

Review article

Bladder cancer – A review of its pathology, diagnosis and treatment

Saurabh, Vijay Pal Singh*, Sanjay Singh and Ritu Sanwal

Siddhartha Institute of Pharmacy, Veer Madho Singh Bhandari Uttarakhand Technical University, Dehradun, Uttarakhand, India

*Corresponding author. E-mail: vijayng6@gmail.com

Article history

Received : July 28, 2022

Accepted : September 07, 2022

Keywords

Anatomy
Cancer
Diagnosis
Pathogenesis
Pathophysiology
Urinary system

ABSTRACT

Urinary tract infections (UTIs) are among the most frequent bacterial infections, affecting an estimated 150 million individuals globally each year. In elderly people, urinary retention is a common condition in which the people in their 70s and 80s have respectively 10% and 30% possibility of acute urinary retention. Inadequate care for the disease can result in unnecessarily high morbidity and, in rare cases, death. The management has substantially improved as the understanding of its pathophysiology has grown through time. Bladder cancer is a frequent malignant tumour of the urinary system, with a subsequent high rate and high prevalence. While the incidence of bladder cancer has been rising in recent decades, the widespread of bladder carcinoma is growing in younger people. There are various techniques for detecting bladder cancer, but each approach has a varied rate of precision, which is determined by the accuracy and precision of the procedure. The present study aimed to comprehensively review existing bladder cancer investigative techniques found in the literature and, at the very same time, to determine the optimal mixture of several successful methods capable of finding the occurrence of malignant cells in the bladder with a reasonable level of accuracy. The review also covered a comprehensive knowledge of the urinary system, pathophysiology, pathogenesis, diagnosis, and assessment of bladder cancer. The findings of this study can aid in the development of a reliable approach for identifying bladder cancer and the identification of problem areas to be again improved for upcoming research.

DOI: 10.53517/CMDR.2581-5008.612022224

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INTRODUCTION

Urinary tract infections (UTIs), which are characterized microbiologically as the incendiary reaction of the urothelium to microorganisms, are among the most well-known bacterial diseases influencing an expected 150 million individuals every year around the world. The frequency of UTIs in men is significantly lower than that in women, with an expected lifetime prevalence of 13.7%. Likewise, UTIs are the most widely recognized reason for contamination in hospitalized patients, representing 17.2% of all nosocomial diseases in England. Moreover, UTIs bring about impressive patient bleakness and time off work; thus, the administration of this condition causes enormous monetary expenses, assessed at \$3.5 billion in the USA each year. UTIs are profoundly pervasive, represent huge quantities of short-term and crisis division counsels and are the main source of clinic-obtained disease and resulting dreariness, accordingly causing enormous monetary expenses for medical services frameworks, featuring the general well-being weight of this condition. In any case, more significant than these elements is the developing gamble of antimicrobial opposition because of our ongoing strategy for dealing with these patients as ~25% of all antitoxin solutions are for UTIs. Antimicrobial

opposition is presently one of the most significant dangers to patient security around the world. The European Center for Disease Prevention and Control has assessed that antimicrobial obstruction costs the European Union \$1.5 billion in medical care costs and lost efficiency every year and contamination with antimicrobial-safe microbes can prompt more extreme diseases, longer clinic stays and expanded mortality (Neha et al., 2018).

ANATOMY OF BLADDER

The bladder is an instinctive organ made out of a syncytium of smooth muscle filaments and a bodily fluid layer. The buildup of smooth muscles at the bladder neck frames the inner sphincter, while the outer sphincter structures from the urogenital stomach around the membranous urethra. The bladder work is constrained by sets of fringe nerve supply, the spinal engine mix focus, supraspinal focus, pontine and suprapontine focus. The physiologic practical properties of the bladder are subject to a suitable limit, great consistency, convenience, and sensation with intentional control to start or stop the activity of micturition. Interruption along the above brain processes or physical impediment to the bladder outlet might prompt urinary maintenance.

The urinary tract comprises two ureters, a urinary bladder and a urethra (Fig. 1).

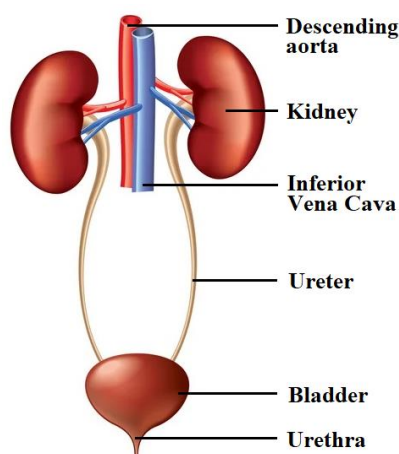


Fig. 1. Anatomy of the urinary system

The urinary bladder is an empty, distensible organ that sits on the floor of the pelvic pit, suspended by an overlay of the parietal peritoneum. It breaks down when void, yet when extended, it becomes pear formed and can hold up to around 700-800 ml of pee in guys (somewhat less in females because of the place of the uterus). The mass of the urinary bladder has three tissue layers. From shallow to profound, these layers are as the following.

Adventitia

The adventitia, the shallowest layer, is made out of areolar connective tissue. On the predominant surface of the urinary bladder is an extra serosa, which is a crease of the parietal peritoneum.

Detrusor muscle

The centre tissue layer is made out of smooth muscle known as the detrusor muscle. The muscle strands are organized into internal longitudinal, centre round, and external longitudinal layers. The detrusor muscle frames a roundabout band around the launch of the urethra, called the inward urethral sphincter.

Mucosa

The mucosa is made out of momentary epithelium with a hidden basal lamina. A mucous layer produces bodily fluid to shield the bladder epithelium from pee. At the point when the bladder isn't full, folds of mucosa called rugae are noticeable.

The floor of the urinary bladder contains a three-sided region called the trigone. The trigone needs rugae and seems smooth because its mucosa is firmly bound to the fundamental muscularis. The two back corners of the trigone are shaped by the two ureteral holes (openings). These holes have mucosal folds that go about as valves to forestall the discharge of pee during disposal. The peak of the trigone is framed by the opening to the urethra, the inner urethral hole. The place of the urinary bladder is different in males and females. In males, it is in front of

the rectum and above the prostate gland whereas, in females, it is in front of the vagina and below the uterus.

PATHOLOGY OF BLADDER CANCER

Urothelial (momentary cell) carcinoma is the most known type of bladder malignant growth, representing roughly 90% of cases (Bellmunt et al., 2014). Non-urothelial bladder malignant growths incorporate squamous cell carcinoma, adenocarcinoma, little cell carcinoma, and blended histology cancers, with squamous cell and adenocarcinomas making up most of the non-urothelial growths (Grignon, 2009). Even though squamous cell carcinoma addresses just a little part of bladder malignant growth cases in the created world, it is the most considered normal type where schistosomiasis is endemic, representing up to 81% of cases (Badawi et al., 1995).

Muscle invasive bladder carcinoma

Given the forceful idea of muscle-invasive bladder malignant growth, opportune finding and treatment are pivotal. Revolutionary cystectomy with reciprocal pelvic lymphadenectomy and cisplatin-based neoadjuvant chemotherapy are emphatically suggested for all patients with resectable nonmetastatic muscle-invasive bladder malignant growth. Five-year endurance rates with cystectomy alone are just around half; neoadjuvant chemotherapy can further develop endurance, particularly in patients at high gamble of movement or repeat (those with nodal contribution, high-grade growths, or transmural or vascular attack). At the point when utilized related to cystectomy, cisplatin-based neoadjuvant chemotherapy exhibited a flat-out five-year endurance advantage of 5% to 8% across a few preliminaries, meaning a number expected to treat of 9.29 Segmental (halfway) cystectomy and neoadjuvant cisplatin-based chemotherapy might be proper for select patients. Broad lymph hub analysis is related to upgrades in movement-free and general endurance. Contrasted and open a medical procedure, a laparoscopic approach is related to comparative repeat and endurance rates that may diminish torment and the requirement for blood bonding and may speed recuperation. Revolutionary cystectomy further develops endurance rates of contrasted and outer shaft radiotherapy and is the favoured therapy for muscle-invasive bladder disease (DeGeorge et al., 2017). Radiotherapy might be considered as a component of a multimodal bladder-saving methodology or for concealment in patients who are not contenders for cystectomy. Chemotherapy is the favoured therapy for patients with metastatic infection or unresectable bladder malignant growth. The two accessible medicines (blend gemcitabine and cisplatin, and mix methotrexate, vinblastine, doxorubicin, and cisplatin) are related with a middle endurance season of about complete 14 months. Bladder reproduction might include landmass supply or ileal conductor urinary redirection, contingent upon cancer qualities and patient inclinations. Notwithstanding, neither one of the methodologies has proof of progress in long-haul results. By and large endurance for patients with muscle obtrusive bladder disease is 66% at five years after revolutionary cystectomy

and broad lymph node analysis, and a half to 60% with bladder safeguarding therapy. Radical cystectomy and reproduction are related with 90-day postoperative death rates of 3% to 9%, highlighting the accentuation on personal satisfaction for patients more seasoned than 80 years and those with huge comorbidities (Witjes et al., 2014; Fedeli et al., 2011).

Non-muscle invasive bladder carcinoma

About 70% to 80% of bladder diseases present as non-muscle-obtrusive cancers. Of these, 60% to 70% are restricted to the bladder mucosa (stage Ta), 20% to 30% show attack to the subepithelial connective tissue (stage T1), and around 10% present as carcinoma in situ. The essential therapy for non-muscle-invasive bladder malignant growth is TURBT, normally followed by prompt instillation of BCG or intravesical chemotherapy (mitomycin C, epirubicin/ Ellence, or doxorubicin/ Adriamycin). The choice to impart BCG or potentially chemotherapy depends on the gamble of disease movement or repeat. For generally safe cancers (second rate Ta), TURBT with the quick establishment of chemotherapy is suggested as complete treatment. Patients with high-risk non-muscle-obtrusive growths (high-grade Ta and T1) have about a half opportunity of repeating with muscle-intrusive infection whenever treated with TURBT alone and are in this manner regularly treated with TURBT and intravesical BCG (liked) or mitomycin C. In patients with high-grade Ta or T1 cancers, 10-year repeat free endurance after TURBT and BCG immunotherapy is around 80%. Around one-half of patients with non-muscle-obtrusive carcinoma in situ will advance to muscle-obtrusive sickness without therapy. Restaging of high-risk non-muscle-obtrusive cancers (high-grade Ta, T1, and Tis) with rehash TURBT two to about a month and a half after determination and ideally before BCG instillation is suggested and is related to diminished repeat, with a number expected to treat forestall repeat at 90 days (DeGeorge et al., 2017). Patients with high-grade T1 non-muscle intrusive growths, particularly those with high-risk highlights (e.g., numerous grade 3 T1 cancers with Tis, expanded profundity of attack, sickness movement with BCG therapy), ought to be considered for prompt cystectomy with instillation of BCG or mitomycin (Bellmunt et al., 2013; Hall et al., 2007; Clark et al., 2013).

Non-urothelial bladder carcinoma

Cystectomy, fractional cystectomy, or radiation is the backbone of therapy for most non-urothelial bladder diseases. Fundamental chemotherapy is for the most part not utilized for these cancers (Clark et al., 2013).

PATHOPHYSIOLOGY OF UTI

The common pathophysiology of urinary tract infection is given in Fig. 2 and 3. Urinary care might be intense, intense on-constant, or persistent. Intense maintenance could be encouraged or unconstrained, while persistent maintenance could be low tension or high strain. Urinary maintenance usually results from a physical check from benign prostatic hyperplasia (BPH), carcinoma of the

prostate, urethral injury; iatrogenic causes, for example, in the intraurethral infusion of building specialists in the treatment of intrinsic sphincter deficiency and psychogenic causes (Jacobsen et al., 1997; Tanagho et al., 2008). Expanded outlet obstruction as found in patients with bladder outlet obstruction (BOO) is the commonest system of urinary maintenance. Patients might show a scope of side effects from the resultant urinary bladder brokenness and periodic renal deficiency, notwithstanding the mechanical impact of the check. There might be just gentle obstructive side effects at first, nonetheless, the patient may frequently not notice a massive change in voiding design, particularly with the alleged high strain maintenance. Expanded outlet obstruction might bring about bladder dilatation, hypertrophy, trabeculations, sacculations and diverticulitis. The drawn-out expanded lingering voiding pressure, in the long run, prompts bladder brokenness and may appear as detrusor flimsiness with diminished consistency and split the difference of the stockpiling capacity demolishing the lower urinary parcel side effects. Such a useless bladder can unexpectedly decompensate, finishing in AUR, or does it guilefully with moderate distention of the bladder, bringing about persistent maintenance. The specific systems liable for steady or abrupt decompensation have not been clarified (Kaplan et al., 2008). Persistent maintenance might be a high strain (30 cm of H₂O) or low tension. The bladder becomes harsh, hypocontractile, permitting distension past the limit that might present as flood incontinence or nighttime enuresis (Mitchell, 1984). In the high-pressure maintenance, bladder changes may likewise bring about the utilitarian disappointment of ureteral three-sided complex, coming about in vesicoureteric reflux, with the resultant back tension on the ureters and gathering framework prompting the improvement of hydronephrosis. With time, steady raised intrarenal strain might prompt cylindrical epithelial decay and possible glomerular capacity and inevitable persistent renal distress. This might additionally be convoluted by calculi arrangement and intermittent urinary parcel disease (O'Reilly et al., 1986).

Patient's evaluation

This should be speedy, orderly, and intensive to guarantee a legitimate conclusion and commencement of suitable therapy. Beginning assessment is pointed toward portraying the sort of deterrent as one or the other intense or constant maintenance. Following the crisis shown in AUR, the need should be to assuage maintenance and avoidance or control of sepsis with adjustment of conceivable liquid and electrolyte derangements. Appropriate history ought to incorporate a portrayal of the voiding side effects including self-restraint, the span and beginning, past voiding side effects, and the history of hematuria. Side effects in patients with BOO are variable, with a moderately unfortunate connection between Singular side effects and the presence of BOO (Kaplan et al., 1996). Just about a portion of men who decided to be clinically impeded on a clinical premise will have urodynamic proof of outlet deterrent (Sirls et al., 1996). In this way, while side effect scores give a valuable device for directing administration methodologies and follow-up

reactions to treatments, they are for the most part not prescient of outlet check or impeded contractility. History of any type of sexual brokenness, weight reduction, summed up body shortcoming, and anorexia might recommend prostate malignant growth. Neurological assessment is pivotal to bar neurogenic bladder. Past clinical history might disclose hypertension, diabetes, and other huge comorbid conditions. It ought to be laid out assuming the intense maintenance is hastened (delayed deferment of micturition, ingestion of enormous volume of liquids, or diuretic misuse) or unconstrained. Encouraged maintenance has a superior guess following preliminary without a catheter (George et al., 1984). On assessment, patients with intense maintenance are normally in serious torment and anxiety, while those with constant maintenance are quiet. Facial puffiness, pedal oedema, pallor, acidotic breath, and raised circulatory strain might be tracked down in patients with hampered renal function.

The mid-region ought to be analyzed for suprapubic expanding and delicacy. A rigidly extended enlarging in the suprapubic district could be intense, intense on-persistent, or high-pressure constant maintenance. In low-pressure constant maintenance, the bladder framework might be ambiguously unmistakable due to the limp bladder, yet the region is dull to percussion. Urethral release or tangible inductions in addition to highlights of epididymo-orchitis are reminiscent of urethral injury. Perianal and perineal sensations as well as butt-centric sphincter tone and bulbocavernosus reflex test the uprightness of the tangible and engine efferent filaments in the pudendal nerves. The prostate might be broadened with harmless or dangerous elements. Lower appendage engine and tactile assessment including profound ligament and plantar reflexes are the significant parts of genitourinary neurological assessments.

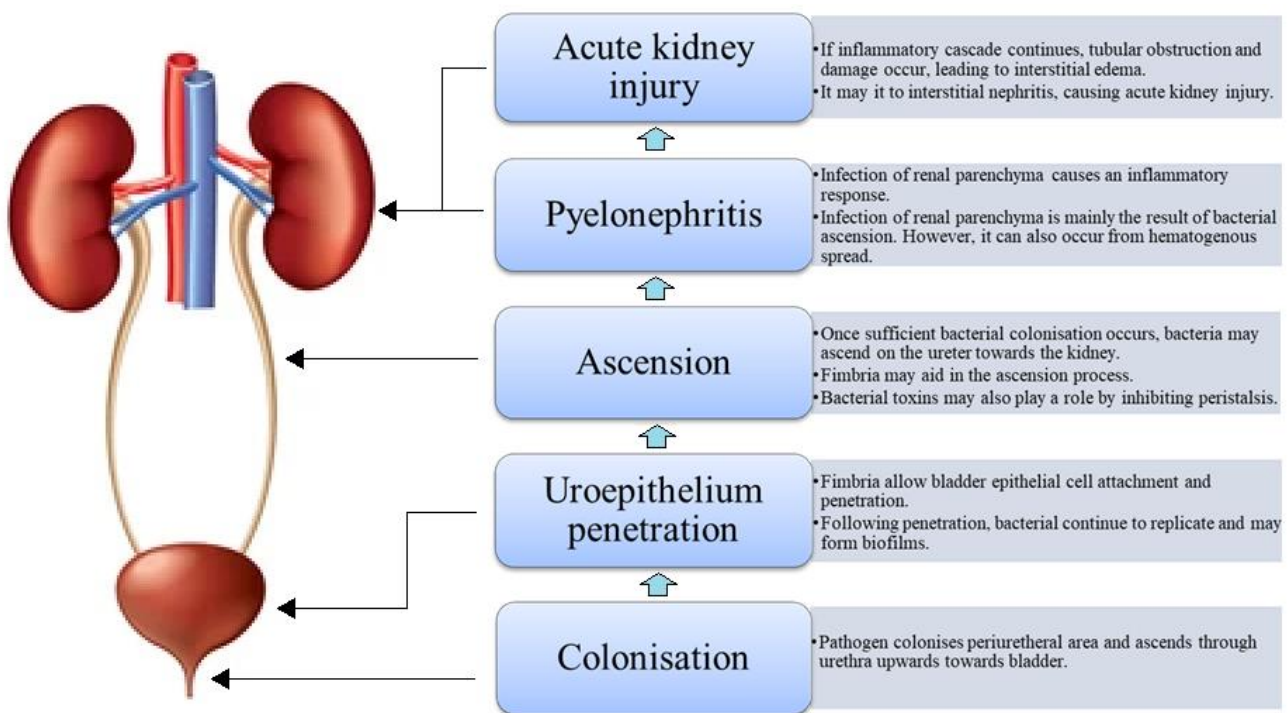


Fig. 2. Pathogenesis of urinary tract infection

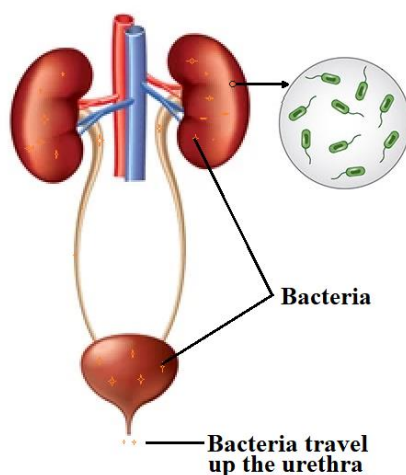


Fig. 3. Bacteria (*E. coli*) entering the urinary tract through the urethra

Examinations

The fundamental research centre examination incorporates serum urea, electrolytes, creatinine, pee investigation, pee microscopy and culture, glucose, and Prostate Specific Antigen (PSA). Patients in constant maintenance with raised urea and creatinine risk postobstructive diuresis. These patients additionally risk postobstructive hematuria and further weakening of the renal debilitation. Abdominopelvic ultrasound will quantify remaining pee in ongoing maintenance as well as divulge a portion of the confusions following persistent maintenance, for example, hydronephrosis, bladder stone, and loss of corticomedullary separation related to disabled kidney work. Transrectal ultrasound evaluates the prostate size, echogenicity, and honesty of the case. Urethroscopy and urodynamic studies may be generally shown (Muhammed and Abubakar, 2012).

Treatment

Treatment starts with brief bladder waste through urethral catheterization; on the off chance that this comes up short, seepage ought to be done using a suprapubic cystostomy. In patients with unhinged renal capacity, close observation for post-obstructive diuresis, hematuria from hyperemia or crack of enlarged veins, and the gamble of additional movement of the hindered kidney work are significant. To diminish the gamble of these difficulties, a few ways of thinking advocate that the bladder ought to be depressurized gradually in all patients with ongoing urinary maintenance. In principle, slow decompression ought to free the abrupt engorgement from the bladder mucosa and the advancement of petechial haemorrhages. By and by, nonetheless, slow decompression is very challenging to accomplish; the initial not many millilitres of pee removed from an inelastic bladder will lessen the tension at an extensive rate. The customary sluggish decompression of the bladder by progressively delivering a door cut on the seepage tube, or by eliminating little amounts of pee at normal spans, doesn't accomplish its point of continuous decrease in intravesical pressure (Arner et al., 1990) because right off the bat withdrawal of just 50 ml of pee from a rigidly stretched inelastic bladder prompts near half decrease in vesical strain; furthermore, delayed waste of stale pee at high tension with an inhabiting catheter inclines toward urinary parcel disease which could demolish the generally compromised renal capacity; and thirdly it is tedious and works serious (Levin et al., 1995). As of late, Perry, et al. recommended sluggish decompression of the bladder with a suprapubic intravenous fluid giving set; nonetheless, it is likewise defenceless to similar impediments specified previously. George and colleagues have displayed from isotope renography that there is an emotional change in isotope waste of time from the upper urinary lot as the bladder pressure reduces, and there appears to be no legitimization for postponing this improvement by sluggish decompression (Arner et al., 1990).

These patients ought to have an intravenous line in situ with severe information and results observed; it is important to screen the serum and urinary electrolytes each 6-12 h to suitably supplant the sodium and potassium intravenously, forestalling hyponatremia and hypokalemia. These patients can be begun on intravenous liquid 0.45% NaCl at a 2-hourly rate, supplanting a portion of the past 2 h pee yield once there is proof of hemodynamic flimsiness. When the patient's urea and creatinine have standardized, then, at that point, all intravenous liquid treatments can be halted. Notwithstanding, there is exploratory proof that keeping up with canines in a volume-packed extended state during block assisted them with accomplishing their pre-obstacle standard serum creatinine after the help of a deterrent (Kato et al., 1990).

DIAGNOSIS OF BLADDER CARCINOMA

The underlying assessment of a patient with thought bladder disease depends on cystoscopy, evaluation of renal capacity, and imaging of the upper urinary plot, ideally with processed tomography (CT) urography (Clark et al., 2013; Sharp et al., 2013).

Laboratory tests

To assess for renal disability, serum blood urea nitrogen and creatinine levels ought to be gotten for all patients in whom bladder malignant growth is thought. On the off chance that metastatic sickness is thought, a total blood count and complete metabolic board, including basic phosphatase level and evaluation of liver capacity, are suitable (Davis et al., 2012).

Cytology and urine tumour markers

Urine cytology isn't suggested as a business-as-usual assessment for asymptomatic minute hematuria (Davis et al., 2012) because renal calculi and urinary parcel diseases can prompt misleading positive outcomes. It has high responsiveness (more prominent than 90%) for high-grade urothelial growths and carcinoma in situ (stage Tis), albeit negative discoveries don't preclude danger (Witjes et al., 2014). Pee cytology is a significant assistant in the assessment of patients at high risk of urothelial cancers because of its positive prescient worth in these patients. Pee cytology is likewise helpful for reconnaissance in patients with known urothelial carcinoma. Routine testing for urinary cancer markers isn't suggested because of the absence of clinical unwavering quality (Davis et al., 2012).

Cystoscopy and TURBT

Cystoscopy ought to be acted on in all patients with gross hematuria and those 35 years and more established with tiny hematuria, and it tends to be considered for more youthful patients with minuscule hematuria (Davis et al., 2012). Patients with hematuria and hazard factors for bladder malignant growth (e.g., tobacco use, irritative voiding side effects, compound openings) ought to be assessed with cystoscopy paying little mind to age.21 Patients with unusual discoveries on bladder wash cytology or tissue pathology ought to go through transurethral resection of the bladder cancer (TURBT). This method gives fundamental histopathologic data important to authoritative analysis, arranging, and evaluation, and takes into account evacuation of apparent growth and examining of encompassing muscle to survey profundity (Hall et al., 2007).

Upper urinary tract imaging

Multiphasic CT urography with and without intravenous differentiation media and excretory imaging ought to be remembered for the underlying workup for bladder malignant growth (Clark et al., 2013). It has the most elevated awareness (95%) and particularity (92%) of all upper urinary plot imaging modalities, and it can assess the urothelium of the upper parcels as well as distinguish renal masses. Attractive reverberation urography and ultrasonography are elective imaging choices for patients with contraindications to CT urography, like pregnancy, contrast sensitivity, or renal inadequacy (Davis et al., 2012). Renal ultrasonography might be viewed as notwithstanding CT urography for patients who have thought renal parenchymal disease.30 Renal ultrasonography isn't suggested all alone for assessment of

hematuria without a known reason, because its low responsiveness (half) may miss urothelial sores, little renal masses, or renal calculi, and it frequently prompts further testing and extra expenses (Sharp et al., 2013). Assuming that metastatic illness is thought, chest radiography and imaging of the midsection and pelvis with CT or attractive reverberation imaging ought to be gotten (Edge et al., 2010). In the screening strategy; there are no significant associations that suggest evaluating for bladder malignant growth in asymptomatic grown-ups. In 2011, the U.S. Preventive Services Task Force reasoned that there was deficient proof to survey the equilibrium between advantages and damages of evaluating for bladder disease in asymptomatic adults, 33 an assertion supported by the American Academy of Family Physicians. The low certain prescient worth of accessible screening tests and the absence of top-notch proof to propose that early therapy of bladder disease further develops long haul results block a suggestion for screening (Bellmunt et al., 2013; Hall et al., 2007; Clark et al., 2013).

Adjuvant chemotherapy

There is deficient excellent proof to help routine utilization of adjuvant chemotherapy for patients with bladder malignant growth. In any case, chemotherapy might give benefit specific high-risk patients (Bellmunt et al., 2014; Ruggeri et al., 2016). Platinum-based blend chemotherapy might further develop endurance in patients with obtrusive bladder disease. Cisplatin-based chemotherapy further develops illness-free endurance in those with lymph hub contribution (Leow et al., 2014). Blend gemcitabine and cisplatin are related with comparable by and large endurance as different regimens however might be less poisonous in patients with unresectable, privately progressed, or metastatic temporary cell bladder malignant growth (Shelley et al., 2011).

CONCLUSION

Neurogenic bladder brokenness in people takes in an extremely wide range of conditions that incorporate intrinsically gained conditions that might try and be preventable today, conditions that are related to explicit anatomic irregularities, and obtained conditions that might happen prenatally or from mishaps or sports or engine vehicle-related wounds. In spite of the aetiology, the core values for the board are comparative; guaranteeing and keeping a sufficiently estimated, ordinarily consistent, repository that clears pee, at a generally low strain, is the way to keeping a solid climate for the kidneys. Future possibilities look splendid for impacted people with the general well-being of the individual the most vital objective to be accomplished.

Old age and BOO auxiliary to BPH stay the commonest risk factors for urinary maintenance. Auxiliary bladder brokenness in BOO, detrusor myogenic brokenness, and modification of bladder innervations are the significant components. Quick and complete decompression in both kinds of maintenance is an ongoing practice. The consequences of this survey can decidedly assist with recognizing precise strategies for distinguishing bladder malignant growth and feature regions to be additionally improved for future examination work.

CONFLICTS OF INTEREST

The author(s) declare(s) no conflicts of interest.

DECLARATION

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How to cite this article?

Saurabh, Singh VP, Singh S, Sanwal R (2022). Bladder cancer – A review of its pathology, diagnosis and treatment. *Current Medical and Drug Research*, 6 (1), Article ID 224.
