PROFILE AND TREATMENT OUTCOME OF PATIENTS WITH CARCINOMA OF BLADDER AS SEEN AT MUHIMBILI NATIONAL AND TUMAINI HOSPITALS, IN DAR ES SALAAM, TANZANIA

Deogratius Emmanuel Mahenda, MD

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PROFILE AND TREATMENT OUTCOME OF PATIENTS WITH CARCINOMA OF BLADDER AS SEEN AT MUHIMBILI NATIONAL AND TUMAINI HOSPITALS, IN DAR ES SALAAM, TANZANIA

By,

Deogratius Emmanuel Mahenda, MD

A Dissertation Submitted in Partial fulfillment of the Requirements for the Degree of Master of Medicine (Urology) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certifies that he has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled **Profile And Treatment Outcome of Patients With Carcinoma of Bladder as Seen at Muhimbili National and Tumaini Hospitals, in Dar Es Salaam, Tanzania**, in partial fulfillment of the requirements for the degree of Master of Medicine (Urology) of Muhimbili University of Health and Allied Sciences.

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Prof. Sydney Chalonde Yongolo

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Date

DECLARATION AND COPYRIGHT

I, **Deogratius Emmanuel Mahenda**, declare that, this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for similar or any other degree award.

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DEDICATION

To my dear and lovely wife, Agnes for her support, patience and care. My daughters Anna-Maria and Petronilla who are ten and six year's girls respectively for the encouragement they gave me and for their patience while I was busy with studies. My dear Parents (Deceased) Mr. and Mrs. Emmanuel Mathew Sambila, who wished me to become a doctor, may their souls rest in eternal peace, Amen.

ABSTRACT

Introduction -Bladder cancer is ninth in worldwide cancer incidence. Approximately 356,000 new bladder cancer cases occurred worldwide in 2002. Globally men are more commonly affected than women with a male/female ratio of 10:3. The incidence rate in Tanzania is projected to be more than 3.7/100, 000], but more than 90% of new cases occur in persons 55 years of age or higher [1]. Globally it is estimated that 145,000 patients die from bladder cancer annually. Cigarette smoking and occupational exposure to urothelial carcinogens are the main risk factors in the US and Europe, but *Schistosoma haematobium* infestation is the main risk factor in Schistosoma endemic areas. Bladder cancer presents with haematuria and irritative symptoms. Transitional cell carcinoma is the commonest histological finding in the developed world and squamous cell carcinoma is associated with Bilharzial bladder cancer are more in the developing countries.

Objectives- This study documents on the profile and early treatment outcome of patients with carcinoma of the urinary bladder as seen in two hospitals (Muhimbili National hospital and Tumaini) in Dar es Salaam from March 2012 to December 2012.

Methodology – A descriptive, prospective, hospital-based study involving observation of patients from admission to outcome of management at discharge or death was carried out. Consecutive admissions of patients with bladder cancer attended at urology unit at the department of surgery Muhimbili National Hospital, and Tumaini hospital were enrolled in the study. The study was conducted from March to December 2012. The data were analyzed using SPSS version 16 software.

Results: A total of 67 bladder cancer patients were enrolled during the study period. Males were 25 and females were 42 with male to female ratio of 1:1.7. The age range was from 30 to 80 years with the mean age of 54.31 years. Twenty two patients (32.8%) were in the age group of 60 to 69. Fifteen (34.9%) of patients in age group between 60 and 69 lived in high risk areas and twenty one (35.6%) in the same age group had high risk occupation. Cigarette smoking and Schistosoma infestation were common

associated factors among patients who had squamous cell carcinoma. All patients who had transitional cell carcinoma presented with blood in urine while 39(58.2%) of squamous cell carcinoma patients had blood in urine as their clinical presentation.

The ultrasound scan was able to pick bladder mass in 60 patients among the 67.However cystoscopy detected tumour in all 67 patients. There were four histological types in all patients of bladder cancer, squamous cell carcinoma 47 (70.1%), transitional cell carcinoma 16(23.9%), Adenocarcinoma 3 and Adenosquamous 1. the tumours were either well or moderately differentiated.

In this study nearly half of the patients presented with clinical stage 4 diseases (46.3%). Among all 67 patients 13 (26.5%) had cystectomy and 3 (6.1%) had TURBT, the rest had palliation either in the form of chemoradiotherapy or home palliative care (16(12.2%) and 27 (55.1%) respectively. Anaemia was the leading complication (30.5%). Among 67 bladder cancer patients 33 (49.3%) died. Five (15.2%) died of renal failure and 18 (54.5%) died of advanced bladder cancer. There was no patient who absconded as all patients were called using either their personal telephone number or their close relative's telephone number.

Conclusions: Women were more affected by the disease than men, Schistosoma infestation was the commonest risk factor for bladder cancer development. Haematuria was the commonest clinical presentation followed by irritative urinary symptoms; the disease was detected by ultrasound scan which was readily available, and affordable. Punch biopsy was the leading method of obtaining tissue specimen for histology diagnosis, and SCC was the leading histological type of bladder cancer. Most of the patients came at an advanced stage, thus few of them had surgical treatment. Wound sepsis and dehiscence were the commonest complication for those who underwent cystectomy and urinary diversion, and 49% of all patients died before treatment.

Recommendations: The findings of this study with limitation of short duration have come up with the following recommendations:

- There is a need for a long duration study especially to get proper treatment outcome of a disease
- Monitor for possible exposure to *Schistoma heamatobium* infestation and advice the prevention measures.
- Mass campaign for possible elimination of *Schistoma heamatobium* infestation.
- Early diagnosis of patients with bladder cancer will improve their treatment outcome.
- Create awareness to primary and secondary referring health facilities on early diagnosis of bladder cancer.
- CT scan for clinical staging of a disease can be used to supplement examination under anesthesia for clinical staging of a disease.

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ABBREVIATIONS

BTA	-	Bladder tumor antigen
CIS	-	Carcinoma in Situ
NMP	-	Nuclear Matrix Protein
TUR	-	Transurethral Resection
PUNLMP	-	Papillary Urothelial Neoplasm of Low Malignancy Potential.
ISUP	-	International Society of Urologic Pathology
MIBC	-	Muscle Invasive Bladder Cancer
NMIBC	-	Non Muscle Invasive Bladder Cancer
SCC	-	Squamous Cell Carcinoma.
TURBT	-	Trans Urethral Resection of Bladder Tumor
UBC	-	Urinary bladder cancer.
TCC	-	Transitional cell carcinoma
IVU	-	Intravenous urogram
USS	-	Ultrasound scan
CT scan	-	Computerized tomography scan
HRR	-	High risk residence –schistosoma endemic areas
LRR	-	Low risk residence-non schistosoma endemic areas
HRO	-	High risk occupation - fishing, paddy cultivation, chemical industry
LRO	-	Low risk occupation-nor fishing,paddy cultivation or chemical industry

DEFINITION OF TERMS

Low risk occupation

This is the occupation which does not render an individual at risk of bladder cancer.

High risk occupation

This is an occupation which renders an individual at risk of bladder cancer.

High risk residence

This is the schistosomal endemic area.

Low risk residence

This non schistosomal endemic area

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1.0 Background

Bladder cancer is ninth in worldwide cancer incidence. It is the seventh most common cancer in men and the seventeenth most common cancer in women. Approximately 356,000 new bladder cancer cases (274,000 males and 83,000 females) occurred worldwide in 2002[1]. Globally men are more commonly affected than females with a male/female ratio of 10:3[1].

Worldwide, the incidence of bladder cancer varies significantly, with Egypt, Western Europe, and North America having the highest incidence rates, and Asian countries the lowest rates [1]. The incidence rate in Tanzania is projected to be more than 3.7/100, 000 [1] and the disease is 3.3% of all registered cancers in Tanzania [2]. The disease may occur rarely in young persons before the age of 40 years [1], but more than 90% of new cases occur in persons 55 years of age or higher [1].

Globally it is estimated that 145,000 patients die from bladder cancer annually. The worldwide mortality rate among males is 4 per 100,000 versus 1.1 per 100,000 among females. The difference in bladder cancer mortality around the world is not as large as that in bladder cancer incidence [3].

1.1.1 Aetiology.

The most well-established risk factors for bladder cancer are cigarette smoking and occupational exposure to urothelial carcinogens and probably chronic bladder infections or infestattion [1, 4], in the US and Europe, but risk factors in other parts of the world may be different [1, 5].

Cigarette smoking is the most important risk factor, accounting for 50% of cases in men and 35% in women [1]. In fact, cigarette smokers have a 2- to 4-fold increased risk of bladder cancer compared to non-smokers [1, 6], and the risk increases with increasing intensity and/or duration of smoking. Upon cessation of cigarette smoking, the risk of bladder cancer falls >30% after 1–4 years and more than 60% after 25 years but never returns to the level of risk of non-smokers [1, 6, and 7].

The second most important risk factor is occupational exposure to urothelial carcinogens accounting for 5–20% of all bladder cancers. The relative risk of occupational exposure to carcinogens is likely underestimated and varies from country to country [1]. The current or historical exposure to aromatic amines (e.g. Benzedine, 2-naphthylamine, 4 aminobiphenyl,otoluidine, and 4-chloro-o toluidine) which are used in the chemical, rubber, and dye industries, and polycyclic aromatic hydrocarbons (PAHs) used in the aluminum, coal, and roofing industries have all been associated with the development of bladder cancer. An increased risk of bladder cancer has also been reported in painters, varnishers, and hairdressers [1, 6, 8].

Chronic cystitis following indwelling catheters or calculi is associated with an increased risk of squamous cell carcinoma (SCC) of the bladder. Similarly, *Schistosoma haematobium* cystitis seems to be causally related to the development of bladder cancer [9]. About 80% of SCCs in Egypt are associated with chronic infestation with S. haematobium. These cancers occur in patients who are, on the average, 10 to 20 years younger than patients with TCC [10].

Carcinoma of the bilharzial bladder is probably related to bacterial and viral infections, commonly associated with bilharzial infestation, rather than the parasite itself. Urinary bacteria have a double action, namely (i) secretion of β-glucuronidase enzyme which may clear conjugated carcinogens, yielding free carcinogenic products, (ii) the production of carcinogenic nitrosamines from their precursors in urine, such as nitrates and secondary amines. Local mechanical irritation by Schistosoma eggs appears to be an important promoting factor. Two thirds of the cancers show squamous cell differentiation. This tumour is of high grade, invasive and more aggressive than transitional cell carcinoma. Most patients present for treatment at an advanced stage. The explanation for the late presentation may be the overlapping of symptoms of simple bilharzial cystitis with early malignant cystitis [11]. Non-bilharzial SCCs are usually caused by chronic irritation from urinary calculi, long-term indwelling catheters, chronic urinary infections, or bladder diverticula [9, 10]. Approximately 80% of paraplegics with chronic infections and/or indwelling catheters have squamous changes in the bladder, and about 5% of them develop SCC. Cigarette smoking has also been reported to be significantly associated with an increased risk of bladder SCC. In general, its prognosis is poor because most patients have advanced disease at the time of diagnosis [10].

Human papilloma virus (HPV) infection, plays a role in cell tumorigenesis in immunocompromised patients to develop bladder cancer[9], and patients treated with cyclophosphamide have up to nine-fold increased risk of developing bladder cancer [9].

Other environmental factors that are associated with development of bladder cancer are exposure to pelvic irradiation in females treated with radiation for carcinoma of the uterine cervix or ovary. Patients with such exposure have a two- to four-fold increased risk of developing bladder cancer subsequently compared with women undergoing only surgery [1, 9]. Recently, the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) group study has found an increased incidence of bladder cancer in men with prostate cancer treated with radiotherapy [1].

High intake of soy food is significantly associated with an elevated risk of bladder cancer [9], as a result of soy secondary metabolites such as isoflavones [12] and a high intake of carotenoids was associated with an overall decrease in bladder cancer risk [9].

An intake of coffee (more than 4 cups/day) was observed to increase bladder cancer risk [1, 6, and 9]. Relationship of consumption of tea was not established with the risk of bladder cancer [6]. Use of large quantities (5 to 15 kg over a period of ten years) of analgesic combinations containing phenacetin is associated with an increased risk of bladder cancer [9].

Bacon is the major food source of preformed nitrosamines. Frequent consumption of bacon was associated with an increased risk of bladder cancer [9].

The consumption of adequate amount of water is a protection against bladder cancer. Large volumes of water in the bladder reduce the concentration and stay time of chemicals by frequent urination. A high fluid intake is associated with a decreased incidence of bladder cancer in males, and lesser intake of daily fluids proportionally increases the risk of bladder cancer. Total daily fluid intake was inversely associated with the risk of bladder cancer [6, 9].

Consumption of fried foods is significantly associated with bladder cancer. Subjects who are consuming fried foods more than 2 days per week have 5.9 times more risk of bladder cancer as compared to those who consume fried foods 2 or fewer days per week [6]. Consumption of fruits more than 2 days per week has 0.173 times risk reduction of bladder cancer, i.e., 83% protection against bladder cancer as compared to those who consume fruits 2 or less than 2 days per week. The risk of bladder cancer was inversely associated with the high consumption of fruits and vegetables [1, 6].

Many studies have evaluated the role of alcoholic beverage consumption on bladder cancer risk and have provided inconsistent results, however a recent meta-analysis indicated no evidence for alcohol consumption [9]. Geographic variations in bladder cancer risk,

observed in the United States and other countries, have been ecologically related to soil selenium levels. However, in a randomized, double-blind, placebo controlled prevention trial, observed no association between toenail selenium concentrations and bladder cancer risk among male smokers [9]. In a prospective study, it was demonstrated that there was no statistically significant association between baseline total fish or marine fatty intake and the risk of bladder cancer among men or women [9]. Dietary supplements, macronutrients, micronutrients in a prospective cohort study involving cases of bladder cancer found no association for total caloric or macronutrient intake and bladder cancer risk, and they also found no association for dietary intake of potassium, sodium, calcium, magnesium, phosphorus, iron, or water-soluble vitamins and bladder cancer risk [9]. Total vitamin E intake and vitamin E supplements were inversely associated with the risk. Finally, a suggested inverse association was seen with the dose of vitamin C supplement used [9].

1.1.2 Symptoms and Signs

The most common presenting symptom of TCC is painless hematuria, which occurs in about 85% of patients [10, 13]. In reality, nearly all patients with cystoscopically detectable bladder cancer have at least microhematuria if enough urine samples are tested. However, hematuria is often quite intermittent so that a negative result on one or two specimens has little meaning in ruling out the presence of bladder cancer. Thus, if a patient in the bladder cancer age range has unexplained hematuria on a urine specimen (either microscopically or grossly evident) and a "confirmatory" second specimen is free of any hematuria, cystoscopic examination is still usually warranted [10].

The symptom complex of bladder irritability and urinary frequency, urgency, and dysuria is the second most common presentation and is usually associated with diffuse carcinoma in situ or invasive bladder cancer. However, these symptoms almost never occur without (at least) microscopic hematuria [10, 13]. The duration of symptoms varies between one and 12 months [13]. Other symptoms and signs of bladder cancer include flank pain from ureteral obstruction, lower extremity edema, and pelvic mass [10, 14]. Symptoms of advanced disease include bone pain from bone metastases or flank pain from

retroperitoneal metastases [14]. Patients with SCC present with symptoms of advanced stage, and they tend to have invasive and more aggressive disease than transitional cell carcinoma patients. Most patients present for treatment at an advanced stage. The explanation for the late presentation may be the overlapping of symptoms of simple bilharzial cystitis with early malignant cystitis [9].

1.1.3. Histopathology

1.1.3.1 Papilloma

The World Health Organization recognizes a papilloma as a papillary tumor with a fine fibrovascular stalk supporting an epithelial layer of transitional cells with normal thickness and cytology. Papillomas are a rare benign condition usually occurring in younger patients [15]. Benign tumours of the bladder, including the inverted papilloma and the nephrogenic adenoma, are uncommon [16].

1.1.3.2 Transitional cell carcinoma

Regardless of name, urothelial (transitional cell) cancers differ from normal urothelium by having an increased number of epithelial cell layers with papillary folding of the mucosa, loss of cell polarity, abnormal cell maturation from basal to superficial layers, increased nuclear cytoplasmic ratio, prominent nucleoli, clumping of chromatin, and increased number of mitoses [10]. These tumors most commonly appear as papillary, exophytic lesions less commonly, they may be sessile or ulcerated. Whereas the former group is usually superficial in nature, sessile growths are often invasive. Carcinoma in situ (CIS) is recognizable as flat, anaplastic epithelium [15]. Carcinoma in situ may appear as a velvety patch of erythematous mucosa, although quite often it is endoscopically invisible. Histologically, it consists of poorly differentiated TCC confined to the urothelium [10]. The urothelium lacks the normal cellular polarity, and cells contain large, irregular hyperchromatic nuclei with prominent nucleoli [14].

1.1.3.3 Squamous cell carcinoma

These tumors are often nodular and invasive at the time of diagnosis. Histologically they appear as poorly differentiated neoplasms composed of polygonal cells with characteristic intercellular bridges. Keratinizing epithelium is present, although often in small amounts [10, 14]. Keratinizing epithelium is present in islands that contain eccentric aggregates of cells called squamous pearls. They may show varying degrees of histologic differentiation [10].

1.1.3.4 Undifferentiated carcinomas

Undifferentiated bladder carcinomas, which are rare (accounting for <2%), have no mature epithelial elements. Very undifferentiated tumors with neuroendocrine features and small cell carcinomas tend to be aggressive and present with metastases [14].

1.1.3.5 Mixed carcinoma

Mixed carcinomas constitute 4–6% of all bladder cancers and are composed of a combination of transitional, glandular, squamous, or undifferentiated patterns. The most common type comprises transitional and squamous cell elements. Most mixed carcinomas are large and infiltrating at the time of diagnosis [14].

1.1.3.6 Rare epithelial & nonepithelial cancers

Rare epithelial carcinomas identified in the bladder include villous adenomas, carcinoid tumors, carcinosarcomas, and melanomas. Rare nonepithelial cancers of the urinary bladder include pheochromocytomas, lymphomas, choriocarcinomas, and various mesenchymal tumors (hemangioma, osteogenic sarcoma, and myosarcoma). Cancers of the prostate, cervix, and rectum may involve the bladder by direct extension. The most common tumors metastatic to the bladder include (in order of incidence) melanoma, lymphoma, stomach, breast, kidney, lung and liver [14].

1.1.3.7 Adenocarcinoma

Adenocarcinomas account for less than 2% of primary bladder cancers. They are classified into three groups: (1) primary vesical; (2) urachal; and (3) metastatic. Adenocarcinomas also occur in intestinal urinary conduits, augmentations, pouches, and ureterosigmoidostomies [10].

Primary vesical adenocarcinoma

Adenocarcinomas usually arise in the bladder base area or in the dome, but they can occur anywhere. It is the most common type of cancer in exstrophic bladders. These tumors develop in response to chronic inflammation and irritation. All histologic variants of enteric adenocarcinoma occur in the bladder. Most are mucin producing. Signet-ring carcinomas characteristically produce linitis plastica of the bladder. Most adenocarcinomas are poorly differentiated and invasive. They are more commonly associated with cystitis glandularis than with carcinoma in situ. The generally poor prognosis associated with adenocarcinomas is due primarily to their advanced stage at diagnosis. There is no evidence to indicate that, stage for stage, their prognosis is markedly different from that of urothelial carcinoma [10].

Urachal carcinoma

Urachal carcinomas are extremely rare tumors that arise outside the bladder, and they are usually adenocarcinomas, although they may be primary TCCs or SCCs and, rarely, even sarcomas. Urachal carcinomas have a sharp demarcation between the tumor and the adjacent bladder epithelium, with the tumor being located in the bladder wall beneath the normal epithelium. They may appear with a bloody or mucoid discharge from the umbilicus or produce a mucocele, occurring as a palpable mass. Many urachal tumors have stippled calcifications on radiographs. Tumors invading the bladder lumen may produce mucus in the urine. Patients with urachal carcinomas have a worse prognosis than do those with primary bladder adenocarcinomas. Histologically, these tumors exhibit wider and

deeper infiltration of the bladder wall than expected, compromising the results of partial cystectomy. Urachal carcinomas metastasize to iliac and inguinal lymph nodes, omentum, liver, lung, and bone [10].

Metastatic adenocarcinoma

One of the most common forms of adenocarcinoma of the bladder is metastatic (or invasive) adenocarcinoma. The primary sites for these tumors include the colon, stomach, endometrium, breast, prostate, and ovary [10].

1.1.4 Grading and clinical staging

Grading

There is no uniformly accepted grading system for bladder cancer. The most commonly used systems are based on the degree of anaplasia of the tumor cells [10]. Traditionally, bladder carcinomas have been graded according to the World Health Organization (WHO) 1973 grading of urothelial papilloma: well differentiated (G1), moderately differentiated (G2), or poorly differentiated (G3) [14, 15]. In 2004, the WHO and the International Society of Urological Pathology (ISUP) published a new grading system that employs specific cytologic and architectural criteria [14]. The new WHO/ISUP classification differentiates between papillary urothelial neoplasms of low malignant potential (PUNLMP) and low-grade and high-grade urothelial carcinomas [14]. Use of the 2004 WHO/ISUP classification should result in more uniform diagnoses of tumours that are better stratified according to risk potential. WHO classifications should be used for tumour grading until the 2004 grading system is validated in more clinical trials [14].

A strong correlation exists between tumor grade and stage, with most well-differentiated and moderately differentiated tumors being superficial and most poorly differentiated ones being muscle invasive [10]. Stage for stage, there is a significant correlation between tumor grade and prognosis; however, the correlation between tumor stage and prognosis is even stronger. A papilloma (grade 0) is a papillary lesion with a fine fibrovascular core covered by normal bladder mucosa [10].

Well-differentiated tumors have a thin fibrovascular stalk with a thickened urothelium containing more than seven cell layers, with cells exhibiting only slight anaplasia and pleomorphism. The disturbance of the base-to-surface cellular maturation is mild, and there are only rare mitotic figures. When they are mucosally confined, these have been termed papillary urothelial tumors of low malignant potential by the WHO and the ISUP [10]. However, even when detected alone, they often recur, and recurrences may be of higher histologic grade and stage [10]. Lesions with this appearance (similar to those formerly called grade 1) are urothelial cancers. They are found in the same bladders and frequently in the same individual tumors) as higher-grade cancers and share similar molecular and prognostic features with low-grade cancers [10].

Moderately differentiated tumors have a wider fibrovascular core, a greater disturbance of the base-to-surface cellular maturation, and a loss of cell polarity. The nuclear-cytoplasmic ratio is higher, with more nuclear pleomorphism and prominent nucleoli [10]. Mitotic figures are more frequent. These have been termed low-grade urothelial carcinomas in the new WHO and ISUP classification [10].

Poorly differentiated tumors named high-grade urothelial carcinoma in the new WHO and ISUP system (old grade 3), have cells that do not differentiate as they progress from the basement membrane to the surface. Marked nuclear pleomorphism is noted, with a high nuclear-cytoplasmic ratio. Mitotic figures may be frequent [10].

World Health Organization (WHO) grading of Urinary bladder tumours in 1973 and 2004 [1]

WHO 1973	
Urothelial papilloma	
Grade 1	Well differentiated
Grade 2:	Moderately differentiated
Grade 3	Poorly differentiated
WHO 2004	
Urothelial papilloma	
PUNLMP	
Low-grade papillary urothelial carcinoma	
High-grade papillary urothelial carcinoma	
PUNLMP = papillary urothelial neoplasms of low malignant potential	

Staging

Tumor stage is important in determining therapy. Accurate staging of bladder cancer is desirable [16]. The tumour-node-metastases (TNM) classification for tumour staging and both the World Health Organization (WHO) 1973 and 2004 grading systems should be applied for appropriate staging and grading of NMIBC [1]. Stage and grade are significant prognostic factors for survival, progression, and recurrences therefore are critical for the appropriate treatment and management of NMIBC [1]. The most widely used and universally accepted staging system is the tumour-node-metastases (TNM) system [1, 14]. This staging system allows for a precise and simultaneous description of the primary tumor stage [14]. Thus NMIBC includes (1) papillary tumours confined to the epithelial mucosa (stage Ta); (2) tumours invading the subepithelial tissue (ie, lamina propria; T1); and (3) Tis (CIS) [1].

2002 TNM classification of urinary bladder cancer [1]

Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumour
Ta	Non-invasive papillary carcinoma
Tis	Carcinoma in situ: ‘‘flat tumour’’
T1	Tumour invades sub epithelial connective tissue
T2	Tumour invades muscle
T2a	Tumour invades superficial muscle (inner half)
T2b	Tumour invades deep muscle (outer half)
T3	T3 Tumour invades perivesical tissue:
T3a	T3a: Microscopically
T3b	T3b: Macroscopically
T4	T4 Tumour invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall
T4a	T4a: Tumour invades prostate, uterus, or vagina
T4b	T4b: Tumour invades pelvic wall or abdominal wall
N	Lymph nodes
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single lymph node $\leq$ 2 cm in greatest dimension
N2	Metastasis in a single lymph node >2 cm but not >5 cm in greatest dimension, or multiple lymph nodes, not >5 cm in greatest dimension
N3	Metastasis in a lymph node >5 cm in greatest dimension
M	Distant metastasis
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

1.1.5 Diagnostic work up

Laboratory investigations.

The most common laboratory abnormality is hematuria. It may be accompanied by pyuria, which on occasion may result from concomitant urinary tract infection. Renal insufficiency may be noted in patients with ureteral occlusion owing to the primary bladder tumor or lymphadenopathy. Anemia may be a presenting symptom owing to chronic blood loss, ureamia or replacement of the bone marrow with metastatic disease [14].

Exfoliated cells from both normal and neoplastic urothelium can be readily identified in voided urine. Larger quantities of cells can be obtained by gently irrigating the bladder with isotonic saline solution through a catheter or cystoscopy (barbotage). Cytologic examination of exfoliated cells may be especially useful in detecting cancer in symptomatic patients and assessing response to treatment. Detection rates are high for tumors of high grade and stage as well as CIS but not as impressive for low grade superficial tumors [14]

Several new tests have been developed in order to overcome the shortcomings of urinary cytology Commercially available tests include, the Bladder Tumour Antigen (BTA) test , BTA stat test , the BTA TRAK assay, determination of urinary nuclear matrix protein (NMP) 22 , Immunocyt and UroVision. These tests can detect cancer specific proteins in urine (BTA/NMP22) or augment cytology by identifying cell surface or cytogenetic markers in the nucleus [14].

Imaging

Although bladder cancers may be detected by various imaging techniques, their presence is confirmed by cystoscopy and biopsy. Imaging is therefore used to evaluate the upper urinary tract and, when infiltrating bladder tumors are detected, to assess the depth of muscle wall infiltration and the presence of regional or distant metastases. Intravenous urography remains one of the most common imaging tests for the evaluation of hematuria. However, intravenous urography is increasingly being replaced by computed tomography

(CT) urography, which is more accurate, for evaluation of the entire abdominal cavity, renal parenchyma, and ureters in patients with hematuria. Bladder tumors may be recognized as pedunculated, radiolucent filling defects projecting into the lumen, nonpapillary, infiltrating tumors may result in fixation or flattening of the bladder wall [14]. However Mwashambwa and Yongolo concluded that ultrasound is an effective method for evaluating patients presenting with haematuria or suspected to have bladder tumours. It is cheap, available, affordable and non-invasive; has a high sensitivity, and therefore it can also be useful in the follow-up of patients with bladder cancer [17].

Hydronephrosis from ureteral obstruction is usually associated with deeply infiltrating lesions and poor outcome after treatment. Superficial (Ta, Tis) bladder cancers staged with a properly performed TUR and examination under anesthesia do not require additional imaging of the bladder or pelvic organs. However, higher stage lesions are often under staged, and the addition of imaging may be useful. Both CT and magnetic resonance imaging (MRI) have been used to characterize the extent of bladder wall invasion and detect enlarged pelvic lymph nodes, with overall staging accuracy ranging from 40% to 85% for CT and from 50% to 90% for MRI. Both techniques rely on size criteria for the detection of lymphadenopathy: Lymph nodes more than1 cm are thought to be suggestive of metastases; unfortunately, small-volume pelvic lymph node metastases are often missed [13]. Because invasive bladder cancers may metastasize to the lung or bones, staging of advanced lesions is completed with chest x-ray and radionuclide bone scan [14].

Cystoscopy

Cystoscopic examination of the bladder continues to be the primary diagnostic tool since urinary cytology and imaging studies have high false negative rates [14]. However in SCC cytology has been of limited utility in the diagnosis of this tumor [10]. The diagnosis and initial staging of bladder cancer is made by cystoscopy [14]. Tumors discovered on cystoscopy will need to be biopsied for diagnosis and treatment. Deep resection of the entire tumor with underlying muscle is necessary [14]. Resection should be followed by superficial random cold cup biopsies from the anterior wall or dome, each lateral wall, the posterior wall, trigone, and the prostatic urethra (in males), looking for field changes consistent with carcinoma in situ. Tumors within diverticula should be removed by cold cup biopsy and fulguration or open surgery [19]. Cystoscopy can be done with either flexible or rigid instruments, although the former is associated with less discomfort and only requires local anesthesia. Superficial, low-grade tumors usually appear as single or multiple papillary lesions. Higher grade lesions are larger and sessile. CIS may appear as flat areas of erythema and mucosal irregularity. Use of fluorescent cystoscopy with blue light can enhance the ability to detect lesions by as much as 20% [14]

Once a tumor is visualized or suspected, the patient is scheduled for examination under anesthesia and TUR or biopsy of the suspicious lesion. The objectives are tumor diagnosis, assessment of the degree of bladder wall invasion (staging), and complete excision of the low-stage lesions amenable to such treatment. Patients are placed in the lithotomy position and a careful bimanual examination is performed. The presence of any palpable mass and mobility of the bladder are noted, along with any degree of fixation to contiguous structures [14].

1.1.6.0 Treatment of Bladder Cancer

1.1.6.1 Treatment of Non Muscle Invasive Bladder Cancer

Successful treatment of bladder cancer is still a challenge for urologists and oncologists. Once a tumor has been clinically and pathologically staged and graded, treatment options vary according to disease stage and severity [18]. Patients with superficial transitional cell carcinoma -bladder can be treated with TUR followed by selective intravesical chemotherapy or immunotherapy [14]. Patients with initial low-grade small tumors are at low risk of progression and may be treated by TUR alone followed by surveillance or intravesical chemotherapy. Patients with T1, high-grade, multiple, large, recurrent tumors or those associated with CIS on bladder biopsies are at a higher risk of progression and recurrence and should be considered candidates for intravesical chemotherapy or immunotherapy after complete and careful TUR. A second resection of the same area may be required to accurately stage disease and determine treatment [14, 18]. However well-differentiated, superficial SCC can be managed by transurethral resection. Locally invasive tumors are managed by radical cystectomy. Patients with lymph node involvement generally survive only 3 to 6 months. No effective chemotherapy has yet been identified [19].

It is recommended to administer a single dose of immediate intravesical mitomycin C within 24 h of the resection to lower the risk of recurrence in Ta low-grade tumors [19]. The first year recurrence rate is significantly decreased if Mitomycin (MMC) -40 is instilled following TUR [20]. Most low grade, low volume tumours would not require any further treatment if MMC-40 is given immediately following TUR [20]. Following TURBT, all patients with high-grade Ta or Tis tumors should be treated with intravesical instillation of bacillus Calmette-Guérin (BCG) or mitomycin C [21]. Patients with multiple recurrent high-grade tumors, high-grade T1 tumors, high-grade tumors with concomitant carcinoma in situ, or who have not responded to intravesical BCG or MMC should undergo immediate cystectomy [18]

Due to the risk of recurrence and progression urothelial bladder carcinoma, patients with non-muscle invasive bladder tumors need to be followed according to the individual patient's degree of risk. In Europe patients with tumors at low risk of recurrence and progression should have a cystoscopy at 3 months. If it is negative, the following cystoscopy is advised at 9 months and consequently yearly for 5 years [18]. Patients with tumors at high risk of progression should have a cystoscopy and urinary cytology at 3 months. If negative, the following cystoscopies and cytologies should be repeated every 3 months for a period of 2 years, every 4 months in the third year, every 6 months thereafter until 5 years, and yearly thereafter [18]. However, patients with Tis should be followed lifelong due to the high risk of recurrence and progression, both within the bladder and extravesically. Urine cytology together with cystoscopy (and bladder biopsies in cytology positive cases) is essential for monitoring of treatment efficacy and the follow- up schedule is the same as for patients with high-risk tumors [18].

1.1.6.2.0 Treatment of Muscle Invasive Bladder Cancer

Cystectomy is the recommended therapy for patients with carcinoma in situ (CIS) or T1 tumors who are either at high risk for progression or have failed to respond to intravesical therapy [18].

1.1.6.2.1 Partial Cystectomy

Patients with solitary, infiltrating tumors (T1–T3) localized along the posterior lateral wall or dome of the bladder are candidates for partial cystectomy, as are patients with cancers in a diverticulum [14]. Disease remote from the primary tumor must be excluded by random bladder biopsies preoperatively. To minimize tumor implantation resulting from contamination of the wound with cancer cells at the time of surgery, short-course, limited-dose (1000–1600 cGy) irradiation can be used, and an intravesical chemotherapeutic agent can be instilled preoperatively[14]. Partial cystectomy has been successful for T2a lesions localized to the dome of the bladder, with 5-year survival rates of 50% to 70% [19].

1.1.6.2.2 Radical Cystectomy

Radical cystectomy with urinary diversion is the most effective treatment for eradication of curable muscle-invasive TCC, SCC and adenocarcinoma, either primarily or when radiotherapy has failed. It is also used to treat G3pT1 TCC and CIS, refractory to BCG [15].

Radical cystectomy with bilateral pelvic lymphadenectomy is considered the standard treatment for patients with clinically localized muscle-invasive bladder cancer [18]. Radical cystectomy implies removal of the anterior pelvic organs: in men, the bladder with its surrounding fat and peritoneal attachments, the prostate, and the seminal vesicles; in women, the bladder and surrounding fat and peritoneal attachments, cervix, uterus, anterior vaginal vault, urethra, and ovaries, however lymphadenectomy is done in both male and female UBC patients This remains the "gold standard" of treatment for patients with muscle invasive bladder cancer [14]. In selected female patients, the vaginal vault and urethra can be spared along with the uterus, fallopian tubes, and ovaries, particularly in those who are premenopausal. Sparing of the urethra allows for construction of a neobladder that can be anatomized to the urethral remnant [14]. Urinary diversion may be accomplished using a variety of techniques [14]. The choice of procedure may depend on the socio-economic and environmental factors [22]. In UK urinary diversion is most commonly attained by formation of an ileal conduit [18], however in a study done by Aboud, he pointed out that in Tanzania the procedure of urinary diversion preferred is Mainz pouch 2. Generally, the early results of Mainz pouch 2 were excellent; all the patients were continent and there were no cases of pyelonephritis or metabolic derangement. The upper tracts were preserved or improved in the 18 patients that survived. He concluded that, Mainz pouch II has been well accepted in our society and the results were comparable favorably with those reported from elsewhere [22].

1.1.6.3 Radiotherapy

External beam irradiation (5000–7000 cGy), delivered in fractions over a 5- to 8-week period, is an alternative to radical cystectomy in well-selected patients with deeply infiltrating bladder cancers [13]. However SCC and adenocarcinoma are less sensitive to radiotherapy than TCC [15].

1.1.6.4 Chemotherapy

Owing to high local and systemic failure rates after definitive irradiation, several investigators have explored the possibility of combining irradiation with systemic chemotherapy to decrease recurrence rates, improve patient survival, and allow bladder preservation. Trials of single agent chemotherapy and irradiation have shown better local response rates than are found in historical series of irradiation alone[14]. Combination chemotherapy is recommended for treatment of metastatic bladder cancer in patients fit enough to tolerate its toxicity. A response rate of 30% is seen [15].

1.1.6.5 Palliative Measures

This will include radiotherapy for metastatic bone pain, formalin instillation or internal iliac artery ligation for intractable hematuria and ureteric stenting for obstruction [15].

1.1.7 Prognosis

Invasive cancer involving detrusor muscle, which is present at diagnosis in 25% of patients [21], is an aggressive tumor with a poor prognosis. Superficial disease recurs in up to 80% of patients [23, 24]. There are considerable variations in surgical and non-surgical management. The fact that both pTis and pT1 have a poorer prognosis than pTa tumours [25, 26]. Patients with pT1a tumours have a better prognosis, as the characteristics of these tumours are often similar to pTa tumours. pT1c tumours are more aggressive and may lead to a prognosis similar to that of patients with pT2a tumours. There is evidence from two cohort studies that an assessment of micro invasion is predictive of recurrence, with pT1b tumours having a significantly greater recurrence than pT1a [27, 28].

Some patients may be cured following complete TURBT but prognosis after recurrence is poor. Progression to muscle invasive disease (pT2-4) has been reported in 40% of patients [26]. Close follow up and early definitive treatment is common practice although some practitioners advocate immediate cystectomy. Several large cohort studies had an overall five year survival rate of 60% after radical cystectomy [29, 30]. Observational studies indicate that five year survival of patients treated with radiotherapy is between 30% and 50%, with a salvage cystectomy rate of around 20% [31, 32].

In a study done by Aboud, early complications, generally defined as occurring within 30 days of urinary diversion, were seen in 5 of the 19 patients. Only two complications were serious. One death occurred in a patient who had wound infection and wound dehiscence. The second serious complication was peritonitis whose cause was not established. Wound infection was the most common early complication. The day time continence rate of 100% and a single case of mild night soiling was noted. Hyperchloraemic acidosis has been reported in a few patients with urinary diversion, especially if they have impaired renal function. The problem is caused by absorption of chloride and ammonium ions and urea from the urine and by loss of potassium. This was not a serious problem in their series. The mixture of faeces and urine in the bowel is associated with a high risk of neoplasia at 20-30 years of follow up [22]

1.2. PROBLEM STATEMENT

Bladder cancer has been well documented in most parts of developed world including Europe and North America [1, 6]. In East Africa countries including Tanzania there was few data, though Bilharzial bladder cancer patients are being attended in different tertiary hospitals including Urology unit at Muhimbili National Hospital, which is a public University teaching hospital and a National referral Centre for Tanzania, and Tumaini hospitals.

Data from a one year pilot study done by Kivambe (unpublished) found that among all patients (1002) admitted at MNH urology unit between July 2009 and June 2010 , one hundred fifty five (15.5%) had bladder cancer. Among them 89 (57.4%) were females and 66 (42.6%) were males. Thirty eight (24.5%) were surgically treated and 28 (18%) of all BC patients died of it. He also found a 2.9 fold increase of BC patients when he compared urological services a year before and after establishment of a unit in July 2009. From the studies mentioned above, it is clear that bladder cancer is an important surgical problem in Tanzania and therefore there is a need to study its risk factors, clinical presentation, diagnosis and early surgical treatment outcome. This study has documented the clinical and pathological presentation and early treatment outcome of bladder cancer patients in Dar es Salaam.

1.3. RATIONALE

This study reports on associated factors, clinical presentation, diagnosis and early surgical treatment outcome of bladder cancer patients in MNH and Tumaini hospital. The study findings have shown that patients were diagnosed at advanced stage of a disease as a results the surgical outcome were poor, hence it calls for early diagnosis which will improve the surgical outcome of bladder cancer patients. Lastly, this study has also fulfilled the completion of study programme, Masters of Medicine Degree in Urology.

1.4. OBJECTIVE

1.4.1 Broad Objective

To document the profile and treatment outcome of patients with carcinoma of the bladder as seen at MNH and Tumaini Hospital.

1.4.2 Specific Objectives

1) To determine the demographic characteristics of bladder cancer patients as seen at MNH and Tumaini Hospital.
2) To identify the associated factors in patients with bladder cancer as seen at MNH and Tumaini Hospital.
3) To document clinicopathological presentation of bladder as seen at MNH and Tumaini Hospital.
4) To document the treatment and early treatment outcome of bladder cancer patients seen at MNH and Tumaini Hospital.

CHAPTER TWO

2.0 METHODOLOGY

2.1. Design:

This was a hospital based prospective descriptive study that involved all patients presenting at MNH urology unit and Tumaini Hospital confirmed to have bladder cancer during the period of study from March 2012 to December 2012.

2.2. Setting:

The study was conducted at Department of surgery of Tumaini Hospital which is a private hospital located in Upanga opposite the headquarter of the Tanzania Peoples' Defence Force, among other disciplines of medicine it offers surgical and urology services, and Muhimbili National Hospital (MNH), which is the national referral hospital receiving patients from districts and regional hospitals within the country but in addition it serves as city hospital by receiving more patients from the three municipal hospitals (Amana, Temeke and Mwananyamala) in the city and nearby district hospitals of Coast Region due to its geographical location. The hospital is also a teaching hospital for Muhimbili University of Health and Allied Sciences (MUHAS) students both Undergraduates and Postgraduates located within Dar es Salaam city, which has a population of about 4 million people out of approximately 40 million Tanzanians. The hospital bed capacity is 1500, and surgical wards have 220 beds.

Urology unit at Muhimbili National Hospital has 54 beds out of 220 beds of surgical wards in Kibasila block. Ward 9 and 10 admit female surgical patients each with a capacity of 32 beds, among them 8 beds in each ward have been reserved for urology patients. Ward 14 admits male urology patients and has a capacity of 32 beds. Ward 15 and 16 are private wards which admit female and male surgical patients respectively; each with a capacity of 16 beds, among them 6 beds has been reserved for urology patients.

Urology unit has two days for outpatient clinic in a week, in which Tuesday is for follow up clinic and Wednesday is for new case clinic. The clinics are run on Tuesday and Wednesday in room number 48 to 52 and 19 to 24 respectively located in left wing first floor and ground floor respectively.

2.3. Patients recruitment:

The recruitment was of in- patients and outpatients attending urology service at MNH, and Tumaini hospital, and their age ranged from 20 to 80 years. The disease can occur rarely in young persons, thus the age range taken had a purpose of catching even the young patients before the age of 40years. Both female and male patients presenting with symptoms and signs of bladder cancer then confirmed by histology were recruited for the study. The participants were well informed on the study purpose and expected outcome. Once agreed they signed consent form and then a face to face questionnaire was administered**.** However patients confirmed to have bladder cancer were recruited by convenient sampling technique and there was no randomization.

2.4. Ethical Consideration:

Ethical clearance was sought for conducting the research from the Research Ethics Committee of Muhimbili University of Health and Allied Sciences. Before carrying out the study, permission was also sought from the management of Muhimbili National Hospital, Tumaini Hospital, patients themselves or relatives and guardians of those unconscious or very ill were informed about the purpose of the study. This was done at any point during inpatient period once a patient met the inclusion criteria. Data were extracted from the patient, relative or guardian and from the case hospital record. The data were entered in the data collection tool. Patients were assured that the information extracted from them will be confidential, privacy during physical examination and even if they did not participate in the study standard care of treatment was offered

2.5. Exclusion Criteria:

Patients who died before confirmation of definitive diagnosis and those whose data were incomplete

2.6. Variables Studied:

These included age, sex, occupation, and associated factors leading to bladder cancer clinical presentation, diagnostic workup, clinical stage, histology and grading, treatment offered and early outcome of treatment of bladder cancer.

2.8. Data Processing and Analysis:

Manual analysis was carried out through sorting out all the questionnaires collected. Data were entered in the computer by the principal investigator followed by data cleaning. Data analysis was done using SPSS program version16.0. Demographic data, risk factors, clinical and pathological presentation, treatment and its outcome after three months were used to determine frequencies distribution and proportions.

2.9. Study Limitations

This study was done at Muhimbili National Hospital which is a tertiary care referral centre, and Tumaini hospital thus the findings may not reflect a true image of the magnitude of bladder cancer in Dar es Salaam. The follow up of patients after treatment had limitation to patients who came from upcountry and those who went for chemoradiotherapy at Ocean Road Cancer Institute, also to patients who went for home palliative therapy.

CHAPTER THREE

3.0 RESULTS

A total of 67 bladder cancer patients were enrolled during the study period in the surgical department urology units of MNH and Tumaini hospitals. Males were 25(37.3%) and females were 42 (62.7%); therefore the male to female ratio was 1:1.7. The age range was from 30 to 80 years with the mean age of 54.31 years. Twenty two patients (32.8%) were in the commonest age group (60 to 69). The younger age group (30 to 39) had 11(16.4%) patients (table 1a).

Table 1a: Age distribution by sex of 67 studied bladder cancer patients

Age group (years)	Sex		Total
	Male	female	
30-39	2	9	11 (16.4%)
40-49	3	11	14(20.9)
50-59	5	5	10(14.9%)
60-69	9	13	22(32.8%)
≥70	6	4	10(14.9%)
total	25 (37.3%)	42(62.7%)	67(100%)

The table shows the commonest age group was 60 to 69 years and more female patients had bladder cancer than males (62.7% and 37.3% respectively)

Table1b: Age and Residence, Occupation distribution of the 67 Studied Patients

Age group in years	Residence		Occupation	
	High risk	Low risk	High risk	Low risk
30-39	7(16.3%)	4(16.7%)	11(18.6%)	0(0%)
40-49	9(20.9%)	5(20.8%)	14(23.7%)	0(0%)
50-59	5(11.6%)	5(20.8%)	6(10.2%)	4(50%)
60-69	15(34.9%)	7(29.2%)	21(35.6%)	1(12.5%)
≥70	7(16.3%)	3(12.5%)	7(11.9%)	3(37.5%)
Total	43(100%)	24(100%)	59(100%)	8(100%)

This table shows the association of residence and occupation of an individual to develop cancer of the bladder. Fifteen (34.9%) of patients in age group between 60 and 69 lived in high risk areas and twenty one (35.6%) in the same age group had high risk occupation (table 1b). Staying in a high risk residence and working in high risk occupation had nearly the same proportion to age group 60 to 69.

Among the associated factors identified cigarette smoking 25(37.3%) and Schistosoma infestation 32(47.8%) were common among patients who had SCC, other histological types showed less association with cigarette smoking (TCC 5(7.5%), and Adenosquamous carcinoma 1(1.5%). Patients who had exposure to alcohol had risk of developing SCC 13(19.4%), and less risk to other three histological types

Table 2: Distribution of Associated Factors among 67 Studied Patients with Bladder Cancer

Risk Factors	**Histological Type**								
	Squamous cell Carcinoma		**Transitional Cell Carcinoma**		**Adenocarcinoma**		**Adenosquamous Cell Carcinoma**		**Total**
	Yes	No	Yes	No	Yes	No	Yes	No	
Cigarette Smoking	25(37.3%)	22(32.8%)	5(7.5%)	11(16.4%)	0(0%)	3(4.5%)	1(1.5%)	0(0%)	67(100%)
Alcohol Intake	13(19.4%)	34(50.7%)	4(6%)	12(18%)	3(4.5%)	0(0%)	1(1.5%)	0(0%)	67(100%)
Paddy Farming	32(47.8%)	15(22.4%)	12(18%)	4(6%)	1(1.5%)	2(3%)	1(1.5%)	0(0%)	67(100%)
Sexual Transmitted Infection	5(7.5%)	42(62.7%)	6(9%)	10(15%)	2(3%)	1(1.5%)	1(1.5%)	0(0%)	67(100%)
Working In a Chemical /Dye Industry	0(0%)	47(70.1%)	1(1.5%)	15(22.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
Schistosomiasis Infestation	32(47.8%)	15(22.4%)	9(13.4%)	7(10.4%)	2(3%)	1(1.5%)	1(1.5%)	0(0%)	67(100%)
Indwelling	1(1.5%)	46(68.7%)	1(1.5%)	15(22.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)

Catheterization									
Bladder Stone	0(0%)	47(70.1%)	1(1.5%)	15(22.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
Chronic Cystitis	23(34.3%)	24(35.8%)	6(9%)	10(15%)	1(1.5%)	2(3%)	0(0%)	1(1.5%)	67(100%)
Radiotherapy	1(1.5%)	46(68.6%)	1(1.5%)	15(22.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
Chemotherapy	0(0%)	47(70.1%)	0(0%)	16(23.9%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
HIV Infection	0(0%)	23(71.9%)	0(0%)	8(25%)	1(3.1%)	0(0%)	0(0%)	0(0%)	32(100%)
Family History Of Bladder Cancer	4(6%)	43(64.2%)	0(0%)	16(23.9%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
Use Of Analgesics	42(62.7%)	5(7.5%)	14(21%)	2(3%)	2(3%)	1(1.5%)	1(1.5%)	0(0%)	67(100%)
Fried Food	28(41.8%)	19(28.4%)	13(19.4%)	3(4.5%)	1(1.5%)	2(3%)	0(0%)	1(1.5%)	67(100%)
Soy food	45(67.2%)	2(3%)	14(21%)	2(3%)	3(4.5%)	0(0%)	0(0%)	1(1.5%)	67(100%)
Bacon	3(4.5%)	44(65.7%)	7(10.4%)	9(13.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67(100%)
Vegetables	46(68.7%)	1(1.5%)	16(23.9%)	0(0%)	3(4.5%)	0(0%)	0(0%)	1(1.5%)	67(100%)
Total	300	522	110	170	19	33	5	11	1206(100%)

The patients who were cultivating paddy had risk of developing SCC 32(47.8%) this was probably due to Schistosoma infestation 32 (47.8%) to those who had SCC ,the second was patients who had TCC 9(13.4%) also were cultivating paddy and got Schistosoma infestation, this had less impact to other histological types

Of patients with SCC 4(6%) reported BC history in their family, however, use of analgesic drugs like non steroid anti-inflammatory drugs showed association to patients with SCC 42(62.7%), TCC 14 (25%), others had less association. Chronic cystitis was observed as a associated factor to patients who had SCC 23(34.3%). Consumption of alcohol associated with development of both SCC and TCC (13(19.4% and 4(6%) respectively).

STI had no clear association with bladder cancer. Exposure to chemicals was seen in only one patient of TCC. He had exposure to agricultural pesticides. Two patients were exposed to radiation as occupational exposure and therapy for cancer of cervix developed SCC and TCC respectively. HIV and chemotherapy had no association with bladder cancer, however almost half of the patients reported their HIV status and the rest did not know their status.

The consumption of soy food showed association with development of all four histological types but more in SCC 45(67.2%). Consumption of bacon had association to development of bladder cancer more in TCC 7 (10.4%). Consumption of fried food had association to development of SCC 28(41.8% and TCC 13(19.4%). The consumption of vegetables had association to patients who had SCC 46(68.7%), and TCC 16(23.9%)

The Indwelling catheter was not a marked risk factor for development of bladder cancer; two patients had this risk factor SCC 1(1.5%) and TCC 1(1.5%) (Table 2).

Patients who took water more than one liter a day developed bladder cancer, 55(82%) had bladder mass by ultrasound scan ,water was not protective as patients started taking plenty of water after being diagnosed with bladder cancer.

Table 3a: Distribution of Clinical Features and Histological Types of studied Bladder Cancer patients

Clinical features	Histology types									
	Squamous cell carcinoma		Transitional cell carcinoma		Adenocarcinoma		Adenosquamous carcinoma		Total	Total proportion of sympt&signs
	Yes	No	Yes	No	Yes	No	Yes	No		
Haematuria	39(58.2%)	8(11.9%)	16(23.9%)	0(0%)	2(3.0%)	1(1.5%)	1(1.5%)	0(0%)	67	58(86.6%)
Frequency	43(64.2%)	4(6%)	13(19.4%)	3(4.5%)	3(4.5%)	0(0%)	1(1.5%)	0(0%)	67	60(89.6%)
Urgency	42(62.7%)	15(22.4%)	14(20.9%)	2(3.0%)	3(4.5%)	0(0%)	1(1.5%)	0(0%)	67	60(89.6%)
Urge incontinence	26(38.8%)	21(31.3%)	11(16.4%)	5(7.5%)	2(3.0%)	1(1.5%)	1(1.5%)	0(0%)	67	40(59.7%)
Dysuria	43(64.2%)	4(6%)	13(19.4%)	3(4.5%)	3(4.5%))	0(0%)	1(1.5%)	0(0%)	67	60(89.6%)
Nocturia	43(64.2%)	4(6%)	13(19.4%)	3(4.5%)	3(4.5%)	0(0%)	1(1.5%)	0(0%)	67	60(89.6%)
Flank pain	30(44.8%)	17(25.4%)	9(16.4%)	7(10.4%)	2(3.0%)	1(1.5%)	1(1.5%)	0(0%)	67	42(62.7%)
Supra pubic mass	20(29.9%)	27(40.3%)	4(6%)	12(17.9%)	3(4.5%)	0(0%)	0(0%)	1(1.5%)	67	27(40.3%)
Lower limb edema	2(3.0%)	45(67.2%)	1(1.5%)	15(22.4%)	0(0%)	3(4.5%)	0(0%)	1(1.5%)	67	3(4.5%)
Bone pain	13(19.4%)	34(50.7%)	3(4.5%)	13(19.4%)	1(1.5%)	2(3.0%)	0(0%)	1(1.5%)	67	17(25.4%)
Anaemia	29(43.3%)	18(26.9%)	8(11.9%)	8(11.9%)	1(1.5%)	2(3.0%)	0(0%)	1(1.5%)	67	38(56.8%)
Renal insufficiency	9(16.4%)	38(56.7%)	5(7.5%)	11(16.4%)	2(3.0%)	1(1.5%)	0(0%)	1(1.5%)	67	16(23.9%)
Total	296	336	110	82	25	11	7	5	872	

Irritative symptoms were more marked to patients who had SCC than other histological types of bladder cancer. The irritative symptoms reported were frequency, urgency, urge incontinence, dysuria, and nocturia. Patients with- SCC presented with features of advanced disease (flank pain 30(44.8%), suprapubic mass 20(29.9%), lower limb oedema 2 (3.0%) and bone pain 13(19.4%). Renal failure features were seen in 9(16.4%) of SCC and 5(7.5%) of TCC (table 3a). All patients who had TCC presented with blood in urine while 39(58.2%) of SCC patients had blood in urine as their clinical presentation.

Haematuria and irritative urinary symptoms had high proportion of more than 50% among 67 studied bladder cancer patients, lower limb oedema showed small proportion (4.5%).

Table 3b: Distribution of Imaging and Endoscopic Investigations Done To 67 Studied Bladder Cancer Patients

Investigation	Bladder tumour		Total
	Yes	No	
Ultrasound scan	60(89.6%)	7(10.4%)	67(100%)
Cystoscopy	67(100%)	0(0%)	67(100%)

Ultrasound scan was routinely done to majority of patients suspected to have bladder cancer. Other imaging methods were expensive and were only done to patients whom ultrasound was not able to detect the presence of bladder mass. Ultrasound detected 60(89.6%) of all patients and the rest were detected by CT scan 7(10.4%). One patient underwent IVU 1(1.5%) as supplementary imaging. The endoscopic examination of bladder (cystoscopy) was performed to all patients by different urologists, and it was able to detect presence of bladder mass in all 67 patients studied (Table 3b)

Table 3c: Types of Biopsy Taken and Histology Results

Type of biopsy taken	**Histology results**				**Total**
	SCC	**TCC**	**Adenocarcinoma**	**Adenosquamous carcinoma**	
TURBT	3(75%)	1(25%)	0(0%)	0(0%)	4(100%)
Punch biopsy	44(69.8%)	15(23.8%)	3(4.8%)	1(1.6%)	63(100%)
Total	47(70.1%)	16(23.9%)	3(4.5%)	1(1.5%)	67(100%)

Two methods were used to take biopsy of bladder mass during cystoscopy, punch biopsy was the commonest method employed in all types of bladder tumour, in patients who had SCC accounted for 44(69.8%), TCC 15(23.8%) , three patients of adenocarcinoma and one with Adenosquamous carcinoma, however only four patients had their biopsy taken by TURBT method. Out of 67 patients studied, SCC accounted for 47(70.1%) the rest were TCC 16(23.9%), three Adenocarcinoma and one Adenosquamous carcinoma (table 3c).

Table 3d: Frequency distribution of Location of Bladder Tumour and Their Histological Results

Location of bladder tumour	Frequency	Percentage	Histology type			
			SCC	TCC	adenocarcinoma	Adenosquamous carcinoma
Base	15	22.4	10(21.3%)	5(31.3%)	0(0%)	0(0%)
Lateral walls	15	22.4	13(27.7%)	2(12.5%)	0(0%)	0(0%)
Fundus	6	9.0	5(10.6%)	1(6.3%)	1(33.3%)	0(0%)
Whole bladder cavity	31	46.3	23(48.9%)	8(50%)	2(66.7%)	1(100%)
Total	67	100	47(100%)	16(100%)	3(100%)	1(100%)

The urinary bladder tumour was located in different locations in the bladder cavity, however majority of them were filling the whole bladder cavity 31(46.3%), and this was also observed in all histological results studied (table 3d).

Table 3e: Histological Types and Their Grades

Histology types	Histology grades				
	PNMP	G1	G2	G3	Total
SCC	0(0%)	19(40.4)	22(46.8%)	6(12.8%)	47
TCC	4(25%)	2(12.5%)	7(43.8%)	3(18.8%)	16
Adenocarcinoma	0(0%0	1(33.3%)	1(33.3%)	1(33.3%)	3
Adenosquamous	0(0%)	1(100%)	0(0%)	0(0%)	1
Total	4(5.9%)	23(34.3%)	30(44.8%)	10(14.9%)	67(100%)

This table shows the frequent histological grade is G2.

Table 3f: Local Tumour Stage and Histological Outcome

Local tumour Stage	Histological results				Total
	SCC	TCC	Adenocarcinoma	Adenosquamous	
T1	0(0%)	1(50%)	0(0%)	1(50%)	2
T2	2(33.3%)	4(66.7%)	0(0%)	0(0%)	6
T3	21(75.0%)	7(25.0%)	0(0%)	0(0%)	28
T4	24(77.4%)	4(12.9%)	3(9.7%)	0(0%)	31
Total	47(70.1%)	16(23.9%)	3(4.5%)	1(1.5%)	67

Majority of bladder cancer patients with squamous cell carcinoma were diagnosed at late local clinical stage (T3, T4) (Table 3f)

Table 4a: Treatment Modalities According To Clinical Stage among 49 Patients

Treatment modality	Clinical stage				
	T1	T2	T3	T4	Total
TURBT	1(50%)	2(40%)	0(0%)	0(0%)	3(6.1%)
Cystectomy	1(50%)	1(20%)	9(47.4%)	2(8.7%)	13(26.5%)
Radiotherapy	0(0%)	0(0%)	0(0%)	3(13.0%)	3(6.1%)
Chemotherapy	0(0%)	0(0%)	0(0%)	3(13.0%)	3(6.1%)
Home	0(0%)	2(40%)	10(52.6%)	15(65.2%)	27(55.1%)
Total	2(100%)	5(100%)	19(100%)	23(100%)	49(100%)

Among 67 patients 49(73.1%) underwent various forms of treatment, including 13 (26.5%) who had cystectomy and 3 (6.1%) had TURB. The rest had palliation either in the form of chemo radiotherapy 3(6.1%), radiotherapy 3(6.1%) or home palliative care 27 (55.1%)). Surgical treatment was offered to patients whose clinical stage ranged from early to an advanced clinical stage disease so long as the mass was not fixed to the pelvic walls. However, those who had palliation therapy, the disease were advanced and non operable (Table 4a). Among 67 patients 18 died before being treated.

Table 4b: Cystectomy According to Histology Results

Histological results	Cystectomy		Total
	Yes	No	
SCC	8(17.0%)	39(83%)	47(100%)
TCC	4(25%)	12(75%)	16(100%)
Adenocarcinoma	0(0%)	3(100%)	3(100%)
Adenosquamous	1(100%)	0(0%)	1(100%)
Total	13(19.4%)	54(80.6%)	67(100%)

Cystectomy and urinary diversion was done to 13(19.4%) of studied urinary bladder cancer patients, eight patients (17.0%) had SCC followed by 4(25%) who had TCC and one had Adenosquamous (table 4b).

Table 4c: Frequency Distribution of Bladder Cancer Complications.

Complications	Frequency	Percentage	Cystectomy		TURBT	
			Yes	No	Yes	No
Post operative Sepsis	1	1.7	0	10	0	3
Anaemia	18	30.5	3	7	0	3
Renal failure	11	18.6	6	4	0	3
Loin pain	12	20.3	3	7	0	3
Metabolic disturbance	3	5.1	2	8	0	3
Hydroureteronephrosis	14	23.8	8	12	0	6
Total	59	100	22	48	0	21

Anaemia was the leading complication (30.5%). However for patients who underwent cystectomy, renal failure was a major complication. There were no observed complications to patients who underwent TURBT (table 4b).

Among 67 bladder cancer patients 33 (49.3%) died. Five (15.2%) died of renal failure and 18 (54.5%) died of advanced bladder cancer causing anemia, metabolic disturbance. The cause of death for remaining 10 patients was not determined.

CHAPTER FOUR

4.0 DISCUSSION

This study reported on the profile and early treatment outcome of bladder cancer patients.

4.1 Sex and Age

Males were 25(37.3%) and females were 42 (62.7%). The study identified women are more affected than men, and the male to female ratio was 1:1.7. Globally men are more commonly affected than females with a male/female ratio of 10:3[1]. In this study the age range was from 30 to 80 years with the mean age of 54.3 years. This can probably be explained by exposure to schistosomiasis is more on women than men due to their activities, for example in lake zones females are the one who cultivate paddy and males are pastoralists. Globally 90% of the disease occurs in persons 55 years or more which concurs with this study. A study done in France found the median age at diagnosis to be 60 years (48-76years) and male to female ratio of 9 to 1[35]. A study done in Upper Egypt found the mean age of their patients to be 58.34 ± 12.13[36], and males were four times than the number of females [5].

4.2 Risk factors.

4.2.1 Cigarette Smoking

Cigarette smoking was identified in 25(37.3%) patients of SCC, five (7.5%) of TCC and one patient who had Adenosquamous carcinoma. Worldwide smoking has a risk of 50% in males and 35% in females to develop bladder cancer [1]. A study done in Egypt identified that among men cigarette smoking was associated with TCC (OR = 1.8, 95% CI = 1.4, 2.2) but not SCC [37].

4.2.2 Schistosomiasis Infestation

Schistosoma infestation (32(47.8%)) was common among patients who had SCC. In our set up this was expected to be the common association because of schistosomiasis endemicity. In Egypt history of schistosomiasis was found to be associated with increased risk of both TCC (OR = 1.9, 95% CI = 1.2, 2.9) and SCC (OR = 1.9, 95% CI = 1.2, 3.0) in females and less in males (OR = 1.4, 95% CI = 1.2, 1.7 and OR = 1.4, 95% CI = 1.1, 1.7, for TCC and SCC respectively) [37].

4.2.3 Alcohol.

Patients who had exposure to alcohol associated with development of SCC 13(19.4%), and less risk to other three histological types. In Pakistan they found no one used alcohol [38]. Consumption of alcohol is associated with development of both SCC and TCC (13(19.4% and 4(6%) respectively).

4.2.4 Paddy Cultivation.

Patients who had history of cultivating paddy were found to have association with development of SCC 32(47.8%) this was probably due to Schistosoma infestation 32 (47.8%) to those who had SCC. Paddy cultivation accounted 9(13.4%) patients of TCC. Paddy cultivation had less impact to other histological types. In Tanzania human exposure to schistosomiasis is mostly related to occupational activities such as fishing, farming, or recreational activities around the basin or within the permanent or temporal water bodies such as lakes, rivers, dams, swampy areas, or road side ditches [39].

4.2.5 Exposure to Chemical and Irradiation.

Exposure to chemical was seen in only one patient of TCC. He had exposure to agricultural pesticides. Worldwide exposure to occupational carcinogen accounts for 5-20% of all bladder cancers [1]. Two had exposure to radiation as occupational exposure (one was a radiographer) and the other one radiation therapy for cancer of cervix. One developed SCC and the other one TCC. In an international cancer registry study it was reported that out of

49828 women who had radiation therapy for cervical cancer, 3750 survived for 30 or more years and a two-times risk of cancer of heavily irradiated organs was seen. Most of the cancer was of the rectum, vagina, ovary and bladder [40].

4.4.6 Family and Non Steroid Anti-Inflammatory Drugs.

Patients with SCC 4(6%) reported BC history in their family. In Pakistan of all the subjects studied 34(22.5%) reported history of BC in their family [38], however, use of analgesic drugs like non steroid ant-inflammatory drugs showed association to patients with SCC 42(62.7%), TCC 14 (25%): and it was reported that use of large quantities of analgesic combination containing phenacetin is associated with an increased risk of bladder cancer [9]. In Hampshire state department of health and human services' cancer registry, bladder cancer patients reported regular use of phenacetin than control subjects (odds ratio (OR) =2.2, 95% CI = 1.3-3.8). In contrast use of paracetamol did not relate overall to risk of BC. They also found regular use of any NSAIDS was associated with statistically significant decrease a BC risk (OR =0.6, 95% CI = 6.4-0.9 and specifically aspirin [41].

4.4.7 Chronic Bladder Irritation

Bladder stone was associated with development of TCC in one patient. In USA bladder stone is associated with an increased risk of SCC [10]. Chronic cystitis was observed as a association in patients who had SCC 23(34.3%). However in Iran they found 103(52.5%) of the study subjects who had bladder cancer had history of urinary tract infection [42].

Indwelling catheter was not a marked associated factor for development of bladder cancer; one had SCC 1(1.5%) and the other one had TCC 1(1.5%). In America they reported about 5% of paraplegics who were managed by indwelling catheter had SCC [10].

4.3 Clinical and Pathological Presentation

4.3.1 Clinical Presentation.

All patients who had TCC presented with blood in urine while 39(58.2%) of SCC patients had blood in urine as their clinical presentation. In this study majority of patients with SCC presented with features of an advanced disease (flank pain 30(44.8%), suprapubic mass 20(29.9%), lower limb oedema 2 (3.0%) and bone pain 13(19.4%), this was similar to other study findings [10, 14]. The renal failure features were seen in 9(16.4%) of SCC and 5(7.5%) of TCC. Generally hematuria is present in 85% of patients [10, 13]. In Pakistan haematuria was present in 54.5% [43]. However irritative symptoms were more marked in patients who had SCC than other histological types of bladder cancer. The irritative symptoms reported were frequency, urgency, urge incontinence, dysuria, and Nocturia. In the previous studies it was reported that the symptom complexes of bladder irritability almost never occur without microscopic haematuria [10, 13].

4.3.2 Investigations and Histology Diagnosis.

4.3.2.1 Imaging

Ultrasound scan was routinely done to majority of patients suspected to have bladder cancer. Other imaging methods were expensive and were only done to patients whom ultrasound was not able to detect the presence of bladder mass. Ultrasound scan is readily available, cheap, affordable and non invasive as pointed out in Mwashambwa and Yongolo study [16]. Ultrasound detected 60(89.6%) of all patients and the rest were detected by CT scan 7(10.4%).

4.3.2.2 Endoscopy and Biopsy.

The endoscopic examination of bladder (cystoscopy) was performed to all patients by different urologists, and it was able to detect presence of bladder mass in all 67 patients studied. This was equally saying cystoscopy was a primary diagnostic tool as was seen in a study done in USA [14].

Two methods were used to take biopsy of bladder mass during cystoscopy, punch biopsy was the commonest method employed in all types of bladder tumour. In patients who had SCC it accounted for 44(69.8%), TCC 15(23.8%), three patients of adenocarcinoma and one with Adenosquamous carcinoma. However, only four patients had their biopsy taken by TURBT method. Out of 67 patients studied, SCC accounted for 47(70.1%) the rest were TCC 16(23.9%), three Adenocarcinoma and one Adenosquamous carcinoma.

In developed world TUR is the commonly used method of biopsying bladder tumour. The diagnosis is enhanced by use of florescent cystoscopy [14]. Unlike this study the TCC was the commonest histological type in Pakistan accounting for 86% of studied bladder cancer patients and the second histological diagnoses were both SCC and adenocarcinoma making 6.4% of all bladder cancer patients [43]. In Egypt reported a decrease in proportion of SCC cases and increasing proportion of TCC [44].

4.3.2.3 Histology.

Among the four histology diagnoses (SCC=47(70.1%), TCC= 16(23.9%), Adenocarcinoma= 3(0.04%) and Adenosquamous carcinoma= 1(0.01%)) papillary neoplasia of low malignant potential was only seen in TCC, others show grades were ranging from well to poorly differentiated. The grading system used was the WHO 2004. In Iran they reported most of their patients had low grade malignancy 56(39.7%) and less had high grade 44(31.2%) [41].patients with aggressive tumors have poor prognosis [23,24].

4.3.2.4 Staging.

In this study majority of the patients were seen at advanced clinical stage irrespective of histological stage (Table 3f). In Pakistan the commonest clinical stage was T2 18.3% and T1 17.3%, however they had few patients who had advanced stage T3 14.2% and metastatic T4 12.5% and non metastatic T4 12.5% [43].

4.4 Treatment and Its Early Outcome.

Among all 67 patients 49(73.1%) underwent various forms of treatment, among them 13 (26.5%) had cystectomy and 3 (6.1%) had TURBT, the rest had palliation either in the form of chemoradiotherapy or home palliative care (16(12.2%) and 27 (55.1%)) respectively. surgical treatment was offered to patients whose clinical stage ranged from early to an advanced clinical stage disease so long as the mass was operable. However, those who had palliation therapy had an advanced non operable mass (Table 4). In Iran surgical treatment was offered to 193(89.4%) of studied patients, among them one hundred and forty two (73.6%) underwent TURBT and 51(26.4%) had cystectomy [42].

In patients who underwent cystectomy, renal failure was a major complication. One patient had wound infection followed by wound dehiscence, and prolonged hospital stay. There was no observed complication to patients who underwent TURBT. Follow up to patients who went for palliative therapy wasn't reliable enough to comment on (table 4b). Among 67 bladder cancer patients 33 (49.3%) died. Five (15.2%) died of renal failure and 18 (54.5%) died of advanced bladder cancer. The cause of death for remaining patients was not determined. Aboud observed two serious complications after cystectomy and urinary diversion. The first complication was peritonitis whose cause was not established. The second complication was one death which occurred in a patient who had wound sepsis and dehiscence [22].

CHAPTER FIVE

5.0 CONCLUSIONS

Women were more affected by the disease than men. Schistosoma infestation was the commonest association factor for bladder cancer development. Haematuria was the commonest clinical presentation followed by irritative urinary symptoms. The disease was detected by ultrasound scan which was readily available, cheap and affordable. Punch biopsy was the leading method of obtaining tissue specimen for histology diagnosis, and SCC was the leading histological type of bladder cancer. Majority of patients were seen at an advanced clinical stage irrespective of histological type, thus few of them had surgical treatment. Wound sepsis and dehiscence were the commonest complications in those who underwent cystectomy and urinary diversion, and 49% of all patients succumbed before treatment.

5.1. RECOMMENDATIONS

The findings of this study with limitation of short duration have come up with the following recommendations:

- There is a need for a long duration study especially to get proper treatment outcome of a disease
- Monitor for possible exposure to *Schistoma heamatobium* infestation and advice the prevention measures.
- Mass campaign for possible elimination of *Schistoma heamatobium* infestation.
- Early diagnosis of patients with bladder cancer will improve their treatment outcome.
- Create awareness to primary and secondary referring health facilities on early diagnosis of bladder cancer.
- CT scan for clinical staging of a disease can be used to supplement examination under anesthesia for clinical staging of a disease.

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APPENDICES

Appendix i: Questionnaire

ID No. ……

A. IDENTIFICATION

- Date of interview……
- Name of the hospital……..

B. BACKGROUND DATA

1. Age ……
2. Sex …….
3. Permanent address…….
4. Current address……
5. Telephone number……..
6. Occupation……..

C. RISK FACTORS.

7. Do you smoke cigarettes? (active or passive) a) yes / b) no

   If yes a. how long ……..

   b. how many cigarette per day…….

   If no, did you ever smoke in the past? (Active or passive) a. yes b. no

   If yes a. how long ……..

   b. how many cigarette per day…….

8. Do you drink alcohol? a) yes / b) no

   If yes a type of alcohol…….

   b. amount per day……

   c. how often per week……..

   d. for how long……..

If no, did you ever drink alcohol in the past? A. yes b. no

If yes a. amount per day……

b. type of alcohol……

c. how often per week……..

d. for how long……

9. History of working in a pad farm a) yes b) no

10. History of STI a. yes b. no

11. History of working in a chemical or dye industry a) ye b) no

12. History of chronic bladder irritation

I. Urinary Schistosoma infection a. yes b. no
II. History of indwelling catheter a. yes b. no
III. History of bladder stone a. yes b. no
IV. Chronic cystitis a. yes b. no

13. History of being treated for cancer (apart from BC) by radiotherapy.

a. yes b. no

14. History of being treated for cancer (apart from BC) by chemotherapy.

a. yes b. no

15. HIV status a. Positive b. negative c. not known

16. Is there family history of bladder cancer? A. yes b. no

If yes, who has/had bladder cancer (relationship)…….

17. How frequently do you take the following food stuffs?

I. Fried food a. high b. less
II. Vegetables a. high b. less
III. Bacon a. high b. less
IV. Soy products a. high b. less

18. Type of analgesics commonly used…….

I. How much per day……
II. How often per week…….
III. For how long…….

19. Oral fluid intake behavior.

I. How much per day…….
II. Type of fluid (s)……...

20. Beverages taken.

I. Type of beverage……
II. How much per day……
III. For how long…….

D. **CLINICAL PRESENTATION**.

21. Haematuria a. yes b. no

If yes for how long ……..

22. Irritative symptoms

a) Frequency b) urgency c) urge incontinence d) dysuria e) Nocturia.

23. Flank pain a. yes b. no

24. Suprapubic mass a. yes b. no

25. Lower limb oedema a. yes b. no

If yes a. bilateral b. unilateral

26. Bone pain a. yes b. no

27. Anaemia a. yes b. no

28. Renal insufficiency a. yes b. no

E. **INVESTIGATIONS.**

29. HB……..

30. RFT a. normal b. abnormal

31. Ultrasound……

32. IVU……

33. CT SCAN…….

34. MRI……..

35. CYSTOSCOPY

a. number of lesions……...

b. type of lesions……..

c. location…….

d. configuration……

e. type of biopsy taken a. TUR b. punch biopsy

f. clinical staging…….

36. Histology results……

37. Histological grade…….

F. **TREATMENT.**

38. TURBT a. yes b. no

If yes a. Intravesical immunotherapy (BCG) a. yes b. no

b. intravesical chemotherapy (MMC) a. yes b. no

c. BCG + MMC a. yes b no

39. Cystectomy a. yes b. no

If yes a. partial cystectomy a. yes b. no

b. radical cystectomy a. yes b. no

c. Total cystectomy

40. Radiotherapy a. yes b. no

If yes a. indication……

b. duration…….

41. Chemotherapy a. yes b. no

If yes a. indication……

b. duration…….

42. Chemoradiotherapy a. yes b. no

If yes a. indication……

b. duration…….

43. Home base palliation a. yes b. no

If yes a. indication……

b. duration…….

G. **3 MONTHS POST TREATMENT FOLLOW UP**.

a. survival a. yes b. no

If no what was the cause of death……..

b. complications

a) Sepsis

b) Anaemia and number of BT…….

c) Renal insufficiency

d) Loin pain

e) Metabolic disturbance

THANK YOU.

Appendix ii: Informed Consent Form

Introduction

The aim of this study is to document risk factors, clinical presentation, diagnostic process, treatment options and early treatment outcome for urinary bladder cancer at Muhimbili National Hospital. The participation is freely and voluntarily. If you decide not to participate in the research it will not affect the access to the health services at any health facility in the United Republic of Tanzania including MNH.

Benefits

There are no direct benefits participant's gets in this research but you will be appreciated as one of contributors in findings about the facts on the profile of risk factors, clinical presentation, diagnostic process, treatment options and early treatment outcome for urinary bladder cancer at Muhimbili National Hospital

Risks

The participants will not get any serious risks from this research since the cystoscopy procedure will be performed in standard procedure by a specialist followed by biopsy taking then followed by standard histopathological procedure work at Central Pathology Laboratory. Minimal bleeding may be anticipated.

Confidentiality

The information obtained from this research will be confidential and will only be used for improvement of our national health policy management on bladder cancer and knowledge to health personnel.

I will be glad to receive your consent in the participation for this research.

Dr Mahenda Deogratius Emmanuel.

Signature …….. Investigator

Communication

For any query concerning this research, please do not hastate to contact

Dr Mahenda, Deogratius Emmenauel who is the principal investigator, Muhimbili University of Health and Allied Sciences (MUHAS). P.O Box 65492. Mobile number +255 712 740 630

If you have queries concerning your rights as a participant in the research, please contact:

Prof. Aboud, MD, MMed, The Director of research and publications

Muhimbili University of Health and Allied Sciences (MUHAS). P.O Box 65001 Dar es salaam. Tel.022 2151489.

I will be grateful if you will agree to participate in this study.

I…… (Participant)

I have read and understood the information provide to me as it is written also my questions have been properly answered by the investigator. I personally without any coercion I agree to participate in this research.

Name of Participant ……..Tel…….
Signature…… (Participant) Date……

Appendix iii: Fomu ya Ridhaa ya Kushiriki katika Utafiti

Utangulizi

Lengo la utafiti huu ni kujua hali halisi ya tatizo la saratani ya kibofu cha mkojo,visababishi vyake,dalili zake,namna ya kufanya vipimo tiba na hatimaye matokeo ya muda mfupi baada ya tiba. Ushiriki katika utafiti huu ni hiari. Iwapo utahiari kutoshiriki utafiti, haitaathiri huduma upatazo katika kituo/hospitali yoyote katika Jamhuri ya Muungano wa Tanzania ikiwemo MNH.

Faida

Hakuna faida ya moja kwa moja utakayopata kutokana na kushiriki katika utafiti huu bali utathaminiwa kama mojawapo wa watu waliochangia kupatikana kwa taarifa juu ya ukweli kuhusu hali halisi na kwa kiasi gani juu ya tatizo la saratani ya kibofu cha mkojo katika jamii yetu

Madhara

Washiriki hawatapata madhara yoyote makubwa kutokana na utafiti huu kwa kuwa tendo la kufanyiwa kipimo cha kuchunguza kibofu cha mkojo kitafanywa na daktari bingwa na pia kutolewa kinyama kwa ajili ya uchunguzi katika maabara kuu ya pasolojia. Damu kidogo pengine inaweza kutoka.

Usiri

Taarifa zote zipatikanazo kutokana na utafiti huu zitatunzwa kwa usiri mkubwa na zitatumika kuboresha taaluma kwa watoa afya na utungwaji wa sera za kuboresha matibabu ya saratani ya kibofu cha mkojo Tanzania.

Nitashukuru kupata ridhaa yako ya kushiriki utafiti huu.
DR MAHENDA DEOGRATIUS EMMANUEL,

Sahihi ……Mtafiti

Mawasiliano

Kwa maswali yoyote yahusuyo utafiti, tafadhali usisite kuwasiliana na mtafiti DR Mahenda Deogratius Emmanmuel simu ya mkononi +255 712 740 630 Chuo Kikuu cha Afya na Sayansi za Tiba(MUHAS) SLP 65492 DSM. Iwapo una swali juu ya haki yako kama mshiriki katika utafiti wasiliana na:

Prof. ABOUD, Mkurugenzi wa machapisho na utafiti, S.L.P 65001 Dar es salaam. Simu .2151489.

Mimi …… (Mshiriki)

Nimesoma na kuelewa habari zilizotolewa kwangu kama zilivyoandikwa na pia nimejibiwa maswali yangu kwa usahihi na mtafiti. Mimi bila kushawishiwa nimekubali kushiriki utafiti huu.

Jina la Mshiriki …… Simu……

Sahihi…… (Mshiriki) Tarehe……