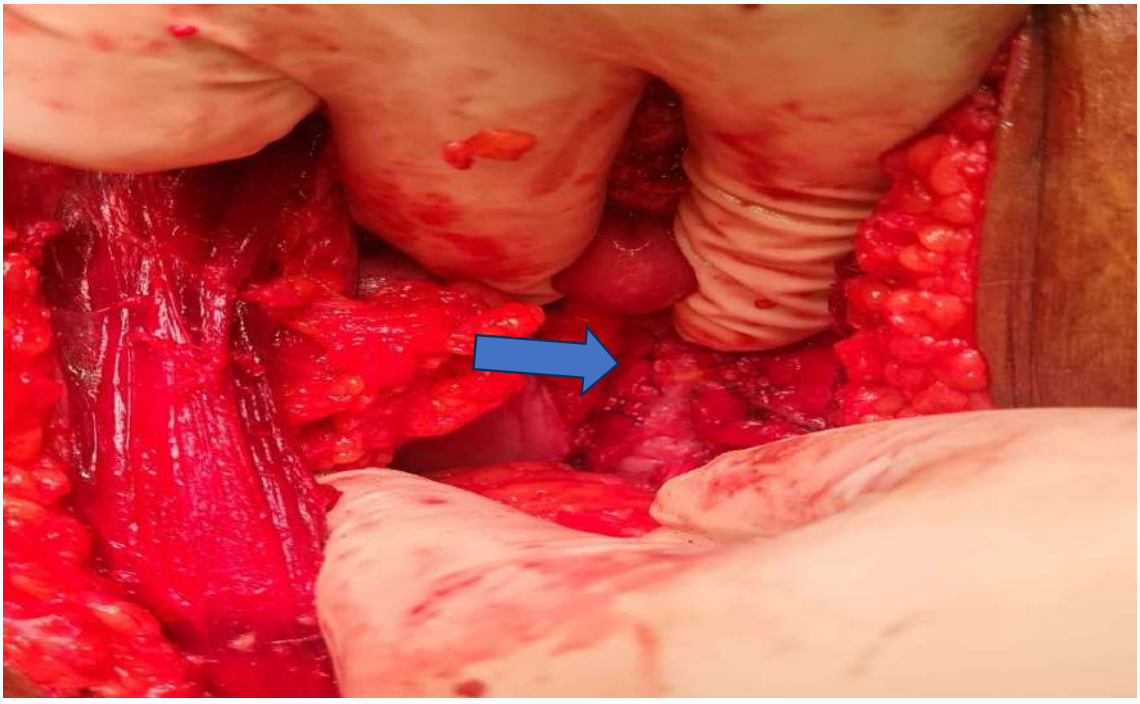

Figure 5. Intraoperative image showing sutured pyelolithotomy incision after retrieval of DJ stent and the calculus.

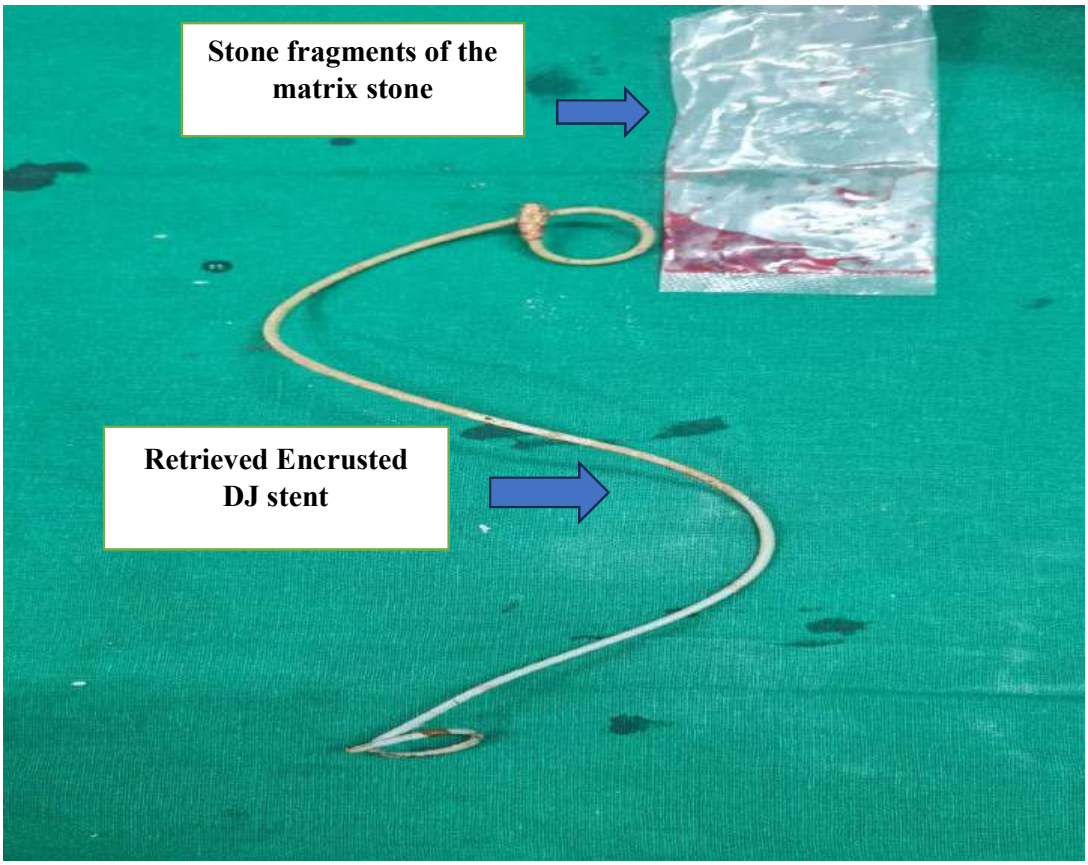

Figure 6. Final postoperative image showing the retrieved DJ stent along with the encrustations and the stone fragments of the matrix stone in the polythene bag.

The post-operative course was uneventful and the patient was discharged after removal of drain. The newly placed DJ stent was removed after 4 weeks. Patient's last follow up was after 3 months after surgery and he is doing well.

Discussion

Renal ectopia in the form of pelvic kidney is one of the described anomalies in the spectrum of the described term "CAKUT" (Congenital anomalies of the Kidney and Urinary Tract).

Thus, CAKUT presents with unique challenges and suprises for the practising urologist due to the variations in their anatomy. So, a careful planning after detailed study of the anatomy by using different available imaging techniques is advisable pre-operatively [1,2].

Double J stent is like a double edged sword and hence, precautions and guidelines should be followed for its appropriate use. Patient should be well counselled that they have double J stent inside their body and they will have to undergo procedure for its removal and or exchange depending on the clinical scenario after a particular period of time. Nowadays DJ stents are used as a therapeutic option for different urological conditions and allows urine to drain from from kidney to bladder and they are considered generally safe and well tolerated. However, if the DJ stent is kept for a prolonged period in situ, then they are

bound to develop hazardous complications in the form of encrustations, fragmentation, infection, migration and stone formation. Forgotten DJ stent presents differently. Damiano et al observed flank pain in 25 %, irritative bladder symptoms in 18.8%, hematuria in 18% of patients. It is believed that asymptomatic patients, poorly compliant patients are more prone to neglect or forget their stents [3]. A calcified forgotten stent or retained ureteral stent is defined as one that cannot be removed with cystoscopy in the first attempt without aid of other auxiliary measures due to encrustation or formation of a stone within the stent [4]. Among various mechanism of encrustation mostly Urinary tract infection (UTI), prolonged duration, urinary composition, congenital urinary tract anomaly is responsible.

At upper coil

Extracoproreal Shock wave Lithotripsy (ESWL), Ureteroscopy, Percutaneous nephrolithotomy (PCNL), Retrograde Intrarenal Surgery (RIRS) and open surgery are the various options available depending on the clinical situation.

At lower coil

Endovesical procedures (cystolithotripsy, cystolitholapaxy). In case of congenital anomalies, one should remember that there are certain precautions to be followed. Retained stent with stone or encrustations is a surgical challenge for urologists and if it occurs in congenital abnormal kidney as in our case, the challenge and the complexity increases further. Our case report presents ectopic pelvic kidney with retained DJ stent with stone formation which was managed by open pyelolithotomy. As per our review of literature, there are very few cases published with retained DJ stent in ectopic kidneys. Management of forgotten stent by endourological methods is well established and there are scoring systems and algorithms developed for management and predictability of clearance in retained DJ stent [5].

Conclusion

Retained DJ stent can be a challenge to remove in some cases especially if there is variation in the anatomy of the kidney and in case of stone formation within the stent. Open Surgery offers an effective approach in the scenario of Retained DJ stent with ectopic pelvic kidney as demonstrated by our case presented here.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable

Author Contributions

Ojas Vijayanand Potdar: Design, patient history taking and writing the manuscript of the case report. Akash Shah: Writing the manuscript of the case report. Mohammed Ayub Karamnabi Siddiqui: Design of the case report. Kaustubh Vaidya- Images of the radiological investigations. Darshan Rathi: Patient history taking. Amrita Vikram Patkar: Writing the manuscript of the case report.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 541–548, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.007

CASE REPORT

Sjogrens Syndrome Presenting as a Case of Cerebro Vasular Accident with Thrombocytopenia – A Case Report

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Accepted: 01-July-2023 / Published Online: 04-August-2023

Abstract

Auto immune disorders have a wide range of presentations. Often, they are missed due to difference in their spectrum of presentations. Hence any slight suspicion of autoimmunity should be thoroughly ruled out. Multiple system involvement like joints, renal, vascular events simultaneously presenting should always rise a suspicion of autoimmunity and prompt investigations should be paged that could be effectively contributing to decrease mortality and morbidity of the patient. Thorough history, if possible, pedigree charts should be evaluated for any clues of autoimmunity. All first-degree relatives of the patient should also be evaluated for any possibility of autoimmune diseases.

Keywords: Autoimmune diseases, Sjogren's syndrome, Acute cortical infract, Thrombocytopenia

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Abbreviations

SS-A, B ANTIBODIES – ANTI SJOGRENS SYNDROME RELATED ANTIGEN A, B ANTIBODIES
OPD – OUT PATIENT DEPARTMENT
BP – BLOOD PRESSURE
HB – HEMOGLOBIN
LMWH – LOW MOLECULAR WEIGHT HEPARIN
CVE – CEREBRO VASULAR EPISODE
AFI – ACUTE FEBRILE ILLNESS
SLE – SYSTEMIC LUPUS ERYTHEMATOSUS
ITP – IMMUNE THROMBOCYTOPENIA
RTA – RENAL TUBULAR ACIDOSIS

Introduction

Sjogren's syndrome is an autoimmune disorder with lymphocytic infiltration of exocrine glands most commonly involving salivary and lacrimal glands. Female are affected more than males at ratio of 20:1 [1].

Patients usually present with dryness of mouth and dry eyes. Extra glandular symptoms like fatigue, arthritis, weight loss. It might also present with proximal myopathy, peripheral neuropathy, and interstitial lung disease.

Pan cytopenic picture might be seen on haematological examination. SS-A, SS-B antibodies will be seen in 40- 80% cases. Diagnosis is mostly based on clinical and immunological analysis.

Steroids, higher immunosuppressants like rituximab, cyclophosphamide have promising role in treatment of Sjogren's syndrome.

Case Presentation

A 50-year-old female came to opd with chief complaint of generalized weakness, fatigue, vomiting, nausea, low appetite since last one week. Nausea is persistent whole day and increasing on food intake. Patient had 2–3 episodes of vomiting which are non-blood or bile stained, non-projectile and mostly contain food and mucous. Patient has severe fatigue, not interested to do any work or house hold activity. Patient had an episode of acute febrile illness one month back for which patient for hospitalised for three to five days.

Patient is a known case of hypothyroidism has been using medication for the same (eltroxin 75 mg). Patient was once diagnosed with hypertension and was not adherent to her medication. No significant family history has been found. Patient reached menopause 3 years back. No addictions. Normal bowel and bladder movement.

On admission pulse – 84/ minute, BP – 138/84 mm/hg right hand supine position. Oxygen saturation – 99% on room air. Patient is pale but no cyanosis, rash, lymphadenopathy, clubbing, icterus seen. Mild periorbital oedema seen.

On systemic examination no significant findings are seen.

Laboratory investigations revealed hb- 10.5gm/dl, TLC – 8000 gm/dl, platelets – 36000 / cumm. Serum bilirubin – 1.80 mg/dl, direct bilirubin – 0.35 mg/dl, indirect bilirubin – 1.45 mg/dl. Patient has

normal blood sugars. Urine routine revealed turbid appearance, 4+ albumin, 8-10pus cells. Blood urea – 78 mg/dl, bun – 36 mg/dl, serum creatinine 1.5 mg/dl.

Ultrasound abdomen has shown bilateral increased cortical echogenicity with poor corticomedullary differentiation and perirenal fluid collection with19*16mm cortical cyst. Echocardiography revealed presence of bicuspid aortic valve.

Next day morning around 4:00 am patient had severe weakness on right side upper and lower limb, patient is aphasic, right sided mouth deviation seen. MRI shown acute non haemorrhagic cortical infract in bilateral occipital lobe more on left lobe. Repeat platelet count shown a value of 9000 /cumm.

Patient has been treated with antibiotics, fresh frozen plasma, platelet concentrates, LMWH, anti-platelets and thyroid supplements.

There is no much rise in platelet count even after platelet concentrate transfusion and subsequent development of CVE along with the presence of 4+ proteinuria, has led to suspicion of autoimmune disorder and hence antibody panel has been sent. SS-A, Ro 52KD, SS-B are found to be positive.

Patient has been treated with steroids, antibiotics, fresh frozen plasma, platelet concentrates, LMWH, anti-platelets and thyroid supplements.

Repeat platelet shown a value of 13000/cumm on day three. Patient has been questioned about symptoms of Sjogren's syndrome and then she revealed lack proper salivation while eating from many months.

Even though patient is still in recovery, on request of the relative's, patient has been referred to another hospital near their hometown.

Discussion

We present a case of 50-year women with Sjogren's syndrome who presented with chief complaint of generalized weakness, fatigue, vomiting, nausea, low appetite, thrombocytopenia in the last one week and subsequently developed stroke. Initially patient is thought to be a case of thrombocytopenia post-acute febrile illness as patient has a history of AFI one month back.

In Sjogren's syndrome patient with anti-Ro antibodies present with higher frequency of systemic manifestations and haematological alterations like anemia and thrombocytopenia [1]. In autoimmune disorders like SLE, Sjogren's with ITP there will be circulating auto antibodies causing peripheral destruction of platelets leading to thrombocytopenia [2].

Type 2 mixed cryoglobulinemia associated with Sjogren's syndrome may lead to peripheral neuropathy, Raynaud's phenomenon, and renal injury. Purpura and arthralgia might also be seen [3].

The management of Sjogren's syndrome mainly focusses on dryness of eyes and oral cavity. Patient should be given lacrimal supplements like hydroxy methyl cellulose, polyvinyl alcohol, hypo tears. Patient should be encouraged to take more fluids. Topical anti-inflammatory solutions with cyclosporine are shown to be promising in some studies [4]. Pilocarpine and cevimeline can be used to stimulate oral secretions.

Renal manifestations like RTA can be treated with soda bicarbonate. Glucocorticoids and monoclonal antibodies like rituximab (anti CD 20) are effective in controlling manifestations of the disease by partial depletion of B cells in salivary glands [5] (Figures 1 to 4).

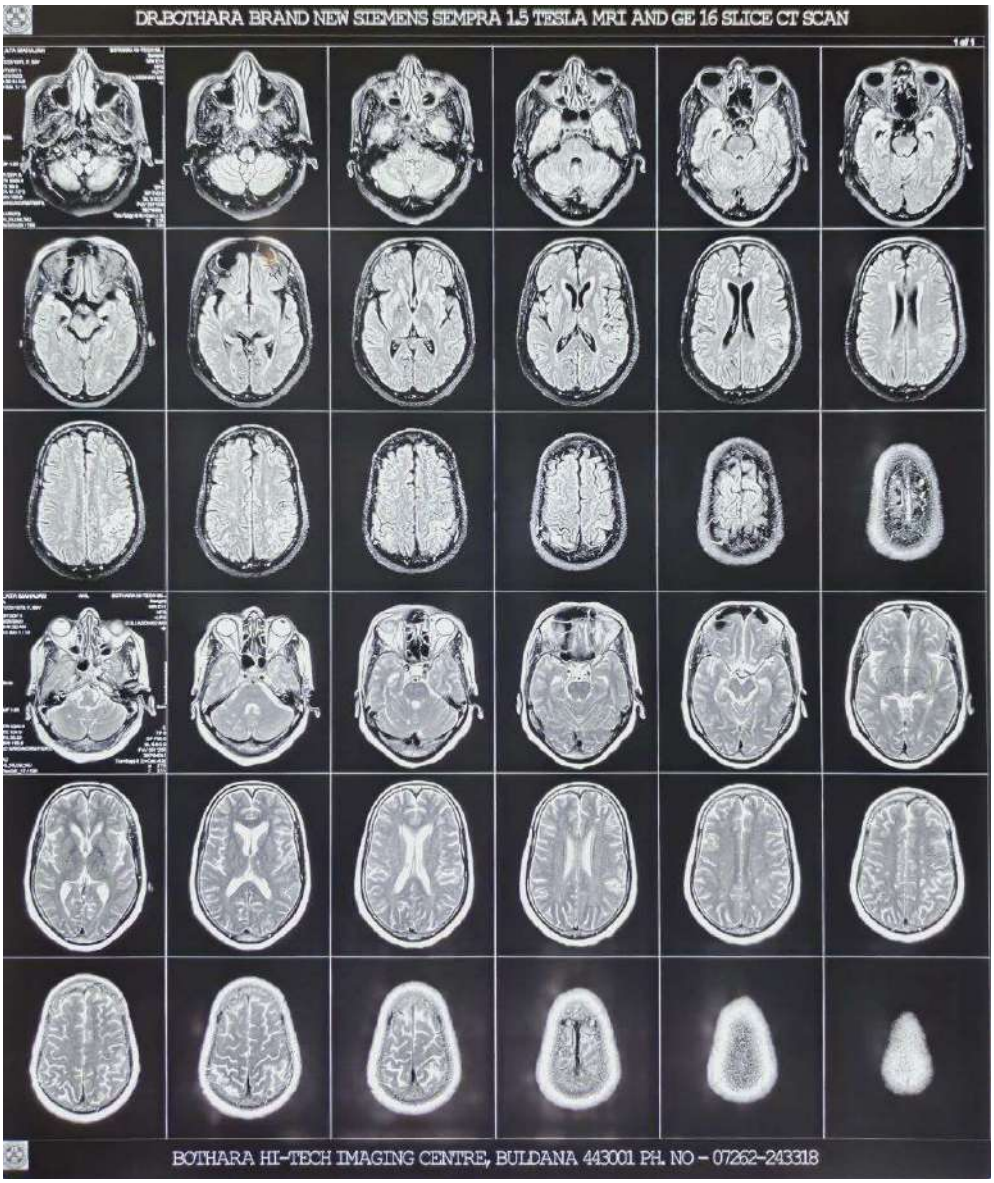

Figure 1. T1 weighted MRI with flair axial with lower T2.

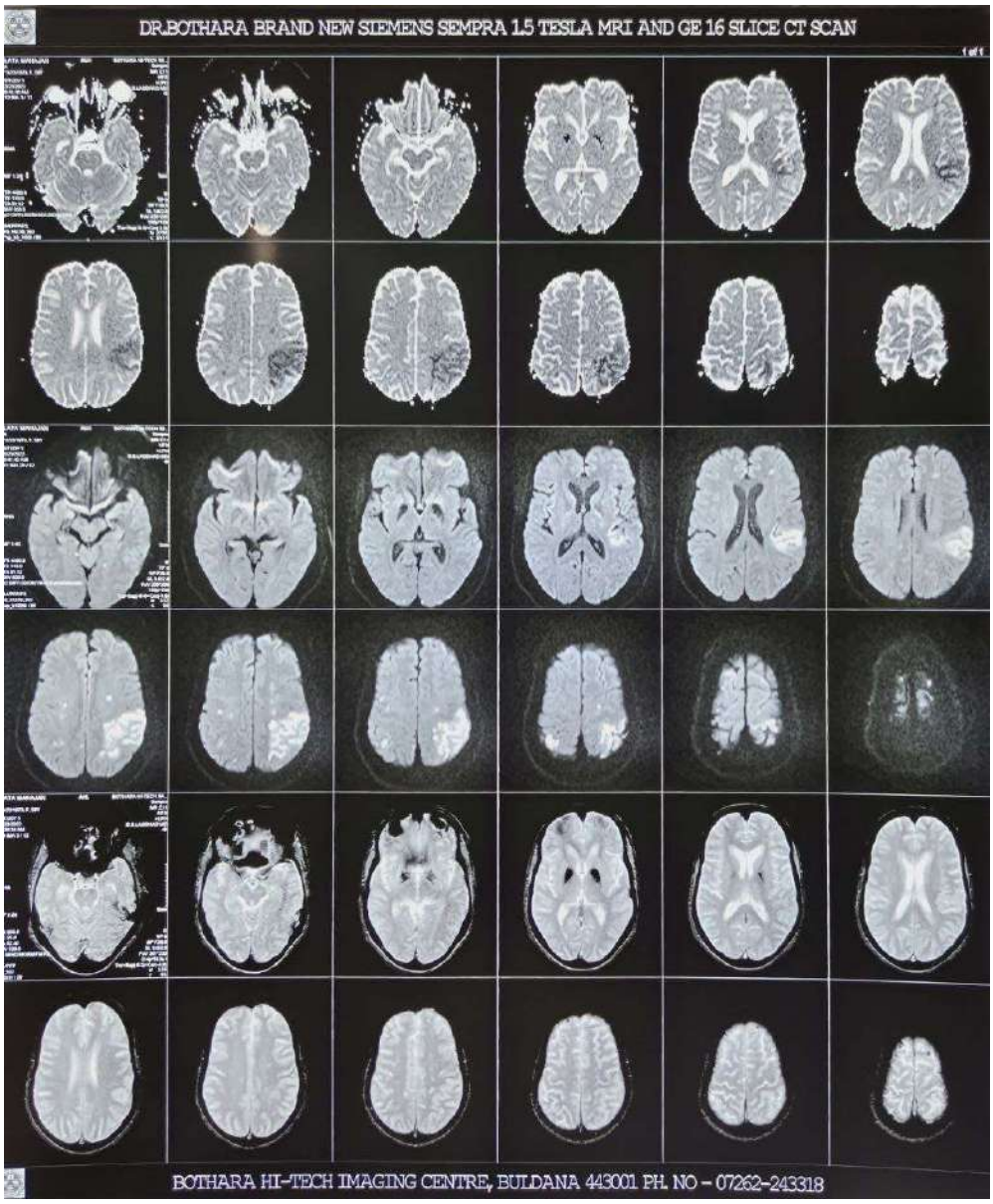

Figure 2. MRI with dwi/swi/gre sequencing.

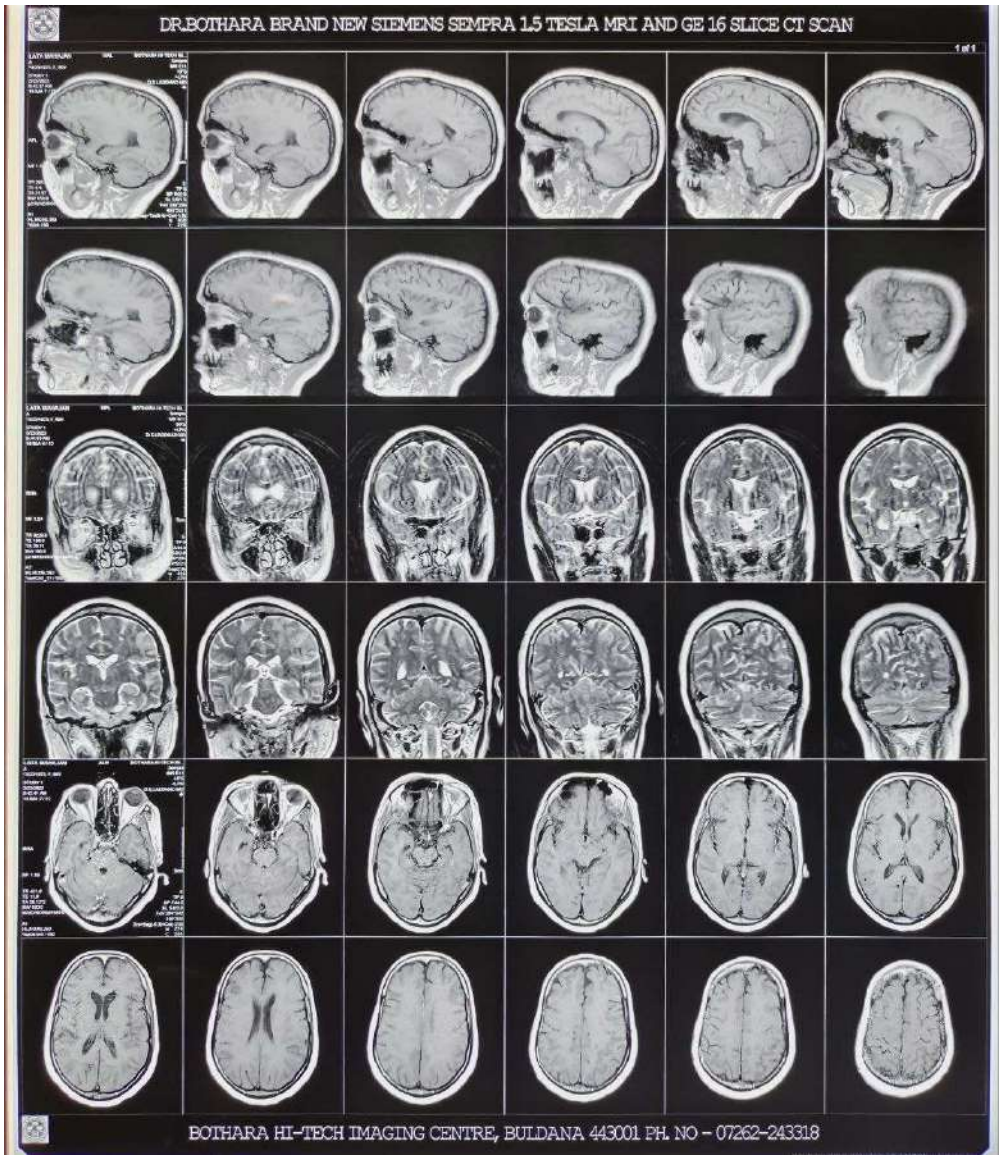

Figure 3. T2 SEQ with axial T1.

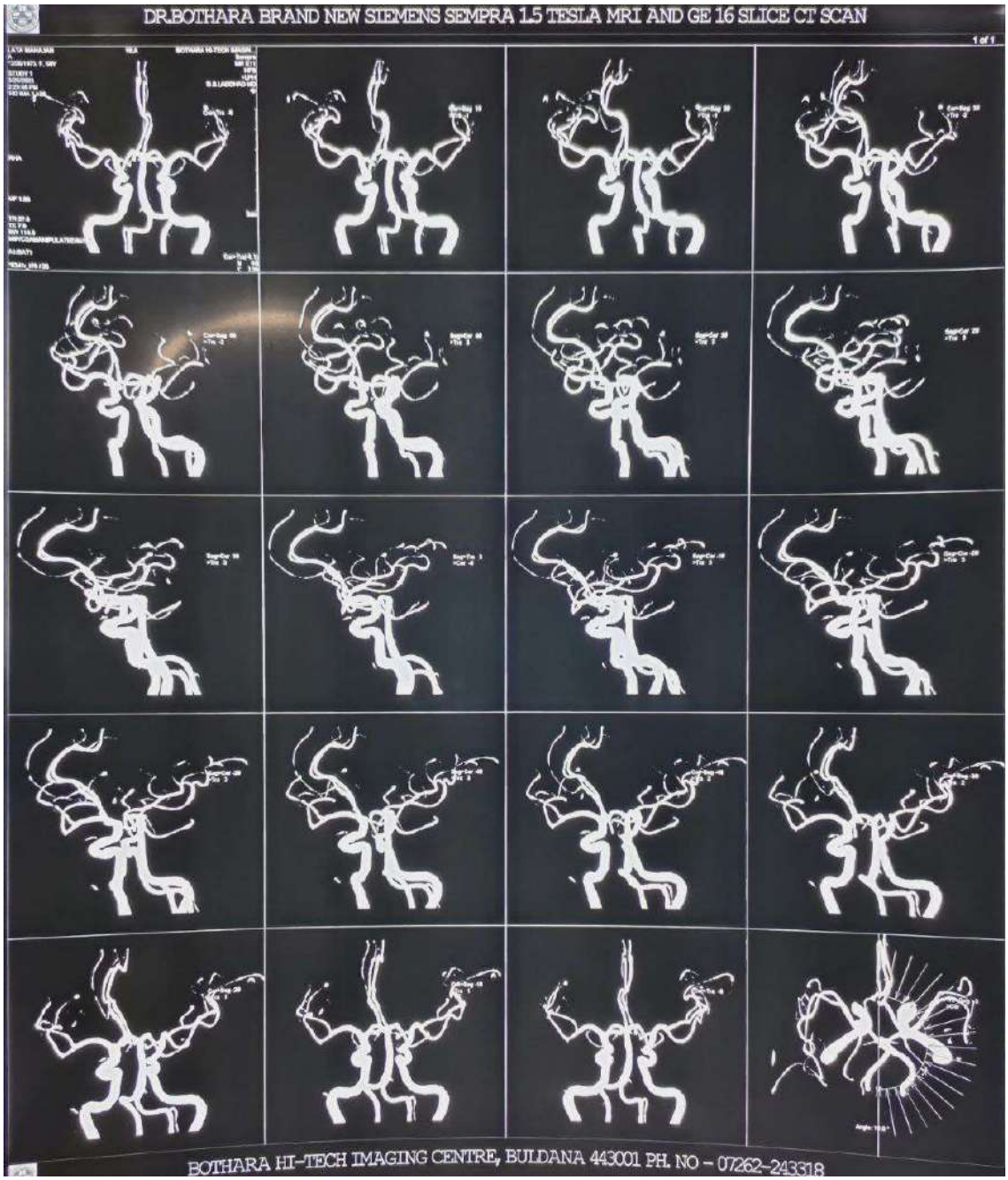

Figure 4. MR venogram.

Conclusion

Auto immune disorders have a wide range of presentations. Hence any slight suspicion of autoimmunity should be thoroughly ruled out. Multiple system involvement like joints, renal, vascular events simultaneously presenting should always rise a suspicion of autoimmunity and prompt investigations should be paged that could be effectively contributing to decrease mortality and morbidity of the patient.

Statements and Declarations

We declare that we have no financial interests or funding for this case report. This has been done only as a part of academical interest.

Author Contributions

Deepak Laddhad: final review and approval of the study; Rushikesh Subash Joshi; final review and approval of the study; Ruthvick Bantu: Reviews of literature, detailing the study; Shantanu Deepak Laddhad: Reviews of literature, detailing the study

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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National Board of Examination - Journal of Medical Sciences
Volume 1, Issue 8, Pages 549–555, August 2023
DOI 10.61770/NBEJMS.2023.v01.i08.008

CASE REPORT

A case of successful repair of urethrocutaneous fistula post proximal hypospadias repair managed by Johanson's 2 stage urethroplasty

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Accepted: 20-May-2023 / Published Online: 04-August-2023

Abstract

Urethrocutaneous fistula (UCF) after hypospadias repair remain a frustrating Problem for all the practicing urologists. Furthermore, with the improvement in suture materials and surgical techniques, complications if they may arise also present with litigations for the urologist. We present a case of a 18 year old boy with 46 XY mixed gonadal dysgenesis who had undergone proximal hypospadias repair with Duckett's tube urethroplasty with resultant complication of subcoronal urethrocutaneous fistula which failed first attempt at repair and resulted in two urethrocutaneous fistulas which was successfully managed by two stage Johanson's urethroplasty.

Keywords: Urethrocutaneous fistula, Johanson's urethroplasty, hypospadias, DSD

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Introduction

Urethrocutaneous fistula (UCF) after hypospadias repair remain a frustrating Problem for all the practicing urologists. Furthermore, with the improvement in suture materials and surgical techniques, complications if they may arise also present with litigations for the urologist. The occurrence of UCF precludes a goal of hypospadias surgery, i.e., an early one-stage repair of the defect. During the last decade, experts have proposed many principles of an ideal repairing technique. Delicate tissue handling, inversion of the urethral mucosa after excising the epithelialized tract of the fistula, a multilayer repair with well-vascularized tissues, avoiding overlapping sutures and nonabsorbable or thick suture materials, a tension-free closure, use of optical magnification and needle-point cautery for coagulation are currently considered mandatory [1]. However, unfortunately there is no single technique that can guarantee success in all cases. Also, UCF tend to recur again and multiple procedures again and again in the same patient cause all the potential harmful physical and psychological consequences [2]. We present a case of a 18 year old boy with 46 XY mixed gonadal dysgenesis who had undergone proximal hypospadias repair with Duckett's tube urethroplasty with resultant complication of subcoronal urethrocutaneous fistula which failed first attempt at repair and resulted in two urethrocutaneous fistulas which was successfully managed by two stage Johanson's urethroplasty.

Case report

A 18-year-old boy presented to the urology outpatient department of a tertiary care centre with complaints of three streams while passing urine. On enquiring about the past history, it was discovered that the patient had a proximal hypospadias with presence of uterus and fallopian tubes and left side streak ovary and right-side scrotal streak testis and on karyotype analysis, he was discovered to have 46 XY karyotype and hence, was diagnosed to have mixed gonadal dysgenesis. His previous medical records reveal that he underwent genitoscopy and Laparoscopic bilateral Hystero-salpingo-oophorectomy with excision of streak gonad on the right side with Duckett's tube urethroplasty. As per his previous clinical notes, at the time of infancy when he was examined, he had a proximal hypospadias with the meatal opening at the penoscrotal junction with the urethral plate well developed and evidence of ventral chordee and dorsal prepucial skin hood with the length of the phallus being 2 cm. The left side testis was not palpable and on the right side there was a streak gonad. On further evaluation by imaging, it was found that the child had a uterus and fallopian tubes and a left side rudimentary ovary. At the age of 2 years, child underwent Genitoscopy and Laparoscopic Hystero-salpingectomy with excision of left sided streak ovary and Duckett's tube urethroplasty for the management of proximal peno-scrotal hypospadias. Then the child developed a subcoronal urethrocutaneous fistula which was repaired by excision of the fistulous tract and flap closure from the surrounding area at the age of 3 years. However, the surgery failed and the patient developed two fistulous openings after which the patient was lost to follow up. Finally at the age of 16 years, patient presented to the urology department with the complaints of three streams while passing urine.

On local examination, penile shaft was of adequate length. There was evidence of puckered scarred skin over the ventral aspect of penile shaft with multiple buttonholes appreciated over it (Figure 1).

Figure 1: Clinical picture showing the ventral aspect of the penile shaft with multiple openings, puckered skin, empty left scrotum and right sided streak gonad.

The patient was asked to void and the three streams were documented (Figure 2).

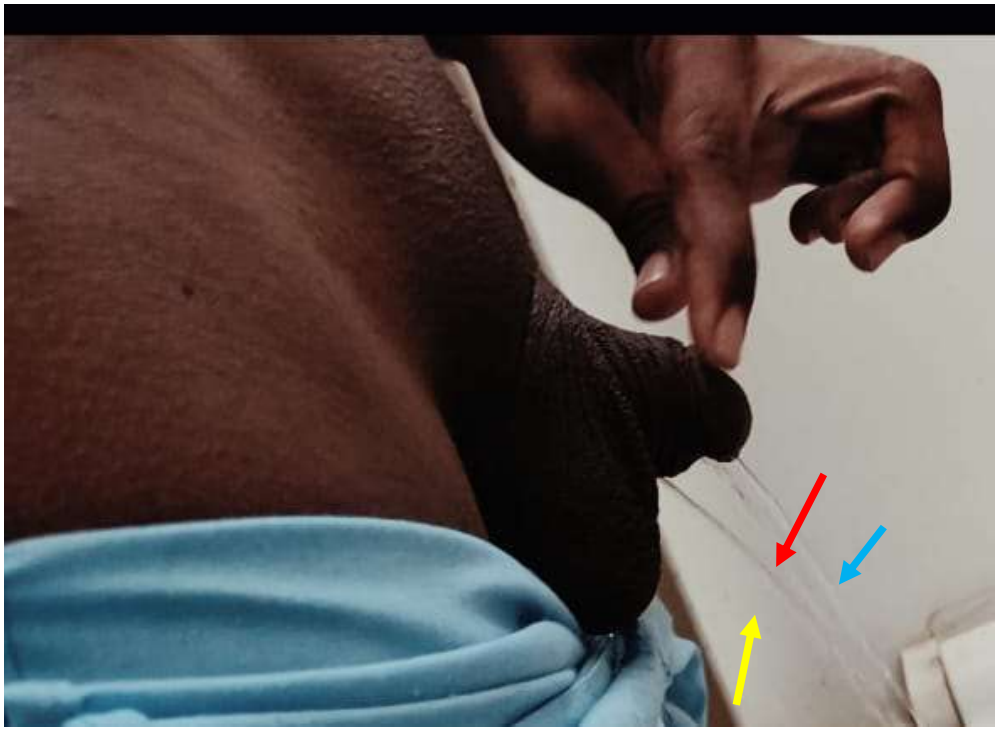

Figure 2. Clinical picture of the patient showing three urinary streams while voiding.

The patient then underwent retrograde urethrogram to visualise the urethrocutaneous fistulous tracts (Figure 3).

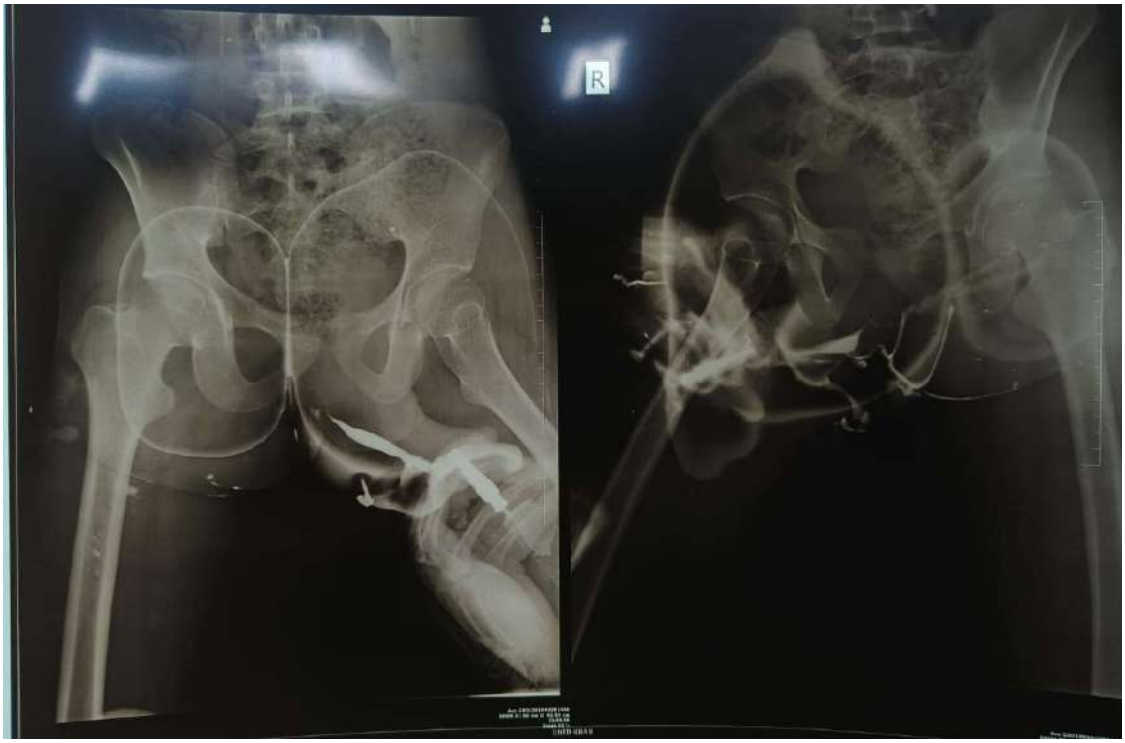

Figure 3. Retrograde urethrogram showing two urethrocutaneous fistulas along the proximal shaft of penis.

In view of the previous history of failed fistula repair and the scarred puckered skin over the ventral aspect of penile shaft, decision was made to go ahead with two stage Johanson's staged urethroplasty. A cystourethroscopy done using 4.5 F ureteroscope revealed a normal posterior urethra and bladder neck and evidence of prominent prostatic utricle. In the first stage, the urethra was laid open ventrally till the level of most proximal urethrocutaneous fistula opening and a buccal mucosal graft was harvested and anchored to the laid open urethra with quilting done to the underlying corpora cavernosa using PDS 4-0 sutures (Figures 4 and 5).

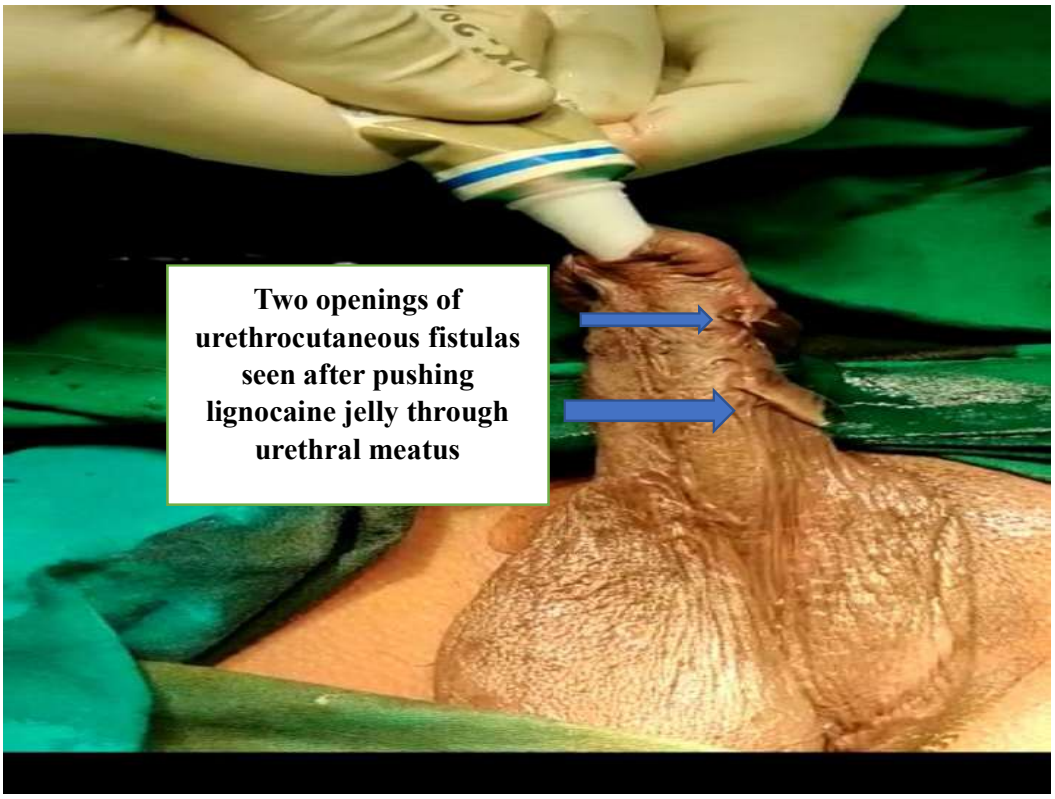

Figure 4. Clinical picture showing two openings of urethrocutaneous fistula seen after pushing lignocaine jelly through urethral meatus.

Figure 5. Clinical picture of patient after first stage of Johanson's first stage urethroplasty showing the buccal mucosal graft anchored to the graft bed.

Patient then underwent second stage of Johanson's urethroplasty where the buccal mucosal graft was tubularised and a second layer of tunica vaginalis flap from the scrotum was used to cover it. (Figure 6).

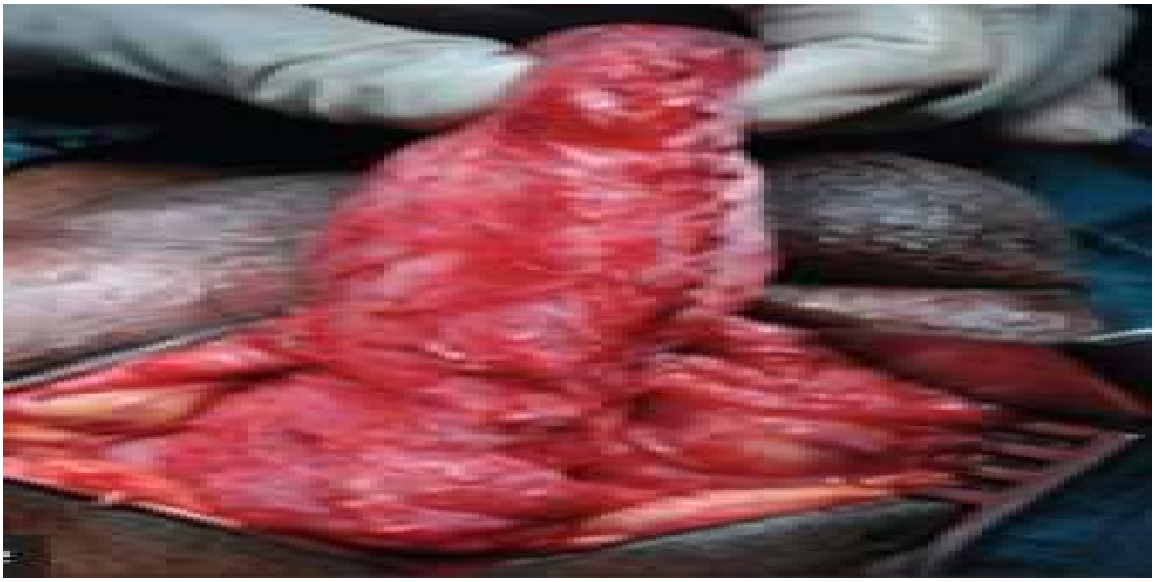

Figure 6. Clinical picture showing second stage of Johanson urethroplasty with additional coverage from tunica vaginalis from right scrotum.

After 4 weeks, the catheter was removed and the patient voided with a single stream. A follow up retrograde urethrogram was done which revealed a normal well healed urethra (Figure 7).

Figure 7. Follow up retrograde urethrogram revealed a normal well healed urethra.

Discussion

There are no perfect techniques for repairing UCF. Many variables could influence the surgical management and outcome, i.e. the time of occurrence after urethroplasty, the location (glanular, coronal, mid-shaft, etc.), size (pinpoint,large), the number and the conditions of local tissue [3]. However, Waterman et al. reported no significant difference in outcomes comparing some variables, e.g. the use or not of a stent or catheter, optical magnification, patient age and interval between surgery at time of fistula repair, type of original hypospadias procedure, and number of previous fistula repairs [4]. As no one technique is effective some failure rate is expected in every series [5-8]. In our case report, in view of the puckered skin and previous failed repair, decision was made to do a 2 staged repair and resulted in a successful outcome.

Conclusion

Thus, urethrocutaneous fistula is a challenging and frustrating complication to manage for a practicing urologist. The management of each case needs to be individualised. We put forth Johanson's two stage urethroplasty with use of buccal mucosal graft as an effective technique for the management of the same.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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