



KENYA JOURNAL OF
UROLOGY

FEBRUARY 2023

Vol: 01
No.: 3

**Closing the Care Gap: Improving Cancer
Outcomes - The Role of Urology**

**Urethral Injury from an Impacted
Urethral Stone: A case report**

Kenya Journal of Urology

The Kenya Journal of Urology (KJU) will be published quarterly and the next issue is expected to be published in May - June 2023. The Editor-in-Chief is calling for manuscripts for consideration. All manuscripts submitted will undergo peer review so it's advisable to submit them in good time. Manuscripts should be submitted to: kausorg@gmail.org

KJU is the Official Journal of the Kenya Association of Urological Surgeons

EDITORIAL BOARD

Editor-in-Chief

Prof. Peter Mungai Ngugi
Nairobi, Kenya

Issue Editor

Dr. Aideed A Kahie
Nairobi, Kenya

Associate Editors

Prof. Peter Larry Ndaguatha
Nairobi, Kenya

Dr. Francis O Osawa
Nairobi, Kenya

Dr. Aideed A Kahie
Nairobi, Kenya

Dr. Samuel Kagiri
Nairobi, Kenya

Dr. Dedan Opondo
Kisumu, Kenya

Editorial Board Members

Dr. Edward Mugallo
Kisumu, Kenya

Dr. Pius Musau
Eldoret, Kenya

Dr. Patrick Mburugu
Nairobi, Kenya

Dr. Joshua Matu
Kitui, Kenya

Contents

Editors note

Prof. Peter Mungai Ngugi 4

Advancing Urological Knowledge through Education and Publications - A KJU perspective

Aideed Kahie 5

A tribute to a Great Kenyan Surgeon: Dr. J C Munene

Aideed Kahie 7

A tribute to Professor George Albert Omoro Magoha

Aideed Kahie, Patrick Mburugu 8

Closing the Care Gap: Improving Cancer Outcomes - The Role of Urology

Miriam Mutebi 9

Nephro-urological issues in obstetrics and gynecology: time to rethink the silo approach – Part one: Obsteric considerations

Koigi, Paul Kamau, Kihara, Anne Beatrice, Kahie, Aideed, Soki, Khalida Bulhan 13

Management of neurogenic bladder in low resource setting: the challenges of service provision. A case series and discussion

Mugalo E. Lumadede, Akello W. Abila, Miima E. Ashiundu, Musau Pius 22

Evaluation and management overactive bladder syndrome: A review

Dr. Abdirashid A Mohamed, Dr. Aideed Kahie 26

Challenges in management of bladder neurofibroma: A case report

James A. Ikol, Ernest N. Kimani, Jeremiah Njogu, Brigid Monda, Wairimu Waweru 35

Orthotopic renal transplantation on splenic vessels: A case report

Dr. Aideed Kahie, Dr. Abdirashid A Mohamed, Dr. Hussein Bagha,
Dr. J C Munene, Dr. Ahmed Twahir 40

Urethral Injury from an Impacted Urethral Stone: A case report

Mustafa O, Ismail H, Jumbi T, Osawa F 43

Editor's note

The landscape of urological publications in resource-limited countries can be quite different from that in developed countries. While developed countries may have many publications in urology, less developed countries may have different levels of resources or infrastructure to support research and academic publishing.

Despite these challenges, urological research in underdeveloped countries has shown significant progress in recent years. The focus of urological research in these regions is diverse, ranging from infectious diseases, urogenital malignancies, and reproductive health to bladder dysfunction and trauma. The outcomes of urological research in these regions have been impactful, leading to improved patient care and outcomes.

With the third issue of KJU since its launch, there has been considerable enthusiasm for publishing from the membership and other professional associations, as seen in the number of articles in this edition. At KJU, we are dedicated to providing a platform for them to share their valuable insights and findings with the wider urological community.

In this country, there have been deliberate efforts by the KAUS leaders to improve the landscape of urological publications. These include initiatives to increase access to funding and training for researchers through EAKI (East African Kidney Institute), collaborations with international organizations and developed countries like SIU and PAUSA, and technology to connect researchers and facilitate communication and collaboration.

Prof. Peter Mungai Ngugi
Editor-in-Chief

Advancing Urological Knowledge through Education and Publications - A KJU perspective

Aideed Kahie

MBChB, MMed Surg. MRCS, FMAS, DMAS, EBU

Consultant Urological and Kidney Transplant Surgeon

Email: aideed@kaatun.com

The adage of 'publish or perish' holds to the individual in academic practice and to the professional body at large. Therefore, research, mentorship, and innovation are critical guiding pillars for professional societies. These ensure the progressive accumulation of new knowledge, dissemination of information, and the opportunity to directly influence the skills acquisition of junior colleagues and opportunities for intergenerational learning.

Publications are a reality, in that they are a widely accepted and used, means of disseminating information, research findings, and other forms of written content. They can take many forms, including books, academic journals, magazines, and online articles, and serve as a crucial platform for sharing knowledge, opinions, and ideas with a broader audience. It also serves through a continuing discourse, in helping to build and engage a community of practice. KJU endeavors to provide this platform.

Not long ago, the editorial board discussed two potential avenues to encourage both readership and authorship. The first, named 'From my desk,' takes an illustrative platform that aims to describe specific, simplified steps of a standard procedure with the intent of utilizing locally available resources. Though intended for teaching, these descriptions should stay within the established international standard of cares and patient safety. The second, a renal 'Stone competition' was recently launched to highlight the burden of stone disease and the available skills to manage them locally, brought out various innovative ways of dealing with challenging scenarios in our setting. These anecdotal activities demonstrate the inherent ability to solve patient concerns even in resource-limited settings. It is worth cataloguing these efforts to develop local solutions to local problems.

Writing, too, is often a daunting assignment. It is a challenge from observation, questioning, and constructing a hypothesis to conducting the research, analyzing data, and composing a manuscript. These can be complicated by the field of study, type of article, and stringent guidelines to reflect the standards and expectations of the scientific community. However, inculcating these tenets into our practices early, whether in academia or in private practice, begins to provide us all with the building blocks of becoming reflective practitioners. The humble audit, frequently forms the basis of many scientific enquiries and approaches and provides the basis for observation and generation of new knowledge. It also provides avenues for iteration, where we can continue to strive to improve on our outcomes.

Choosing urolithiasis as the first condition for the competition was perhaps informed by its frequency amongst our patients and the relative sophistication required in its treatment. Recently, advancements in imaging and diagnostic technologies have allowed for more accurate detection and characterization of urinary stones, leading to a better understanding of the underlying causes and risk factors, including genetics, poor dietary habits, and sedentary lifestyle.

Equally, the treatment options are modern, miniaturized, and varied. They range from non-invasive measures, such as increased fluid intake, pain management, and propulsive therapy, to invasive procedures, such as ureteroscopy, percutaneous nephrolithotomy (PCNL), shockwave lithotripsy, and a later entrant of laparoscopic pyelolithotomy. These choices are guided by the size and location of the stones, the surgeon's skill, and the patient's overall health.

These approaches offer superior outcomes over traditional open surgery, including faster recovery times and reduced risk of complications. Therefore, KAUS has made deliberate efforts to provide shared information about these modern practices to our members. Recently, a series of PCNL workshops have been done for the members to actualize these advantages for the patient, and many more are planned.

Like the infamous stone passing, KAUS's painful but rewarding efforts among the members are slowly paying off. The results of these shine brilliantly through the continued contribution and engagement with the KJU. In this issue, there are articles covering a wide range of urological topics from rare urological tumors like bladder neurofibroma discussed by Dr. J Ikol et al., functional urology by Dr. Mugalo et al. with a case series discussing the challenges of management neurogenic bladder in a resource-limited setting to a review on overactive bladder syndrome by Dr. A Mohamed, et al. Other uncommon cases of urethral injury by impacted stone

in a child and orthotopic kidney transplant on splenic vessels are presented by Dr. O Mustafa et al. and Dr. A Kahie et al. respectively. There are also exciting submissions from guest authors. For example, Dr. Miriam Mutebi, a renowned continental cancer surgeon, advocate and health system researcher, gives an overview of cancer prevalence and the urologist's unique position in impacting a select population. Likewise, Dr. Paul Koigi, an equally prolific writer, gives the first part of a series on nephron-urological issues in Obstetrics and Gynecology.

Therefore, whether writing on topical issues or imparting skills and knowledge, much is still to be learned in this field. The research will only continue to improve our understanding, treatment, and, ultimately our patient's quality of life. In whichever form, the urologists must lead the way in providing value based care that is of the highest quality and cost effective. Here's to the continued sharing of all your efforts, around these strategies, on this forum.

A tribute to a Great Kenyan Surgeon: Dr. J C Munene

Dr. James Chege Munene, popularly going among theatre fraternities as simply JC, was a man of many firsts, a teacher, mentor, and a reliable colleague when things go 'south' in vascular surgeries! Many surgeons in Kenya will agree that he epitomized simpleness in thought and deed, always willing to lend a hand or raise the spirit of the younger colleagues, who would otherwise be repudiated for their shortcomings.

He was born on 5th March 1960 in Nyeri and attended his medical education through the 80's to a specialist cardiothoracic surgeon in Madras Medical in India and Japan for the pediatric subspecialty. He contributed enormously to the field of cardiac surgery in Kenya (in both the private and the public health sectors) and around Africa. Notably in Namibia, where he founded their cardiac surgery unit. His commitment to excellence in all areas of his work, from patient care to education, earned him a reputation as one of the top surgeons in the field.

To the Kenyan urologist, Dr. Munene will be remembered for his contribution to kidney transplant services and vascular access for dialysis in Kenya. Dr. Munene was always the permanent member of any transplant team in all the hospitals where this service was available in this country.

He was a highly skilled and dedicated surgeon who significantly impacted countless patients' lives. His expertise and compassionate care helped many people overcome their struggles with kidney disease and regain their health and independence.

Patients and colleagues held him highly for his technical skill, clinical judgment, and compassionate bedside manners. However, nothing emphasizes his selfless nature, as we experienced firsthand when he agreed to lead a complex orthotopic kidney transplantation on splenic vessels barely two weeks before his scheduled surgery.

In recognition of his outstanding contributions to the field of transplant surgery and cardiothoracic surgery in general, we pay tribute to Dr. Munene and express our deep appreciation for all he has done to improve the lives of those he has treated. He is an inspiration to us all and a testament to the power of dedication and hard work.

This towering figure departed unexpectedly on 5th November, Saturday afternoon ~4 pm, 2022, and was joined by an equally highly decorated founding member of KAUS, the late Prof. George Albert Omore Magotha, whose tribute appears elsewhere in this journal.

May they rest in eternal peace.

Aideed Kahie

A tribute to Professor George Albert Omore Magoha

Professor Magoha is widely recognized as a pioneering urologist and a distinguished academic who has made remarkable contributions to the medical profession and practice in Kenya and beyond. He has been an inspiration to many, and his work has saved countless lives and improved the quality of life for many patients.

Professor Magoha has also made significant contributions to medical education. He has held several leadership positions in academic institutions, including serving as the Chairman of the Department of Surgery, Dean of the Medical School and as the Vice-Chancellor of the University of Nairobi.

Throughout his career, Professor Magoha has been a strong advocate for public health and has worked tirelessly to improve healthcare services in Kenya. He has been involved in several initiatives aimed at improving access to medical care, especially for the underprivileged.

In his distinguished career in medicine and surgery spanning over four decades, Prof. Magoha has saved countless lives through his expert skills and dedication to his craft, and as an academic, training numerous doctors who have gone on to become respected medical professionals in their own right. Many of these mentees relished being referred to 'Nyangao', prof's catchword for not high-achieving resident.

Closer home in urology, Professor Magoha's contributions have been significant and wide-ranging. Particularly alleviating the suffering of the male patient. His contribution in research and publications touching on various areas of urology and specifically in the male sexuality is well known.

Professor Magoha has received numerous awards and recognitions for his contributions to medicine and surgery. In 2003, he was awarded the Order of the Grand Warrior of Kenya, one of the highest honors in the country.

Though departed from the physical world, his legacy will continue to have a profound impact on the medical profession for generations to come.

Aideed Kahie and Patrick Mburugu

Closing the Care Gap: Improving Cancer Outcomes-the Role of Urology

Miriam Mutebi,

Consultant Breast Surgical Oncologist at Aga Khan University

President of Kenya Society of Haematology and Oncology,

President elect African Organization for Research and Training in Cancer

INTRODUCTION

Across the world there is an increasing incidence and mortality of cancers, particularly in low and middle income countries, such as Kenya. The recent Lancet commission on cancer in sub-Saharan Africa in 2021, (1) showed that over the past 30 years, there has been a doubling in cancer incidence, with over half a million deaths in 2020. This number is predicted to double by 2030 thus underscoring a need for urgent action. This incidence may be attributed to a combination of factors such as an increase in life expectancy combined with the adoption of unhealthy dietary habits, consumption of tobacco and alcohol and lack of physical exercise and environmental factors and exposure, infections (a quarter of cancers in Africa are associated with infectious diseases such as hepatitis B and c and human papilloma virus) and genetics.

The recently released 'Status of Cancer in Kenya Report' by the National Cancer Institute of Kenya (2), noted that there are 27,000 cancer related deaths are recorded every year in Kenya, with about 75 deaths a day. The leading cause of cancer deaths are esophageal, followed by cervix, breast and liver cancers. Globocan Data from 2020 (3) shows that Breast cancer is the most commonly diagnosed cancer in Kenya, with an annual incidence of about 6,700 new cases and 2,500 cancer-related deaths. The other top 5 cancers are cervical, prostate, esophageal and colorectal cancers.

The government of Kenya has made considerable strides in improving access to cancer services and has launched many initiatives to address this rising cancer burden. The national hospital insurance fund now covers some of the costs of treatment such as chemotherapy and radiotherapy. There have been commendable efforts to decentralize access to chemotherapy, having established 10 fully functional county-level chemotherapy centers, and to radiotherapy services with the development of regional comprehensive cancer centers in Nairobi, Mombasa, Nakuru and Garissa.(4) There has also been an increase in the diagnostic equipment in a number of counties, including CT-Scans, ultrasonography, and mammography etc

There has been an expansion of enabling policy with the launch of the New Cancer Control Strategy 2017-2022, (5) by the Ministry of Health and its current ongoing revision. This is a national effort to address the growing burden of the disease in the country. In addition, there has been development of Palliative and supportive care policy, a national cancer taskforce report and the launch of a Breast Cancer Action Plan outlining deliberate steps and strategies to improve access to cancer care.

The care and treatment of cancer involves three major aspects: systemic treatments like chemotherapy and immunotherapy, and local treatments like radiotherapy and surgery. These are frequently used in combination to treat and potentially cure or palliate patients. This year's world cancer day theme, 'Closing the care gap' requires us all to pause, reflect and rethink strategies to make all these treatment modalities more accessible to all patients.

LOCAL ADVANCES IN CANCER THERAPIES

The government's efforts in increasing chemotherapy and radiotherapy services are laudable. We have now developed the capacity to provide brachytherapy and external beam therapy to the prostate and other pelvic malignancies. However, surgical services as a whole continue to lag behind the progress made in the other aspects of cancer care. We have also had a promising expansion in local and regional training in both medical oncology and clinical oncology, but there has not been much surgical oncology training in the East African Region.

ROLE OF SURGERY

Surgery is one of the major pillars of cancer care and control. More than 80 per cent of all cancer patients will require surgical procedures and one third of patients will require multiple surgical procedures thus underscoring the need to develop these critical services. (6) Surgery can be preventive, for instance, removing a polyp before it turns into a cancer, diagnostic: when biopsies are performed, curative when a breast lump or colonic tumor is completely removed or supportive, palliative or reconstructive (e.g. reconstructing a limb or breast after removal of a cancer).

The Lancet Commission on global surgery in 2014 showed that nine out of ten people (5 billion people) have no access to safe timely and affordable surgery with an additional 143 million more surgical procedures needed in lower medium income countries every year, to prevent death and disability. (7). Safe surgery does not refer to the actual surgery only, but also includes the peri-operative care, anesthesia and diagnostics that help to support successful surgical outcomes. This is particularly pertinent in Africa, where data from the African Surgical Outcomes Study (ASOS) shows that patients are twice as likely to die from routine, planned, common surgeries as compared to the global standard. (8)

The Lancet Commission on Cancer Surgery in 2015 showed that less than a quarter of patients globally had access to affordable, safe, timely cancer surgery with 15.2 million new cancer patients requiring surgery in 2015 and a projected estimation of 48 million cancer surgeries being required by 2030. (7) In the sub-Saharan region, there is a huge deficit in health care workers and more so in the field of oncology, and even more so, in surgical oncology. There is need to train more cancer surgeons to strengthen health systems, if we are to offer patients comprehensive, curative and palliative cancer services.

Cancer surgery involves a multi-disciplinary team of surgeons, medical and oncology radiologists, pathologists and anesthesiologists. Before any cancer surgery is done, the team will discuss and decide on a treatment plan which is then communicated to the patient. Sometimes this plan may involve chemotherapy first to shrink the cancer and make surgery safer. At the time of surgery, the intent is usually to remove the entire cancer, with a margin of normal tissue, in order to prevent local recurrence and is often the definitive (curative) treatment for many solid cancers like breast, colon or prostate tumors. Good cancer surgery is thus a key component of effective cancer treatment.

In many lower and middle income countries, general surgeons form the center of cancer treatment. However, the training may vary and the skills sets to do good cancer surgery may also differ. In many parts of Africa, due to deficits in both surgical oncology and medical oncology, general surgeons are involved in the diagnostics, cancer surgeries and in some cases, even administering chemotherapy and giving follow-up care to cancer patients. Despite this gap, there have been little large scale efforts to improve access to oncological surgical services and training.

To mitigate this, the African Organization for Research and Training in Cancer (AORTIC), the Pan African Women Association of Surgeons (PAWAS) and Kenya Society for Hematology and Oncology (KESHO) in partnership with the Aga Khan University Hospital have designed surgical trainings to impart skill sets to general surgeons to enable them to operate safely on cancer patients and to provide a better understanding of the multidisciplinary approach to cancer management.

The Pan African Women Association of Surgeons in collaboration with Kenya Association of Breast Surgery, through the Surgical Society of Kenya, have also been holding a series of training workshops to educate and empower health care providers to give quality surgical services. These initiatives are in anticipation that with time, a more sustainable long term training will be provided.

The Aga Khan University is also in the process of developing a training program for general surgeons for breast cancer surgery locally and in the region. This capacity building, will consequently help to bridge some of the gaps that patients face in accessing quality and timely surgical cancer care in our region.

IMPLICATIONS FOR UROLOGY

Prostate cancer is the most commonly diagnosed cancer in men locally and in the East African region. However, the majority of our patients are diagnosed with advanced disease and frequently do not complete their care. How can we shift narratives around this and improve uptake of cancer services for our patients?

There is a clear need for more surgical advocacy at the community level. KAUS has made strides through the introduction of multi-disciplinary urology camps that try to educate and impact communities. What is needed is a key amplification of common signs and symptoms of prostate cancers and other common urological conditions. Sustainable approaches and message to the communities will be key. Having these conversations in more public spaces will help increase awareness and combat sociocultural barriers that exist. These conversations need to be culturally appropriate and sensitive and involve having a nuanced discussion of barriers to care including the stigma and shame that exists around a diagnosis of prostate cancer and its management. A thorough understanding of the patient's interpretation and understanding of the disease and its treatment implications are paramount. Many of us are aware of patients who decline to have sub capsular orchiectomies in lieu of not being able to afford long term chemical castration, because of the social contexts and connotations of these procedures.

WORKFORCE EDUCATION AND EXPANSION

Primary health care providers are still the gate keepers to care and we know that on average in sub-Saharan Africa patients will see 3-5 health care providers before a definitive diagnosis of their cancer is made. (9) Educating the workforce is key to getting early recognition and timely referral of patients. The Kenya Society for Haematology and Oncology (KESHO) is involved in disseminating weekly CMEs for all cancer types to all cadres of health care workers. We have also had the opportunity to run joint prostate cancer symposiums in collaboration with KAUS, highlighting advances and best practice in management of prostate cancers. Going forward, it would be critical to explore platforms that provide this consistent education for all health workers.

SURGICAL SKILLS DEVELOPMENT

Cancer surgeries require multi-disciplinary approaches and inculcating these tenets to residents and all practitioners is key. Beyond prostate cancers, urologists play a key role in the management of all genitourinary malignancies like kidney and bladder cancers and in the management of most pelvic malignancies like cervical, ovarian, colorectal or retroperitoneal malignancies. In all these, collaborative efforts are needed with oncology medical oncology, gynaecology, radiation oncology and radiation oncology and diagnostics (pathology and radiology) to devise optimal personalized therapies for patients. The multi-disciplinary tumor board approach is the gold standard of care and should be encouraged in the management of all genitourinary and pelvic malignancies. (10). With the expansion of oncology services and the availability of virtual platforms there is now increased access to these services, and healthcare providers should be encouraged to tap into the virtual tumor boards in their regions, before commencing treatment for patients. In line with the findings from the ASOS trial it would be important to develop perioperative care including surgical nursing and critical care for complex surgical procedures. Expansion of the skills sets including laparoscopic procedures must go hand in hand with development of surgical and oncology nursing.

A CALL TO ARMS!

Urologists are uniquely placed to be able to impact cancer outcomes at all levels of the continuum from prevention, active treatment all the way through to cancer survivorship and its outcomes. Collaborative efforts and multisectoral approaches will be key in improving outcomes for patients.

REFERENCES

1. Ngwa, W., Addai, B. W., Adewole, I., Ainsworth, V., Alaro, J., Alatise, O. I., Ali, Z., Anderson, B. O., Anorlu, R., Avery, S., Barango, P., Bih, N., Booth, C. M., Brawley, O. W., Dangou, J. M., Denny, L., Dent, J., Elmore, S. N. C., Elzawawy, A., ... Kerr, D. (2022). Cancer in sub-Saharan Africa: a Lancet Oncology Commission. *The Lancet Oncology*, 23(6), e251-e312. [https://doi.org/10.1016/S1470-2045\(21\)00720-8](https://doi.org/10.1016/S1470-2045(21)00720-8)
2. Status of cancer in Kenya – A National Cancer Institute of Kenya report
3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
4. Development of cancer centres- <https://www.health.go.ke/government-sets-up-10-cancer-centres/>
5. National Cancer Control Strategy Kenya 2017-2022 https://www.iccp-portal.org/system/files/plans/KENYA%20NATIONAL%20CANCER%20CONTROL%20STRATEGY%202017-2022_1.pdf
6. Sullivan R, Alatise OI, Anderson BO, Audisio R, Autier P, Aggarwal A, Balch C, Brennan MF, Dare A, D'Cruz A, Eggermont AM, Fleming K, Gueye SM, Hagander L, Herrera CA, Holmer H, Ilbawi AM, Jarnheimer A, Ji JF, Kingham TP, Liberman J, Leather AJ, Meara JG, Mukhopadhyay S, Murthy SS, Omar S, Parham GP, Pramesh CS, Riviello R, Rodin D, Santini L, Shrikhande SV, Shrime M, Thomas R, Tsunoda AT, van de Velde C, Veronesi U, Vijaykumar DK, Watters D, Wang S, Wu YL, Zeiton M, Purushotham A. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. *Lancet Oncol*. 2015 Sep;16(11):1193-224. doi: 10.1016/S1470-2045(15)00223-5. PMID: 26427363.
7. Meara JG, Hagander L, Leather AJM. Surgery and global health: a Lancet Commission. *Lancet*. 2014 Jan 4;383(9911):12-13. doi: 10.1016/S0140-6736(13)62345-4. Epub 2013 Dec 11. PMID: 24332309.
8. Biccadd BM, Madiba TE, Kluyts HL, Munlemvo DM, Madzimbamuto FD, Basenero A, Gordon CS, Youssef C, Rakotoarison SR, Gobin V, Samateh AL, Sani CM, Omigbodun AO, Amanor-Boadu SD, Tumukunde JT, Esterhuizen TM, Manach YL, Forget P, Elkhogja AM, Mehyaoui RM, Zoumeno E, Ndayisaba G, Ndasi H, Ndonga AKN, Ngumi ZWW, Patel UP, Ashebir DZ, Antwi-Kusi AAK, Mbwele B, Sama HD, Elfiky M, Fawzy MA, Pearse RM; African Surgical Outcomes Study (ASOS) investigators. Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *Lancet*. 2018 Apr 21;391(10130):1589-1598. doi: 10.1016/S0140-6736(18)30001-1. Epub 2018 Jan 3. PMID: 29306587
9. Mutebi M, Dehar N, Nogueira LM, Shi K, Yabroff KR, and Gyawali B Cancer Groundshot: Building a Robust Cancer Control Platform in Addition To Launching the Cancer Moonshot American Society of Clinical Oncology Educational Book 2022 :42, 100-115
10. Taylor C, Munro AJ, Glynne-Jones R, Griffith C, Trevatt P, Richards M, Ramirez AJ. Multidisciplinary team working in cancer: what is the evidence? *BMJ*. 2010 Mar 23;340:c951. doi: 10.1136/bmj.c951. PMID: 20332315.

Nephro-urological issues in obstetrics and gynecology: time to rethink the silo approach – Part one: Obsteric considerations

**Koigi, Paul Kamau^{1,2,3}, Kihara, Anne Beatrice^{4,5,6},
Kahie, Aideed^{7,8}, Soki, Khalida Bulhan⁹**

Affiliations:

¹ Consultant Obstetrician & Gynaecologist & Head of Research, The Nairobi Hospital

² Deputy Editor-in-Chief, Journal of Obstetrics and Gynaecology of East and Central Africa (JOGECA)

³ Editor-in-Chief, The Nairobi Hospital Medical Journal (TNH Med J)

⁴ Past President, Kenya Obstetrical and Gynaecological Society (KOGS)

⁵ President Emeritus, African Federation of Obstetrics and Gynaecology (AFOG)

⁶ President Elect, International Federation of Gynecology and Obstetrics (FIGO)

⁷ Senior Urologist, Kaatun Urology Centre and Male Executive Clinics

⁸ Kenya Association of Urological Surgeons (KAUS)

⁹ Consultant Nephrologist, The Nairobi Hospital

ABSTRACT:

Introduction: The management of pregnancy in the context of new or ongoing urological disease is often fraught with angst due to the lack of robust ubiquitously applicable data and uncertainty regarding the ideal approach to take in order to optimize outcomes of the maternal-fetal dyad. This imbroglio occurs despite the context of the conjoined triplet specialties of urology, nephrology, obstetrics and gynecology.

Methodology: This is the first of a two-part cross-cutting narrative literature review that facilitated the evaluation of several cross-cutting physio-pathological entities amongst gravid patients. The second part shall address gynecological considerations.

Discussion: Specific conditions reviewed include: pregnancy-induced urinary tract changes; hyperemesis gravidarum; abortion; urinary tract infections in pregnancy; hypertensive disease of pregnancy; nephrolithiasis in pregnancy; autoimmune diseases in pregnancy; diabetes in pregnancy; pregnancy after renal transplantation; glomerular disease in pregnancy; chronic kidney disease in pregnancy; reflux nephropathy and congenital abnormalities in of the kidney and urinary tract; pregnancy-associated atypical hemolytic uremic syndrome; and iatrogenic risk during caesarean section. The risk of adverse obstetric outcomes is also stratified according to the degree of renal derangement.

Conclusion: The substantial complexity of these physiological and pathological entities, coupled with their preponderance to cross-cutting reciprocal synergistic adverse affection of multilateral outcomes warrants a change of the current silo approach to the management of obstetric patients.

INTRODUCTION

The urological and reproductive systems develop from a common mesodermal urogenital ridge along the posterior wall of the abdominal cavity. Despite growing and differentiating into distinct systems under endocrine and non-endocrine influence, they remain intimately interwoven due to their anatomical juxtaposition and physiological interdependence (1,2).

Professionally, the surgical specialties of Urology and Obstetrics & Gynaecology are similar to siblings conjoined by a parapagus. Conversely, the specialties of Urology and Nephrology may be thought of as being conjoined by a cephalopagus, resulting in what may have been otherwise considered the extremely rare instance of viable conjoined triplets (3). However, the three specialties have a tendency to operate in silos, as it has been anecdotally rare to have all three specialties represented in the management of a case, save for two instances that typically demand collaborative input: multidisciplinary tumor boards (4); and cases involving malformation of the urinary and reproductive tracts (5,6). This siloed paradigm to provision of care creates an imbroglio that results in failure to optimize patient outcomes due to inability to crystallize research-informed integration of cross-cutting best evidence-based practices (7). This is typically because there is a tendency to adjoin specialists in Urology/ Nephrology to the management of reproductive health patients when complications have already occurred, hence an inability to effect primary prevention (8).

METHODOLOGY

This article will briefly review several significant physiological and pathological entities in Obstetrics that have a significant bearing on Urology and Nephrology. A narrative literature review of available literature published over the last 50 years available on Medline, PubMed, Embase and Google Scholar was undertaken. The most pertinent issues that merit consideration in relation to these physio-pathological entities in Obstetrics shall be highlighted, and the key messages of this article shall be conveyed in the conclusion and recommendations. The entities that are pertinent to Urology and Nephrology in Gynecology will be reviewed in a subsequent article, with some the cross-cutting inferences and recommendations being deferred for integration in the conclusion of the second article of this two-part series.

KEY ENTITIES IN OBSTETRICS

1. Pregnancy-induced urinary tract changes:

The actions of progesterone and relaxin instigate dilation of the urinary collecting system that predisposes pregnant women to developing urinary tract infections due to urinary stasis (9). There is an increase in glomerular filtration rate by up to 50% results in increased renal clearance that reduces serum concentrations of creatinine and medications that are cleared via urine. Increased aldosterone levels in pregnancy result in sodium and water retention, resulting in a significant increase in total body water (10). Additionally, there is an increase in renal blood flow that results in an increase in renal size by up to 1.5cm. This is associated with an increase in renal vasculature, interstitial volume, urinary dead space and ureteric dilation that instigates a physiological hydronephrosis in 4 out of every 5 pregnant women. The hydronephrosis tends to be worse on the right due to the right ureter crossing the iliac and ovarian vessels before entering the pelvis, while the urinary stasis predisposes gravidae to development of pyelonephritis (9).

2. Hyperemesis gravidarum:

This refers to nausea and vomiting in pregnancy that is severe enough to prevent retention of feeds and is associated with dehydration, >5% pre-pregnancy weight loss, electrolyte imbalance and metabolic derangements (11). It afflicts up to 3% of pregnancies and is typically more common in the first trimester, and has a high propensity to deleteriously afflict the mother and fetus (ibid). Hyperemesis gravidarum has been associated with Pregnancy-related acute kidney injury (PRAKI) (12,13)the indications and clinical outcomes of patients with Pregnancy-Related Acute Kidney Injury (PRAKI). In order to avoid this adverse outcome, it is vital to enforce strict input-output and electrolyte monitoring; judicious fluid management; and effective control of the nausea/vomiting (14)health-care providers should be aware of the likelihood of such a complication. The aim of the study was to report a case of HG complicated by AKI. A 35-year-old G2P1+0 (one alive.

3. Abortion:

Whether spontaneous or induced (medically or surgically), abortions carry the inherent potential for significant morbidity and mortality. Of particular relevance is the risk of acute tubular necrosis due to severe hemorrhage; collateral injury to the bladder following inadvertent perforation during surgical abortion that requires prompt surgical repair; and the propensity of septic abortion to instigate renal failure due to septicemia and septic shock (15)therapeutic abortions, as well as spontaneous miscarriages, can lead to a variety of complications. Most complications are considered minor such as pain, bleeding, infection, and post-anesthesia complications. Others are major, including uterine atony and subsequent hemorrhage, uterine perforation, injuries to adjacent organs (bladder or bowels. Acute renal failure following abortion may be due to renal artery stenosis often due to Takayasu arteritis (16) or due to renal cortical necrosis (17). The sepsis requires culture-guided antibiotic therapy, and renal failure may require renal replacement therapy if the patient is to survive (15)therapeutic abortions, as well as spontaneous miscarriages, can lead to a variety of complications. Most complications are considered minor such as pain, bleeding, infection, and post-anesthesia complications. Others are major, including uterine atony and subsequent hemorrhage, uterine perforation, injuries to adjacent organs (bladder or bowels.

4. Urinary tract infections in pregnancy:

The anatomical proximity of the urethra to the anus and the physiological changes of pregnancy raise the prevalence of all urinary tract infections (UTI) to up to 15% (18). Common etiologic pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, *Providencia* species, *Pseudomonas aeruginosa*, *Enterobacter* and *Serratia* (19). The occurrence of UTI in pregnancy is associated with a myriad of adverse outcomes, including preterm labor and delivery, anemia, pulmonary edema, acute respiratory distress syndrome and progression into septic shock (20). These complications are avoidable with appropriate timely culture-guided antimicrobial therapy (ibid) inspired by a high index of suspicion for UTI amongst both the symptomatic and asymptomatic, hence a need for routine antenatal screening (19).

5. Hypertensive disease in pregnancy:

Despite already being the most common morbidity in pregnancy (up to 15%), the prevalence of hypertension in pregnancy continues to rise due to: intentional deferral of childbearing to a later age; increased number of younger patients living with kidney disease; and the reducing age of renal transplant (21). The spectrum of hypertensive disease in pregnancy includes: pre-existing hypertension; pregnancy-induced hypertension; pre-eclampsia; eclampsia and Hemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome (ibid). There is a quagmire of factors that increase the predilection towards early development of hypertensive disease in pregnancy and more severe forms (22).

The core derangement that underlies the pathophysiologic basis of pre-eclampsia is thought to be failed arborization of the uteroplacental vasculature due to a defective second wave of trophoblastic invasion in the early second trimester of pregnancy (23). This failure to convert from a high-resistance low-capacity spiral arterioles to a high-capacity low-resistance state. This necessitates a physiological maladaptive rise in blood pressure that results in target end-organ damage (24) if left unchecked. We infer that the management of hypertension in pregnancy necessitates the application of four key principles (25):

- i. Close monitoring of the pregnancy (clinical, laboratory and ultrasonographic)
- ii. Judicious control of blood pressure using anti-hypertensives
- iii. High index of suspicion for development of collateral target end organ damage
- iv. Readiness to promptly intervene to effect delivery if indicators of severity materialize in order to minimize immediate and residual morbidity and mortality.

6. Nephrolithiasis in pregnancy:

Nephrolithiasis is a particularly challenging condition that afflicts an average of 1 in 1,500 obstetric patients (26), amongst whom a majority are multiparas in or beyond the second trimester of pregnancy (27). However, the prevalence is higher amongst those who are obese &/ or diabetic (28). The challenge instigated by this condition is because the investigations and treatments pose a predilection to harming the fetus, hence the challenge in defining optimum protocols of management of these patients (27). Given the potential quagmire that this condition generates, it is feasible to infer that a core principle of management of such a patient (27,29).

Presently, the first-line evaluation recommended for nephrolithiasis in pregnancy is a Renal-bladder ultrasound that ensures evaluation of ureteral jets to detect potential obstruction. Transvaginal ultrasonography is valuable for suspected distal ureteral stones (ibid). Magnetic resonance imaging is preferred to low-dose computed tomography due to an objectively lower risk to the fetus (26). Upon diagnosis, medical expulsive therapy with α 1 blockers, low-dose, short-term opioid analgesia, antiemetics and hydration are preferred (ibid). In event of a septic obstructing stone, decompression with or ureteroscopy with laser lithotripsy, ureteral stenting (26,29) or nephrostomy (30) are indicated.

7. Autoimmune diseases in pregnancy:

Systemic lupus erythematosus (SLE) is due to derangement of T Helper Cell Type 2 (TH2) immunity. Because pregnancy upregulates TH2 immunity, patients with SLE experience clinical deterioration during pregnancy, with renal function often being worst affected (31–33). Because of this, women with SLE are advised to avoid pregnancy until disease quiescence is sustained for at least 6 months prior to conception (13,34). Additionally, hydroxychloroquine and steroids recommended in pregnancy for these patients, with close monitoring of renal function by a multidisciplinary team (34,35), as gravidity has been associated with a 26% risk of lupus flare (13,36) which may necessitate hemodialysis (37). Extra-renal flares tend to be more common during the second and third trimesters, with renal flares being more prevalent post-partum (13).

8. Diabetes in pregnancy:

The physiological changes of pregnancy result in variations in insulin sensitivity that enable the mother to be able to appropriately respond to the glycemic demands of the growing fetus (38). During the first trimester, there is increased insulin sensitivity to facilitate glucose uptake to prime the adipose stores for the energy demands of the latter portion of the pregnancy (ibid). Thereafter, hyperglycemia is promoted by the presence of progesterone, leptin, cortisol, placental growth hormone, human placental lactogen and human chorionic gonadotropin due to the establishment of insulin resistance (38,39).

Diabetes mellitus (DM) refers to a state of chronic hyperglycemia due to an absolute (Type 1) or relative (Type 2) deficiency of insulin (38). In addition, the increased presence of multiple risk factors such as obesity, advanced maternal age, and a positive family history have instigated a sharp rise in the prevalence of diabetes in pregnancy to roughly 1 in every 7 pregnancies (38). During gravidity and delivery, the significant maternal complications include pre-eclampsia, the need for early induction of labor, increased risk of Caesarean section, increased risk of perineal injury and a dramatically increased risk of post-partum hemorrhage (40), alongside the potential to develop acute renal failure (41). From the fetal-neonatal perspective, macrosomia, birth trauma, stillbirth, shoulder dystocia, hypoglycemia and respiratory distress syndrome are the preponderant complications. Dysglycemia and hyperglycemia in pregnancy predisposes both the mother and fetus to additional later adverse outcomes that have a strong tendency to converge at the focal point of microvascular disease following the development of Type 2 DM, often with attendant severe renal and urological complications (ibid). Therefore, the value of maintaining tight optimal glycemic control using the binary approach lifestyle behavior change and insulin cannot be overemphasized. Metformin may be added if required (42). Equally vital is the prevention of hypoglycemia and diabetic ketoacidosis – two potentially fatal diabetic emergencies (ibid).

For those with established pre-existing diabetic nephropathy, the following are the pertinent considerations to make if pregnancy is planned (34):

- a. Glycemic control and blood pressure should be optimized prior to conception so as to minimize the risk of pregnancy loss and congenital malformations.
- b. Angiotensin converting enzyme inhibitors and angiotensin 2 receptor antagonists should be discontinued upon conception.
- c. Specialist multidisciplinary care should be offered throughout the pregnancy.

9. Pregnancy after renal transplantation:

Following definitive renal replacement therapy (transplantation), a woman desiring pregnancy should wait for at least one year after the transplant. This is to allow time for better graft survival/ function and the attainment of maintenance on medications that are safe in pregnancy (34). This has been associated with improved fertility and reduced risk of pregnancy complications (13). Additionally, the management of the pregnancy and delivery should be managed by a multidisciplinary team at a transplant centre (34).

10. Polycystic kidney disease in pregnancy:

This is often an autosomal dominant condition that affects up to 1 in 1000 people (43). It is recommended that patients with autosomal dominant polycystic kidney disease (ADPKD) should be offered genetic and pre-implantation counselling (34). ADPKD is has been associated with increased risk of hypertension, proteinuria, edema, urinary tract infection, renal dysfunction, pre-eclampsia and non-reassuring fetal status (43,44).

11. Glomerular diseases in pregnancy:

There is a significant hiatus of data regarding the prevalence and type of glomerular diseases in pregnancy and their individualized pregnancy outcomes (33,45). On account of this, any currently available figures are considered underestimates of the true incidence and prevalence (ibid). Patients with pre-existing glomerulonephritis will often have nephrologists routinely involved in their care prior to pregnancy. They will often have been advised that their pregnancy outcomes can be optimized by having their disease in remission in the setting of preserved renal function in the absence of proteinuria and hypertension (46,47).

Currently, any pregnancy in a patient with pre-existing or new glomerular disease is considered high-risk due to the independent association with adverse obstetric outcomes (45) and the inherent risk of escalation towards end-stage renal disease (33). The common adverse gestational affections that have been associated with glomerular disease include preeclampsia, prematurity and intrauterine growth retardation (ibid). Presently, the empirical approach towards glomerular disease in pregnancy is to administer steroids and azathioprine or a calcineurin inhibitor. However, in the setting of severe/ life-threatening maternal disease, termination/ delivery is indicated, depending on whether or not viability has been attained (33,46). Renal biopsy in pregnancy should only be done if the results will alter the course of management (46). These principles are thought to apply across the board in multiple glomerular diseases, including IgA nephropathy, membranous nephropathy, focal segmental glomerulosclerosis and ANCA-associated vasculitis (ibid).

Gestational nephrotic syndrome has been associated with a high risk of developing maternal (pre-eclampsia, acute kidney injury, premature rupture of membranes) and fetal (low birth weight, intrauterine growth retardation, and need for neonatal intensive care unit admission) complications (48). However, these adverse gestational affections are less prevalent in the absence of uncontrolled hypertension and renal insufficiency (ibid).

12. Chronic kidney disease in pregnancy:

Chronic kidney disease afflicts up to 10 % of the world's population (49) & 3% of women of childbearing age in high-income countries (34,50). Gestational hypertension almost triples the odds of development of chronic kidney disease (CKD) (51). There is an apparent symbiotic interaction between adverse obstetric and renal outcomes amongst women with chronic kidney disease who become pregnant (13). There is therefore an absolute need for multidisciplinary management of these patients by a team that includes a minimum of high-risk obstetrics specialist and a nephrologist, whether the CKD is new or was preexisting (ibid). Overall, there is an undeniable need for careful pregnancy planning amongst those

13. Reflux nephropathy and congenital abnormalities of the kidney and urinary tract:

It is recommended that women with previous bladder surgery due to congenital anomalies or reflux nephropathy should have a urologist with expertise in bladder reconstruction as part of the team managing the pregnancy so as to evaluate the options for delivery (34).

14. Pregnancy-associated atypical hemolytic uremic syndrome (p-aHUS):

Atypical hemolytic uremic syndrome (aHUS) is characterized by microangiopathic hemolytic anemia, thrombocytopenia and decreased kidney function instigated by systemic uncontrolled complement activation. This may occur in pregnancy, and particularly in the postpartum period, and raises the risk of fetal loss, pre-eclampsia and rapid escalation to end-stage renal disease (13) in up to 7 out of every 10 of patients with p-aHUS (52).

Patients with aHUS who have conceived are thought to have high probability of achieving a live birth if the condition is well controlled (53). Currently, the mainstay of management of this condition has been the use of eculizumab and renal replacement therapy, which have significantly improved the hitherto dismal prognosis of this condition (13,54). However, a high index of suspicion, accurate diagnosis (that rules out significant differentials) and timely management are vital if these patients are to survive in both the short- and long-term (52), each and all of which require multidisciplinary management. However, since relapse and recurrence after transplantation are common (28% & 54% respectively) (54), it may be preferable to avoid conception amongst these patients.

15. Iatrogenic risk during Caesarean Section:

Bladder injury is the most common urological injury during obstetric surgery due to the juxtaposition of the bladder and the lower segment of the term gravid uterus. The vital issue is to immediately recognize and promptly repair the injury in order to avoid sepsis and the development of a fistula (8).

INTEGRATION OF RENAL DISORDERS AND ASSOCIATED MATERNAL AND FETAL RISKS

In obstetrics, the maternal and fetal risks and outcomes associated with renal disease in pregnancy can be stratified by the degree of renal impairment as shown in Table 1. Since serum creatinine varies with gestational age and has the potential to predict the propensity toward adverse obstetric outcomes, there is a pressing need to develop local population-specific reference ranges (55).

Table 1: **Maternal and fetal risk by degree of renal impairment (25)***

Maternal and fetal risk by degree of impairment		
Stage	Pregnancy/fetal outcomes	Renal/maternal outcomes
Early CKD I - II sCr < 1.4 mg/dL eGFR < 70 ml/min Normal BP	Higher risk than general population for preeclampsia, SGA, preterm delivery Counseling: May need specialized care Generally good outcome	Lower risks for accelerated progression
Minimal proteinuria Moderate CKD II - III sCr 1.4 - 2.4 mg/dl eGFR 40 - 70 mL/min	With more advanced CKD and higher proteinuria: Higher risks of caesarian section, preterm delivery, SGA, and need for NICU	Increased risk of progression during pregnancy and within 6week postpartum Counseling: Pregnancy termination doesn't reduce risks for progression Increased risk of progression during pregnancy and within 6 week postpartum
Severe CKD III - IV sCr > 2.4 mg/dL eGFR < 40 mL/min ESRD	With more advance CKD and higher proteinuria: Higher risks of caesarian section, preterm delivery, SGA, and need for NICU care Decreased fertility and high fetal mortality except with more intensive hemodialysis Higher risks of preeclampsia, SGA, cervical incompetence, and need for NICU care persist ± increased risk of fetal loss	Increased need for transfusion, worsening hypertension
Post-transplant	Increased risk of low birth weight and preterm delivery Significantly increased risk of preeclampsia if hypertensive	Blunted renal physiologic adaptations No anticipated decrease in graft survival but may be associated with decreased maternal life span Increased risk of diabetes, urinary tract infection (due to anatomy, insulin resistance, and immunosuppression)

SGA: Small for gestational age; NICU: Neonatal intensive care unit; CKD: Chronic kidney disease; ESRD: End-stage renal disease.

* This table has been reproduced from the work by Berry and Atta (2016) under the creative-commons attribution Non Commercial license (CC BY-NC 4.0).

CONCLUSION:

The substantial complexity of these physiological and pathological entities, coupled with their preponderance to cross-cutting reciprocal synergistic adverse affection of multilateral outcomes warrants a change of the current silo approach to the management of obstetric patients. Collaborative management is therefore vital to the realization of the potential to optimize obstetric, renal and urological outcomes.

ETHICS:

Since this was a narrative literature review that did not involve direct contact with patients or access to identifiable patient data, there was no indication to seek ethical approval to conduct this review.

DECLARATION:

The authors declare that they have no conflicts of interest in association with the publication of this article.

REFERENCES

1. Sadler TW, editor. Urogenital System. In: Langman's Medical Embryology. 12th Editi. Philadelphia: Lippincott Williams & Wilkins; 2012. p. 232–59.
2. Libretti S, Aeddula NR. Embryology, Genitourinary. StatPearls [Internet] [Internet]. 2022 May 8 [cited 2023 Feb 5]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK559309/>
3. Oostra RJ, Schepens-Franke AN, Magno G, Zanatta A, Boer LL. Conjoined twins and conjoined triplets: At the heart of the matter. *Birth Defects Res.* 2022;114(12):596–610.
4. Ezzi MS, Abinya NAO. The Tumor Board experience at The Nairobi Hospital from 2016 to 2018. *Nairobi Hosp Med J.* 2022;1(2):84–8.
5. Guerrero-Fernández J, Azcona San Julián C, Barreiro Conde J, Bermúdez de la Vega JA, Carcavilla Urquí A, Castaño González LA, et al. Management guidelines for disorders / different sex development (DSD). *An Pediatr.* 2018;89(5):315.e1-315.e19.
6. Nicolaou N, Renkema KY, Bongers EMHF, Giles RH, Knoers NVAM. Genetic, environmental, and epigenetic factors involved in CAKUT. *Nat Rev Nephrol* 2015 1112 [Internet]. 2015 Aug 18 [cited 2023 Feb 5];11(12):720–31. Available from: <https://www.nature.com/articles/nrneph.2015.140>
7. Sacristán JA. Clinical research and medical care: Towards effective and complete integration. *BMC Med Res Methodol.* 2015;15(1):1–7.
8. Lee JS, Choe JH, Lee HS, Seo JT. Urologic complications following obstetric and gynecologic surgery. *Korean J Urol.* 2012;53(11):795–9.
9. Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovasc J Afr* [Internet]. 2016 Mar 1 [cited 2023 Feb 5];27(2):89. Available from: [/pmc/articles/PMC4928162/](https://pubmed.ncbi.nlm.nih.gov/2728162/)
10. Costantine MM. Physiologic and pharmacokinetic changes in pregnancy. *Front Pharmacol.* 2014 Apr 3;5 APR:65.
11. RCOG, The Royal College of Obstetricians and Gynaecologist. The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum: Green-top Guideline No. 69. RCOG Green-top Guidel No 69. 2016;(1):1–27.
12. Awowole IO, Omitinde OS, Arogundade FA, Bola-Oyebamiji SB, Adeniyi OA. Pregnancy-related acute kidney injury requiring dialysis as an indicator of severe adverse maternal morbidity at a tertiary center in Southwest Nigeria. *Eur J Obstet Gynecol Reprod Biol* [Internet]. 2018 Jun 1 [cited 2023 Feb 10];225:205–9. Available from: <http://www.ejog.org/article/S0301211518302136/fulltext>
13. Gonzalez Suarez ML, Kattah A, Grande JP, Garovic V. Renal Disorders in Pregnancy: Core Curriculum 2019. *Am J Kidney Dis.* 2019;73(1):119–30.
14. Archibong MS, Adeniyi OA, Nana FO, Olayemi OJ. Hyperemesis Gravidarum as a cause of pregnancy-related acute kidney injury: a case report from Ile-Ife, South West Nigeria. *Niger J Med.* 2020;29:741–3.
15. Sajadi-Ernazarova KR, Martinez CL. Abortion Complications. StatPearls [Internet]. 2022 May 23 [cited 2023 Feb 11]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK430793/>
16. Jabbar Z, Jha V, Bali HK, Kohli HS, Gupta KL, Sakhuja V. Looking beyond the obvious - A young woman with septic abortion and acute renal failure. *Nephrol Dial Transplant.* 2007;22(3):923–5.
17. Lim LM, Tsai KB, Hwang DY, Kuo MC, Chiu YW, Chen HC. Anuric acute renal failure after elective abortion. *Intern Med.* 2011;50(16):1715–8.
18. Ansaldi Y, Martinez de Tejada Weber B. Urinary tract infections in pregnancy. *Clin Microbiol Infect.* 2022 Aug 27;
19. Rahiman F, Balasubramanian T, Shejina M, Musambil M. A Review on Urinary Tract Infection in Pregnancy. *Int J Pharma Res Rev.* 2015;4(2):26–33.
20. Habak PJ, Griggs, Jr RP. Urinary Tract Infection In Pregnancy. StatPearls [Internet]. 2022 Jul 5 [cited 2023 Feb 5]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK537047/>
21. Palma-Reis I, Vais A, Nelson-Piercy C, Banerjee A. Renal disease and hypertension in pregnancy. *Clin Med* [Internet]. 2013;13(1):57–62. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5873710/#__ffn__sectitle
22. Staff AC. The two-stage placental model of preeclampsia: An update. *J Reprod Immunol.* 2019;134–135(March):1–10.
23. Schiffer V, Evers L, de Haas S, Doha-Ghossein C, Al-Nasiryp S, Spaanderman M. Spiral arterial blood flow during pregnancy; a systematic review and meta-analysis. *BMC Pregnancy Childbirth.* 2020;20:680.
24. Gyselaers W. Preeclampsia is a syndrome with a cascade of pathophysiologic events. *J Clin Med.* 2020;9(7):1–25.
25. Berry C, Atta MG. Hypertensive disorders of pregnancy. *World J Nephrol.* 2016;5(5):418–28.
26. Cardoso PAS, Neto ACL. Update on approaches to urinary lithiasis in pregnancy. *Ital J Gynaecol Obstet.* 2022;34(2):103–11.
27. Thakur APS, Sharma V, Ramasamy V, Choudhary A, Patel P, Singh S, et al. Management of ureteric stone in pregnancy: a review. *African J Urol* [Internet]. 2020;26(1). Available from: <https://doi.org/10.1186/s12301-020-00070-5>
28. Semins MJ, Matlaga BR. Management of urolithiasis in pregnancy. *Int J Womens Health.* 2013;5(1):599–604.
29. Lee MS, Fenstermaker MA, Naoum EE, Chong S, Van de Ven CJ, Bauer ME, et al. Management of Nephrolithiasis in Pregnancy: Multi-Disciplinary Guidelines From an Academic Medical Center. *Front Surg.* 2021;8(December):1–10.

30. Juliebø-Jones P, Somani BK, Baug S, Beisland C, Ulvik Ø. Management of Kidney Stone Disease in Pregnancy: A Practical and Evidence-Based Approach. *Curr Urol Rep*. 2022 Nov 1;23(11):263–70.
31. Antony KM, Racusin DA, Aagaard K, Dildy III GA. Maternal Physiology. In: Gabbe SG, Niebyl JR, Simpson JL, Landon MB, Galan HL, Jauniaux ERM, et al., editors. *Obstetrics: Normal and Problem Pregnancies*. 7th ed. Philadelphia: Elsevier; 2017. p. 38–63.
32. Waldorf KMA. Maternal-Fetal Immunology. In: Gabbe SG, Niebyl JR, Simpson JL, Landon MB, Galan HL, Jauniaux ERM, et al., editors. *Obstetrics: Normal and Problem Pregnancies*. 7th ed. Philadelphia: Elsevier; 2017. p. 64–82.
33. Hladunewich MA, Bramham K, Jim B, Maynard S. Managing glomerular disease in pregnancy. *Nephrol Dial Transplant*. 2017;32:148–56.
34. Wiles K, Chappell L, Clark K, Elman L, Hall M, Lightstone L, et al. Clinical practice guideline on pregnancy and renal disease. Vol. 20, *BMC Nephrology*. *BMC Nephrology*; 2019. 1–43 p.
35. Blom K, Odutayo A, Bramham K, Hladunewich MA. Pregnancy and glomerular disease: A systematic review of the literature with management guidelines. *Clin J Am Soc Nephrol*. 2017;12(11):1862–72.
36. Smyth A, Oliveira GHM, Lahr BD, Bailey KR, Norby SM, Garovic VD. A Systematic Review and Meta-Analysis of Pregnancy Outcomes in Patients with Systemic Lupus Erythematosus and Lupus Nephritis. *Clin J Am Soc Nephrol* [Internet]. 2010 Nov 1 [cited 2023 Feb 12];5(11):2060. Available from: /pmc/articles/PMC3001786/
37. Daza JL, Cruz Y de la, Galindo JF, Puello L, Gutiérrez G, Correcha MC, et al. Hemodialysis in Pregnant with Systemic Lupus Erythematosus: Case Report and Review. *Open J Nephrol*. 2022;12(01):48–59.
38. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci*. 2018;19(11):1–21.
39. Johnson MS, Jackson DL, Schust DJ. Endocrinology of pregnancy. In: *Encyclopedia of Reproduction* [Internet]. Elsevier; 2018 [cited 2021 Mar 31]. p. 469–76. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK278962/>
40. Gray SG, Sweeting AN, Mcguire TM, Cohen N, Ross GP, Little PJ. Changing environment of hyperglycemia in pregnancy: Gestational diabetes and diabetes mellitus in pregnancy. *J Diabetes*. 2018 Aug 1;10(8):633–40.
41. Khorsandi B, Rad MK, Moradi M. Early Manifestations of Acute Renal Failure in a Pregnant Woman with Diabetes. 2020;27–33.
42. Care D, Suppl SS. 15. Management of diabetes in pregnancy: Standards of medical care in diabetesd - 2022. *Diabetes Care*. 2022;45(Suppl. 1):S232-243.
43. McBride L, Wilkinson C, Jesudason S. Management of autosomal dominant polycystic kidney disease (ADPKD) during pregnancy: Risks and challenges. *Int J Womens Health*. 2020;12:409–22.
44. Wu M, Wang D, Zand L, Harris PC, White WM, Garovic VD, et al. Pregnancy outcomes in autosomal dominant polycystic kidney disease: A case-control study. *J Matern Neonatal Med*. 2016;29(5):807–12.
45. Fakhouri F, Schwotzer N, Cabiddu G, Barratt J, Legardeur H, Garovic V, et al. Glomerular diseases in pregnancy: pragmatic recommendations for clinical management. *Kidney Int*. 2023;103(2):264–81.
46. Gleeson S, Lightstone L. Glomerular Disease and Pregnancy. *Adv Chronic Kidney Dis* [Internet]. 2020;27(6):469–76. Available from: <https://doi.org/10.1053/j.ackd.2020.08.001>
47. Marinaki S, Tsiakas S, Skalioti C, Kapsia E, Lionaki S, Vallianou K, et al. Pregnancy in Women With Preexisting Glomerular Diseases: A Single-Center Experience. *Front Med*. 2022;9(February):1–10.
48. De Castro I, Easterling TR, Bansal N, Jefferson JA. Nephrotic syndrome in pregnancy poses risks with both maternal and fetal complications. *Kidney Int* [Internet]. 2017;91(6):1464–72. Available from: <http://dx.doi.org/10.1016/j.kint.2016.12.019>
49. Piccoli GB, Alrukhaimi M, Liu ZH, Zakharova E, Levin A. What We Do and Do Not Know about Women and Kidney Diseases; Questions Unanswered and Answers Unquestioned: Reflection on World Kidney Day and International Women’s Day. *Am J Nephrol*. 2018;47(2):103–14.
50. Fitzpatrick A, Mohammadi F, Jesudason S. Managing pregnancy in chronic kidney disease: Improving outcomes for mother and baby. *Int J Womens Health*. 2016;8:273–85.
51. Carvalho BTB, Borovac-Pinheiro A, Morais SS, Guida JP, Surita FG. Gestational hypertension as a factor associated with chronic kidney disease: the importance of obstetric history of women undergoing hemodialysis. *Brazilian J Nephrol*. 2023;1–8.
52. Saad AF, Roman J, Wyble A, Pacheco LD. Pregnancy-Associated Atypical Hemolytic- Uremic Syndrome. 2016;1(212).
53. Rondeau E, Ardissino G, Caby-Tosi MP, Al-Dakkak I, Fakhouri F, Miller B, et al. Pregnancy in Women with Atypical Hemolytic Uremic Syndrome. *Nephron*. 2022;146(1):1–10.
54. Bruel A, Kavanagh D, Noris M, Delmas Y, Wong EKS, Bresin E, et al. Hemolytic uremic syndrome in pregnancy and postpartum. *Clin J Am Soc Nephrol* [Internet]. 2017 [cited 2023 Feb 12];12(8):1237–47. Available from: https://journals.lww.com/cjasn/Fulltext/2017/08000/Hemolytic_Uremic_Syndrome_in_Pregnancy_and.7.aspx
55. Kang J, Hwang S, Lee TS, Cho J, Seo DM, Choi SJ, et al. Gestational age-specific serum creatinine can predict adverse pregnancy outcomes. *Sci Rep* [Internet]. 2022;12(1):1–9. Available from: <https://doi.org/10.1038/s41598-022-15450-w>

Management of neurogenic bladder in low resource setting: the challenges of service provision. A case series and discussion.

**Mugalo E. Lumadede¹, Akello W. Abila²,
Miima E. Ashiundu³, Musau Pius⁴**

Affiliations

¹ Department of Surgery & Anesthesiology Moi University, School of Medicine, Eldoret, Kenya.

² Faculty of Health Sciences, Egerton University, Nakuru, Kenya.

³ Faculty of medicine, Masinde Muliro University of Science and Technology, Kakamega, Kenya.

⁴ Department of Surgery & Anesthesiology Moi University, School of Medicine

Corresponding author: Dr. Mugalo Edward Lumadede.

Email : edwardmugalo@gmail.com, emugalo@mu.ac.ke

ABSTRACT

Healthcare workers in resource-poor sectors face many challenges in managing patients with neurogenic bladders. These subsets of patients do not get optimum care due to the unavailability of specialized personnel and equipment. Healthcare providers in these regions use clinical knowledge and basic imaging procedures to make management decisions. Both pharmacological and non-pharmacological treatment is available, and it has been cited that solid social support contributes to patients' care, improves the quality of life, and limits morbidities. Two cases are discussed in this report.

Key Words: Neurogenic bladder, continence, urodynamic studies, quality of life

INTRODUCTION

A Neurogenic Bladder (NB) has dysfunctional storage and or micturition functions due to disordered activities of the central and peripheral nervous systems. This leads to either bladder underactivity or overactivity, referred to as a Neurogenic Lower Urinary Tract Dysfunction (NLUTD). Supra-spinal lesions cause Detrusor Overactivity (DO) and Detrusor Sphincter Dyssynergia (DSD), leading to back pressure, upper urinary tract dilatation, and compromised renal function. It requires long-term or lifelong bladder care and regular medical assessments to provide social continence and prevent upper urinary tract damage, life-threatening urinary tract infections, and renal failure. NB is not considered a priority in Sub-Saharan Africa because of the more significant burden of infectious diseases that take up a bigger budgetary allocation.

Africa has the lowest physician index at 2.7 per 10,000 population compared to other regions. This further complicates the allocation of resources to the management of NB [1]. Because of the high financial and health service needs, access to comprehensive medical care

is affected. Multiple bladder management interventions have been proven beneficial, the gold standard being clean intermittent catheterization (CIC) [2]

[3] Despite the varied challenges in terms of the number of cases, competing interests in the care of patients, limited infrastructural support, and personnel hindrances, the general supervision of patients in Sub-Saharan Africa can ensure good quality of life and prevention of complications.

CASE 1.

A 65-year-old male with a history of a fall from a height 30 years earlier suffered a C4-C5 spine injury. He developed quadriplegia. He first attended our urology clinic in 2015 as a referral with a right renal oncocytoma. The patient was on assisted clean intermittent catheterization from when he suffered the injury and was initiated at the Spinal Injury Hospital. He suffers several episodes of Urinary tract infection (UTI) managed after a urine culture and sensitivity. The last urine culture grew E. coli, and the latest bladder capacity was 360cc from the most recent ultrasound. Table 1 shows preserved renal function.

Table 1: Renal function test for patient case 1.

	Results	Normal range
urea	3.53 mmol/L	0.30 - 8.30 mmol/L
creatinine	84 µmol/L	62 – 106 µmol/L
Na	136.7mmol/L	136.0 – 148.0mmol/L
K	3.90mmol/L	3.50 – 5.10 mmol/L
Cl	108.2mmol/L	98.0 – 107.0 mmol/L

CASE 2.

A 19-year-old female attended the urology clinic for the first time at the age of 12 years. She had suffered from voiding dysfunction since early childhood, managed by clean intermittent catheterization (CIC). Referring Micturating Cysto-urethrogram showed increased bladder capacity, bilateral hydronephrosis, and bladder trabeculations. Her current ultrasound showed a bladder capacity of 344mls with grade 1 hydronephrosis.

Table 2: Renal function test for patient case 2

	Results	Normal range
Urea	6.0mmol/L	0.30 - 8.30 mmol/L
Creatinine	61.0µmol/L	62 - 106µmol/L
Na	139	137-145Mmol/L
K	3.9	3.5-5.1Mmol/L
Cl	103	98-107Mmol/L

DISCUSSION

Sub-Saharan Africa has an enormous burden of urological diseases for which optimum treatment is still unavailable for most patients [4]. The burden of the neurogenic bladder (NB) parallels diseases of the central and peripheral nervous systems, as many patients manifest urinary bladder dysfunction. The 2016 global incidence and prevalence of spinal cord injury (SCI) were 934, 000 and 27 million, respectively [5]. Low and low-middle development index countries had SCI incidence and prevalence of 330 000 and 7 million, respectively. The estimates showed about 82,000 new cases of SCI and under 2 million total cases in Sub-Sahara Africa and 4,000 and 83,000, respectively, for Kenya. About 70 % - 80 % of these patients are expected to have some degree of bladder dysfunction attributable to the SCI.

NB was shown to affect 40% to 90% of patients with multiple sclerosis, 37% to 72% of 6 patients with Parkinsonism, and 15% of patients with cerebrovascular accidents [6, 7]. NB is less commonly seen in autonomic neuropathy of diabetes mellitus, as a complication of pelvic surgery, and as part of cauda equina syndrome [6].

The complete evaluation of patients with NB requires the availability of a laboratory to conduct urinalysis, urine culture and sensitivity, and renal function tests. Further evaluation requires an ultrasound, cystometry, electromyography, cystoscopy, and video urodynamics [8]. The Sub-Saharan experience includes the most basic of these requirements, complemented with clinical acumen.

Urology practice faces challenges just like other health service provisions in developing countries. There are limited trained urologists, specialized urology units, and limited availability of drugs and specialized equipment. There are two National Referral Hospitals in Kenya, yet none can perform video urodynamics, cystometry, or electromyogram (EMG) studies. This limits the comprehensive evaluation of patients with NB. Diagnosis is based on the first principles of clinical evaluation and basic imaging studies in understanding the nature of bladder dysfunction. A thorough urodynamical evaluation to evaluate bladder and sphincter behavior is recommended to better assess urinary dysfunction before therapy initiation. NB patients and their family members and caregivers need specific information and training. Most of these needs remain unmet with low numbers of staff in the few urology units.

The availability of guidelines provides a resource of reference for management within a given environment considering the available resources in the setting. However, except for South-Africa, Sub-Saharan African countries still need guidelines for the management of NB [9]. This may either indicate a failure to recognition of NB as a problem of concern or a lack of capacity to manage the condition.

Africa, however, still has a solid social structure and good family support for patients with chronic diseases, including NB. This is exemplified in our two patients. Case 1 patient continually undergoes assisted CIC, while the Case 2 patient was assisted to do CIC as a child until she was grown enough to do it herself. Both patients have prolonged survival, preserved renal function, and minimal complications (Tables 1 and 2). Evidence suggests that higher levels of social support influence more positive outcomes in patients with NB [10, 11]. As a result of the growing gap between the need for self-care support and existing resources, family members are increasingly recognized as essential allies in the care of chronically ill patients [12].

The options in the management of NB include conservative (non-pharmacological, non-surgical), pharmacological, and surgical methods. Principal management goals are preserving renal function, improving continence, and reducing urinary complications such as kidney failure and urinary tract infection (UTI). Recurrent UTI has been the main complication that our two patients experience. It is, however, managed guided by culture and sensitivity results.

Bladder management focuses on therapy to facilitate bladder filling and storage of urine and treatment to facilitate bladder emptying that assists in preserving both renal function and social functioning that affords patients

acceptable quality of life. A comprehensive diagnosis and assessment of bladder dysfunction are required for appropriate individualized treatment pathways. In Sub Sahara Africa, the options are, however, limited.

There are few studies on the region's management and outcomes of NB. In a study conducted at the Botswana SCI center, of the 27 patients who were on follow-up, 60 % required bladder management, and up to 30 % had suffered UTIs at one point during follow-up [13]. Notably, up to 30 % of CIC was used, which was reported as increased uptake. Another 30 % either used an indwelling or suprapubic catheter. The study did not report on the use of drugs alongside bladder emptying. Catheters were reported to be available, allowing single use. Lofvenmark et al. had a follow-up rate of 77 %, and the high rate was attributed to the facilitation of transport for patients and dedicated staff to contact patients. A dedicated center for the care of NB would probably be a starting point in the effective management of patients with NB.

In a Dutch study consisting of 282 participants, CIC was most commonly used as the primary bladder-emptying method (42.6%, excluding the catheterized pouches and channels), followed by condom catheter drainage (11.3%), indwelling suprapubic catheterization (11.3%) and voluntary bladder reflex triggering (11.0%) [14]. In the same study, they report a variety of surgical interventions, including bladder augmentation and conduits, as well as non-surgical, non-pharmacological methods such as sacral anterior root stimulation. During follow-up, they reported a UTI rate of 33 % in the preceding three months. An array of possible interventions would be the next step in the care of NB, but this is only possible in a setting where the infrastructural support would ensure detailed patient evaluation with individualized care based on the ultimate diagnosis.

CIC is the gold standard for bladder emptying in patients with NB, but studies have shown that it is not without problems, including impacting the quality of life and risk for UTIs and urethral strictures [14,15]. The benefit of hydrophilic catheters over ordinary catheters, touch vs. no-touch techniques, and single over multiple-use catheters insofar as UTI risk is concerned remains controversial [15]. For our two cases, low-friction reusable Nelaton catheters are used after cleaning with

clean water and applying the lubricating jelly. After each use, the catheters are cleaned with water and stored in an antiseptic solution. Proper adherence to the needed aseptic techniques and patient dexterity is required. Social support will come in handy when the patient is incapable of these, as shown by the two cases presented.

The benefit of botulinum toxin and antimuscarinics in detrusor overactivity has been proven in multiple studies. However, intravesical botulinum has been shown to increase UTI risk. Oxybutynin and the newer generation antimuscarinics are available in low and middle-income countries, although the cost might be prohibitive [9].

Pediatric NB is primarily a result of spinal dysraphism. The mainstay of management is the immediate commencement of clean intermittent catheterization and oxybutynin therapy where there is detrusor overactivity [8]. Our case 2 was diagnosed with NB from early childhood, and CIC was immediately commenced. She has maintained good renal function over time. CIC commencement should be followed or preceded by urodynamic studies. Subsequent management consists of regular clinical assessments, maintained bladder diaries, urinalysis, renal function tests, imaging of the urinary system, and cystoscopy where indicated. The absence of guidelines in developing countries and the capacity for urodynamics negatively impact the likelihood of recommended care for children [8].

CONCLUSION

Management of neurogenic bladder is mainly lifelong, and the financial and health service needs of NB are high. They are expected to affect access to the comprehensive medical care of patients. Despite limited resources in low-resource settings, there are options for patient assessment and bladder management that are inexpensive, require minimal expertise, and can produce comparable results if adopted. A robust social structure in Sub-Sahara Africa is an essential factor in determining our patients' quality of life and survival. Recognition of NB and the development of relevant guidelines will likely improve care in resource-poor settings.

REFERENCES

1. WHO-GlobalHealth Observatory (2020) Medical doctors (per 10 000 population). [https://www.who.int/data/gho/data/indicators/indicator-details/GHO/medical-doctors-\(per-10-000-population\)](https://www.who.int/data/gho/data/indicators/indicator-details/GHO/medical-doctors-(per-10-000-population)). Accessed 6 Feb 2021.
2. Mihnert, U., Chartier-Kastler, E., de Wachter, S. et al. The management of Urine Storage Dysfunction in Neurological Patients. *SN Compr Clin. Med.*1,160-180 (2019).<https://doi.org/10.1007/s42399-0118-0005-8>].

3. Di Benedetto P. Clean Intermittent self-catheterization in neuro-urology. *Eur J Phys Rehabil Med.* 2011 Dec;47(4):651-9. PMID:2222962].
4. Juvet T, Hayes JR, Ferrara S, Goche D, Macmillan RD, Singal RK (2019) The burden of urological disease in Zomba, Malawi: A needs assessment in a sub-Saharan tertiary care center. *Can Urol Assoc J.* <https://doi.org/10.5489/cuaj.5837>.
5. James SL, Theadom A, Ellenbogen RG, et al (2019) Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 18:56–87.
6. Dorsher PT, McIntosh PM (2012) Neurogenic bladder. *Adv Urol.* <https://doi.org/10.1155/2012/816274>.
7. Ruffion A, Castro-Diaz D, Patel H, Khalaf K, Onyenwenyi A, Globe D, LeReun C, Teneishvili M, Edwards M (2013) Systematic review of the epidemiology of urinary incontinence and detrusor overactivity among patients with neurogenic overactive bladder. *Neuroepidemiology.* <https://doi.org/10.1159/000353274>.
8. Stein R, Bogaert G, Dogan HS, et al (2020) EAU/ESPU guidelines on the management of neurogenic bladder in children and adolescent part I diagnostics and conservative treatment. *NeuroUrol Urodyn* 39:45–57.
9. Theron F, Wilson V, Scriba E, Campbell R, Van Zyl M, Terry D, Visser A, Louw G, Seirlis A (2019) Best practice recommendations for bladder management in spinal cord-afflicted patients in South Africa. *S Afr Med J* 109:12569.
10. Strom JL, Egede LE (2012) The Impact of social support on outcomes in adult patients with type 2 diabetes: A systematic review. *Curr Diab Rep.* <https://doi.org/10.1007/s11892-012-0317-0>.
11. Costa DC, Sá MJ, Calheiros JM (2012) The effect of social support on the quality of life of patients with multiple sclerosis. *Arq Neuropsiquiatr.* <https://doi.org/10.1590/s0004-282x2012000200007>.
12. Rosland AM, Piette JD (2010) Emerging models for mobilizing family support for chronic disease management: A structured review. *Chronic Illn.* <https://doi.org/10.1177/1742395309352254>.
13. Löfvenmark I, Wikmar LN, Hasselberg M, Norrbrink C, Hultling C (2017) Outcomes 2 years after traumatic spinal cord injury in Botswana: A follow-up study. *Spinal Cord* 55:285–289.
14. Adriaansens JJE, van Asbeck FWA, Tepper M, Faber WX, Vissers-Meily JMA, de Kort LMO, Post MWM (2017).
15. Kennelly M, Thiruchelvam N, Averbek MA, Konstantinidis C, Chartier-Kastler E, Trøjgaard P, Vaabengaard R, Krassioukov A, Jakobsen BP (2019) Adult Neurogenic Lower Urinary Tract Dysfunction and Intermittent Catheterisation in a Community Setting: Risk Factors Model for Urinary Tract Infections. *Adv Urol.* <https://doi.org/10.1155/2019/2757862> .

Evaluation and management overactive bladder syndrome: A review

Dr. Abdirashid A Mohamed¹
Dr. Aideed Kahie^{1,2}

Affiliations:

¹ Kaatun urology & male executive clinics and 3RD Park Hospital

² Corresponding author

ABSTRACT

Overactive bladder syndrome (OAB) is a chronic medical condition that has a significant physical and psychosocial consequences to the patients and on the quality of their lives. Most patients do not seek medical help due to embarrassment or the thought of it being part of a normal life. The cause of OAB is not yet fully understood and many theories have been postulated. Establishing the correct diagnosis and initiating effective therapies is paramount in these patients. Therefore, the patient should be clearly explained to about the disease and the fact that complete cure is difficult so as to manage his/her expectations. Although there are several treatment modalities, it still remains a significant challenge for specialists and patients.

INTRODUCTION

Overactive bladder syndrome (OAB) is a chronic medical condition that severely affects the quality of life of the patient (1, 2). It is defined by the international groups as urine urgency with/without incontinence, associated with increased frequency and nocturia with no underlying pathology(3-5) .

OAB commonly affects adults over 40 years, but has also been reported in pediatric and young adults(1, 6, 7). It is a symptomatic diagnosis unlike other types of incontinence which are noted on urodynamic studies. The overall prevalence is 12-16.5%, but this increases with age and at 65 years it rises up to 30.9% (2, 8, 9). This number is still believed to be an underestimate as many patients down play their symptoms or do not seek help initially because of embarrassment or ignorance as many think it is part of the ageing process(1, 8). Al Edwan et al noted only 13 % of the women with symptoms suggestive of OAB were receiving treatment(8).

Urgency, urgency incontinence, frequency and nocturia are the symptoms of overactive bladder(1, 5, 10, 11). Urgency is defined as a sudden compelling desire to void that cannot be deferred as the patient fears leakage of urine. This should

not be confused with urgency due to fear of pain which is seen in bladder pain syndrome(10). Urgency incontinence is involuntary leakage of urine immediately preceded by urgency. OAB can be categorized as OAB 'dry' and OAB 'wet'. OAB 'dry' means urgency without associated incontinence, while OAB 'wet' is urgency with associated incontinence. OAB wet is seen in 1/3 of the OAB patients and predominantly in females and older patients(1, 10). The difference is presumed to be due to relative weakness of bladder neck and urethral sphincter mechanism(10).

Urinary Frequency which is the number of times the patient voids during the waking hours has been define as >7 episodes. While nocturia is interruption of sleep because of need to void and more than 3 episodes per night is defined as bothersome. Both nocturia and frequency episodes are highly variable depending on sleep, type and amount of fluid intake and comorbidities(1, 5, 10).

Overactive bladder syndrome affects patients' quality of life and has far reaching consequences that affect the mental, physical and social well-being of the patient(1, 10, 12, 13). The

patient can develop sleep disturbances, depression, recurrent Urinary tract infections (UTI), skin excoriations due to urine leakage, longer hospital stay, multiple physician visits, reduction of sexual activity and marital satisfaction(1, 10, 14).

Over active bladder syndrome also affects patients' social functions leading to most of them limiting their public outings, social gatherings and outdoor activities which can lead to depression and other psychological disorders(12, 15, 16). Moreover, it affects the patients job performance due to frequent loss of time due to illness, physician visits and hospitalization. This can lead to decreased productivity at work and loss of employment. This is detrimental both directly with cost of therapy of this condition and indirectly with the economic burden of time off work and unemployment(13, 17, 18).

While OAB is difficult to completely cure, symptoms can be controlled and patients' quality of life changed for the better without excess cost or morbidity(1, 19, 20). OAB bladder diagnosis is made after excluding pathological conditions such as UTIs, bladder outlet obstruction, metabolic disorders, neurological disorders, side effect of some medication (neuroleptics, benzodiazepines, Parkinson's medication, beta-blockers), radiotherapy and urinary stress incontinence(1, 10).

PATHOPHYSIOLOGY

The etiology and pathophysiology of OAB is not well known and several theories have been postulated. Initial theories focused on detrusor overactivity (DO) suggesting the sensory mechanism of the bladder is affected which leads to patient developing urgency when bladder capacity is smaller than normal conditions(21, 22). However, it was noted that only 50% of patients with OAB have objective evidence of DO and this led to further research into alternative mechanisms(22).

The theories proposed include are:

- a. The myogenic theory – here the symptoms are initiated from contraction of the detrusor muscle. The detrusor muscle becomes more sensitive to cholinergic stimulation. This leads to increased spontaneous and uninhibited contractions(1, 9, 22);
- b. Urotheliogenic theory – The lower urinary tract nerve endings are densely concentrated under the urothelium and are exposed to different urothelium mediators. Thus, urothelial and suburothelia sensory dysfunction leads to urgency due to the altered sensory input(9, 10, 22, 23);
- c. Urethrogenic theory - here the urgency arises from the urethra. Activation of urethral afferent fibers can modulate the micturition reflex(24). Thus, entry of urine into the proximal urethra in patients with stress urinary incontinence (SUI) may induce/increase DO. Most of the patients experience urgency when moving from a sitting or lying position to a standing position(22, 25);
- d. Supraspinal theory – here the urgency arises due to white matter damage in elderly patients which results in severe functional urinary impairment(9, 22, 26, 27);
- e. Detrusor underactivity (DU) - which is defined urodynamically and overlaps with OAB with the most common symptom being is urgency. This urgency is attributed to be a result of increased postvoid residual volume and consequent reduced functional bladder capacity and recurrent urinary infection due to prolonged chronic urine retention(28). Current data suggest that detrusor underactivity may be as a result of previously mentioned hypothesis i.e. the urotheliogenic and myogenic hypothesis(22, 29).

EVALUATION

As there are no specific OAB clinical signs during examination, a detailed focused history is necessary(30, 31). Specific details of the symptoms (urgency, urgency incontinence, nocturia, frequency) should be explored with a symptom-based questionnaire. The questionnaires are validated and can determine the severity and burden (ICIQ-OAB questionnaire) and quality of life with urge incontinence (OAB- questionnaire)(1, 10, 19).

The history should also include thorough assessment of risk factors of pathological conditions causing the OAB and that may be reversible. Such risk factors include metabolic conditions (Diabetes mellitus), neurological conditions (stroke, Parkinsons disease, dementia, spinal cord injury, multiple sclerosis) psychiatric history, pelvic organ prolapse, pelvic surgery, obstetric history, multiparity per vaginal deliveries, prostatic enlargement, prostatitis, malignancy (urothelial carcinoma), systemic diseases (hypertension, heart disease), arthritis, previous treatment of OAB, medications (diuretics, neuroleptics, B-blockers, narcotics), radiotherapy of pelvic organs and lifestyle factors (smoking, obesity, caffeine, alcohol, carbonated beverages)(1, 10, 19, 32).

On physical examination a general assessment and focused thorough systemic examination of organs that may lead to incontinence. The organs to be examined include – abdominal examination (scars, lower abdominal masses, distended bladder, hernias), vaginal examination (prolapse, cystocele, rectocele which may impair bladder emptying), digital rectal examination (anal tone, fecal impaction, occult blood or lesions that distends rectum and sigmoid), neurological examination (check for Upper and lower motor neuron lesions) and spinal examination(1, 10, 32-35).

A bladder diary and frequency volume charts filled by the patient are used to assess frequency of voiding, nocturia and pattern of voiding. On the frequency volume chart, the number of voids recorded during the day i.e., from the waking time until last void before sleeping. The maximum voided volume recorded can indicate the severity of OAB and detrusor overactivity, because in OAB the pattern of voiding is erratic. On the other hand, a bladder diary is an easy-to-use tool that captures the symptoms i.e., frequency, urinary volume, pattern of voiding, urgency and incontinence episodes. The diary can also generate a symptom score such as the international consultation on incontinence questionnaire (ICIQ) bladder diary score or the patient perception of intensity of urgency scale (PPIUS)(36, 37). The score generated for every void depending on the severity of the symptoms for example a score of 0 (no urgency) up to a score of 4 (urgency incontinence). A further quantitative analysis can be obtained from the diary – Total urgency and frequency score (TUFS)(36, 38).

Laboratory tests that are recommended include are necessary to rule out pathologies that may cause OAB-like symptoms: urine analysis and culture for infection, hematuria. Blood test including creatinine level for renal function tests, glycosylated hemoglobin (HbA1C) and electrolyte levels(33, 35).

Ultrasound is used to measure post-void residual volume; the patients are advised to void immediately before the test if the last void was more than half an hour prior. If available uroflowmetry studies should be done prior to post-void residual volume test. In complicated or therapy refractory cases other additional tests such as – urodynamics evaluation should be carried out. This tool is important in patients with neurological symptoms or concomitant voiding dysfunction. upper genito-urinary tract (GUT) Imaging and cystoscopy are important in patients with recurrent UTI and hematuria(1, 10, 19, 39).

TREATMENT

The objective here is to educate the patient about OAB so that he/ she can be able to understand the symptoms of OAB and develop strategies to manage the symptoms(10). It is important to be clear with the patient and inform them the process will take long period of time and they must remain tolerant and motivated to achieve long-term results. As well one needs to manage the patients' expectations from the beginning and be honest with them due to the nature of the syndrome a "cure" is not realistic(10, 35, 40, 41).

The management strategies of OAB as agreed in the guidelines is to start with non-invasive treatment (first- and second-line therapies) and invasive treatment in refractory cases (third line therapy)(1, 10, 35).

First line therapy – Non pharmacological therapy

This is mainly behavioral therapy which have been proven to be effective and are associated with minimal risk(35, 42, 43). This includes:

- a. Lifestyle modification – weight loss, exercise and cessation of smoking, stop consumption of alcohol, coffee, acidic foods and sour drinks, reduced fluid intake and no fluids 2 hrs before bed time, bowel regulation(1, 10, 35, 44).
- b. Bladder training which involves urination at regular intervals disregarding the normal urge to void. Initially start with short intervals of 30 minutes and gradually increase the intervals periods of 3-4 hrs. This procedure leads to a slow gradual increase in bladder capacity. The patient must understand every minute they postpone the urination is an important gain(45, 46). Certain motivational and visual feedback tools can be used to keep the patient engaged and compliant such as a micturition calendar(43, 47).
- c. Pelvic floor muscle training (PFMT) which includes Kegel exercises, pelvic floor exercises with biofeedback, vaginal weight training and pelvic floor electrical stimulation. They have been shown to be highly effective especially in reducing urge and incontinence by reducing detrusor contraction through inhibitory reflection of the pelvic floor and improving urethral stability(19, 40, 48). As there is no single effective PFMT regime therapy should be individualized under supervision of a specialist. Combination of PFMT and bladder training produces optimal results as patients are able to gain control gradually and increase the urination intervals(42, 48).

Behavioral therapy was found to be most effective when combines with pharmacological therapy(1, 35, 49).

Second line therapy – Pharmacological therapy

Pharmacological treatment is initiated once behavioral therapies have been tried. There are three groups of drugs used anti-cholinergic, beta -3 adrenergic agonists and phosphodiesterase-5 inhibitors(1, 10, 35, 50).

Anticholinergics are the initial drugs used in patients with OAB and they help achieve detrusor relaxation and improve patient symptoms(1, 10, 35, 51). The mechanisms by which they achieve this is by competitively blocking the cholinergic-muscarinic receptors at the Neuro-muscular junction thus preventing parasympathetic stimulation of the detrusor muscle contraction and by inhibiting afferent nerve fibers from stimulating urothelial sensory receptors. The most common anticholinergics are: oxybutynin, tolterodine, trospium, solifenacin. These drugs are available in tablet form as extended release (ER) and immediate release (IR). when prescribing the ER form is preferred to the IR as it may have superior efficacy. Oxybutynin is available as a transdermal patch and ointment.

Several high-grade studies have demonstrated anticholinergic drugs produced significant improvement of OAB symptoms(51-53). However, these drugs have associated side effect such as dryness of mucous membranes, constipation, urine retention, tachycardia, palpitations, arrhythmias and cognitive impairment (e.g. somnolence, blurred vision, confusion, hallucinations, and memory problems) (35, 54-56). Many patients discontinue these medications due to their side effects with rates of 48-83% in the first 30 days(1, 35, 57, 58). The most common reason for discontinuation were constipation (approximately 50%) and dry mouth (approximately 30%) (1, 35, 48, 59). Transdermal oxybutynin although associated with lower systemic side effects as it avoids liver first pass effect with time it is associated with erythema and pruritus(35, 40).

Contraindication to anticholinergics use are patients with: narrow angle glaucoma, myasthenia gravis, intestinal obstruction, urine retention, severe ulcerative colitis and toxic megacolon(1, 35, 40). Thus, the treatment should be individualized and patients be co-managed with the physicians caring for these disorders. As cognitive effects of anticholinergics are cumulative (so called anticholinergic burden/load) they should be used with caution in elderly patients or patients with cognitive impairment (10, 35, 50, 60).

Beta -3 adrenergic agonist acts by binding the receptors which are predominantly responsible for detrusor relaxation during the filling phase(61, 62). They are considered second line therapy and used in patients who do not respond to first line pharmacological anticholinergic treatment, those who cannot tolerate side effects or those in whom they are contraindicated. Mirabegron was the first beta -3 adrenergic agonist introduced in 2013 (63) and several studies have shown favorable outcomes and effectiveness is comparable to anticholinergics with minimal side effects(50, 64, 65). Studies have demonstrated a higher adherence to mirabegron compared to anticholinergics(66).

Mirabegron can be used in treatment of elderly population, as a phase IV study demonstrated its safety and tolerability in this group. In the BESIDE study, the authors found that there was no different between combining solifenacin 5mg and mirabegron 50mg vs solifenacin 10mg (67). In fact, the higher dose of solifenacin is associated with increased anticholinergic load and more side effects (67). In another study they found that mirabegron was not associated with significant changes in cognitive function from baseline after 12 weeks(68). In September 2018, Vibegron was approved in Japan for treatment of OAB(69). Several multicenter prospective studies have demonstrated vibegron was associated with significant improvement in OAB symptoms and quality of life(50, 70, 71).

Low dose Tadalafil has been investigated for its safety and efficacy in OAB(72). A double blinded placebo-controlled RCT of 96 female patients with OAB demonstrated a significant improvement in the OAB symptom score and the Indevus urgency severity scale(50, 72, 73).

Third Line Therapy – refractory patients

Refractory patients are those that fail to achieve clinical improvement on pharmacological therapies (whether monotherapy or combined therapy) or those who do not tolerate the side effects or have contraindications to pharmacological therapy (1, 35, 50). Third line therapy includes: temporary chemical denervation of bladder detrusor muscle with intravesical botulinum toxin A, posterior tibial nerve stimulation (PTNS) and sacral neuromodulation (1, 40, 48, 50).

Temporary chemical denervation of bladder detrusor muscle with intravesical botulinum toxin A works by selectively blocking the presynaptic release of acetylcholine from nerve endings which results in a temporary paralysis of the muscle and by directly inhibiting release of neurotransmitters from

the urothelium (35, 43, 50, 74). The technique is by injecting it into 20 places on the posterior bladder wall above the trigone using a cystoscope. Trigone injection is avoided as it has been shown to be associated with higher incidences of voiding difficulties, urine retention and urinary tract infection(35, 50).

A systematic review and metaanalysis have shown significant reduction in incontinence episodes and mean number of micturition(75). The optimal dose of the toxin is 100 U. Higher doses (200-300U) have been shown to be effective but associated with side effects such as urine retention and increased residual volume which require clean self-intermittent catheterization(76). The duration of the toxin effect is 6-9 months after which a re-injection may be necessary(1, 35).

Posterior tibial nerve stimulation (PTNS) is a form of neuromodulation used to improve urinary symptoms(35, 77). This is a weekly 30 min session over a 12-week period and the technique is by intermittent stimulation of tibial nerve at the level of the medial aspect of the ankle(35, 40, 78). Favorable effects can last up to 1 year and repeated treatments may be required for sustained effect. It is associated with minimal temporary local side effects (local inflammation, pain, minimal bleeding) (79). PTNS is contraindicated in pregnancy, bleeding disorders, implantable defibrillators and pacemaker. Recently there is an option of transcutaneous stimulation and implantable devices(35, 50, 80, 81).

Sacral neuromodulation (SNM) involves implanting a device which generates continuous low frequency electrical impulses which stimulate S3 nerve root and modulate bladder/pelvic floor function(1, 35, 39, 47, 50). A preliminary phase (phase 1) is required to see if the patient has significant improvement in symptoms (>50% from baseline symptoms) prior to the permanent implant being inserted (phase 2). It was initially approved for use in 1997 with success rates of 62-90% with patients having a marked improvement in quality of life, and favorable effects being maintained for 3-5 years. It does have adverse effect such as pain, bleeding, infection, device migration and device failure. The rates of surgical revision due to these adverse effects is 3-16%(82, 83).

There are two models approved for use in the market. The first one was approved in 1997 and needs to be replaced after the battery runs its life span, which on average is 62.5 months(50, 83). The device is contraindicated in patients who require frequent MRI. The manufacturers recommend if an MRI is necessary only an MRI brain can be done using a 1.5 Tesla magnet or lower and the device should be turned

off(50, 84). A more recent rechargeable smaller size system has come to the market which can last up to 15 years or more and requires 2 weekly recharging via wireless charger and takes 1-2 hours to fully charge(50, 85). The advantages of the newer rechargeable system over the older model is it is smaller size is more comfortable for the patients especially those with lower BMI and it is safer to use with MRI scans(50, 85). The recommendation is to use 1.5 Tesla MRI for full body scan and 3 Tesla head scan(50, 85).

If SNM fails treatment of refractory OAB is difficult, some authors have reported improvement with botulinum toxin injection. One study of 52 patients in whom SNM did not work, 27% of them improved with botulinum toxin injection(86).

Recent studies have been looking at using selective denervation and use of laser therapy in treatment of OAB(87, 88). Selective denervation involves radiofrequency ablation (RFA) of different points on the urothelium of the bladder subtrigone which contains afferent sensory nerves. In one study of 63 patients with refractory OAB who underwent this treatment at 12 weeks there was a significant improvement in OAB questionnaire score and quality of life score(50, 87). Laser treatment was in menopausal patients with OAB and vulvovaginal atrophy in prospective studies with one using CO2 laser and erbium: YAG (Er: YAG) laser. The CO2 team gave 3 treatments 30 days apart and the Er: YAG team gave three treatment 1 month apart. There was significant improvement in urgency and urge incontinence episodes, bladder diaries and OAB Questionnaire scores(50, 88, 89). At present the results are promising, but larger controlled studies are needed.

Fourth line therapy – Augmented cystoplasty and urinary diversion

Surgical therapy is done in rare severe cases where all else have failed. These procedures are a major undertaking, associated with significant morbidity and are irreversible(35, 47). Augmentation cystoplasty involves adding a 10-15 cm loop of detubularised small bowel to the wall of the bladder to increase its intraluminal surface. Urinary diversion involves implanting the ureter to an ileal segment and creating a stoma. The complications include dehiscence of anastomotic site with consequent leaks, sepsis, abscess formation and metabolic derangement(10, 35, 48, 50, 90). These procedures are contraindicated in patients who are unable or unwilling to perform life-long intermittent self-catheterization, because of the high likelihood that catheterization will ultimately be required and patients with inflammatory bowel disease (especially Crohn disease), a short or irradiated bowel, severe radiation cystitis, or severe renal insufficiency(35).

CONCLUSION

Overactive bladder is a common problem which has a significant impact on quality of life. The cause of OAB is not yet fully understood and symptoms may not always be apparent. Its assessment involves exclusion of serious disorders and risk factors. Management is initially conservative with behavioral therapy being the key and followed by tailored pharmacological therapy. In patients who are refractory then specialist reassessment and management with invasive therapies such as botulinum injection, tibial nerve stimulation and sacral neuromodulation are warranted. In rare severe cases surgical intervention in the form of augmented cystoplasty and urinary diversion maybe needed. In every step of the management the patient should be fully involved, counselled and understand that a complete cure is rare so as to manage his/her expectations.

REFERENCES

1. Leron E, Weintraub AY, Mastrolia SA, Schwarzman P. Overactive bladder syndrome: evaluation and management. *Current Urology*. 2017;11(3):117-25.
2. Stewart W, Van Rooyen J, Cundiff G, Abrams P, Herzog A, Corey R, et al. Prevalence and burden of overactive bladder in the United States. *World journal of urology*. 2003;20(6):327-36.
3. Abrams P, Blaivas JG, Stanton SL, Andersen JT. Standardisation of terminology of lower urinary tract function. *Neurourology and Urodynamics*. 1988;7(5):403-27.
4. Drake MJ. Do we need a new definition of the overactive bladder syndrome? ICI-RS 2013. *Neurourology and urodynamics*. 2014;33(5):622-4.
5. Haylen BT, De Ridder D, Freeman RM, Swift SE, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourology and Urodynamics: Official Journal of the International Continence Society*. 2010;29(1):4-20.
6. Ramsay S, Bolduc S. Overactive bladder in children. *Canadian Urological Association Journal*. 2017;11(1-2Suppl1):S74.
7. Franco I. Overactive bladder in children. *Nature Reviews Urology*. 2016;13(9):520-32.
8. Al Edwan G, Abdelazim MS, Salhab SE, Jamal YM, Soliman MA. The prevalence of overactive bladder symptoms in women in Algeria, Egypt, Jordan and Lebanon: A cross-sectional population-based survey. *Advances in therapy*. 2021;38(2):1155-67.
9. Meng E, LIN WY, LEE WC, CHUANG YC. Pathophysiology of overactive bladder. *LUTS: Lower Urinary Tract Symptoms*. 2012;4:48-55.
10. Wallace KM, Drake MJ. Overactive bladder. *F1000Research*. 2015;4.
11. Lose G, Griffiths D, Hosker G, Kulseng-Hanssen S, Perucchini D, Schäfer W, et al. Standardisation of urethral pressure measurement: report from the Standardisation Sub-Committee of the International Continence Society. *Neurourology and Urodynamics: Official Journal of the International Continence Society*. 2002;21(3):258-60.
12. Irwin DE, Milsom I, Kopp Z, Abrams P, Cardozo L. Impact of overactive bladder symptoms on employment, social interactions and emotional well-being in six European countries. *BJU international*. 2006;97(1):96-100.
13. Irwin DE, Mungapen L, Milsom I, Kopp Z, Reeves P, Kelleher C. The economic impact of overactive bladder syndrome in six Western countries. *BJU international*. 2009;103(2):202-9.
14. Coyne KS, Sexton CC, Irwin DE, Kopp ZS, Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. *BJU international*. 2008;101(11):1388-95.
15. Lai H, Gardner V, Vetter J, Andriole GL. Correlation between psychological stress levels and the severity of overactive bladder symptoms. *BMC urology*. 2015;15(1):1-7.
16. Kinsey D, Pretorius S, Glover L, Alexander T. The psychological impact of overactive bladder: a systematic review. *Journal of health psychology*. 2016;21(1):69-81.
17. Hu T-W, Wagner TH, Bentkover JD, LeBlanc K, Piantentini A, Stewart WF, et al. Estimated economic costs of overactive bladder in the United States. *Urology*. 2003;61(6):1123-8.
18. Durden E, Walker D, Gray S, Fowler R, Juneau P, Gooch K. The direct and indirect costs associated with overactive bladder within a commercially-insured population in the United States. *Journal of Occupational and Environmental Medicine*. 2018;60(9):847-52.
19. Willis-Gray MG, Dieter AA, Geller EJ. Evaluation and management of overactive bladder: strategies for optimizing care. *Research and Reports in Urology*. 2016;8:113.
20. Lee UJ, Scott VC, Rashid R, Behniwal A, Wein AJ, Maliski SL, et al. Defining and managing overactive bladder: disagreement among the experts. *Urology*. 2013;81(2):257-62.
21. Roosen A, Chapple CR, Dmochowski RR, Fowler CJ, Gratzke C, Roehrborn CG, et al. A refocus on the bladder as the originator of storage lower urinary tract symptoms: a systematic review of the latest literature. *European urology*. 2009;56(5):810-20.
22. Peyronnet B, Mironska E, Chapple C, Cardozo L, Oelke M, Dmochowski R, et al. A comprehensive review of overactive bladder pathophysiology: on the way to tailored treatment. *European urology*. 2019;75(6):988-1000.

23. Kushida N, Fry CH. On the origin of spontaneous activity in the bladder. *BJU international*. 2016;117(6):982-92.
24. Shafik A, Shafik AA, El-Sibai O, Ahmed I. Role of positive urethrovesical feedback in vesical evacuation. The concept of a second micturition reflex: the urethrovesical reflex. *World journal of urology*. 2003;21(3):167-70.
25. SERELS SR, RACKLEY RR, APPELL RA. Surgical treatment for stress urinary incontinence associated with valsalva induced detrusor instability. *The Journal of urology*. 2000;163(3):884-7.
26. Tadic SD, Griffiths D, Schaefer W, Murrin A, Clarkson B, Resnick NM. Brain activity underlying impaired continence control in older women with overactive bladder. *Neurourology and urodynamics*. 2012;31(5):652-8.
27. Apostolidis A, Wagg A, Rahnama'i MS, Panicker JN, Vrijens D, von Gontard A. Is there "brain OAB" and how can we recognize it? International Consultation on Incontinence-Research Society (ICIRS) 2017. *Neurourology and urodynamics*. 2018;37(S4):S38-S45.
28. Chapple CR, Osman NI, Birder L, van Koeveeringe GA, Oelke M, Nitti VW, et al. The underactive bladder: a new clinical concept? *European urology*. 2015;68(3):351-3.
29. Kerdraon J, Peyronnet B, Gamé X, Faton B, Haddad R, Hentzen C, et al. Pathophysiology of detrusor underactivity in the elderly. *Progres en Urologie: Journal de L'association Francaise D'urologie et de la Societe Francaise D'urologie*. 2017;27(7):402-12.
30. Lucas MG, Bosch RJ, Burkhard FC, Cruz F, Madden TB, Nambiar AK, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *European urology*. 2012;62(6):1130-42.
31. Nambiar AK, Bosch R, Cruz F, Lemack GE, Thiruchelvam N, Tubaro A, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *European urology*. 2018;73(4):596-609.
32. Nitti V. Clinical testing for overactive bladder. *Canadian Urological Association Journal*. 2011;5(5 Suppl 2):S137.
33. Millman AL, Cheung DC, Hackett C, Elterman D. Overactive bladder in men: a practical approach. *British Journal of General Practice*. 2018;68(671):298-9.
34. Gratzke C, Bachmann A, Descazeaud A, Drake MJ, Madersbacher S, Mamoulakis C, et al. EAU guidelines on the assessment of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *European urology*. 2015;67(6):1099-109.
35. Scarneci I, Lupu S, Bratu OG, Teodorescu A, Maxim LS, Brinza A, et al. Overactive bladder: A review and update. *Experimental and Therapeutic Medicine*. 2021;22(6):1-8.
36. Cartwright R, Srikrishna S, Cardozo L, Robinson D. Validity and reliability of the patient's perception of intensity of urgency scale in overactive bladder. *BJU international*. 2011;107(10):1612-7.
37. Bright E, Cotterill N, Drake M, Abrams P. Developing and validating the International Consultation on Incontinence Questionnaire bladder diary. *European urology*. 2014;66(2):294-300.
38. Chapple CR, Drake MJ, Van Kerrebroeck P, Cardozo L, Drogendijk T, Klaver M, et al. Total urgency and frequency score as a measure of urgency and frequency in overactive bladder and storage lower urinary tract symptoms. *BJU international*. 2014;113(5):696-703.
39. Milsom I, Kaplan SA, Coyne KS, Sexton CC, Kopp ZS. Effect of bothersome overactive bladder symptoms on health-related quality of life, anxiety, depression, and treatment seeking in the United States: results from EpiLUTS. *Urology*. 2012;80(1):90-6.
40. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019. *The Journal of urology*. 2019;202(3):558-63.
41. Ljungberg B, Albiges L, Bensalah K, Bex A, Giles R, Hora M. EAU guidelines. Edn. presented at the EAU annual congress Amsterdam 2020. *Eur Urol*. 2020;67(5):913-24.
42. Burgio KL. Update on behavioral and physical therapies for incontinence and overactive bladder: the role of pelvic floor muscle training. *Current urology reports*. 2013;14(5):457-64.
43. Osman NI, Chapple CR. The management of overactive bladder syndrome: a review of the European Association of Urology Guidelines. *Clinical Practice*. 2013;10(5):593.
44. Imamura M, Williams K, Wells M, McGrother C. Lifestyle interventions for the treatment of urinary incontinence in adults. *Cochrane Database of Systematic Reviews*. 2015(12).
45. Funada S, Yoshioka T, Luo Y, Sato A, Akamatsu S, Watanabe N. Bladder training for treating overactive bladder in adults. *The Cochrane Database of Systematic Reviews*. 2020;2020(4).
46. Cardozo L. Systematic review of overactive bladder therapy in females. *Canadian Urological Association Journal*. 2011;5(5 Suppl 2):S139.
47. Abboudi H, Fynes MM, Doumouchsis SK. Contemporary therapy for the overactive bladder. *The Obstetrician & Gynaecologist*. 2011;13(2):98-106.
48. Burkhard F, Bosch J, Cruz F, Lemack G, Nambiar A, Thiruchelvam N, et al. EAU guidelines on urinary incontinence in adults 2018. *European Association of Urology Guidelines*. 2018.
49. Burgio KL, Locher JL, Goode PS. Combined behavioral and drug therapy for urge incontinence in older women. *Journal of the American Geriatrics Society*. 2000;48(4):370-4.
50. Araklitis G, Baines G, da Silva AS, Robinson D, Cardozo L. Recent advances in managing overactive bladder. *F1000Research*. 2020;9.
51. Novara G, Galfano A, Secco S, D'Elia C, Cavalleri S, Ficarra V, et al. A systematic review and meta-analysis of randomized controlled trials with antimuscarinic drugs for overactive bladder. *European urology*. 2008;54(4):740-64.

52. Herbison P, Hay-Smith J, Ellis G, Moore K. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. *Bmj*. 2003;326(7394):841.
53. Nabi G, Cody JD, Ellis G, Hay-Smith J, Herbison GP. Anticholinergic drugs versus placebo for overactive bladder syndrome in adults. *Cochrane database of systematic reviews*. 2006(4).
54. Rosenberg MT, Newman DK, Tallman CT, Page SA. Overactive bladder: recognition requires vigilance for symptoms. *Cleveland Clinic journal of medicine*. 2007;74(3):S21.
55. Olshansky B, Ebinger U, Brum J, Egermark M, Viegas A, Rekedal L. Differential pharmacological effects of antimuscarinic drugs on heart rate: a randomized, placebo-controlled, double-blind, crossover study with tolterodine and darifenacin in healthy participants \geq 50 years. *Journal of Cardiovascular Pharmacology and Therapeutics*. 2008;13(4):241-51.
56. Abrams P, Andersson KE, Buccafusco JJ, Chapple C, De Groat WC, Fryer AD, et al. Muscarinic receptors: their distribution and function in body systems, and the implications for treating overactive bladder. *British journal of pharmacology*. 2006;148(5):565-78.
57. Sexton C, Notte S, Maroulis C, Dmochowski R, Cardozo L, Subramanian D, et al. Persistence and adherence in the treatment of overactive bladder syndrome with anticholinergic therapy: a systematic review of the literature. *International journal of clinical practice*. 2011;65(5):567-85.
58. Shamliyan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Benefits and harms of pharmacologic treatment for urinary incontinence in women: a systematic review. *Annals of internal medicine*. 2012;156(12):861-74.
59. Peeker R, Samsioe G, Kowalski J, Andersson A-S, Bergqvist A. A prospective observational study of the effects of treatment with extended-release tolterodine on health-related quality of life of patients suffering overactive bladder syndrome in Sweden. *Scandinavian journal of urology and nephrology*. 2010;44(3):138-46.
60. Gray SL, Anderson ML, Dublin S, Hanlon JT, Hubbard R, Walker R, et al. Cumulative use of strong anticholinergics and incident dementia: a prospective cohort study. *JAMA internal medicine*. 2015;175(3):401-7.
61. Hashim H. Profile of mirabegron in the treatment of overactive bladder: place in therapy. *Drug design, development and therapy*. 2017;11:463.
62. Niitti VW, Rosenberg S, Mitcheson DH, He W, Fakhoury A, Martin NE. Urodynamics and safety of the β 3-adrenoceptor agonist mirabegron in males with lower urinary tract symptoms and bladder outlet obstruction. *The Journal of urology*. 2013;190(4):1320-7.
63. TA290 N. Mirabegron for treating symptoms of overactive bladder. June; 2013.
64. Khullar V, Amarengo G, Angulo JC, Cambronero J, Høye K, Milson I, et al. Efficacy and tolerability of mirabegron, a β 3-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European–Australian phase 3 trial. *European urology*. 2013;63(2):283-95.
65. Wu T, Duan X, Cao C-X, Peng C-D, Bu S-Y, Wang K-J. The role of mirabegron in overactive bladder: a systematic review and meta-analysis. *Urologia internationalis*. 2014;93(3):326-37.
66. Wagg A, Franks B, Ramos B, Berner T. Persistence and adherence with the new beta-3 receptor agonist, mirabegron, versus antimuscarinics in overactive bladder: early experience in Canada. *Canadian Urological Association Journal*. 2015;9(9-10):343.
67. Gibson W, MacDiarmid S, Huang M, Siddiqui E, Stözel M, Choudhury N, et al. Treating overactive bladder in older patients with a combination of mirabegron and solifenacin: a prespecified analysis from the BESIDE study. *European Urology Focus*. 2017;3(6):629-38.
68. Griebing TL, Campbell NL, Mangel J, Staskin D, Herschorn S, Elsouda D, et al. Effect of mirabegron on cognitive function in elderly patients with overactive bladder: MoCA results from a phase 4 randomized, placebo-controlled study (PILLAR). *BMC geriatrics*. 2020;20(1):1-10.
69. Keam SJ. Vibegron: first global approval. *Drugs*. 2018;78(17):1835-9.
70. Yoshida M, Takeda M, Gotoh M, Nagai S, Kurose T. Vibegron, a novel potent and selective β 3-adrenoreceptor agonist, for the treatment of patients with overactive bladder: a randomized, double-blind, placebo-controlled phase 3 study. *European Urology*. 2018;73(5):783-90.
71. Yoshida M, Kakizaki H, Takahashi S, Nagai S, Kurose T. Long-term safety and efficacy of the novel β 3-adrenoreceptor agonist vibegron in Japanese patients with overactive bladder: A phase III prospective study. *International Journal of Urology*. 2018;25(7):668-75.
72. Chen H, Wang F, Yu Z, Zhang Y, Liu C, Dai S, et al. Efficacy of daily low-dose tadalafil for treating overactive bladder: results of a randomized, double-blind, placebo-controlled trial. *Urology*. 2017;100:59-64.
73. Dell'Atti L. Efficacy of Tadalafil once daily versus Fesoterodine in the treatment of overactive bladder in older patients. *Eur Rev Med Pharmacol Sci*. 2015;19(9):1559-63.
74. Mangera A, Andersson K-E, Apostolidis A, Chapple C, Dasgupta P, Giannantoni A, et al. Contemporary management of lower urinary tract disease with botulinum toxin A: a systematic review of botox (onabotulinumtoxinA) and dysport (abobotulinumtoxinA). *European urology*. 2011;60(4):784-95.

75. Cui Y, Zhou X, Zong H, Yan H, Zhang Y. The efficacy and safety of onabotulinumtoxinA in treating idiopathic OAB: a systematic review and meta-analysis. *Neurourology and urodynamics*. 2015;34(5):413-9.
76. Gong Q-Q, Xu Y-Q, Xu J, Ding X-Y, Guo C. Meta-analysis of randomized controlled trials using botulinum toxin A at different dosages for urinary incontinence in patients with overactive bladder. *Frontiers in pharmacology*. 2020;10:1618.
77. Bhide AA, Tailor V, Fernando R, Khullar V, Digesu GA. Posterior tibial nerve stimulation for overactive bladder—techniques and efficacy. *International urogynecology journal*. 2020;31(5):865-70.
78. Ridout A, Yoong W. Tibial nerve stimulation for overactive bladder syndrome unresponsive to medical therapy. *Journal of Obstetrics and Gynaecology*. 2010;30(2):111-4.
79. MacDiarmid SA, Peters KM, Shobeiri SA, Wooldridge LS, Rovner ES, Leong FC, et al. Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. *The Journal of urology*. 2010;183(1):234-40.
80. Yamashiro J, de Riese W, de Riese C. New implantable tibial nerve stimulation devices: review of published clinical results in comparison to established neuromodulation devices. *Research and Reports in Urology*. 2019;11:351.
81. MacDiarmid S, Staskin DR, Lucente V, Kaaki B, English S, Gilling P, et al. Feasibility of a fully implanted, nickel sized and shaped tibial nerve stimulator for the treatment of overactive bladder syndrome with urgency urinary incontinence. *The Journal of Urology*. 2019;201(5):967-72.
82. Michalak JR, Kim S, Funk JT, Twiss CO. Sacral neuromodulation for overactive bladder. *Adult and Pediatric Neuromodulation*: Springer; 2018. p. 25-46.
83. Marcelissen TA, Leong RK, de Bie RA, van Kerrebroeck PE, de Wachter SG. Long-term results of sacral neuromodulation with the tined lead procedure. *The Journal of urology*. 2010;184(5):1997-2000.
84. Medtronic I. MRI guidelines for InterStim therapy. 2017.
85. Cohn JA, Kowalik CG, Kaufman MR, Reynolds WS, Milam DF, Dmochowski RR. Evaluation of the axonics modulation technologies sacral neuromodulation system for the treatment of urinary and fecal dysfunction. *Expert Review of Medical Devices*. 2017;14(1):3-14.
86. Baron M, Perrouin-Verbe MA, Lacombe S, Paret F, Le Normand L, Cornu JN. Efficacy and tolerance of botulinum toxin injections after sacral nerve stimulation failure for idiopathic overactive bladder. *Neurourology and Urodynamics*. 2020;39(3):1012-9.
87. Tu LM, De Wachter S, Robert M, Dmochowski RR, Miller LE, Everaert K. Initial clinical experience with selective bladder denervation for refractory overactive bladder. *Neurourology and Urodynamics*. 2019;38(2):644-52.
88. Robinson D, Flint R, Veit-Rubin N, Araklitis G, Cardozo L. Is there enough evidence to justify the use of laser and other thermal therapies in female lower urinary tract dysfunction? Report from the ICI-RS 2019. *Neurourology and Urodynamics*. 2020;39:S140-S7.
89. Perino A, Cucinella G, Gugliotta G, Saitta S, Polito S, Adile B, et al. Is vaginal fractional CO. *European Review for Medical and Pharmacological Sciences*. 2016;20:2491-7.
90. Veeratterapillay R, Thorpe AC, Harding C. Augmentation cystoplasty: contemporary indications, techniques and complications. *Indian Journal of Urology: IJU: Journal of the Urological Society of India*. 2013;29(4):322.

Challenges in management of bladder neurofibroma: A case report

**James A. Ikol¹, Ernest N. Kimani², Jeremiah Njogu², Brigid Monda³,
Wairimu Waweru⁴**

¹ Urology Unit, Department of Surgery, Kenyatta National Hospital, Kenya

² Department of Surgery, University of Nairobi, Kenya

³ Department of Obstetrics and Gynecology, Kenyatta University

⁴ Department of Pathology, The Nairobi Hospital

Corresponding Author: Ernest N. Kimani. Email: drenk10@gmail.com

ABSTRACT

Neurofibroma is a tumor of the peripheral nerve sheath. Its occurrence in the bladder is rare. With less than 100 cases reported in literature, there is minimal data to guide treatment and follow-up. In this review, a case report of bladder neurofibroma is discussed.

Key words: Bladder Neurofibroma, uterine leiomyoma,

INTRODUCTION

Neurofibroma is the most common benign nerve sheath tumor arising from the connective tissues of the peripheral nerve sheaths (1). Its occurrence in the bladder is rare with approximately 70 cases reported in literature. Males are more affected than females in a ratio of 3:1 (2). Urogenital involvement arises from pelvic and bladder nerves and the prostatic plexus. Urinary bladder is the most commonly affected organ in the urinary tract.

The patient can present with hematuria and lower urinary tract symptoms. Other presentation symptoms include fullness in the lower abdomen, flank pains or incontinence. (3).

The condition has been associated with Neurofibromatosis type I. However, sporadic occurrence without any association with NF-1 has been reported. Bladder neurofibroma in the background of uterine leiomyoma has not been described in literature.

Investigations in such a condition would warrant use of imaging, transurethral resection of bladder tumor (TURBT) (4) and use of immunohistochemistry to characterize the nature of the lesion (5).

In this review we discuss the management of a patient who presents with bladder neurofibroma and uterine leiomyoma.

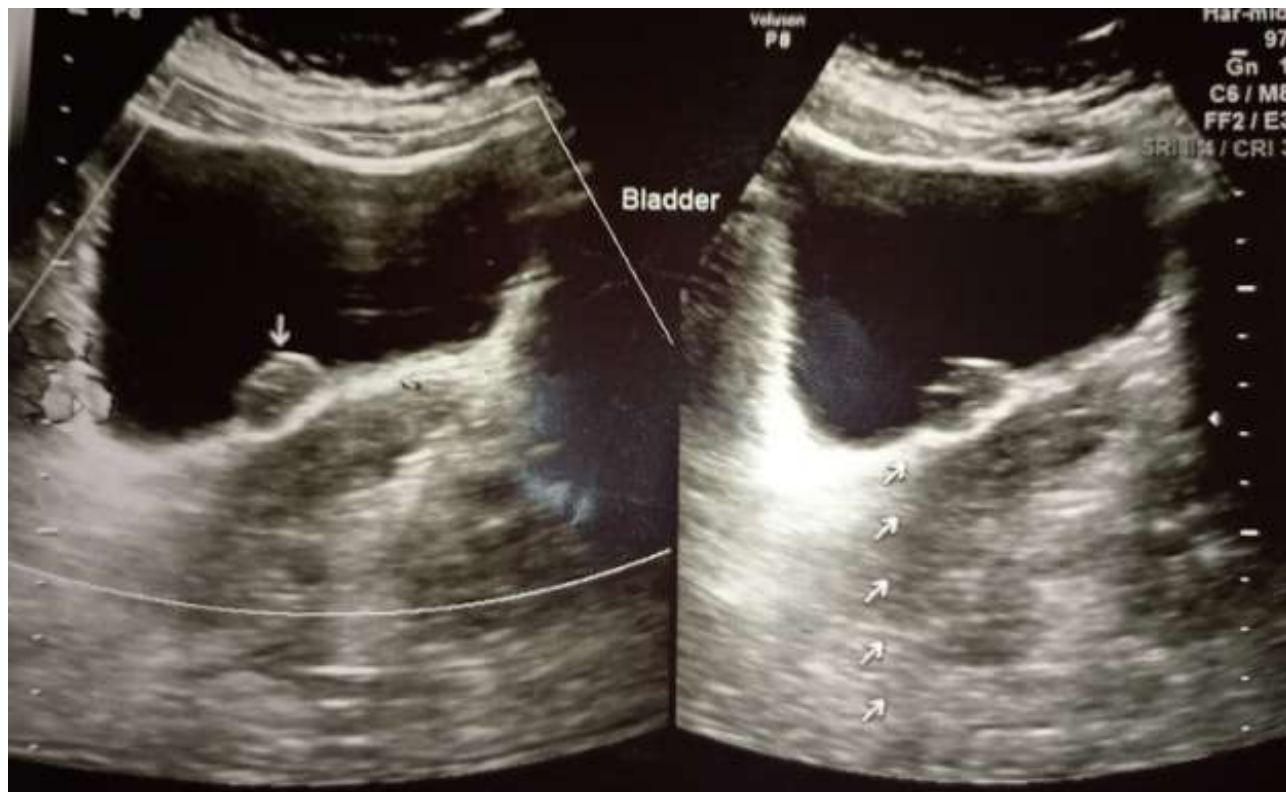
CLINICAL SUMMARY

A female patient, 50 years old, presents with abnormal vaginal/uterine bleeding and perimenopausal symptoms of hot flushes. She has no hematuria or lower urinary tract symptoms (LUTS).

On clinical examination, the skin exam did not show café au lait lesions characteristic of NF-1. She is a business lady, married with 3 children. She is a non-smoker, and has never been exposed to industrial chemicals.

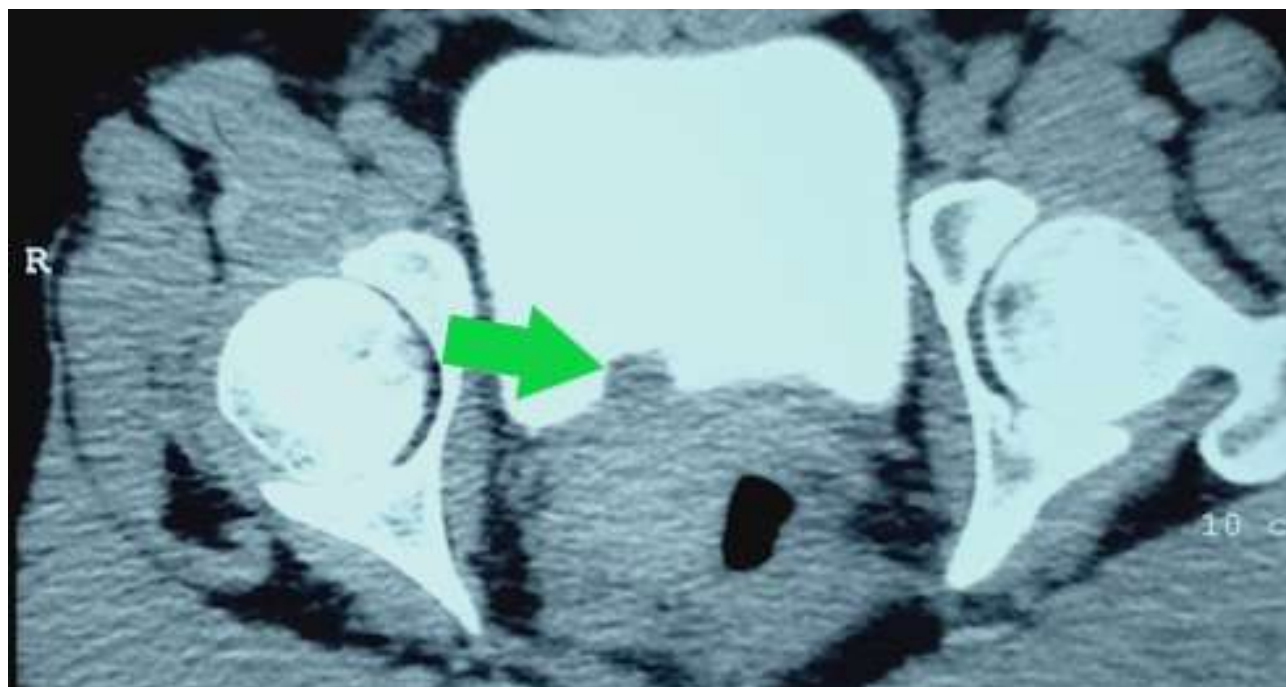
Ultrasound imaging findings demonstrate multiple uterine fibroids, largest 3.2 cm. and hypovascular. Urinary bladder imaging demonstrates an incidental finding of urinary bladder polypoid mass measuring 20 * 12 mm in the right postero-lateral bladder wall. (Figure 1)

Figure 1: **Solid mass demonstrated within the bladder (White arrow)**



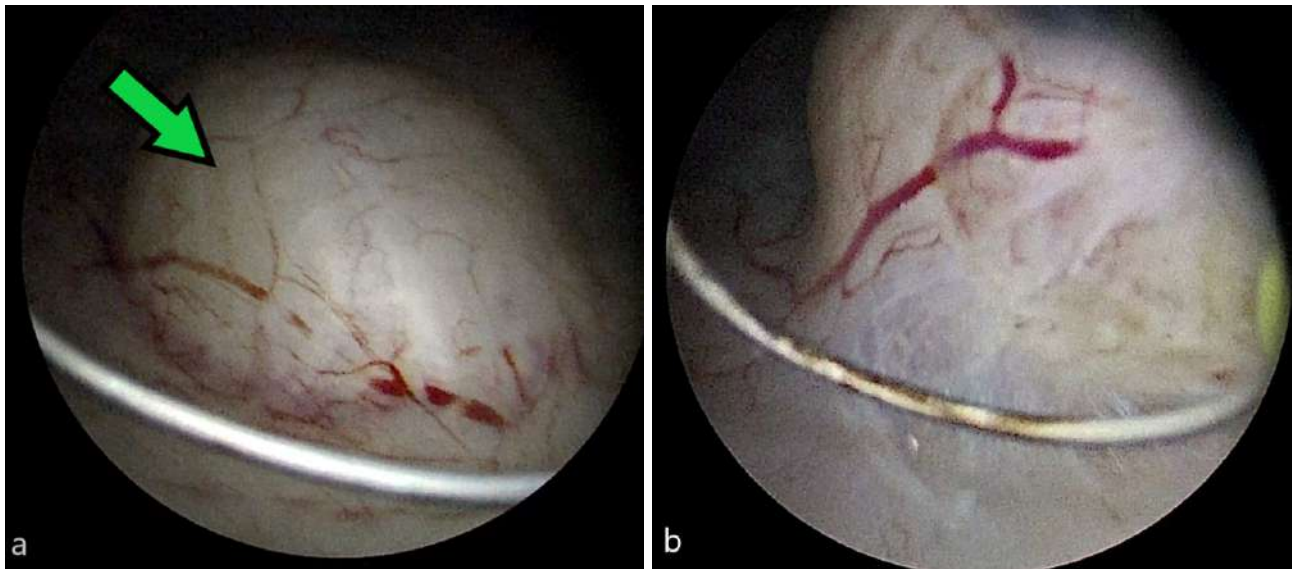
CT Urogram shows normal upper tract. However, a non-enhancing sessile mass measuring 14 * 14 mm is demonstrated in the posterior bladder wall. (Figure 2)

Figure 2: **A non-enhancing sessile mass in the posterior bladder wall on CT scan imaging.**



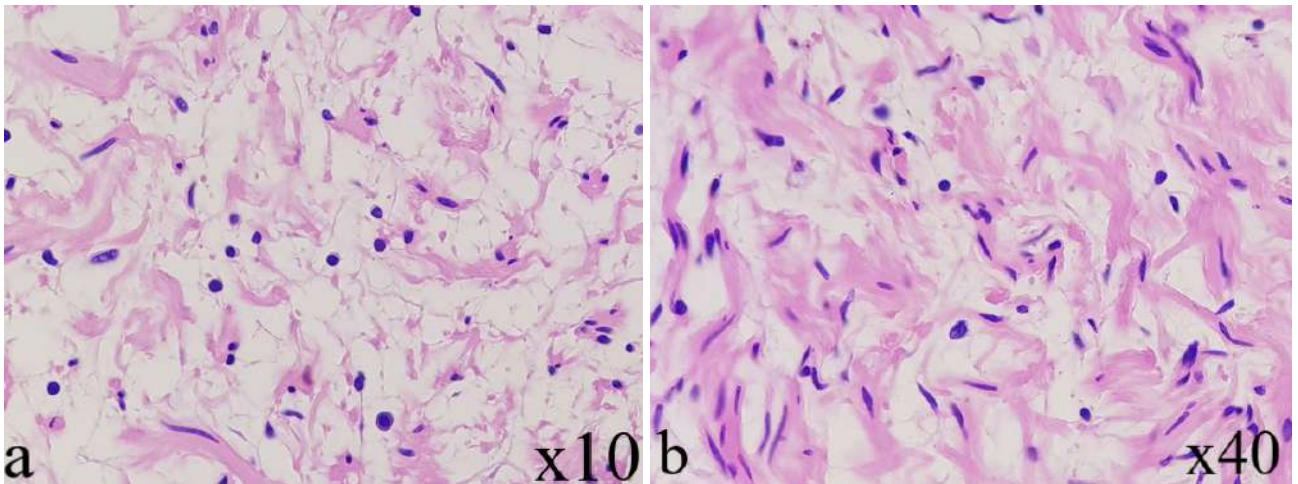
She underwent cystoscopy examination and TURBT where enucleation of the mass was performed. (Figure 3)

Figure 3: Cystoscopy findings of the mass demonstrate a sessile mass (a) in the right posterior wall of the bladder. Figure (b) demonstrates the enucleation of the mass.



Histologically, there was bladder wall tissue with a nodular tumor, composed of sheets of cells with spindle nuclei and collagenous stroma. There was no necrosis. Final diagnosis urinary bladder peripheral nerve sheath tumor characteristic of a neurofibroma (Figure 4).

Figure 4: Histological appearance of the bladder mass consistent with a peripheral nerve sheath tumor, neurofibroma. Cells with spindle nuclei and collagenous stroma are seen. Figure (a) at x10 magnification, (b) at x40 magnification.



DISCUSSION

Neurofibroma of the bladder is a rare tumor occurring with an incidence of less than 0.1% of all bladder tumors. There are less than 100 hundred cases reported in literature with sporadic cases being even more rare. Reports describe a higher occurrence in males than females with a ratio of 3:1 (2).

In this case, the patient was a 50 year old female. Literature describes a varied age presentation of patients with neurofibroma of the bladder ranging from 7 – 54 years (Table 1).

Patients commonly present with hematuria, storage or voiding LUTS, recurrent UTIs, or pelvic mass. Acute urine retention has been reported as a mode of presentation in one patient with a mass growing around the bladder neck (6). However, the presentation in this case was an incidental finding. Similar presentation has been reported by Bryce et al., 2020 (3).

A Kidney-Ureter-Bladder (KUB) ultrasound and a KUB computed tomography (CT) scan are routinely performed as a work up for the mass. Neurofibromas are mostly benign lesions and metastatic work up is not performed routinely at presentation. Further investigation includes a diagnostic cystoscopy and a TURBT. Transurethral resection is mostly employed in treatment. However, partial and complete cystectomy have been reported in some cases (5). Histopathological examination demonstrates a spindle cell neoplasm. Histopathological subtypes can include localized, diffuse, or plexiform. Wang et al., 2008 describes 3 cases of diffuse type with 2 cases having the plexiform type (7).

Immunohistochemistry is advised to further characterize the mass. Neurofibromas stain positive for S-100 for Schwann cells in 50% of the cases. Other immunohistochemical markers that have been utilized include CD34, EMA, myelin basic protein, neurofilament protein and acid mucopolysaccharides (1,4). Genetic screening can be performed to assess the association with NF-1. The patient in this case did not have a family history of neurofibromatosis. Occurrence of the condition in the background of uterine fibroids raises questions about an association between the two. Wang et al., 2008 in a report of 8 cases of neurofibroma of the bladder reports of an occurrence of similar lesions in the uterus (7).

Neurofibroma are largely benign lesions and malignant transformation rarely occurs. However, some authors report that it can occur in upto 10% of the cases for the bladder neoplasms and upto 30% for neoplasms occurring in other sites. Follow-up is warranted to monitor local recurrence or progression (3). However, the follow-up schedule is not defined in literature. In the four patients followed up by Cheng et al for 9.6 years, no malignant transformation was reported (5).

CONCLUSION

Neurofibroma of the bladder is a rare condition. Minimal data is available on the management protocol. The current management pathway mirrors that of other bladder tumors. Standardization of treatment is difficult due to rarity of cases. Further studies would be needed to inform on investigation, treatment and follow-up pathways of patients presenting with the condition.

ACKNOWLEDGEMENT

Authors contributions: James Ikol conceptualized, provided materials, compiled and critically appraised the manuscript. Ernest Kimani and Jeremiah Warutere compiled and critically appraised the data. Brigid Monda and Wairimu Waweru provided materials and critically appraised the manuscript. All authors edited and approved the final version.

CONFLICT OF INTEREST

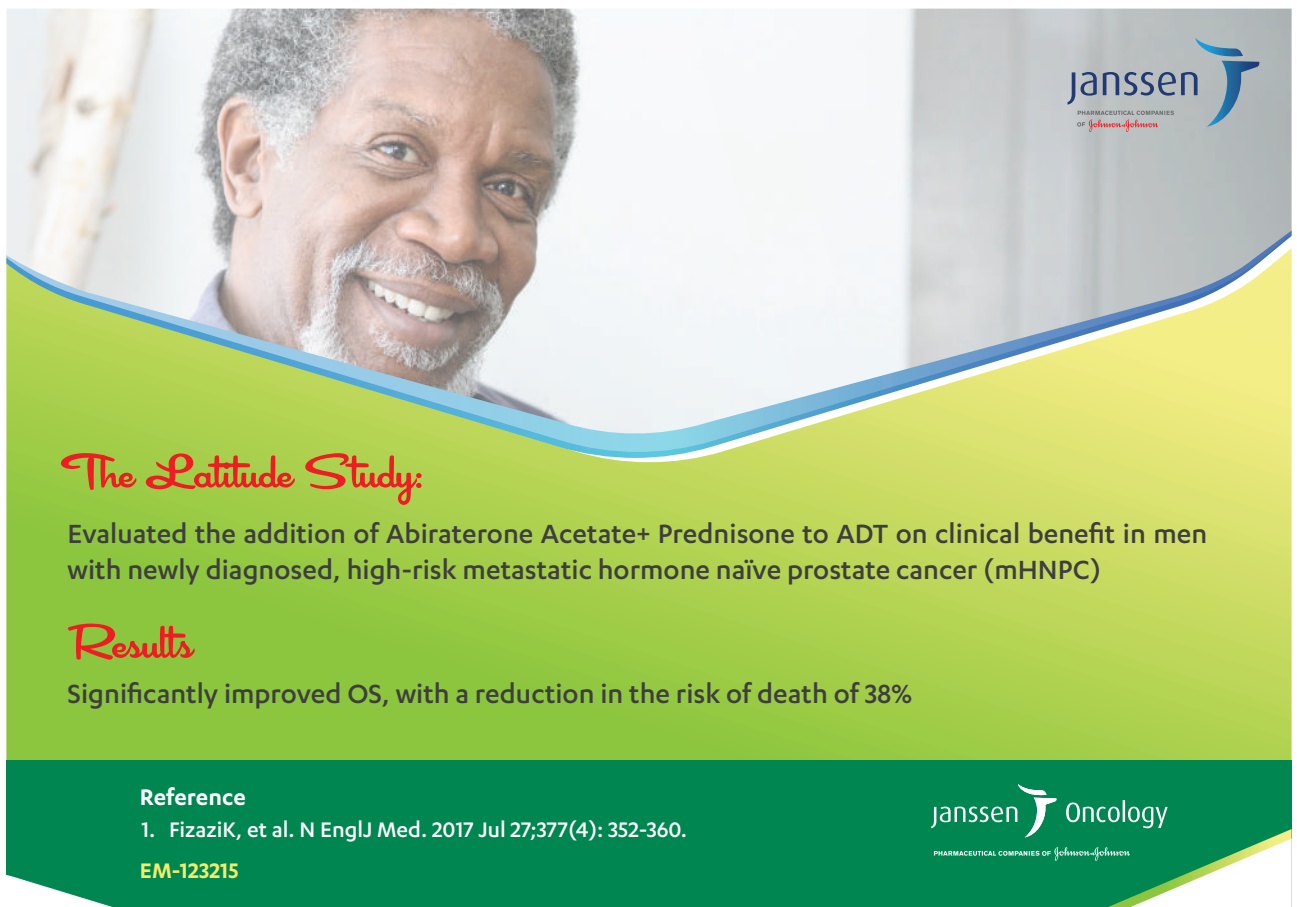
None

REFERENCES

1. Messersmith L, Krauland K. Neurofibroma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 [cited 2023 Jan 18]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK539707/>
2. Cabrera Castillo PM, Alonso y Gregorio S, Cansino Alcaide JR, Aguilera Basan A, De La Peña Barthel JJ. [Bladder neurofibroma: case report and bibliographic review]. *Arch Esp Urol*. 2006 Nov;59(9):899–901.
3. Baugh B, Stencil M, Patel A, Hale N. An isolated case of an incidentally discovered neurofibroma of the urinary bladder. *Urol Case Rep*. 2020 Sep 1;32:101215.
4. Umakanthan S, Naik R, Bukelo MM, Rai S, Prabhu L. Primary Bladder Neurofibroma: A Rare Case with Clinical Implications and Diagnostic Challenges. *J Clin Diagn Res JCDR*. 2015 Sep;9(9):ED05–6.
5. Cheng L, Scheithauer BW, Leibovich BC, Ramnani DM, Cheville JC, Bostwick DG. Neurofibroma of the urinary bladder. *Cancer*. 1999 Aug 1;86(3):505–13.
6. Costa-Martínez MA, Prieto Vita M, Garcés Proaño LE, Carro Rubias C, Ortiz Gorraiz MÁ, De Nova Sánchez E. Neurofibromas in the urogenital system: Report of two cases and literature review. *Arch Esp Urol*. 2017 Nov;70(9):796–9.
7. Wang W, Montgomery E, Epstein JI. Benign nerve sheath tumors on urinary bladder biopsy. *Am J Surg Pathol*. 2008 Jun;32(6):907–12.

Table 1: Patient Characteristics in neurofibroma of the bladder

Study and year	Number of patients	Age	Sex	Presenting complains	Associations	Outcome
Cheng et al., 1999	4	17* (7 - 28)	2 males 2 females	Hematuria (1); Storage luts (2); Pelvic mass (1)	4/4 NF-1	Partial cystectomy (1); Complete cystectomy (1)
Pedro et al., 2006	1	45	Female	Voiding LUTS & Recurrent UTI	Sporadic	NAD
Wang et al., 2008	8		5 females 3 males	Recurrent UTI (6), Hematuria (3), Storage Luts (3)	3/7 – neurofibromas in skin, uterus, mesentry, ureter, 1/7 – stigmata of NF-1	NAD
Duminda et al., 2014	1	54	Female	Obstructed defecation, perineal hernia	NF-1	NAD
Srinkanth et al., 2015	1	52	Male	Hematuria; Storage luts; Pelvic mass	Sporadic	NAD
Maria et al., 2017	1	46	Male	Obstructive LUTs; Acute urine retention	NF-1	NAD
Bryce et al., 2020	1	19	Male	Incidental	Sporadic	NAD



The Latitude Study:
Evaluated the addition of Abiraterone Acetate+ Prednisone to ADT on clinical benefit in men with newly diagnosed, high-risk metastatic hormone naïve prostate cancer (mHNPC)

Results
Significantly improved OS, with a reduction in the risk of death of 38%

Reference
1. FizaziK, et al. N Engl J Med. 2017 Jul 27;377(4): 352-360.
EM-123215

janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Orthotopic renal transplantation on splenic vessels: A case report

**Dr. Aideed Kahie¹, Dr. Abdirashid A Mohamed¹,
Dr. Hussein Bagha³, Dr. J C Munene⁴,
Dr. Ahmed Twahir⁵**

Affiliations:

¹ Kaatun Urology & Male Executive Clinics, Parklands, Nairobi

² Head of Internal Medicine & Nephrology, M P Shah Hospital, Nairobi Corresponding author

³ Former Head of Surgery, Nairobi Hospital, Nairobi. Passed on November, 2022.

⁴ Director, Parklands Kidney Centre and Chairman, Transplant Committee

Corresponding Author: Dr. Aideed Kahie. Email: aideed@kaatun.com

ABSTRACT

Kidney transplant is the treatment option for patients with end-stage renal disease. The standard surgical technique involves using recipient iliac vessels for anastomosis. However, thrombosis of these vessels presents an intraoperative challenge, and alternative anastomotic sites need to be sought. Here we present the case of a patient with iliac vessel thrombosis who underwent orthotopic renal transplantation on splenic vessels.

BACKGROUND

There are several treatment options for ESRD, and kidney transplant (KTx) is the preferred option as it is associated with lower morbidity and mortality compared to others. The standard surgical technique for a kidney transplant is to anastomose renal vessels to recipient iliac vessels. However, one can sometimes not use these vessels due to either thrombosis, pseudoaneurysms, or aberrant anatomy. This thrombosis is a sequela of repeated catheterization for hemodialysis or infection of the catheters (1).

These lesions are commonly noted preoperatively with good imaging, but there are cases where the discovery is made intraoperatively. In such instances, an alternative site for renal graft outflow, such as the common iliac, aorta, IVC, native renal vessels, splenic vessels, and gonadal veins, is used. Here we present a case where the splenic vessels were utilized for revascularization after splenectomy. See Figure 1.

We present a case of a 38-year-old male with ESRD for sixteen months managed on hemodialysis. He has had interval bilateral femoral access causing thrombosis extending to the inferior vena cava. He was admitted on 16th October 2022 with a creatinine of 940umol/l and discharged after seven days, having had the procedure with a creatinine of 144umol/l. During the last visit on 23rd January 2023, creatinine had further fallen to 122umol/l. See Table 1. Intraoperatively, there were challenges in positioning the graft kidney, and we tacked under the transverse colon at the splenic flexure. See Figure 2.

Table 1: Creatinine levels before and after transplant

Date	16/10/2022	23/10/2022	23/01/2023
Creatinine (umol/l)	940	144	122

Figure 1: An illustration showing end-to-end reno-splenic vessel anastomosis and ureteroureterostomy

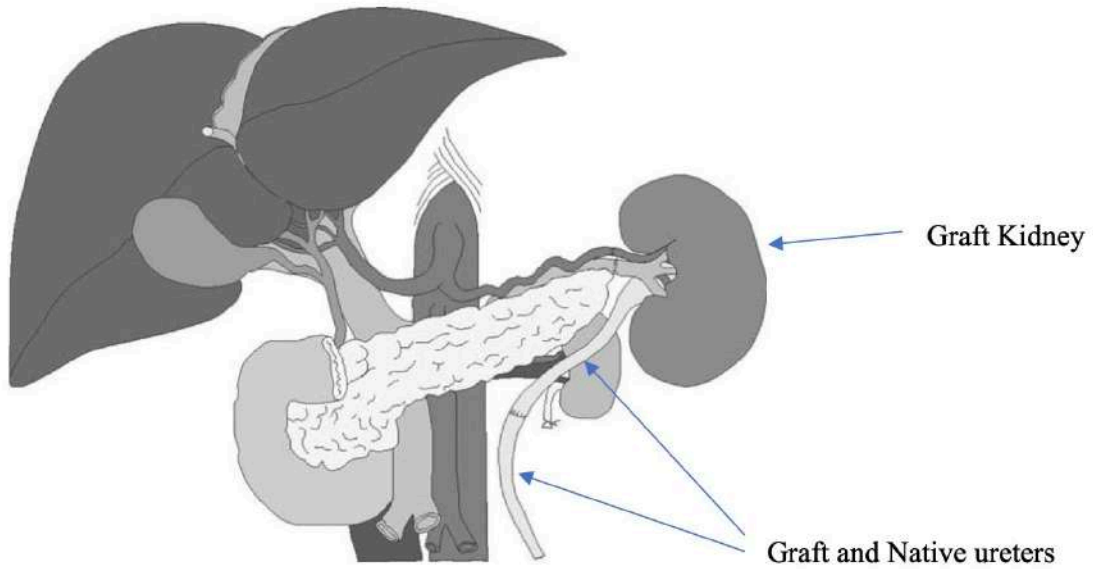
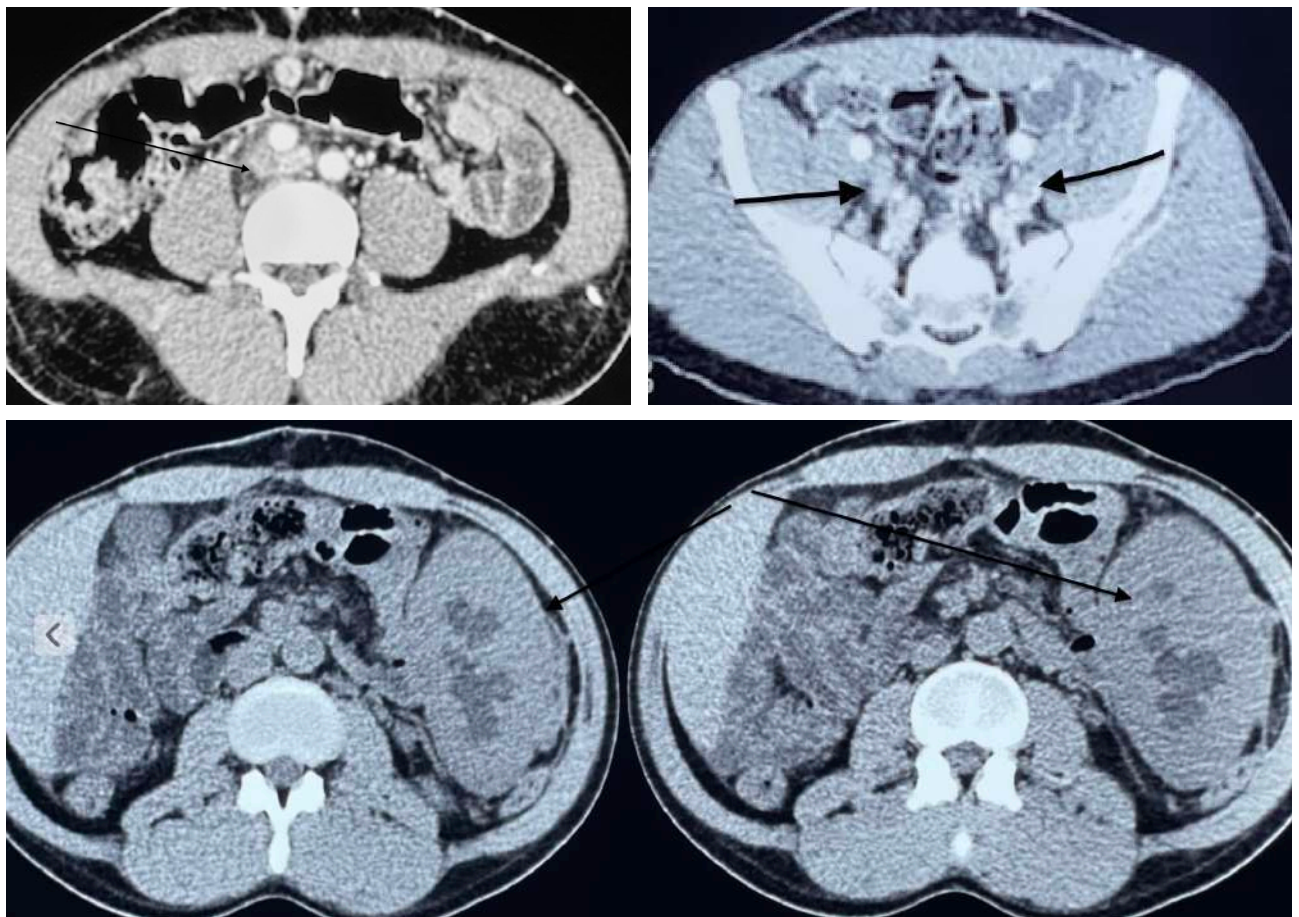


Figure 2: CT scans showing thrombosed IVC at the bifurcation and at common iliac veins, and graft in the left upper abdomen (at splenic flexure)



DISCUSSION

Kidney transplant is the primary therapy for patients with ESRD and has been demonstrated to have low morbidity and mortality compared to other therapies. The anastomosis of the recipient's vessels to native vessels is usually done to iliac vessels. However, there are cases where this is not possible due to either thrombosis of the vessels or congenital anomalies(1). The iliac vein thrombosis may be found in patients with end-stage renal disease (ESRD) on hemodialysis with multiple vascular interventions done while awaiting renal transplant, those with hypercoagulable states, or those with previous renal transplantation. These cases should be identified preoperatively with appropriate imaging of the vasculature. In emergency transplant cases, e.g., cadaveric transplant, thrombosis will be identified intraoperatively in most cases.

The alternative locations for reconstruction in these instances are to use the native renal vein after nephrectomy, systemic or portal venous system. The systemic sites include the inferior vena cava (IVC) (both infra-renal and infra-hepatic IVC), and gonadal vessels (1, 2). Utilization of systemic circulation has been demonstrated by Pirenne et al. (3) and Martinez -Urrutia et al (4), who reported 4 cases of pediatric iliac and distal IVC thrombosis and end-to-end anastomosis was done to the renal vein. This involved nephrectomy and anastomosis to the recipient renal vein. The limitation of this technique being the nephrectomy prolongs the procedure time and leads to prolonged ischemia time of the graft. Wong et al. (5) and Eneriz-Wiemer et al. (6) reported successful anastomosis of the donor's vein to a dilated left ovarian vein draining into the left renal vein. While de Cerqueira et al. reported 5 cases of good clinical outcomes after the use of gonadal vein for anastomosis (7).

The porto-venous system is used in the setting of iliac and caval thrombosis, and the sites used include the splenic vein, inferior mesenteric vein, superior mesenteric vein (SMV), and portal vein (1). The SMV is a good outflow site as it has a favorable caliber and decreased risk of thrombosis and torsion, but its dissection is technically challenging, especially in the setting of porto-systemic collateralization seen in caval thrombosis (1).

The splenic location is more feasible as it is technically easier to access, involves less dissection compared to other sites, and as well provides both inflow and outflow to the graft in the same location (1, 2). This can involve either splenectomy or splenic sparing procedure (8). However, challenges may

occur in these operations during the urinary reconstruction. This is due to the length of the graft ureter, and it may not be long enough to reach the bladder. The options of reconstruction in such instances are end-to-end anastomosis to the native ureter (as done in our patient. see Figure 1) or, if the native ureter is not available, then extensive mobilization of adjacent pancreatic body and tail in order to place the renal graft in an inferior location to allow for ureteroneocystostomy.

CONCLUSION

Kidney transplant is an effective therapy for ESRD. However, in patients with iliac and caval thrombosis, alternative sites for vascular reconstruction are available, and a splenic vein is a viable, feasible, and easily accessible option.

REFERENCES

1. Spaggiari M, Di Bella C, Di Cocco P, Furno S, Benedetti E, Tzvetanov I, editors. Emergency kidney transplantation in recipients with ilio-caval thrombosis using splenic vessel anastomosis after splenectomy: a case series. *Transplantation Proceedings*; 2018: Elsevier.
2. Marinov M, Di Domenico S, Mastrodomenico P, Jacobsen G, Sankary H, Testa G, et al. Use of the splenic vessels for an ABO incompatible renal transplant in a patient with thrombosis of the vena cava. *American Journal of Transplantation*. 2005;5(9):2336-7.
3. Pirenne J, Benedetti E, Kashtan C, Lledo-Garcia E, Hakim N, Schroeder C, et al. Kidney transplantation in the absence of the infrarenal vena cava. 1995.
4. Martinez-Urrutia MJ, Lopez Pereira P, Avila Ramirez L, Lobato Romera R, Alonso Melgar A, Jaureguizar Monereo E, et al. Renal transplant in children with previous inferior vena cava thrombosis. *Pediatric transplantation*. 2007;11(4):419-21.
5. Wong V, Baker R, Patel J, Menon K, Ahmad N. Renal transplantation to the ovarian vein: a case report. *American Journal of Transplantation*. 2008;8(5):1064-6.
6. Eneriz-Wiemer M, Sarwal M, Donovan D, Costaglio C, Concepción W, Salvatierra Jr O. Successful renal transplantation in high-risk small children with a completely thrombosed inferior vena cava. *Transplantation*. 2006;82(9):1148-52.
7. de Cerqueira J, de Oliveira C, Silva B, Santos L, Fernandes A, Fernandes P, et al., editors. Kidney transplantation using gonadal vein for venous anastomosis in patients with iliac vein thrombosis or stenosis: a series of cases. *Transplantation Proceedings*; 2017: Elsevier.
8. Shapira Z, Yussim A, Savir A, Frisher S, Kaikov Y, Zaizov R, et al. The use of the portal system for the transplantation of a neonate kidney graft in a child with Wilms' tumor. *Journal of pediatric surgery*. 1985;20(5):549-51.

Urethral Injury from an Impacted Urethral Stone: A case report

Mustafa O¹, Ismail H², Jumbi T², Osawa F¹.

¹Department of Surgery, University of Nairobi

² Division of surgery, Kenyatta National Hospital

ABSTRACT

Background: Although less prevalent than in adults, urethral stones are not uncommon in pediatric urology. Direct injury to the urinary tract can occur from impacted stones. However inadequate history from the patients and caregivers and a low index of suspicion among clinicians makes the diagnosis of such injuries difficult. Additionally, the limited availability of endourological equipment suited for the management of such urinary stones in small children provides a challenging experience for paediatric urologists when dealing with this disease. Therefore, deployment of innovative management strategies is sometimes necessary.

Method: A case report of a 4-year-old boy with an impacted penile urethral stone who presented with acute urine retention at a teaching and referral hospital in Nairobi, Kenya.

Conclusion: In low middle-income countries with deficient paediatric endourological equipment, innovative management options may need to be employed while managing impacted urinary stones. In this case, retrograde manipulation of urethral stones to the bladder under vision and subsequent open cystolithotomy provided an alternative to minimal invasive procedures.

Keywords: Urethra, stone, urolithiasis

INTRODUCTION

Bladder outlet obstruction is a frequent occurrence in paediatric patients and are mainly due to congenital causes. The most common congenital cause is posterior urethral valves, however, neural tube abnormalities such as neurogenic bladder are sometimes the reason for such obstruction. Bladder bowel syndrome is non congenital common cause of acute urine retention in children. Iatrogenic injuries from urethral catheterization as well as traumatic urethral injuries after pelvic fractures are some of the other causes of acute urine retention (9). Urinary stones though rare in paediatric population can cause obstruction of the bladder outflow, particularly in cases of bladder and urethral stones.

Stones within the urethra presents difficulties with diagnosis and definitive management particularly in low- and middle-income nations where endourologic equipment and diagnostic facilities are not easily accessible. Several treatment options for urethral stones have been mentioned in literature, includ-

ing urethrotomy and meatotomy for urethral meatus stones (5). Transurethral holmium laser ablation is also used to manage impacted urethral stones (8). In our case report, we present a four-year-old boy who presented with acute urine retention which was initially suspected to be due to traumatic urethral injury but turned out to be an impacted urethral stone causing bladder outlet obstruction. In addition, the patient also presented with swelling of the base of the penis and scrotum that was as a result of urinary extravasation.

CASE PRESENTATION

A four-year-old boy presented to the accident and emergency unit with a three-day history of straining while passing urine, dribbling and abdominal pain. He then developed complete failure to pass urine, scrotal swelling and penile swelling a day prior to presentation. The symptoms began after one of his friends forcefully pulled his penile shaft.

There was no history of urethral instrumentation, hematuria, flank pain, fever or urinary frequency. His bowel movements were reported to have been normal. The perinatal and past medical history were unremarkable other than being a known asthmatic on salbutamol inhaler and with the symptoms well controlled.

At the Emergency Department (E.D.), he was found to be in pain, tachycardic with a H.R. of 121 bpm, afebrile at 36.7 degrees Celsius and saturating at 97% on room air. There was a suprapubic abdominal distension up to the level of umbilicus that was tender and dull to percussion. There was scrotal edema that was transilluminable (figure1) Both testes were palpable in the scrotum and there was no tenderness. The penis was edematous and tender but no bruising or hematomas were visible. There was no blood at the urethral meatus. The rest of the systemic exam was normal.

Routine labs were drawn and a total blood count revealed a white cell count of 11.32×10^9 , Hb 12.7gm/dl and a platelet count of 399×10^9 . The renal function tests revealed a urea of 6.02mmol/l, creatinine of 94 μ mol/l and all electrolytes were within normal ranges. Liver function tests were unremarkable.

A KUB ultrasound ordered revealed normal upper tracts and a markedly distended bladder with smooth wall outlines and no features of posterior urethral valves or stones. A scrotal ultrasound revealed normal testes with normal size, shape and vascularity. Marked edema was noted bilaterally.

Figure 1



An initial impression of traumatic urethral injury was made and a 18fr IV cannula inserted at the dome of the bladder to provide temporary drainage (Figure 1). Patient was started on broad spectrum IV antibiotics, analgesia and prepared for emergency urethrocytoscopy. Intraoperatively, a urethral stone was identified at the penile urethra. The stone was approximately 1.5cm in size and was completely obstructing the lumen (Figure 2, 3).

Figure 2

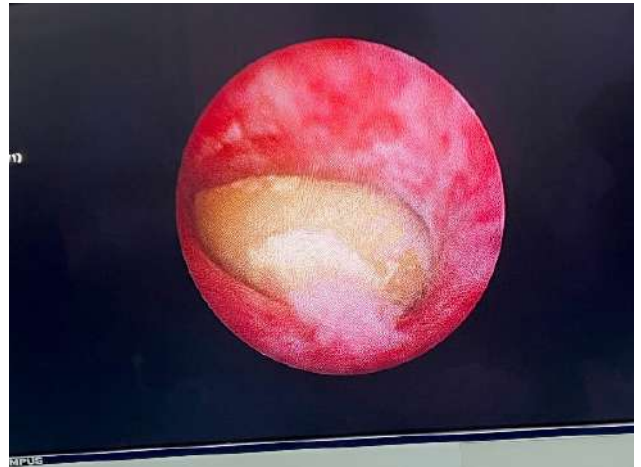
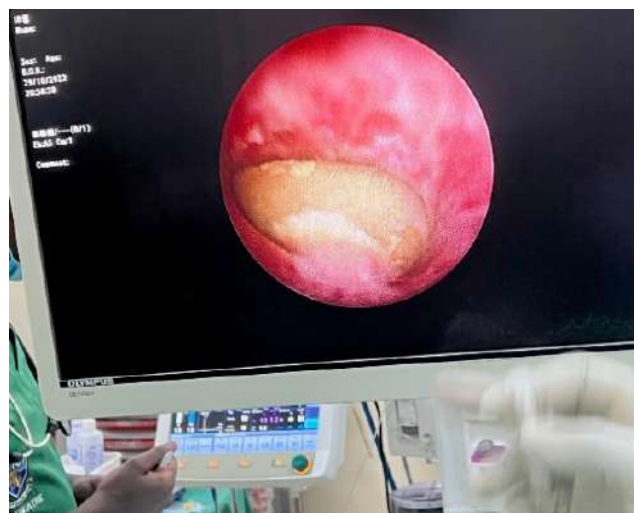


Figure 3



Retrograde manipulation of the stone back to the bladder under direct vision was done. The entire urethra was visualized, no posterior urethral valves, strictures or any injuries noted. The bladder had good capacity, normal mucosa, normal ureteral orifices and no other calculi were noted. An 8FR silicone urethral catheter was inserted (Figure 4) and an open cystolithotomy was performed. A 1.5cm brown calculus was extracted from the bladder and sent for analysis (Figure 6,7). The bladder was closed in two layers and the urethral catheter maintained for 10 days.

Figure 4



Figure 6

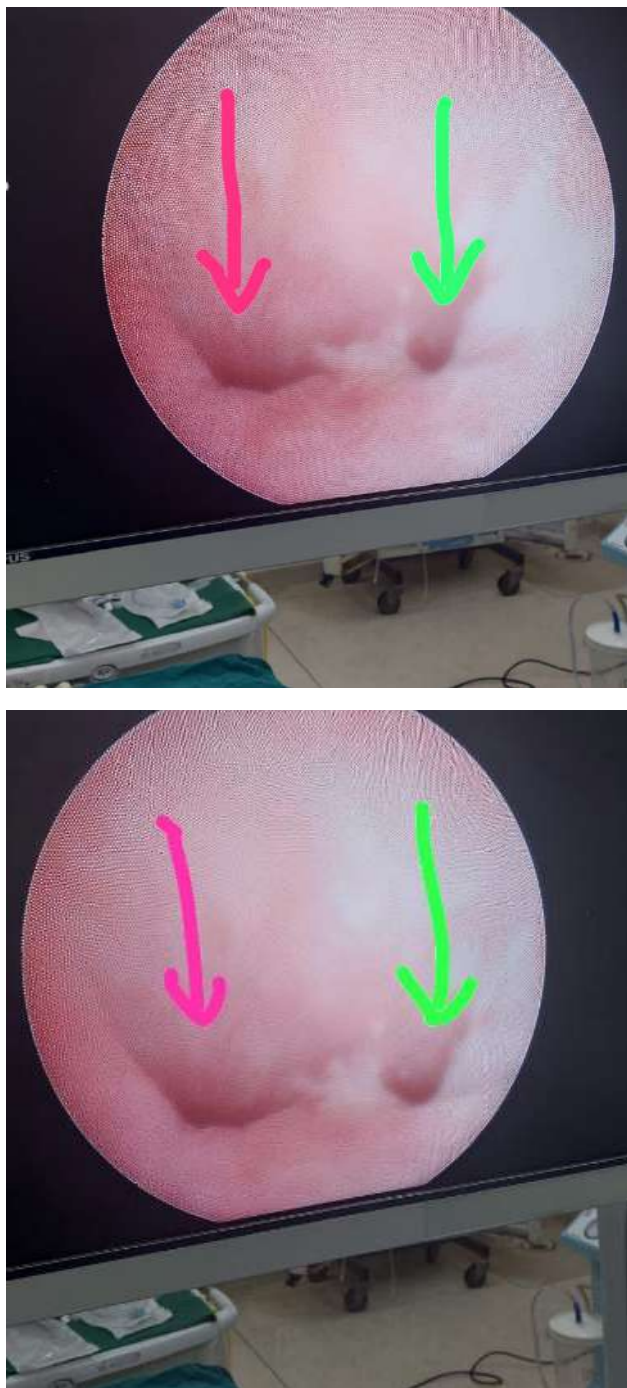


Figure 5



Post operative period was uneventful. Within three days, the penile and scrotal edema subsided. A urine culture report was negative. He completed a five-day course of multimodal analgesia and broad spectrum IV antibiotics. Upon removal of urethral catheter on the tenth post-operative day, it was noted that there was extravasation of urine into the scrotum. A repeat cystoscopy revealed a urethral injury at the point which the urethral stone had been impacted (figure 7,8). A urethral catheter was re- inserted under vision without any further disruption of the injured urethra and left in situ for 21 days. Subsequently he was able to micturate well upon removal of the catheter

Figure 4: Green arrow urethral injury, red arrow: urethra



The retrieved stone composition was confirmed as 50% calcium oxalate monohydrate and 50% ammonium urate. No further metabolic work up was done. The boy is recovering without incident and is doing well.

DISCUSSION

Urolithiasis in the paediatric population is not an uncommon condition. According to literature, the prevalence of bladder stones in Kenya is highest in arid and semi-arid areas and peaks around the age of three (3). Bladder stones are typically linked in developing nations to under-fives, low-protein diets, dehydration, consumption of goat milk, and poor socioeconomic conditions (13). Literature has made reference to an Afro-asiatic stone belt that runs from the Moroccan countries of Mauritania, Algeria, Tunisia, Libya, sub-Saharan Africa (Mali, Chad, Rwanda, Ethiopia, Cameroon, Niger), Sudan, Egypt, Turkey, Saudi Arabia, the United Arab Emirates, Iraq, Iran, Afghanistan, Pakistan, India, Nepal, Myanmar, Thailand, and Indonesia to the Philippine islands (3, 13).

These children usually present with varied symptoms that include hematuria, lumbar pain and dysuria (4). They often also present with lower urinary tract symptoms as well as recurrent urinary tract infections (3). If left untreated, these stones can cause changes to the urinary tract that can predispose to cancer (2).

Management of urolithiasis tends to lean towards use of minimal invasive surgery. Depending on the location of the stones and their sizes, various modalities are available. Extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), Retrograde intrarenal surgery (RIRS) and holmium laser lithotripsy of urethral stones (walker et al). These techniques rely on use of endourological equipment and are more commonly performed in adults. For children, especially in developing countries, access to this equipment that are suited for the paediatric population is not easy. Urethral stones can be pushed back to the bladder by retrograde manipulation and fragmented by ESWL (12).

Several comparative studies have been done pitting open procedures such as cystolithotomy against minimally invasive procedures (1,2,11). A systematic review by Donaldson et al concluded that ESWL offers an inferior stone free rate as compared to open cystolithotomy in children and adults but offers the shortest duration of hospital stay. Bhatia et al found that open surgery resulted in 100% stone removal at one setting but required the longest hospital stay of 5.2 days. ESWL had the shortest hospital stay of 20hrs but several patients required additional SWL treatment for complete fragmentation and two patient had urethral fragment impaction.

These challenges were the same that were faced by the authors in the management of this patient. The initial diagnosis was made intraoperatively since the history and physical examination did not point towards a stone etiology. The stone had actually passed into the urethra and caused bladder outlet obstruction. Since the stone could not be retrieved, the authors opted for a retrograde manipulation into the bladder under vision and retrieve it via open cystolithotomy.

Non conventional methods of dealing with urethral stones are sometimes employed in settings that lack appropriate endourological equipment in low and middle income countries such as Kenya . In a study done in Senegal of 94 cases of bladder stones, open procedures took place in 96% of these cases (14). This is further bolstered by literature that purports good comparable outcomes in terms of stone free rates as well as short and long term complications (1,2,11)

Urethral injuries after impaction of urethral stones are rare complications. These injuries do occur as a result of pressure necrosis from prolonged impacted stones. Trauma to the urethra during laser ablation of the stones can also cause injury. Most urethral stones are migratory (secondary) either from the upper tract or from the bladder. Native (primary) urethral stones may develop with associated anatomic abnormalities or post-surgical changes (8). There are few reports in literature of impacted urethral stones causing urethral injury. Eckstein et al reported of two children aged 2 and 8 who presented with perforation of the urethra and urinary extravasation following impacted urethral stones (6). This is the extreme of this condition if left untreated.

Urethral injury usually presents with extravasation of urine to the penis and scrotum. In our case report, the patient presented with edema of the penis and scrotum. Initially, the edema was suspected to be due to the inflammation as a result of the acute urine retention. However, after removal of the stone and later the urethral catheter, extravasation was noted during micturition.

Diagnosis of urethral injury is clinical like in this case. However, further characterization of the location and grade of injury can be made using contrast urethrography (7,12). Urethroscopy is a viable alternative and can be both diagnostic and therapeutic in cases where primary endoscopic realignment needs to be done.

Management of urethral injuries depend on the grade of injury as per the European Association of Urology (EUA) guidelines (7). In our case, we discovered a grade 2 injury that was managed conservatively by urethral catheterization for three weeks.

CONCLUSION

Paediatric urolithiasis presents a unique diagnostic and management challenge. Young children who cannot clearly express their symptoms, poor history from caregivers and lack of suspicion among clinicians all contribute to a diagnostic quagmire for this disease. Urethral injury with urine extravasation is a complication that the paediatric urologist needs to be on the lookout for in children who have impacted urethral stones. Its management is equally difficult because endourologic equipment suitable for young children is scarce, particularly in developing countries hence the need to adapt and find acceptable solutions to manage this disease. Open procedures are acceptable management options of bladder stones and literature shows that the outcomes of patients treated with these procedures are comparable to those who undergo minimally invasive procedures. Urethral injury should be suspected in children with impacted urethral stones.

REFERENCES

1. Bhatia, V. and Biyani, S.C. (1994) 'Vesical Lethiasis: Open Surgery versus Cystolithotripsy versus Extracorporeal shock wave therapy', *The Journal of Urology*, 151, pp. 660–662.
2. Donaldson, J.F. et al. (2019) 'Treatment of Bladder Stones in Adults and Children: A Systematic Review and Meta-analysis on Behalf of the European Association of Urology Urolithiasis Guideline Panel.', *European Urology*. Elsevier B.V., pp. 352–367. Available at: <https://doi.org/10.1016/j.eururo.2019.06.018>.
3. Jumbi, T. and Lessan, J. (2021) 'Paediatric Bladder Stones in Kenya. A Single Institution Study', *Acta Scientific Pediatrics*, 4(11), pp. 33–37. Available at: <https://doi.org/10.31080/aspe.2021.04.0467>.
4. Sandhu, Dr. U.J., Zia, Dr. H.Z. and Farooq, Dr. F. (2022) 'Analysis of Management of Impacted Urethral Stone in Children', *International Journal of Current Science Research and Review*, 05(04), pp. 1100–1103. Available at: <https://doi.org/10.47191/ijcsrr/V5-i4-32>.
5. Soliman, N.A. and Rizvi, S.A.H. (2017) 'Endemic bladder calculi in children', *Pediatric Nephrology*, 32(9), pp. 1489–1499. Available at: <https://doi.org/10.1007/s00467-016-3492-4>.

6. Eckstein, H., & Kenanoglu, A. (1961). Perforation of the urethra and extravasation of urine caused by a calculus. *The Lancet*, 277(7167), 20–22. doi:10.1016/s0140-6736(61)92187-0.
7. Luis Martínez-Piñeiro, Nenad Djakovic, Eugen Plas, Yoram Mor, Richard A. Santucci, Efraim Serafetinidis, Levent N. Turkeri, Markus Hohenfellner, EAU Guidelines on Urethral Trauma, *European Urology*, Volume 57, Issue 5, 2010, pp. 791-803, ISSN 0302-2838, <https://doi.org/10.1016/j.eururo.2010.01.013>.
8. Brady R. Walker, Blake D. Hamilton, Urethral calculi managed with transurethral Holmium laser ablation, *Journal of Pediatric Surgery*, Volume 36, Issue 9, 2001, pp. 16-17, ISSN 0022-3468, <https://doi.org/10.1053/jpsu.2001.26398>.
9. Amihay Nevo, Roy Mano, Pinhas M. Livne, Bezalel Sivan, David Ben-Meir, Urinary Retention in Children, *Urology*, Volume 84, Issue 6, 2014, pp.1475-1479, ISSN 0090-4295, <https://doi.org/10.1016/j.urology.2014.08.020>.
10. El-Sherif, A. E., & Prasad, K. (1995). Treatment of urethral stones by retrograde manipulation and extracorporeal shock wave lithotripsy. *British Journal of Urology*, 76(6), 761–764. doi:10.1111/j.1464-410x.1995.tb00770.
11. Mohammed S. Al-Marhoon, Osama M. Sarhan, Bassam A. Awad, Tamer Helmy, Ahmed Ghali, Mohammed S. Dawaba, Comparison of Endourological and Open Cystolithotomy in the Management of Bladder Stones in Children, *The Journal of Urology*, Volume 181, Issue 6, 2009, pp. 2684-2688, ISSN 0022-5347, <https://doi.org/10.1016/j.juro.2009.02.040>.
12. Pichler, R., Fritsch, H., Skradski, V., Horninger, W., Schlenck, B., Rehder, P., & Oswald, J. (2012). Diagnosis and Management of Pediatric Urethral Injuries. *Urologia Internationalis*, 89(2), 136–142. doi:10.1159/000336291
13. Lal B, Paryani JP, Memon SU. Childhood Bladder Stones-An Endemic Disease of Developing Countries. *J Ayub Med Coll Abbotabad*. 2015 Jan-Mar;27(1):17-21. PMID: 26182729.
14. Diallo, Abdoulaye & Toure, Balla & Camara, Christine & Barry, Macka & Bah, Ibrahima & Keita, Mamady & Balde, Ibrahima & Diallo, M.P.. (2008). Les accidents de la circoncision: aspects anato-mo-cliniques et thérapeutiques au CHU de Conakry, Guinée. *A propos de 44 cas. Andrologie*. 18. 10-16. 10.1007/BF03040374.



KENYA JOURNAL OF
UROLOGY
Official Journal of the Kenya Association of Urological Surgeons

Kenya Association of Urological Surgeons
www.kaus.or.ke