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FOUR MOST LIFE THREATENING UROGENITAL CANCER AND ITS MANAGEMENT

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ABSTRACT: Now a day's urogenital cancer is the life threatening disease in worldwide, among them most four life threatening urogenital cancers are kidney cancer, bladder cancer, prostate cancer and testicular cancer. Kidney cancer or renal cell carcinoma (also called adenocarcinoma) is a disease in which malignant cancer cells are found in the living of tubules (renal epithelium). The kidney cancer has the highest mortality rate of the genito urinary cancers and the incidence of kidney cancer has risen steadily. Bladder cancer is a disease in which malignant cancer cells form in the tissues of the bladder. The bladder is a hollow organ in the lower part of the abdomen. Bladder cancer is seventh most basic cancer worldwide and fourth basic growth in men. Prostate cancer is a disease in which cancer cells shape in the tissues of the prostate. Prostate cancer is the fourth most common cancer in the world and more than 1.1 million cases of prostate cancer recorded in 2012. Testicular cancer is a disease when testicular cells become abnormal (malignant) in one or both testicles. It is a relatively rare tumour, approximately 1% of all male cancers globally. So, drugs are not only the choice for the management of cancers is required peoples/ patients' awareness, a way of living education is the best choice for the prevention of cancers.

INTRODUCTION: Urogenital cancers are the life threatening disease in worldwide, among them kidney cancer, bladder cancer, prostate cancer and testicular cancer are four most life threatening urogenital cancers. The kidney cancer has the highest mortality rate of the Genito urinary cancers and the incidence of kidney cancer has risen steadily.

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Kidney filters unsafe metabolic waste things from the blood in a couple of hundred thousand for all intents and purpose autonomous units called nephrons. A nephron includes one glomerulus and one twofold latch formed tubule that drains the filtrate into the renal pelvis [1]. Kidney cancer is among the 10 most cancers worldwide.

According to the World Cancer Research Fund International 338000b kidney cancer new cases diagnosed in 2012 [2]. Bladder cancer is seventh most common malignancy worldwide and fourth common cancer in men. The urinary bladder is lined by layers of muscle and its volume is 400 ml to 600 ml. It is a solid sac in the pelvis, simply above and behind the pubic bone.

Urine is made in the kidneys, and goes down and stored in the bladder through two tubes called ureters [3]. The totals of 350000 new cases of bladder cancer are diagnosed worldwide each year. Prostate cancer is a disease in which cancer cells shape in the tissues of the prostate. The prostate gland is the biggest extra organ of the male regenerative framework. It secretes a thin, marginally antacid liquid that structures a part of the original liquid. It is made out of glandular and stromal components which are firmly melded inside a pseudocapsule.

Prostate cancer is the fourth most common cancer in the world and more than 1.1 million cases of prostate cancer recorded in 2012. It is a disease in which malignant cancer cells form in the tissues of the prostate [4]. Burden of this disease in men is rising worldwide. Prostate cancer is the fourth most common cancer in the world and more than 1.1 million cases of prostate cancer recorded in 2012. The risk factors of prostate cancer are non modifiable factors, genetic factors and external factors [5]. Testicular cancer is a disease when testicular cells become abnormal (malignant) in one or both testicles. The testis is secured by a thick stringy connective tissue container called the tunica albuginea. From this structure, thin defective septa keep running a back way to join a sinewy thickening of the back piece of the tunica albuginea called the mediastinum of the testis [6]. Testicular is a relatively rare tumour type accounting for approximately 1% of all male cancers globally [7]. So above this life threatening urogenital cancers in worldwide is the first choice for its management among the pharmaceutical and medical researchers and scientists in world wide.

Kidney Cancer: Kidney cancer or renal cell carcinoma (also called adeno carcinoma) is a disease in which malignant cancer cells are found in the living of tubules (renal epithelium) [8]. The tiny tubule in the kidneys filter and clean the blood, taking out waste products and making urine and it passes into the bladder and then passes from the body [2]. The kidney cancer has the highest mortality rate of the Genito urinary cancers and the incidence of kidney cancer has raised steadily [1] and it is among the 10 most cancers worldwide. According to World Cancer Research Fund International, 338000 kidney cancer new cases diagnosed in 2012 [2]. Total 57760 kidney cancer cases and 12980 deaths occurred in the United States in the year 2009 [1].

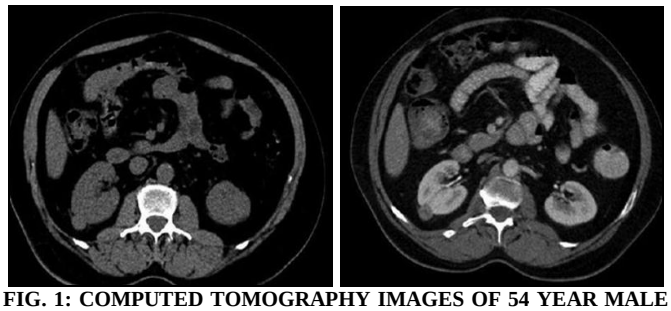

FIG. 1: COMPUTED TOMOGRAPHY IMAGES OF 54 YEAR MALE RENAL CELL CARCINOMA (KIDNEY CANCER); SHOWING A FOCAL LESION IN MEDIAL POLE OF THE RIGHT KIDNEY MEASURING 17MM×16MM WITH CONTRAST ENHANCEMENT [9].

Types: [10] Following types of renal cell carcinoma are clearcell, clearcell papillary, papillary, hereditary leiomyomatosis, chromophobe, mit family trans-location, succinate dehydrogenase-deficient, mucinous tubular and spindle, tubulocystic, unclassified and acquired cystic disease-associated renal cell carcinoma. Following types of cell carcinoma are multi-locularcystic renal neoplasm of low malignant potential, squamous, collecting duct, renal medullary, papillaryadenoma and oncocytoma.

Staging and Size of Cancer Tumours: [11, 12] TX is primary tumour cant not be assessed, T0 is evidence of primary tumour not found, T1 is Tumour≤70 mm, T1a is Tumour≤40 mm, T1b is Tumour >40 mm but≤70 mm, T2 is Tumour >70 mm, T2a is Tumour >70 mm but ≤100 mm, T2b is Tumour >100 mm, T3 is tumour goes into major veins or perinephric tissues but not into the ipsilateral adrenal gland but not far Gerota's fascia, T3a is tumour grossly far into the renal vein or its segmental branches, or tumour invades perirenal or renal sinus fat but not far Gerota's fascia, T3b is Tumour grosslyextends into the venacava below the diaphragm, T3c is tumour grossly extends into the venacava above the diaphragm or invades-thewall of the venacava, T4 is tumour enters beyond Gerota's fascia.

Symptoms: [13 – 17] Blood in the urine, a lump or mass around back, near the kidneys, in the abdomen, abdominal pain, anaemia, nephroliathisis, fatigue, cirrhosis, hypertension, back pain, crohn's disease, von Hippel-Lindau disease, family history, iron deficiency, body mass index, body size, obesity.

Age: The hazard increments altogether after the age of 60 years.

Sex: For each two ladies who get kidney disease, 3 men will do as such.

Smoking: Regular tobacco smokers have a significantly higher hazard; however the hazard drops when the individual stops.

Diagnosis: [15 - 21] Blood and urine tests can discount other conceivable reasons for manifestations, for example, kidney stones or a contamination. Ultrasound scan can enable the doctor to distinguish any adjustment in the state of the kidney that could be caused by a tumour.

CT scan normally involves the patient drinking a dye first. An image guided biopsy includes utilizing a needle to expel a little specimen of kidney tissue for examination under a magnifying instrument for growth cells.

MRI, Excretory Urogram: A dye is infused by means of vein in the patient's arm. The kidneys and urinary framework, prepare the dye, and these empower any indications of malignancy to appear on an X-beam.

Cystoscopy: A long, thin tube with a special lens and light at the end is put into the urethra, to give an image with in the patient's bladder. A biopsy could be taken at the same instance.

Treatment: [22 - 25]

- Partial nephrectomy is suggested for the treatment of all T1 tumors.
- Laparoscopic radical nephrectomy is the favored choice for the treatment of stages-T1, T2.
- Routine adrenalectomy and lymph hub analyzation.
- Partial and radical nephrectomy, Stem Cell, Renal protection treatment, Nedaplatin treatment, gemcitabine treatment.

Drugs: [26 – 29] A conjugate of neocarzinostatin and poly (styrene-comaleic acid), nucleoside, cyclo-phosphamide, sunitinib, pazopanib, bevacizumab, rapamycin, sorafenib, axitinib, cabozanatinib, temsirolimus, everolimus.

Prevention: [19, 30] Physical activity, weight control, blood pressure control, quit smoking and tobacco are the best prevention for the kidney cancer.

Bladder Cancer: Bladder cancer is a disease in which harmful cancer cells form in the tissues of the bladder [31]. The bladder is a hollow organ in the lower some portion of the belly. It is molded like a little inflatable and has a solid divider that enables it to get longer or less. The bladder stores pee until the point that it is passed out of the body [32]. Bladder cancer is seventh most basic threat worldwide and fourth regular disease in men [3]. The aggregate of 350000 new instances of bladder cancer is diagnosed worldwide every year. The most devil hazard factors in the advancement of bladder cancer are smoking and occupational exposure to lethal chemicals [33].

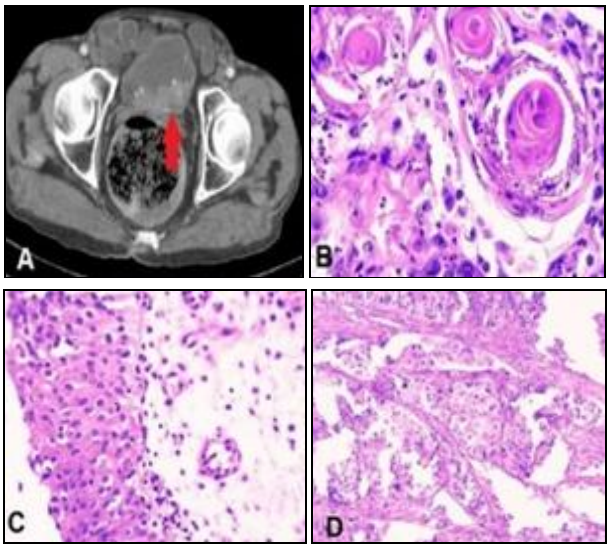

FIG. 2: COMPUTED TOMOGRAPHY IMAGES OF 30 YEAR MALE'S BLADDER CANCER

(A) Showing nodular growth on left postero-lateral aspect of bladder wall (red arrow). (B) Sheets of malignant squamous cells with well-formed keratin pearls. (C) Area of normal appearing transitional epithelium. (D) Muscle bundles infiltrated by malignant cells [34]

Staging: [35 - 39] Stage I is T1, Stage II are T2a and T2b, Stage III are T3a, T3b and T4a, Stage IV is T4b

Causes and Risk Factors: [35 - 53] Occupational risk, aluminium production (polycyclic aromatic hydrocarbons, fluorides), certain aldehydes, aminobiphenyl and its metabolities, aromatic amines, benzidine and its derivative, 2 napthyl-amine, betanapthylamine, ortho toluidine, treatment with cyclophosphamide, chinese herbs- aristolochic, arsenic and arsenic compound- gallium arsenide

contaminated water, schistosoma haematobium bladder infection, neurogenic bladder and associated indwelling cathertes, tobacco, smoking, genetic susceptibility, dietary factors, environmental pollution, medical conditions, Vitamins, physical activities, cruciferous vegetables, citrus fruit.

Sign and Symptoms: [53 - 55] Frank haematuria, pain, urinary frequency, bladder irritability, urinary infection, prostatitis.

Diagnosis: [56 - 58] Urine sediment, urine culture, cytoscopy, intravenous urography, biopsy, trans-urethral resection, bimanual examination.

Treatment: [57 - 59] Intravesical therapy, therapy with Bacillius Calmette Guerin (BCG), intravesical chemotherapy, antituberculous drugs, meticulous pelvic iliac lymphadenectomy, radical cystectomy, urinary diversion, the specific form of urinary diversion, either incontinent or continent, adjuvant therapy, radiation therapy, RNA isolation, DNA isolation, Whole-exome sequencing (WES)

Drugs: [60, 61] Vinflunine, mitomycin, doxorubicin, thiotepa, ethoglucid, valrubicin, cisplatin, gemcitabine, suramin.

Combination Therapy: Cisplatin + methotrexate + vinblastine, gemcitabine + paclitaxel, gemcitabine + cisplatin, methotrexate + vinblastine + doxorubicin + cisplatin.

Prevention: [62, 63]

Vitamin E: This Vitamin confines the cell divides from annihilation. The intake of Vitamin E by patients with bladder cancer may bring about a reduction in tumor recurrence. For the counteractive action of bladder cancer, cruciferous vegetables, allium vegetables, carrots, green vegetables, tomatoes, fruits, dietary fibre, lycopene and selenium intake are important. Physical activity, weight control, blood pressure control, quit smoking and tobacco are the best prevention for the kidney cancer.

Prostate Cancer: Prostate cancer is a disease in which dangerous malignancy cells form in the tissues of the prostate [4]. The prostate gland is the biggest accessory organ of the male regenerative framework. It secretes a thin, marginally soluble fluid that forms a segment of the seminal fluid [64]. The burden of this disease in men is rising around the world. Prostate cancer is the fourth most common cancer in the globe and more than 1.1 million instances of prostate cancer recorded in 2012. The hazard variables of prostate cancer are non modifiable components, hereditary elements and external elements [5].

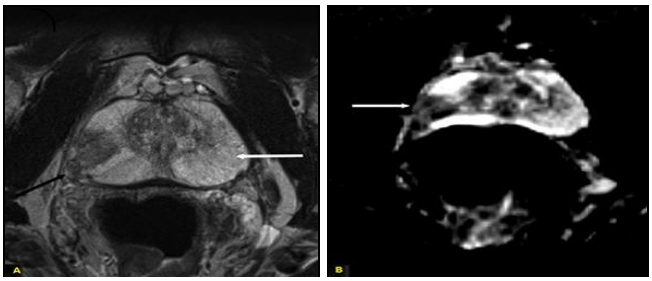

FIG. 3: T2-WI (THE WORKHORSE OF PROSTATE MRI) IMAGES OF 55 YEAR OLD MAN GLEASON PROSTATE CANCER (A) Axial T2-weighted image (T2WI) showing the normal hyperintense T2 signal in the peripheral zone (white arrow) from the high water content with cancer (black arrow) appearing as an area of low signal on T2WI. (B) Apparent diffusion coefficient map at the same level showing low signal from the restricted diffusion at the site of cancer (arrow) [65]

Staging of Cancer Tumours: [66 - 70] TX is primary tumour cannot be assessed, TO is no evidence of primary tumour, T1 is clinically in apparent tumour, T1a is tumour (non-palpable) as incidental histological finding at transurethral resection of prostate in 5% tissue resected, T1b is tumour (non-palpable) as incidental histological finding at transurethral resection of prostate in > 5% tissue resected, T1c is identified by needle biopsy, T2 is tumour confined within prostate that is either palpable or visible on imaging or demonstrated in radical prostatectomy specimen, T2a is tumour involving one-half of one lobe or less, T2b is tumour involving both lobes, T3 is Tumour extends through prostatic capsule, T3a is extra-capsular extension (ECE), T3b is invasion of seminal vesicle(s) and T4 is tumour fixed or invades adjacent structures.

Clinically localized prostate cancer should be categorized as low, intermediate or high risk. Where low risk is T1 to T2a, Gleason <7, PSA <10; high risk equals any of T3 or T4, Gleason >7, PSA >20.

Different Cancer Cells: $CD44^{+}$, $CD44^{-}$, CK5, CK14, LNCaP, PC3, P53, CN706, DU145, Bcl2.

Causes and Risk Factors: [71, 72, 73, 74, 75, 76] Fruits and vegetables, carotenoid lycopene, carotenoids, tocopherols, retinol, genetic, age, smoking, alchohol, family history, sex steroids, neurosporene, phytoene, Vitamin D.

Sign and Symptoms: [77 - 79] Hesitancy, leakage, urgency, dysuria, weak stream, frequency, impotence, nocturia, urinary retention, haemetaria, hyperplasia.

Diagnosis: [30, 80, 81] Engrailed-2 (EN2), Serum Prostate Specific Antigen (PSA), Hypertrophy, Prostatitis, Digital Rectal Examination (DRE), biopsy, prostate size, ethnicity, Transrectal Ultrasound (TRUS), ultrasound-guided trans-perineal and template- guided biopsies, repeat and saturation biopsies, transrectal ultrasonography.

Different Biomarkers Used to Diagnose: [83] IGF2, RSSF1A, GSTP1, AOX1, RARB, EZH2, H3K27, SET9, SMYD3, JHDM2A, JMJD2C, LSD1, HAT , HDAC1, HDAC2, SIRT1, miR-18a, miRNA-129, APC, CRIP3, GSTP1, HOXD.

Treatment: [84 - 89] Surgery, radiation therapy, cryotherapy, brachytherapy, external-beam radiation therapy, primary androgen deprivation therapy, harmonal therapy, androgen-ablation therapy, prostatectomy, cytotoxic chemotherapy, iodine 125 seeds, high dose iridium 192 rods, adjuvant and salvage treatment after radical prostatectomy

Drugs: [90 - 94] Dutasteride, finasteride, flutamide associated with medical (Luteinizing hormone-releasing hormone agonist) enzalutamide, mito-xantrone plus prednisone, prednisone alone, docetaxel, cabazitaxel, mitoxantrone.

Prevention: [95 - 104]

Hormonal Prevention: Finasteride brings down the risk of prostate cancer, however, may likewise change the detection of disease through effects on prostate-specific antigen (PSA). A cochrane efficient survey of every single distributed investigation of clinical outcome examinations of the prostate preventive impacts of 5-alpha-reductase (5AR) inhibitors through 2010 that were no less than one year in length induced that finasteride and dutasteride diminishes the danger of being determined to have prostate among men who are screened routinely for prostate cancer.

Dietary prevention with fruit, vegetables, and a low-fat diet: Intake of vegetables and yellow-orange and cruciferous vegetables was identified with a lower danger of prostate cancer. Clinical and laboratory studies result revealed that, few agents, including alpha-tocopherol, selenium, lycopene, difluoromethylornithine, Vitamin D and isoflavonoids have exhibited potential for chemoprevention of prostate tumor. Lycopene is present as the strongest circulating carotenoid in Americans and has a various potential activities, including a cell reinforcement impact.

Physical activity, weight control, blood pressure control, quit smoking and tobacco are the best prevention for the kidney cancer.

Testicular Cancer: Testicular cancer is a disease when testicular cells, wind up noticeably anomalous (threatening) in one or the two gonads [6]. The balls (testicles) deliver male sex hormones and sperm for proliferation [105]. It is the most widely recognized disease in 15-35 year old men and has two primary sorts, seminoma and non seminoma. Testicular is a moderately uncommon tumor sort representing roughly 1% of all male cancers in the globe [7]. The most vital hazard factors in the improvement of testicular tumor are undescended testicles (cytochordism) uroligical birth defects, family history and Caucasian men [106].

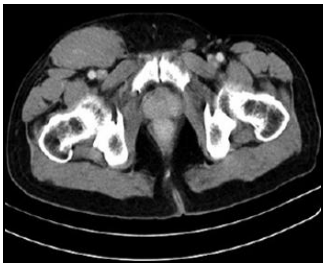

FIG. 4: COMPUTED TOMOGRAPHY IMAGES OF 30 YEAR MALE'S TESTICULAR CANCER; SHOWING RIGHT INGUINAL METASTATIC NODAL MASS [107]

Types: [108, 109] Seminomatou, nonseminomatous, teratoma, embryonal cell carcinoma and yolk sac tumour choriocarcinoma are the different types of testicular cancer.

Staging: T is extent of the primary tumor is classified after radical orchiectomy, TX is primary tumor cannot be evaluated *i.e*. radical orchiectomy not yet performed, T0 is no evidence of primary tumor (histologic scar in the testis), TIS is

carcinoma in situ, pre invasive stage, T1 is tumor limited to the testis, including the rete testis, T2 is Tumor invades beyond the Tunica albuginea or into the epididymis, T3 is tumor invades the spermatic cord and T4 is tumor invades the scrotum.

Symptoms: [6, 110] Anorexia, malaise, weight loss, constipation, cough or shortness of breath, appetite loss, neck mass due to lymph node metastases, sleep disturbance, dyspnoea, lower back pain, lower extremity swelling due to iliac or caval obstruction or thrombosis, nausea, fatigue, vomiting, gastrointestinal haemorrhage, bony pain, diarrhoea.

Causes and Symptoms: [111 - 115] Cryptorchidism, a family history of testis cancer, undescended testis, inguinal hernia, klinefelter syndrome, mumps orchitis, obesity, HIV infection, carcinoma in situ, down syndrome, testis trauma, eepididimytis and hematocele.

Diagnosis: [116 - 118] Hydrocoele, varicocoele, hernia, haematoma, spermatocoele, epididymitis, haemato-cele, ultrasound, biopsy, blood test, testicular self examination, CT scan and MRI.

Different Biomarkers Used to Diagnosed: [119] AFP is α-fetoprotein; β HCG is Human Chorionic Gonadotropin, CA 15-3, CA 19-9, CA 125, CA 549, CA 27-29, Carcinoembrionary antigen, ErbB-2 / HER-2

Treatment: [120 - 123] Sparing surgery, inguinal orchidectomy, cardio therapy and chemotherapy are the treatment of testicular cancer.

Drugs: Bleomycin, etoposide, Cis-platin (BEP), Cis-platinum, vinblastine, bleomycin.

Prevention: Physical activity, weight control, retinol, Vitamin A, adequate hygiene and quit smoking are the best prevention for the testicular cancer.

CONCLUSION: Urogenital cancers are the life threatening disease in worldwide, among them kidney cancer, bladder cancer, prostate cancer and testicular cancer are four most life threatening urogenital cancers. Lots of factors are responsible for the cancers. So, drugs are not only the choice for the management of cancers is required peoples/ patients' awareness, a way of living, education is the best choice for the prevention of cancers.

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CONFLICT OF INTEREST: Nil

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