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**ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES**

**DEPARTMENT OF CLINICAL ONCOLOGY**

**Clinico-pathology and treatment patterns of Urinary bladder Cancer at Tikur Anbessa Specialized Hospital.**

**A Thesis Paper Submitted to the Department of Clinical Oncology of Addis Ababa University in Partial Fulfillment of the Requirements for the Specialization Certificate in Clinical Oncology**

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**February, 2022**

**Addis Ababa, Ethiopia**

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## **Abstract**

### **Back ground:**

Bladder Cancer is the sixth most common cancer in the world, the seventh most common cancer in men, and the seventeenth most common cancer in women. Although the incidence of malignant tumors of the bladder is increasing in developing countries, like Ethiopia, there is a lack of evidence regarding the overall profile of bladder cancer in Ethiopia.

**Objective:** To assess the demography, clinicopathology and treatment patterns of urinary bladder cancer attending at oncology department and Urology unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia during the study period.

**Methods:** An institution based descriptive cross-sectional study was conducted in TASH, department of Oncology and Urology unit, Addis Ababa, Ethiopia, and comprised medical records related to urinary bladder tumors between September 2018 and August 2021.

**Results:** Of 158 cases, 81% were of males while 19% were of females making a male to female ratio of 6.74:1. The mean age was  $57.41 \pm 13.662$  years (ranged from 22 to 88 years). Hematuria was the most common presenting symptom occurring in 143 (90.5%). Transitional cell carcinoma (urothelial carcinoma) was the most common histology which accounted 87.4% followed by Squamous cell carcinoma (6.3%), adenocarcinoma (1.9%), sarcoma (1.3%) and mixed histology variants (1.3%). Overall, 45.6% was non-muscle invasive, 37.3% was muscle invasive and the remaining 17.1% was metastatic at presentation. Majority of patients were treated with radical intent. TURBT was the most commonly practiced type of treatment. Intravesical chemotherapy, perioperative chemotherapy and cystectomy were rarely practiced as compared with standard guidelines and text books.

**Conclusion:** The most common type of bladder cancer in TASH is TCC. Bladder tumor is more frequent in men than in women. Hematuria was the most common presenting symptom. The commonest procedure for bladder tumors was TURBT which is the golden standard for non-muscle invasive tumors.

## *Acronyms and Abbreviation*

AAU..Addis Ababa Univercity .....	5
CT..computed tomography .....	3
GLOBOCAN..Global Burden of Cancer Study Head and Neck cancer .....	3
IAEA..International AtomicEnergy Agency.....	6
LICs:Low Income Countries .....	4
MIBC..Muscle Invasive Bladder Cancer.....	3
NCDs..Non-Communicable Disease .....	11
NMIBC..Non-Muscle Invasive Bladder Cancer .....	5
PAHs..Polycyclic Aromatic Hydrocarbons .....	4
TASH.. Tikur Anbessa Specialized Hospital.....	3
TURBT.. Transurethral Resection of Bladder Tumor.....	5
UCC..Urothelial cell carcinoma .....	4

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# **1.Introduction**

## **1.1 Background**

Cancer ranks as a leading cause of death and an important barrier to increasing life expectancy in every country of the world. The burden of cancer incidence and mortality is rapidly growing worldwide.(1)

Bladder cancer is one of the most-common uro- logical malignancies, and is among the leading causes of cancer deaths worldwide. Approximately 3.0% of all new cancer diagnoses and 2.1% of all cancer deaths are due to bladder cancer. The high incidence, prevalence, mortality, and recurrence rate of Bladder cancer indicate that it remains an unsolved clinical and social problem. (2)

Among the leading cancer sites in Africa, there were an estimated 24 ,437 new cases and 13, 268 deaths from bladder cancer in 2012. The risks of bladder cancer appear to vary across world regions, correlating with smoking and occupational exposures to carcinogens in developed countries, and with chronic bladder urothelial irritation from Schistosoma haematobium infection in Africa and the Middle East.(3)

In Ethiopia, cancer accounts for about 5.8% of total national mortality. Although population-based data do not exist in the country except for Addis Ababa, it is estimated that the annual incidence of cancer is around 60,960 cases and the annual mortality is over 44,000. (4) from the Addis Ababa population-based cancer registry, done in 2015 bladder cancer is the 6<sup>th</sup> and 17<sup>th</sup> commonest cancer in men and women respectively .(5) Unfortunately, owing to multiple barriers to cancer care such as little awareness, improper understanding of the disease, associated stigma, a sense of hopelessness, and the lengthy process of referral to the country's only specialized center (TASH), patients often present with advanced stages of cancer in Ethiopia.(6)

Despite the fact that bladder malignancies appear to constitute a significant burden of uro-logical morbidity and mortality, and the fact that the pattern of cancer varies with factors such as geographical location and people's life style, there is no published study that examine the demographic, clinico-histopathologic profile and treatment patterns of bladder Cancer patients in Ethiopian population. Thus, this study is aimed to assess the clinico-pathology, epidemiology and treatment pattern of bladder cancer patients at Tikur Anbessa Specialized Hospital.

## 1.2. Statement of the problem

Cancer has become the second leading cause of death, behind cardiovascular disease, with more than 8.7 million attributable deaths worldwide in 2015. Low-income countries contribute up to 60% of this death toll. This is an alarming prospect, especially for LICs, where the weak health systems are severely resource constrained and already overwhelmed by the large burden of communicable diseases. Similar to other LICs, the burden of non-communicable diseases (NCDs) is increasing in Ethiopia. Cancer has become the second leading cause of death in the adult population.(5)

Local data on cancer epidemiology in Ethiopia are lacking. There is no reliable cancer registry and data availability is scanty in our country, Ethiopia. The rise in cancer burden in urological tumors in general and bladder cancer in particular has been documented and published by the National Cancer Registry, but it is not thought to depict the accurate situation on the ground because cancer diagnosis and notification from health institutions are not as meticulous as desirable. This increase has not been captured in local studies in bladder carcinomas.

Although a great deal of bladder cancer patients are usually offered palliative and curative therapy by handful of clinical oncologists and urologists at the hospital, there is no well-established and organized approach that focuses on the varying presentations of bladder neoplasms. Fortunately, Urinary bladder cancer patients are more likely treatable in our setup. Chemotherapies used for intravesical, perioperative and palliative treatment are available in TASH. But from day today clinical practice and previously done retrospective study at urology unit, almost all patients did not receive intravesical chemotherapy and perioperative chemotherapy. The pattern of these type of treatments are going to be more elaborated in this study.

Low awareness of the scale of the cancer burden among local and international policy makers contributes to the inadequate attention directed towards the disease in Ethiopia and other African countries. As a result, a significant portion of bladder cancer patients tend to seek appropriate medical care only by their advanced stages, which makes them susceptible to death. These evidences underline the need to assess the contextual situation and characteristics of

patients with bladder neoplasms. So, the purpose of this study is to investigate the overall pattern of bladder cancer at Tikur Anbessa Specialized Hospital mainly focused on clinicopathology and treatment patterns.

### 1.3 Significance of the study

The National Health Sector Transformation Plan (HSTP) 2015/16 in line with our country's second growth and transformation plan, has set ambitious goals to improve equity, coverage and utilization of essential health services, improve quality of healthcare, and enhance the implementation capacity of the health sector at all levels of the system. The plan outlines interventions to reduce the burden of cancer through changes in lifestyle, primary prevention, screening and early diagnosis, appropriate follow-up, treatment and provision of palliative care. In line with this, cognizance of the prominent characteristics of bladder cancer patients will greatly help stakeholders in beating cancer and salvage the overall health cost incurred by these neoplasms. Comprehensive knowledge of bladder cancer characteristics will be of irreplaceable help in early detection of these potentially fatal bladder cancer and allow oncology practitioners to make better clinical decisions for the best end of clients.

Furthermore, it will guide health policy makers and other concerned stakeholders to devise strategic programs on inculcating evidence-based interventional protocol in candidate populations. Hence, the data collected from this study can be a good input to the country's endeavor in handling the several formidable tasks: first, accurately measuring the scale of the national cancer burden and characterizing existing preventive, curative, and palliative care services available at each tier of the health system; second, identifying challenges to the improvement of cancer reporting and specialized oncology services; and finally, designing feasible interventions applicable in a low resource setting.

Finally, the findings obtained from this study will serve as a baseline for other researchers for further in-depth studies.

## **2.Literature Review**

### **2.1. Demographic characteristics of Urinary bladder cancer patients**

Bladder Cancer is the 6th most common cancer in the world, the 7th most common cancer in men, and the 17th most common cancer in women. The rate of bladder cancer diagnosis in men is 4 times greater than in women. Urinary bladder cancer is more common in developed countries and is the fourth and ninth most common cancer in men and women, respectively in the Western world.(7–9). Although the disease may occur in young persons, >90% of new cases occur in persons  $\geq 55$  years of age.(10)Research findings have shown that the geographical and racial distributions of bladder cancer vary in different parts of the world. The highest incidence of bladder cancer in men and women was observed in Europe, the United States, and Egypt, respectively. There was the lowest level in Sub- Saharan Africa, Asia, and South America, respectively. This pattern is due to differences in risk factors for bladder cancer (tobacco epidemic, changes in coding practices, the prevalence of *Schistosoma Haematobium*, especially in Africa, and occupational exposures)(8,11).The two most well-established risk factors for bladder tumors are cigarette smoking and occupational exposure to urothelial carcinogens. Age and male gender are also known risk factors for bladder cancer. Cigarette smoking is the most important risk factor, accounting for 50% of cases in men and 35% in women. In fact, cigarette smokers have a 2- to 4-fold increased risk of bladder cancer compared to non-smokers, and the risk increases with increasing intensity and/or duration of smoking. (7,10) Occupational exposure to urothelial carcinogens is the second most important risk factor, 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.(10)A retrospective study at the King Fahd Hospital, Madinah, Saudi Arabia, from January 2006 to October 2015 was conducted to delineate the frequency and clinicopathological features of urinary bladder cancer involving 116 patients. Of the 116 cases identified, 96(82.7%) were of men while 20(17.3%) were of women, with a male-to-female (M: F) ratio of 4.8:1. The overall mean age was  $62.4 \pm 15.62$  years (range: 20-115 years). The majority of the cases 56(48.3%) were seen in the age group 60-79 years. The young age group ( $\leq 40$  years) and the elderly age group ( $\geq 80$  years) constituted 11(9.5%) and 14(12%) cases, respectively. A retrospective Clinicopathological Study done at three Centers in Khartoum, Sudan involving 106 bladder cancer patients was conducted. The study reported that 87(82.1%) patients

were men. The male to female ratio was 4.6:1. Their mean ( $\pm$ SD) age was 59.49 ( $\pm$ 13.7) range (18-90) years. When the pathology was fractionated; the mean age for TCC was 60.92 and for SCC was 55.47. The peak frequency for all cases was at the age of 60-80 years.

A ten-year retrospective study at Kenyatta National Hospital, Nairobi, Kenya involving 52 bladder cancer (transitional cell carcinoma) patients was done to highlight the pattern of patients with transitional cell carcinoma of the urinary bladder with regards to age, sex, ethnic origin and histopathological classification. The peak incidence was in the 60-69 years age group. The male to female ratio was 4:1. Smoking was found in 28.8% of the patients. One patient was using tobacco snuff. The amount consumed and durations were not recorded in most of the files. A hospital based retrospective cross-sectional analysis was conducted in TASH, department of surgery, Addis Ababa, Ethiopia involving 97 bladder cancer patients. From this retrospective study 60 patients were male and 37 females (M: F of 1.6:1). Their age ranged from 20 to 79 years, with mean age of  $49.73 \pm 1.5$

Therefore, it can be noted from the aforementioned review that patient's factors such as age, sex, lifestyle factors, environmental factor and smoking were documented to be predominant risk factors for malignant neoplasms of the urinary bladder in different settings

## 2.2 Clinical features of Urinary bladder cancer patients

The most common presenting symptom in patients with bladder cancer is microscopic or gross hematuria, although urinary frequency due to irritation or a reduced bladder capacity can also develop. Less commonly, the presenting symptom is a urinary tract infection. Upper tract obstruction or pain may occur in patients with a more advanced lesion. As hematuria is typically transient and the infection and storage symptoms are also attributable to prostate problems, patients often go undiagnosed for considerable periods. Female patients present a more difficult problem because of the higher incidence of urinary infection and the lower risk of bladder cancer. Hematuria is also more likely to be misinterpreted in women of child-bearing age.(12,13) .

The incidence of bladder cancer in a patient with gross hematuria is 20 percent and with microscopic hematuria is 2 percent. Symptoms of bladder irritation, such as urinary frequency and urgency, more commonly occurring patients with bladder carcinoma in situ. Obstructive

symptoms may be present if the tumor is located near the urethra or bladder neck. In advanced disease, patients may present with flank pain caused by ureteral obstruction, or with abdominal, pelvic, or bone pain from distant metastases.(14) From a hospital based retrospective cross-sectional analysis done in TASH, department of surgery, The most common presenting symptoms were hematuria in 91.8% which is often painless, irritative symptoms (dysuria, urgency and frequency) in 74.2%, obstructive symptoms in 39.2% and suprapubic pain in 35.1%. 46.4% of the patients claimed to have weight loss, >10% of their body weight.(15)Hence, bladder cancers can present with a range of symptoms, with significant variation with the site of involvement, stage of the disease, and geographical factors.

### 2.3. Histo-pathologic characteristics of urinary bladder cancer patients

In developed countries 90% of bladder tumors are urothelial cell or transitional cell carcinoma (UCC or TCC). The other 10% of tumors are Squamous cell carcinoma (SCC) (5%), adenocarcinomas (<2%), sarcoma, small cell carcinoma and secondary deposits from cancers elsewhere in the body. But in developing countries 75% are SCC, mostly due to schistosomiasis(15)A hospital based retrospective study was conducted at, Saudi Arabia, the main histopathological types were transitional cell carcinoma (TCC) accounting for 95.7% of cases, followed by adenocarcinoma 2.6% and squamous cell carcinoma (SCC) 1.7%.(16)SCC has two subtypes, schistosomiasis (Bilharzia) associated and non-schistosomiasis associated SCC. Schistosomiasis associated SCC is common in regions where Schistosoma haematobium infection is endemic, such as the Middle East and parts of Africa. SCC was the most frequent subtype of bladder cancer in Northern Nigeria, representing 53% of cases.(17) A study done in Egypt to assess The Impact of Schistosomiasis on the Pathology of Bladder Carcinoma. squamous cell carcinoma was more frequent in egg-positive cases, whereas, transitional cell carcinoma and adenocarcinoma were more frequent in the egg-negative group.(18).A retrospective histopathologic review was done in Nigeria, showed, Squamous carcinoma was the most common histology accounting over 53% of all cases. Transitional cell carcinoma comprised 35.3% of bladder malignancies. Other rare histologic types include anaplastic Carcinoma, adenocarcinoma and leiomyosarcoma. In general the histologic findings are similar to bladder cancer in other Schistosomal endemic regions of Africa.(19)

A retrospective cross-sectional hospital-based study done in TASH surgery department. Of the patients with malignant bladder tumors, 80.4% had TCC, 5.2% SCC, and 3.1% adenocarcinomas.(15)

## 2.4 Assessment and staging

The clinical investigation should begin with a careful history, including any history of cigarette smoking or occupational exposures. Patients with urinary symptoms should have a urinalysis with urine microscopy and a urine culture to rule out infection. Urine cytology is a noninvasive test for the diagnosis of bladder cancer. It is used to identify high-grade tumors and monitor patients for persistent or recurrent disease following treatment. Cystoscopy, an office procedure usually performed under local anesthesia, remains the mainstay of diagnosis and surveillance. Patients presenting with symptoms of bladder cancer should be evaluated with cystoscopy to determine if a lesion is present. Cystoscopy provides information about the tumor location, appearance, and size. Upon detection of a lesion, a bimanual examination under anesthesia and transurethral resection of the tumor is performed and the representative tissue sends for biopsy. The muscle surrounding the tumor should be sampled to assess the depth of muscle invasion. (14) Additional workup for all patients with bladder cancer includes evaluation of the upper urinary tract with intravenous urography (IVU), renal ultrasonography, computed tomography (CT) urography, or magnetic resonance urography. (14) Complete blood count, blood chemistry tests (including alkaline phosphatase tests), liver function tests, chest radiography, and CT or magnetic resonance imaging of the abdomen and pelvis should be included in the metastatic workup for invasive bladder cancer. A bone scan may be performed if the alkaline phosphatase level is elevated or if symptoms suggesting bone metastasis are present.(14)

Most cases (70% to 80%) present with non–muscle-invasive bladder cancer (NMIBC, stage Ta, T1, and carcinoma in situ [Tis]), which is rarely lethal, but shows a high recurrence rate of 50% to 70% after treatment by transurethral resection of the bladder tumor (TURBT). In about 10% to 20% of patients with NMIBC, the disease progresses to muscle invasion ( $\geq T2$  lesions), which can lead to metastasis and death. Approximately 5% of patients have metastatic disease at the time of diagnosis.(12)The aggregate information provided by the imaging and the cystoscopy examination facilitates the staging of the tumor according to the tumor–node– metastasis (TNM)

system. It is by recourse to the TNM stage of the tumor, in addition to the general fitness of the patient, that treatment decisions are ultimately made.

## 2.5 Treatment patterns of urinary bladder cancer

Critical step in the management of non-muscle invasive bladder cancer is to prevent tumor recurrence which include transurethral resection of the bladder tumor (TURBT) for staging and histological diagnosis. A second TURBT for high grade tumor, T1 tumors and intravesical adjuvant chemotherapy and immunotherapy are essential to reduce recurrence rate. Radical transurethral bladder tumor resection is a reliable therapeutic approach for patients with muscle invasive bladder cancer after complete tumor resection and with negative biopsies of the tumor bed. These results are consistent in all age ranges.(20) Nevertheless, variant histology(squamous cell, adenocarcinoma ,sarcoma) multiple, progressive and recurrent high-grade tumors are best treated with early radical cystectomy. The African literature is scanty on the management of NMIBC. Most of the histological types are squamous cell bladder cancer and may not conform to transurethral resection only but rather radical cystectomy. Most of these patients are not suitable for any form of treatment as they present with advanced disease.(21).For muscle invasive bladder cancer cystectomy ,perioperative chemotherapy and radiotherapy/concurrent chemoradiotherapy are possible options of management .(13) A retrospective observational study conducted in America to assess treatment patterns of stage IV bladder cancer. OF 501 patients diagnosed with stage IV bladder cancer who had a first disease progression, systemic therapy consisted of platinum-based therapy (56.3%), with the most common regimen being gemcitabine/carboplatin (23.6%) followed by gemcitabine/cisplatin (17.0%). In the first line treatment period, 35.9% of patients did not receive chemotherapy. Among the 265 patients with a second disease progression, platinum-based therapy was administered to 29.1% of patients. Otherwise, taxane alone, pemetrexed alone, gemcitabine alone, or taxane/gemcitabine were the most frequently used therapies. In the second line treatment period, 44.5% of patients did not receive chemotherapy. (22)

From hospital based retrospective cross-sectional study done at TASH, department of surgery , Surgical techniques employed for bladder tumors were TURBT in 82.5%, trans vesical removal of the mass in 13.4%, open biopsy and fulguration in 2.1%, cyst prostatectomy in 2.1% patients.45% of patients had additional surgery such as repeated TURBT in 16.5.% for recurrent

and residual tumors, cystectomy+ureterosigmoidostomy in 12.4%, cystectomy+neobladder in 8.2%, anti-incontinence procedure (embedding) in 4.1%, partial cystectomy in 4.1%. 4.1% of patients took chemotherapy. (15) Hence urinary bladder cancer treatment is mainly based on stage of the disease, histology type and site of the tumor.

### **3.Objectives**

#### **3.1. General Objective**

- To assess the epidemiology, clinicopathology and treatment patterns of bladder cancer patients at Tikur Anbessa specialized hospital oncology center and Urology Unit surgical department, AAU, Ethiopia

#### **3.2. Specific objectives**

- To describe the demographic characteristics of urinary bladder cancer patients
- To describe the tumor characteristics and stage of the disease
- To describe the treatment pattern

### **4. Methods and materials**

#### **4.1 Study area and setting**

The study was conducted at oncology department and Urology unit surgical department of Tikur Anbessa Specialized Hospital, starting from September 1st, 2021 to January 30<sup>th</sup>, 2022. Tikur Anbessa Specialized Hospital (TASH) is a tertiary hospital located in Addis Ababa which is a capital city of the country. It is the largest & oldest public hospital of the country providing high level of clinical care for millions of people and training to health science students from different parts of the country and from the Horn of Africa. The hospital has the leading oncology center in the country, providing tertiary specialist care for a catchment population of approximately 100 million people from different parts of the country with a range of malignancies. The Radiotherapy center, established 27 years back with the help of International Atomic Energy Agency (IAEA), the center currently has two Cobalt-60 Teletherapy units both are out of service and one HDR Brachytherapy unit dedicated for gynecologic malignancies but it is not working for the past several months. Since December, 2020, the center established one LINAC machine with one CT

simulator and three Varian TPS computers. Activities include palliative and curative therapy for all patients with histopathologically proven cancers, including bladder cancers.

The Urology unit provides tertiary specialist care with referrals from deferent hospitals of the country. Activities include elective surgery and emergency surgery with a range of urologic cases including malignancies.

#### 4.2 Study design

An institution-based descriptive cross-sectional study design was conducted to assess the demography, clinicopathology and treatment patterns of bladder cancer patients that were seen from September 2018 to August 2021 GC attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

#### 4.3 Source population

All histologically-confirmed primary bladder cancer patients that were registered at the oncology department and Urology Unit of Tikur Anbessa specialized hospital between September 2018 - August 2021 G.C are included

#### 4.4 Study population

All cases of histologically-confirmed primary bladder cancer patients seen in Tikur Anbessa Specialized Hospital Oncology center and urology Unit, whose files were available during the study period.

#### 4.5 Inclusion criteria

- Pathologically confirmed urinary bladder cancer at presentation
- Patents who have complete medical record (at least Biopsy, age, sex, treatment,)
- Age  $\geq 18$  years old

#### 4.6 Exclusion criteria

- Patients who have any other confirmed cancer (second primary)

#### 4.7 Sampling procedure

HMIS logbooks used to identify all cases of bladder cancer that were documented after evaluation and treatment at the oncology department and Urology unit. Every case that fulfills the inclusion criteria was included in the study.

#### 4.8 Operational definitions

- **Staging** – the extent of spread of the cancer based on the American Joint Committee on Cancer (AJCC) TNM system. T describes size of the tumor and spread to nearby tissue, N describes spread of cancer to nearby lymph nodes, M explains the distant spread to other parts of the body
- **Non-muscle invasive bladder cancer (NMIBC)** \_cancer found in the tissue that lines the inner surface of the bladder
- **Muscle invasive bladder cancer (MIBC)** \_ cancer that spreads into the detrusor muscle of the bladder.
- **Urothelial cancer**\_ Cancer that begins in cells called urothelial cells that line the urethra, bladder, ureters, renal pelvis, and some other organs

#### 4.9 Variables

- Demographic characteristics such as sex, age, residence, smoking and occupational exposure history
- Clinical profile of bladder cancer patients
- Tumor pathology and stage of the disease
- Type of treatment

#### 4.10 Data collection tools and procedures

Data was collected from oncology center and Urology unit of TASH using a structured checklist containing closed ended questions especially designed for the study. The data was collected from the medical chart of each participant by two trained health professionals, under close supervision and facilitation by the principal investigator. Each day, the collected data was checked for accuracy and completeness.

#### 4.11 Data management and quality assurance

The principal investigator gave training on the relevance of the study and standard operating procedures to the data collectors; was followed closely the data collection procedures and kept hard copy of the completed forms in a protected place.

#### **4.12 Data analysis**

Data was entered and analyzed using SPSS version 25. The demographic, clinical & histopathologic characteristics and treatment patterns of patients were computed by using descriptive statistics such as mean, percentage, frequencies, and standard deviation. Finally, the study finding was presented using tables and figures.

#### **4.13 Ethical consideration**

Ethical clearance was obtained from Institutional Review Board of the Radiation oncology Department. Permission letter was submitted to the medical record unit from the Clinical Oncology Department & Research Directorate to retrieve and review the charts. After this, introduction & familiarization of the data collectors with team unit was secured. The questionnaires were kept anonymous and confidential.

#### **4.14 Dissemination of results**

Upon completion, the study finding will be submitted to Department of Clinical Oncology, College of Health Sciences, Addis Ababa University as a partial fulfillment of specialty degree in Clinical Oncology. Publication of the result on scientific journals will be considered through peer review and presentation on different meetings/conferences.

## 5. Results

### 5.1 Socio-demographic characteristics of patients

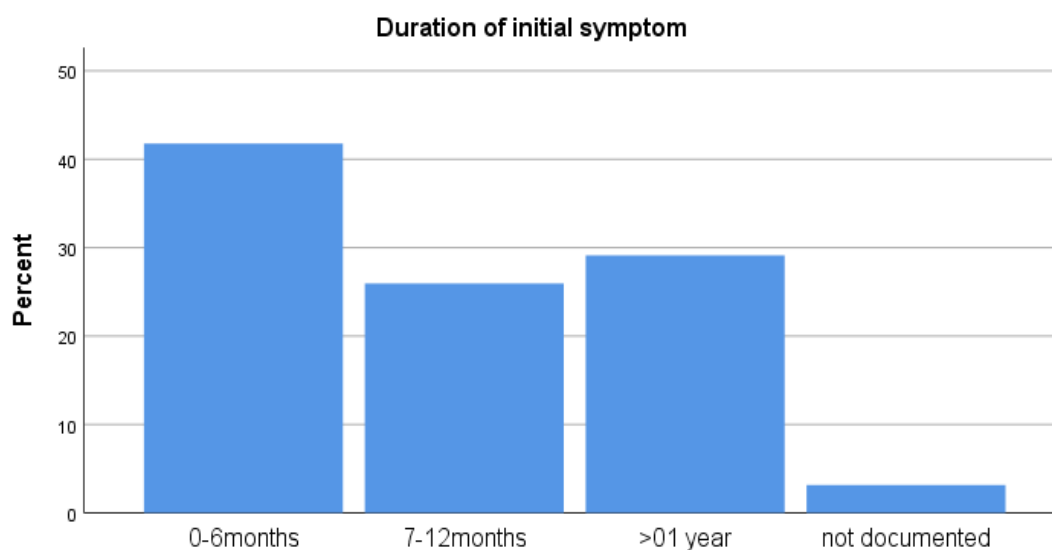
This study included data derived from 158 urinary bladder cancer patients who attended Oncologic clinic and urology clinic of TASH, after excluding 10 patients who didn't fulfill the inclusion criteria. Among the studied patients, most 128(81%) were males while the remaining 30(19%) were females, with a male-to-female (M: F) ratio of 6.74:1. Participants' age ranged from 22 to 88 years with a mean age of  $57.41 \pm 13.662$  years. Majority of cases (81,51.2%) were seen in the age group 50-70 years. Concerning the residence, nearly one-third of (50,31.6%) patients claimed to be dwellers of the capital, Addis Ababa while 47(29.7%) of all patients reported to be residents of Oromia region. The remaining more than one-third of the patients came from different regions of the country, as detailed in Table 1. With respect to history of cigarette smoking, a few numbers of patients (15,9.5%) had documented history of smoking while nearly two- fifth of patients (43%,68/158) have no history of smoking. The remaining 47.5% (75) of patients had missing data about their smoking history. Besides, only 2(1.3%) patients had history of occupational exposure while 63 patients had no exposure. The other 93 patients had no documentations.

**Table 1** :Socio-demographic characteristics of urinary bladder cancer patients attending Oncology clinic and urology unit of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31 2021

Variable (n=158)		Frequency	Percent (%)
Sex	Male	128	81
	Female	30	19
Age strata	18 - 29 years	1	0.6
	30 - 39 years	13	8.2
	40 - 49 years	30	19
	50 - 59 years	37	23.4
	60 - 69 years	44	27.8
	70 - 80 years	27	17.1
	>80 years	6	3.8
Residence	Oromia	47	29.7
	Addis Ababa	50	31.6
	Amhara	31	19.6
	SNNPR	26	16.5
	Harari	1	0.6
	Dire Dawa	0	0
	Afar	1	0.6
	Somali	2	1.3
	Gambella	0	0
	Tigray	0	0
Occupational exposure	Yes	2	1.3
	No	63	39.9
	Unknown	93	58.9
Smoking	Yes	15	9.5
	No	68	43
	Unknown	75	47.5

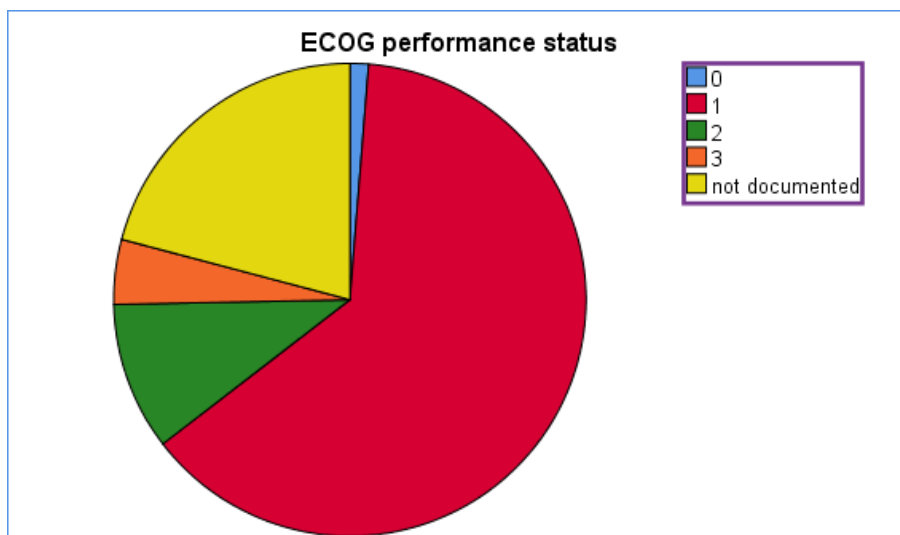
## 5.2 Clinical profile of patients

The presenting symptom was hematuria in 143(90.5%), irritative symptoms (Dysuria, frequency, urgency, urge incontinence) in 103(65.2%), obstructive symptoms (Decreased force of stream, feeling of incomplete voiding) in 71(44.9%), suprapubic pain in 27(17.1%) and weight loss in 13(8.2%). On the other hand, symptoms of advanced or metastatic disease like pelvic pain, abdominal pain and bone pain were mentioned in nearly 20% of all the studied patients. (Table 2).



**Figure 1:** Duration of illness of urinary bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Finally, considering the duration of the illness most patients (41.8%) were presented within 6 months while 25.9% were presented within 7-12 months. The other significant number of patients (29.1%) was late presenters, more than 12 months (Fig. 1). On physical examination: pallor, flank tenderness, suprapubic tenderness, suprapubic mass and bone tenderness were detected in 20.4% of patients. (Table 2). Moreover, with respect to ECOG performance status, the current study showed that majority (100; 63.3%) of the patients belonged the ECOG performance category 1. 16 (10.1%) patients were classified as ECOG performance category 2 while the remaining 9(5.7%) were categorized to either ECOG 0 or 3 category. The other 33(20.9%) patients had missed data about their performance status (Fig 2).



**Figure 2:** ECOG performance status of bladder cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

**Table 2 :** Clinical profile of urinary bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Clinical feature		Frequency	Percent
<b>Symptoms</b>			
Haematuria		143	90.5
Irritative symptoms		103	65.2
Obstructive symptoms		71	44.9
Suprapubic pain		27	17.1
Weight loss		13	8.2
Symptoms of advanced or metastatic disease	pelvic pain	10	11.4
	Abdominal pain	3	6.3
	Bone pain	18	1.9
<b>Signs</b>			
Pallor (Anaemia)		14	8.9
Flank tenderness		8	5.1
Suprapubic tenderness		5	3.2
Suprapubic mass		3	1.9
Bone tenderness		2	1.3

All 158 (100%) studied patients were diagnosed with biopsy. Moreover, most patients had imaging investigations with one or combinations of abdominopelvic CT, abdominopelvic US, pelvic MRI and CXR with patterns listed on table 3. The other 6.3% of patients had no documented imaging.

**Table 3:**Imaging profile of urinary bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Types of imaging modalities used	Frequency	Percent
Abdominopelvic CT, Abdominopelvic US, CXR	46	29.1
Abdominopelvic CT, Abdominopelvic US	35	22.2
Abdominopelvic US, CXR	30	19
Abdominopelvic US	24	15.2
Pelvic MRI, Abdominopelvic US, CXR	7	4.4
CXR	4	2.5
Pelvic MRI	2	1.3
No imaging	10	6.3
Total	158	100.0

Upon initial presentations to oncology and urology clinic and until the time of medical record review, 46(29.1%) patients were developed local recurrence while only 4(2.5%) had both local and distant recurrence. Besides, 25(15.8%) patients were developed distant metastasis at the time of presentation or in the meantime to this medical record review mainly to the lungs (11,7%) and bone (4,2.5%). (Table 4)

**Table 4:** shows Site of recurrence and metastasis of urinary bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

<b>Site of recurrence</b>	<b>Frequency</b>	<b>Percent (%)</b>
Local	46	29.1
Both local and distant recurrence	4	2.5
<b>Site of metastasis</b>	<b>Frequency</b>	<b>Percent (%)</b>
Lung	11	7
Bone	4	2.5
Liver	3	1.9
Lung and bone	3	1.9
Lung and Liver	1	0.6
Other sites	3	1.9

### 5.3 Histo-pathologic tumor characteristics

In our review transitional cell carcinoma (urothelial carcinoma) was the most common histology which accounted 87.4%. Of which ,66(41.8%) was high grade invasive urothelial carcinoma, 60(38%) was low grade non-invasive papillary urothelial carcinoma and 12(7.6%) was high grade non-invasive papillary urothelial carcinoma. The other rare histologies were represented by Squamous cell carcinoma 10(6.3%), adenocarcinoma 3(1.9%), sarcoma 2(1.3%), mixed histology variants 2(1.3%) and other unspecified histologies 3(1.9%). Overall, 45.6% was non-muscle invasive, 37.3% was muscle invasive and the remaining 17.1% was metastatic at presentation.

Furthermore, stage-wise analysis shows that more than one-thirds (56) of the studied patients were diagnosed to have bladder cancer by the time the cancer reached an advanced clinical stage with stage III and stage IV disease accounting for 30 (19%) and 26 (16.5%), respectively. Besides, about one-fifth (32,20.3%) of the patients were diagnosed at clinical stage of 0 while 12 (7.6%) and 22(13.9%) patients were staged to stage I and stage II respectively based on the AJCC TNM staging system by the time of diagnosis.

**Table 5:** Histo-pathologic characteristics of urinary bladder cancer patients attending Oncology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Types of Histology	Frequency	Percent
High grade invasive urothelial carcinoma	66	41.8
Noninvasive papillary urothelial carcinoma, low grade	60	38
Noninvasive papillary urothelial carcinoma, high grade	12	7.6
Squamous cell carcinoma	10	6.3
Adenocarcinoma	3	1.9
Mixed histology	2	1.3
Sarcoma	2	1.3
Others	3	1.9
Total	158	100

Depth of the cancer	Frequency	Percent
Non-muscle invasive bladder ca (NMIBC)	72	45.6
Muscle invasive bladder ca (MIBC)	59	37.3
Metastasis at presentation	27	17.1
Total	158	100.0

Group staging	Frequency	Percent
Stage 0	32	20.3
Stage 1	12	7.6
Stage 2	22	13.9
Stage 3	30	19.0
Stage 4	26	16.5
Unknown	36	22.8
Total	158	100

## 5.4 Treatment patterns

Regarding the intent of treatment at initial presentation, 122(77.2%) patients had radical treatments while 32(20.3%) patients had undergone palliative treatment. Homeostasis and other unspecified treatments constituted less than 5%.

**Table 6:** Intent of treatment for bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Intent of treatment	Frequency	Percent
Radical	122	77.2
Palliative	32	20.3
Homeostasis	2	1.3
Others	2	1.3
Total	158	100

For 158 patients diagnosed with bladder cancer, initial surgery at presentation, additional surgery, intravesical chemotherapy, perioperative chemotherapy, palliative chemotherapy, radiotherapy and chemoradiotherapy was given depending on the stage and clinical conditions of the patients. Initial Surgical techniques employed for bladder tumors were TURBT in 132(83.5%), cystectomy 6(3.8%), trans vesical removal of the mass in 1(0.6%), open biopsy and fulguration in 2(1.3%) and other unspecified procedures were done in 10.8 %. Twenty-one (13%) patients had additional surgery such as radical cystectomy in 15(9.5%), partial cystectomy in 2(1.3%), palliative stent in 2(1.3%) and excision in 2(1.3%). (Table 5). Eight (5.1%) patients took intravesical doxorubicin. Thirteen (8.2%) patients took cisplatin/gemcitabine based perioperative chemotherapy. Only one patient took MVAC based perioperative chemotherapy. The other two patients took unspecified type of perioperative chemotherapy regimen. Twenty-one (13.3%) patients were treated with palliative chemotherapy. Among these the most widely used type of chemotherapy was cisplatin /gemcitabine combination (15,9.5%) followed by carboplatin/gemcitabine (5,3.2%) combination chemotherapy .one patient was treated with unknown type of palliative chemotherapy regimen. Among patients treated with radiotherapy,7(4.4%) patients took palliative radiotherapy while 4(2.5%) patients took radical dose of radiotherapy. Only one patient took homeostatic radiotherapy. Only two patients took concurrent chemoradiotherapy.

**Table 7:** patterns of treatment for bladder cancer patients attending Oncology clinic and urology clinic of TASH, AA, Ethiopia, from Sep 1st, 2018 to Aug 31st, 2021

Types of surgery performed	Frequency	percent
Initial surgery		
TURBT	132	83.5
Cystectomy	6	3.8
Trans vesical (TV) tumor resection	1	.6
Open biopsy and fulguration	2	1.3
Other procedure	17	10.8
Total	158	100.0
Additional surgery	Frequency	Percent
Radical cystectomy	15	9.5
Partial cystectomy	2	1.3
Palliative stent	2	1.3
Excision	2	1.3
Total	21	13.3
<b>Types of intravesical treatment used</b>	<b>Frequency</b>	<b>Percent</b>
Doxorubicin	8	5.1

Types of perioperative chemotherapy used	Frequency	Percent
Cisplatin + Gemcitabine	13	8.2
MVAC	1	0.6
Not specified	2	1.3
Total	16	10.1

Types of palliative chemotherapy used	Frequency	Percent
Cisplatin + Gemcitabine	15	9.5
Carboplatin + Gemcitabine	5	3.2
Unknown	1	.6
Total	21	13.3

Intent of radiotherapy used	Frequency	Percent
Palliative	7	4.4
Hemostatic	1	.6
Radical	4	2.5
Total	12	7.6
Chemoradiotherapy	2	1.3

## 6. Discussion

In this study 158 bladder cancer patients were studied and it was found that 81% were males while 19% were of females making a male to female ratio of 6.74:1, suggesting that urinary bladder cancer has a noticeable propensity of attacking male population. Participants' age ranged from 22 to 88 years with a mean age of  $57.41 \pm 13.662$  years. Majority of cases (81, 51.2%) were seen in the age group 50-70 years. This corresponds to a Saudi Arabian study that found 96 (82.7%) were of men while 20 (17.3%) were of women, with a male-to-female (M: F) ratio of 4.8:1. The overall mean age was  $62.4 \pm 15.62$  years (range: 20-115 years). The majority of the cases 56 (48.3%) were seen in the age group 60-79 years. (16) A similar retrospective Clinicopathological Study done at three Centers in Khartoum, Sudan involving 106 bladder cancer patients was conducted. The study reported that 87 (82.1%) patients were men. The male to female ratio was 4.6:1. Their mean ( $\pm$ SD) age was 59.49 ( $\pm$ 13.7) range (18-90) years. The peak frequency for all cases was at the age of 60-80 years. (23) A hospital based Kenyan study had also similar demographic pattern to current study that reported 41 (78.8%) patients were male while 11 (21.2%) were of female with male to female ratio of 4:1. The peak incidence was in the 60-69 years age group. (24) Another hospital based study from TASH, department of surgery, Addis Ababa, Ethiopia reported similar results to the current study. Of which, 60 (61.9%) patients were male while 37 (38.1%) patients were females with male to female ratio of 1.6:1. Their age ranged from 20 to 79 years, with mean age of  $49.73 \pm 1.5$ . (15) In the current study only a few numbers of patients (9.5%, 15) had documented history of cigar pipe smoking while 75 (47.5%) patients had no smoking history. The remaining 68 (43%) patients had missing data on smoking status. Two patients had history of occupational exposure while 63 (39.9%) patients had no history of occupational exposure. The remaining 93 (58.9%) patients had missed data. In this review, the association between bladder cancer versus cigarette smoking and occupational exposure seems low. But from international study Cigarette smoking is the most important risk factor, accounting for 50% of cases in men and 35% in women and smokers have a 2- to 4-fold increased risk of bladder cancer compared to non-smokers. The risk increases with increasing intensity and/or duration of smoking. From same study Occupational exposure to urothelial carcinogens is the second most important risk factor, accounting for 5–20% of all bladder cancers. Even the relative risk of occupational exposure to carcinogens is likely underestimated and varies from country to country. (10). The reason why the

association between smoking and environmental exposure versus bladder cancer seems low in current study may be due to poor documentation or possibly due to most patients came from contour side where smoking habits and industries were relatively low. Further study is recommended on this area.

The present study revealed that hematuria was the most common presenting symptom occurring in 143 (90.5%) patients followed by irritative symptoms in 103(65.2%), obstructive symptoms in 71(44.9%), suprapubic pain in 27(17.1%), weight loss in13(8.2%) patients and symptoms of advanced or metastatic disease like pelvic pain, abdominal pain and bone pain were mentioned in nearly 20% of all the studied patients. A similar result obtained from Sudanese study that showed clinical presentation of gross hematuria in 75 (84.3%), urgency in 14 (15.7%) and symptoms include suprapubic pain and weight loss.(23). A similar clinical patter also documented in prior Senegalese and Kenyan studies. (24,25)

Another study from TASH, department of surgery, Ethiopia that showed similar clinical presentation to the current study with the most common presenting symptoms were hematuria in 91.8% followed by irritative symptoms in 74.2%, obstructive symptoms in 39.2%, suprapubic pain in 35.1% and weight loss in 46.4%. (15) considering the duration of the illness, this study found most patients (41.8%) were presented within 6 months while 25.9% were presented within 7-12 months. The other significant number of patients (29.1%) was late presenters, more than 12 months. A Sudanese study had similar result to current study in terms of durations in initial presentation which most patients (52.9%) were presented in less than 6 months duration while 47.1%patients had symptoms of >6 months.

In this review transitional cell carcinoma (urothelial carcinoma) was the most common histology which accounted 87.4%. Of which ,41.8% (66) was high grade invasive urothelial carcinoma, 38% (60) was low grade non-invasive papillary urothelial carcinoma and 7.6% (12) was high grade non-invasive papillary urothelial carcinoma. The other rare histologies were represented by Squamous cell carcinoma (6.3%), adenocarcinoma (1.9%), sarcoma (1.3%), mixed histology variants (1.3%) and other unspecified histologies (1.9%). Overall, 45.6% was non-muscle invasive, 37.3% was muscle invasive and the remaining 17.1%was metastatic at presentation. A similar pattern was documented in developed countries with Approximately 90 percent of

epithelial bladder tumors were urothelial carcinomas; the remaining 10 percent were nonurothelial or mesenchymal in origin.(14)A similar histological result was obtained from Yemeni descriptive study(involving 316 patients) that showed urothelial neoplasms in 78%,squamous cell carcinoma in 17% ,adenocarcinoma in 2% and rhabdomyosarcoma in 1%.(26).studies done in Saudi Arabia, Sudan ,Kenya and Ethiopia also had similar histopathological finding with the current study.(15,16,23,24)

However, Schistosomiasis associated SCC is common in regions where Schistosoma haematobium infection is endemic, such as the Middle East and parts of Africa. Studies done in Northern Nigeria (53%) and Egypt; Schistosomiasis associated Squamous cell carcinoma was the commonest histology type. (17,18) In Ethiopia, there are all three known schistosoma haematobium endemic area that is in the middle and lower parts of Awash valley, in the lower Wabe Shebelle valley and along Sudanese border in Wellega but majority of Ethiopians are highlanders. Further study is highly recommended to ascertain the above finding.

The result of the present study showed Initial Surgical techniques employed were TURBT in 132(83.5%), cystectomy 6(3.8%), trans vesical removal of the mass in 1(0.6%), open biopsy and fulguration in 2(1.3%) and other unspecified procedures were done in 10.8 %. Twenty-one (13%) patients had additional surgery such as radical cystectomy in 15(9.5%), partial cystectomy in 2(1.3%), palliative stent in 2(1.3%) and excision in 2(1.3%). Eight (5.1%) NMIBC patients took intravesical doxorubicin after TURBT was done. None of the patients received immunotherapy, simply because the facility is not available at TASH. Study done at TASH ,Ethiopia, had similar result in superficial tumor of which TURBT was commonly done and 4 patients took intravesical chemotherapy.(15) IN Africa the treatment for superficial tumor is unclear but in well-developed countries it needs a great investment and has multiple treatment options like Intravesical immunotherapy(BCG)and chemotherapy.(14,21)Currently 13(8.2%) patients took perioperative chemotherapy (gemcitabine and cisplatin combination regimen). one patient took MVAC chemotherapy regimen and the other two patients took unspecified type of chemotherapy regimen. Twenty-one (13.3%) patients were treated with palliative chemotherapy. Among these the most widely used type of chemotherapy was cisplatin /gemcitabine combination (15,9.5%) followed by carboplatin/gemcitabine (5,3.2%) regimen .one patient was treated with unknown type of palliative chemotherapy regimen. Among patients treated with radiotherapy,7(4.4%) patients took palliative

radiotherapy while 4(2.5%) patients took radical dose of radiotherapy. Only one patient took homeostatic radiotherapy. The other two patients took concurrent chemoradiotherapy. The same treatment pattern result was obtained from study done at TASH, department of surgery, Ethiopia that showed initial Surgical techniques employed were TURBT in 82.5%, trans vesical removal of the mass in 13.4%, open biopsy and fulguration in 2.1% and cystoprostatectomy in 2.1% patients. 45% of patients had additional surgery such as radical cystectomy in 20.6%, partial cystectomy in 4.1%. 4.1% of patients took chemotherapy. The same study was done in Netherlands to know treatment patterns of MIBC and metastatic bladder cancer. Of 470 patients upfront radical cystectomy was done in 64%, neoadjuvant or induction chemotherapy followed by radical cystectomy in 6%. 45 patients took palliative radiotherapy and 24 patients took palliative chemotherapy with same regimen to current study, cisplatin/Gemcitabine and cisplatin/carboplatin regimen. Others were on best supportive care or lost from follow-up. compared to the current study, most patients had radical cystectomy (64%). In our case the number of patients who had radical cystectomy were small. the possible explanation may be lack of skillful personnel to undergo surgery (RC), absence of well-equipped set-up and late presentation of patients. For stage IV bladder ca ,similar study done with comparable pattern to our study in USA.(22)

## **7. Strength and limitations**

### **7.1 Strength**

- The study was done at the leading Oncology unit of the country where the highest numbers of oncologic patients (including Urinary bladder cancer) with varying socio-demographic characteristics are expected to be represented.
- The author was involved in the data quality management personally in order to assure authenticity and completeness of data collected as well as the results obtained.
- The fact that the study was retrospective chart review in its nature, there was no concern of COVID-19 transmission in the process of data collection.
- The establishment of i-care system in the hospital makes every documentation readable and easily accessible in the data collection process
- The data was collected from Oncology center and Urology unit that makes it representative data of the hospital

### **7.2 Limitations**

- This study design was a cross-sectional, and hence it is challenging to make causal inferences and alternative explanations of the findings.
- Being a hospital based retrospective study, some important information in patients' clinical records were missing due to improper filling of patients' particulars. Moreover, the exclusion of incomplete medical records has resulted in smaller sample size which may compromise the statistical power.

## **8. Conclusion and Recommendations**

Most of the bladder cancer patients who attended Oncology center and urology unit of Tikur Anbessa Specialized Hospital were males in their sixth and seventh decade of life. Hematuria was the most common presenting symptom. Transitional cell carcinoma (urothelial carcinoma) was the most common histology. 45.6% was non-muscle invasive while 37.3% was muscle invasive and the remaining 17.1% was metastatic at presentation. Majority of patients were treated with radical intent. TURBT was the most commonly practiced type of treatment. Intravesical chemotherapy, perioperative chemotherapy and cystectomy was rarely practiced as compared with standard guidelines and text books.

It would be prudent for the government and other stakeholders to formulate policies that are targeted to improve treatment options and increase well trained medical staffs. The Uro-Oncology MDT should be strengthened to identify patients who need perioperative chemotherapy and other treatment options from both sides. Treatment options that are available in our hospital should be practiced as per guidelines such as intravesical chemotherapy, perioperative chemotherapy, Radical surgery and radiotherapy. Diagnostic facilities including different level of radiological image and pathological facilities must be give especial attention to determine the stage and plan of appropriate treatment plan. Moreover, health education and improvement of health infrastructures are necessary in order to overcome late disease presentation. Outreach services should also be considered as significant portion of the patients are out of the capital. Further nation-wide studies to assess incidence and prevalence of bladder cancer with consideration of a wide range of potential risk factors, such as detailed smoking, occupational exposure and their management should be projected.

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## 7. Work plan

Activity	July	Aug	Sep	Oct	Nov	Dec
Finalization of proposal	X					
paper submission for department ethics review	X					
Ethical review by AAU- College of Health Sciences	X					
Equipment procurement		X				
Training of data collectors		X				
Data collection		X	X	X		
Data entry					X	
Preliminary Analysis and write up of primary end point					X	
Final analysis and write up						X
Dissemination						X

## 8. Budget break down

Training and pretest	Number	Number of days	Per person in ETB	Total cost
Data collectors	2	5	150	1,500
Supervisor	1	5	250	1,250
<b>Sub total</b>				<b>2,750</b>
Data collection	No	No of days	Per person in ETB	Total cost/ETB
Supervisor	1	30	200	6,000
Data collectors	2	30	50 birr per chart	25,000
Chart finder	2	30	20 birr per chart	10,000

<b>Subtotal</b>	<b>41,000</b>
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<b>Material</b>	<b>Unit</b>	<b>Total needed</b>	<b>Unit cost</b>	<b>Total cost</b>
Duplicating Paper	Pack	5	500	2500
Pen	Pack	1	240	240
Pencil	Pack	1	48	48

Eraser	Each	4	10	40
Sharpener	Each	4	20	80
CD (RW)	Each	3	50	150
Binding	Each	5	80	400
Data collection tools & checklist duplication (Questioner)	Format	1000	2	2000
<b>Sub total</b>				<b>5,458</b>

**Total budget=49,208ETB**

## *9. Annexes*

### **8.1 English Version Questionnaire**

Questionnaire ID: \_\_\_\_\_

MRN: \_\_\_\_\_

<b>Section 1: Demographic data</b>		
<b>S.N.</b>	<b>Question item</b>	<b>Possible answer</b>
01	Age at diagnosis in years	
02	Sex	1. Male                      2. Female

03	Marital status	1. Married 2. single 3. divorced 4. widow
04	Educational level	
05	Religion	1. orthodox 2. protestant 3. Muslim 4. others
06	Region	1. Addis Ababa 2. Dire Dawa 3. Oromia 4. Amhara 5. Tigray 6. Somalia 7. SNNPR 8. Gambela 9. Benishangul gumuz 10. Harari 11. Afar
07	Occupation	1) Employed 2) Unemployed 3) Self-employed
08	Smoking History	1. Yes      2. No    3. unknown
9	History of occupational exposure	1. Yes      2. No

**Section 2: Clinical data of the patient (Signs and Symptoms of Bladder Cancer)**

10	Hematuria	1. Yes      2. No
11	If the answer for Q no12 is yes, type of hematuria	1.painless    2. Painful
12	irritative symptoms (Dysuria, frequency, urge incontinence, urgency)	1. Yes      2. No
13	Obstructive symptoms (Decreased force of stream, feeling of incomplete voiding, intermittent stream, straining)	1. Yes      2. No
14	Suprapubic pain	1. Yes      2. No
15	Weight loss (weight loss, >10% of their body weight)	1. Yes      2. No

16	Signs and symptoms of metastases or advanced disease	1. Abdominal pain 2. bone pain 3. pelvic pain 4. others
17	Signs	1. Suprapubic tenderness 2. Pallor (Anemia) 3. Flank tenderness 4. Suprapubic mass 5. Bone tenderness
18	Duration of initial symptom	1. 0-3 months 2. 3-6 months 3. 6-9 months 4. 9-12 months 5. More than 01 year
19	ECOG performance status	1. 0 2. 1 3. 2 4. 3 5. 4
20	Diagnostic modalities	Biopsy
21	Imaging modalities	1. Abdominopelvic US 2. Abdominopelvic CT 3. CXR 4. Pelvic MRI
22	Metastasis	1. Yes 2. No
23	If the answer is yes, Site of metastasis	
24	Recurrence	1. Yes 2. No
25	If the answer is yes, site of recurrence	

**Section 3: Histo-pathologic findings at diagnosis**

26	Type of histology	<ol style="list-style-type: none"> <li>1. Infiltrative urothelial (transitional cell) carcinoma with its v</li> <li>2. Mixed histology</li> <li>3. noninvasive papillary urothelial carcinoma, low grade</li> <li>4. noninvasive papillary urothelial carcinoma, high grade</li> <li>5. Adenocarcinoma</li> <li>6. squamous cell carcinoma</li> <li>7. Small cell carcinoma</li> <li>8. Melanoma</li> <li>9. Sarcoma</li> <li>10. others</li> </ol>			
27	Depth of the cancer	<ol style="list-style-type: none"> <li>1. non-muscle invasive bladder ca (NMIBC)</li> <li>2. Muscle invasive bladder ca (MIBC)</li> <li>3. Metastasis at presentation</li> </ol>			
28	T,N,M	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td data-bbox="740 909 1409 1398"> <ol style="list-style-type: none"> <li>1. Tx</li> <li>2. T0</li> <li>3. Ta</li> <li>4. Tis</li> <li>5. T1</li> <li>6. T2</li> <li>7. T3</li> <li>8. T</li> </ol> </td> </tr> <tr> <td data-bbox="740 1398 1409 1703"> <ol style="list-style-type: none"> <li>1. Nx</li> <li>2. N0</li> <li>3. N1</li> <li>4. N2</li> <li>5. N3</li> </ol> </td> </tr> <tr> <td data-bbox="740 1703 1409 1824"> <ol style="list-style-type: none"> <li>1. Mo</li> <li>2. M1</li> </ol> </td> </tr> </table>	<ol style="list-style-type: none"> <li>1. Tx</li> <li>2. T0</li> <li>3. Ta</li> <li>4. Tis</li> <li>5. T1</li> <li>6. T2</li> <li>7. T3</li> <li>8. T</li> </ol>	<ol style="list-style-type: none"> <li>1. Nx</li> <li>2. N0</li> <li>3. N1</li> <li>4. N2</li> <li>5. N3</li> </ol>	<ol style="list-style-type: none"> <li>1. Mo</li> <li>2. M1</li> </ol>
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29	Group staging	Stage 0 Stage I Stage II Stage III Stage IV Undocumented
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<b>Section 4. Treatment patterns data</b>			
30	Surgery types (Initial)	Write type of initial surgery-----	
31	Additional surgery	Write type of additional surgery other than TURBT-----	
32	intravesical chemotherapy After TURBT	1. Yes            2. No	
33	If the answer for Q no.27 is yes, write the type of chemotherapy used	-----	
34	preoperative chemotherapy	1. Yes            2. No	Chemotherapy regimen
35	Post-operative chemotherapy	1. Yes            2. No	Chemotherapy regimen
36	Palliative chemotherapy		Chemotherapy regimen
37	Radiotherapy	1. Yes            2. No	intent of treatment if the answer is yes
38	Chemoradiotherapy	1. Yes            2. No	

