Addis Ababa University

Collage of Health Science and School of Medicine

Department of pathology

Histopathologic pattern of neoplastic and non-neoplastic bladder lesions in Tikur Anbessa specialized Hospital, Addis Ababa, Ethiopia, over a 5 year period, 2016-2020

December, 2020

Declaration of Principal Investigator

I the undersigned, Anteneh Belachew agree to accept all responsibilities for the scientific and ethical conduct of this thesis entitled "**Histopathologic study of Bladder lesions: A Hospital Based Retrospective Study, From January 01, 2016 to August 30, 2020.**

The Thesis is my original work and was not prepared by others. All resources and materials used for this research have been dully acknowledged. I was communicating and providing timely progress report to my advisor and seek the necessary advice, comment and approval in the course of this work.

Anteneh Belachew Fantaye(MD), Final Year Pathology Resident:

_____ _____

Signature Date

Approval of Advisor:

The Student had worked on this research and fulfilled all the requirements and hence hereby can submit the thesis to the Department of Pathology, TikurAnbessa Specialized Hospital, School Of Medicine, College of Health Sciences, Addis Ababa University.

Dr Mulugeta Temesgen (MD), Assistant professor of pathology:

_____ _____

Signature Date

A Thesis submitted to the Department of Pathology, College of Health Sciences, School of medicine, Addis Ababa University in Partial fulfillment of the requirements for the Specialty Diploma in Pathology.

Investigator: Anteneh Belachew (MD, Pathology resident)

Advisor: Dr. Mulugeta Temesgen (MD, Assistant professor of pathology)

Acknowledgement

I would like to express my deepest gratitude to my instructor and advisor, Dr Mulugeta Temesgen (MD), Assistant professor of pathology for his expertise, guidance and constructive advice in the course of this study. Next, I would like to extend my sincere gratitude to college of health sciences, Addis Ababa University.

Table of contents

Contents

Lists of tables

Lists of figures

Abbreviation

TCC-Transitional cell carcinoma

SCC-Squamous cell carcinoma

UBC-urinary bladder cancer

BC-bladder cancer

HGPUC-high grade papillary urothelial carcinoma

LGPUC-low grade papillary urothelial carcinoma

PUNLMP-papillary urothelial neoplasm of low malignant potential

TURBT- trans-urethral resection of bladder tumor

LUTS-lower urinary tract symptom

WHO-world health organization

ISUP-international society urological pathology

ASMR-age specific mortality rate

ASIR-age specific incidence rate

ABSTRACT

Background: Urinary bladder lesions, non-neoplastic and neoplastic, are collectively responsible for significant morbidity and mortality throughout the world. Bladder cancer is the 7th most common cancer worldwide, with an estimated 260,000 new cases occurring each year in men and 76,000 in women. Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females. According to Globocan, there were 1455 newly diagnosed bladder cancer cases in Ethiopia in 2018 and accounts for 2.2% of cancer death in the same year. According to Addis Ababa Cancer registry, there were a total of 4139 newly diagnosed cancer cases over the period of two years (2012–2013) and bladder cancer accounts for 5.6% of cases.

Objectives: The aim of this study is to determine histopathologic patterns of neoplastic and non-neoplastic bladder lesions in Tikur Anbessa Specialized Hospital.

Methods: This was a retrospective cross sectional descriptive study conducted on 625 patients having histopathologic evaluation for bladder lesions at Tikur Anbessa Specialized Hospital from January 01, 2016 to August 30, 2020.

Results: From a total of 700 cases reviewed, 625 cases fulfilled the study criteria and included in this study. Out of 625 cases, 597 cases were of TURBT, 27 cases were cystectomy specimens and 1 case was true cut biopsy. The majority of the cases were seen in the age group of 51-60 yrs (28.5) with a male predominance (76.8%).Hematuria was the most common presenting symptom (59%).non neoplastic lesions accounted for 111 cases (17.8%),benign tumors accounted for 16 cases (2.6%) and malignant tumors accounted for 498 cases (79.6%).Urothelial carcinoma (96.4%) were the predominant lesions observed under malignant category, of which low grade non invasive papillary urothelial carcinoma (51.8%) was the most common subtype. urothelial papilloma was the commonest benign tumor accounting for 7 cases(43.8%).Among nonneoplastic lesions, chronic nonspecific cystitis (20.7%) was the commonest lesion noted.

Conclusions: This study demonstrates that majority of the cases were malignant bladder neoplasms of urothelial origin, large number of which was low grade non-invasive papillary urothelial carcinoma.

1. Introduction

1.1Background

The bladder is a hollow viscus with the shape of a four-sided inverted pyramid when empty and of a rounded structure when distended. It is divided into the following portions: superior surface (also known as dome, and covered by the pelvic parietal peritoneum), posterior surface (also known as base), and the two inferolateral surfaces. [1].

Urinary bladder lesions, non-neoplastic and neoplastic, are collectively responsible for significant morbidity and mortality throughout the world. Neoplasm's of the bladder pose biologic and clinical challenges. Despite significant inroads into their origins and improved methods of diagnosis and treatment, tumors of the bladder continue to extract a toll in morbidity and mortality [2].

Urinary bladder lesions constitute an important source of clinical signs and symptoms; these are more disabling than lethal. [3] Both non-neoplastic and neoplastic lesions are quite common. The non-neoplastic lesions include cystitis, malakoplakia, urachal lesions and tuberculosis. [4] Cystitis constitutes an important source of clinical signs and symptoms. Neoplastic lesions are responsible for significant morbidity and mortality throughout the world. [5]

Urinary bladder cancer is an important cause of cancer related morbidity and mortality with a consecutive increase in incidence throughout the world. It is the 7th most common type of cancer worldwide [6]. Among men it is the fourth most common cancer and eighth most common malignancy in women [7]. Bladder cancer is more frequent in developed countries rather than in developing countries.

Every 9 out of 10 bladder cancer cases diagnosed turn out to be transitional cell carcinoma (TCC), thus showing the dominance of TCC over other types that include squamous cell carcinoma (SCC), adenocarcinoma and other less frequent types of bladder cancer which collectively account for the remaining 1 out of 10 bladder cancer cases [8].Exposures to tobacco smoke, occupational toxins, and environmental sources of heavy metals such as arsenic are the major reported risk factors for TCC [9-13].

The primary sign associated with bladder carcinoma is hematuria [14]; however, it is often non-specific and requires further investigation. Although, cystoscopy remains as the primary screening tool for patients that allow a direct visualization of the bladder mucosa and biopsies of the suspected lesions [15], however, it cannot provide the accurate diagnosis and histopathology is the only resort for most accurate and definitive diagnosis.

1.2 Statement of the problem

The increase in the incidence rate of UBC and its recurrent nature has led to massive pressures on health care systems [16]. Bladder cancer is the 7th most common cancer worldwide, with an estimated 260,000 new cases occurring each year in men and 76,000 in women [17]. Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females (ratio worldwide is about 3.5:1) [18].

In both sexes, the highest incidence rates of bladder cancer are observed in Western Europe, North America and Australia [19].In general, the prevalence of bladder tumors in developed countries in approximately 6-times higher compared with that in developing countries. Research findings have shown that the geographical and racial distributions of BC vary in different parts of the world; for instance, it is more dominant in American countries than in Asian countries [20].

According to Globocan, there were 1455 newly diagnosed bladder cancer cases in Ethiopia in 2018 and accounts for 2.2% of cancer death in the same year [21]. According to Addis Ababa Cancer registry, there were a total of 4139 newly diagnosed cancer cases over the period of two years (2012–2013) and bladder cancer accounts for 5.6% of cases [22]. Approximately 550,000 new UBC (almost 425,000 in males and over 125,000 in females) were diagnosed worldwide in 2018,the lifetime risk of getting UBC is 1.1% in men, and 0.27% in women and approximately 200,000 patients died from UBC in 2018 [23].

1.3 Significance of the study

As mentioned earlier, data from the literature shows difference in the relative frequencies of the various neoplastic and non-neoplastic bladder lesions. Several reports on this topic from different part of the world showed difference in geographic prevalence among the neoplastic and non-neoplastic lesions. Since there is limited information in the literatures about the prevalence of the neoplastic and non-neoplastic bladder lesions in Ethiopia, the objective of the current study is to establish the frequency and type of the various neoplastic and non-neoplastic bladder lesions diagnosed in biopsy specimens in Tikur Anbessa specialized Hospital from January 2016 to August 2020 and to compare the results with those found in similar studies done in different part of the world. This study will also be used as a reference for other studies in the future.

2. Literature review

During 2018, 549,393 new cases of bladder cancer were diagnosed worldwide, 125,311 (22.80%) of whom were female and 424,082 (77.19%) were male. In general, the global ASIR of Bladder cancer was 5.7 (2.4 in women and 9.6 in men). There were also 199,922 deaths from bladder cancer, 51,652 (25.83%) of whom were female and 148,280 (74.16%) were male. The global ASMR of bladder cancer was 1.9 (0.87 in women and 3.2 in men [24].

One study done in Bangalore, Karnataka, India in 2017 .A retrospective study conducted in the Department of pathology and Cystoscopic biopsies of 70 cases were included in the study. 73.1% were males and 26.9% were females. The majority of the cases were seen in the age group of 41-50 yrs (29.9%) with a male predominance (73.1%). The common clinical presentation was hematuria followed by dysuria, frequency and suprapubic pain. Three specimens out of 70 biopsies were inadequate for reporting. Of the remaining 67 cases, 38 were (56.7%) neoplastic and 29 (43.3%) were non neoplastic lesions. Of the 29 non neoplastic lesions, 15(51.7%) were chronic nonspecific cystitis, 5(17.2%) were follicular cystitis and 3(10.3%) were granulomatous cystitis of tubercular etiology. Other lesions like eosinophilic cystitis, hemorrhagic cystitis and vonbrunn's nest were observed in 2 (6.9%), 1(3.5%) and 3(10.3%) cases respectively. Urothelial tumors formed the largest group of the neoplastic category. They constituted 94.7% (36 cases) of all neoplastic lesions. The remaining 2 cases (5.3%) were secondary adenocarcinomas. Among all urothelial tumors, invasive papillary urothelial carcinoma was the most common subtype accounting for 29 cases (80.6%) with low grade comprising 8 cases and high grade 21 cases. Four of the high grade tumors showed squamous differentiation and one was clear cell variant of invasive urothelial carcinoma. Out of 5 (13.9%) noninvasive papillary urothelial carcinomas, 4 were low grade lesions and one was high grade lesion. Papillary urothelial neoplasm of low malignant potential was observed in 2 (5.6%) cases [25].

Another study conducted in the Department of Pathology of Teerthanker Mahaveer Medical College, over a period of one and half year (Feb 2017 to Sep. 2018). In this study a total of 50 TURBT were evaluated. Majority of patients were in the age group between 61 and 80 years. Majority of patients were males (84%). Out of 50 cases evaluated, majority were malignant (90%) out of which urothelial carcinoma constituted 84% followed by squamous cell carcinoma (4%) and adenocarcinoma (2%). Remaining 5 cases were diagnosed as cystitis out of which interstitial cystitis and eosinophilic cystitis were two in number followed by one case of granulomatous cystitis. Majority of urothelial carcinoma cases were high grade (73.8%) and low grade comprised (26.2%). Muscle invasion was seen in 77.4% of high grade urothelial carcinoma which was completely absent in low grade urothelial carcinoma [26].

Study done by Baidya R, Sigdel B, and Baidya NL on histopathological study of cystoscopic bladder biopsies, a five year retrospective study from January 2008 to December 2013, carried out at B&B Hospital, Lalitpur. A total of 324 cases were included in this study. Out of 324 patients, 216 (66.66%) were male and 108 (33.33%) were females. The peak age of incidence was between 61-70 years. Non-neoplastic lesions were predominant (61.11%).In this study maximum numbers of cases 58.95% were of chronic nonspecific cystitis. tubercular cystitis was found in 0.93% cases. In this study, TCC accounted 38.28% of all tumors while the adenocarcinoma and paraganglioma were 0.31% respectively. Histological distribution according to WHO grading reveals that the maximum number of cases (16.98%) observed TCC-low grade followed by high grade TCC with 16.67%.Papillary urothelial Neoplasm of low malignant potential was seen in 4.01%.[27].

A Prospective Study done on histomorphologic profile of lesions in Cystoscopic Bladder Biopsies in North Maharashtra over a period of three years between June 2012 – June 2015 and included 139 cases in the study. 71cases (51.1%) were males and 68 cases (48.9%) were females with peak age incidence is between 60-69 years . the majority of the patients with benign lesions presented with LUTS accounting for 82.7% of the cases and those with malignant lesions present with haematuria accounting for 90.8%.the non neoplastic bladder lesions constituted 52(37.41%) Neoplastic lesions constituted 102(73.38). Of the 52(37.41%) non neoplastic lesions, 18(12.94%) were non- specific cystitis,8(5.75%) were squamous metaplesia,6(4.31%) were follicular cystitis 2(1.43%) were cystitis glandularis, 1(0.71%) were cystitis cystica, eosinophilic cystitis and tubercular cystitis each. among neoplastic lesion 15(10.79%) were utothelial papilloma. In this study, majority of the bladder lesions were malignant constituting 62.58% (87 cases) of the cases, among them the most common we found was urothelial carcinoma followed by squamous cell carcinoma and adenocarcinoma constituting 55.39%, 5.03% and 2.15% respectively. As per histological grading WHO/ISUP (2004) used in the study there is high prevalence of high grade urothelial carcinoma followed by low grade urothelial carcinoma, and papillary urothelial neoplasm of low grade malignant potential (PUNLMP) accounting for 55.43%, 22.82%, and 5.43% respectively[28].

Another study was done on 38 cases in department of pathology, Guntur medical college, from August 2012 to July 2015. The commonest age group was seen in the 41-60 years and the male to female ratio was 5:1. Among the 38 cases, 12 were non- neoplastic and 26 were neoplastic lesions. Of the 12 non-neoplastic lesions, there were 8 cases of non-specific cystitis, two cases of exostrophy showing metaplastic changes and one case of Cystitis glandularis. Of the 26 neoplastic lesions, 22 cases were papillary urothelial carcinomas and four cases were squamous cell carcinoma. Of the 22 papillary urothelial carcinomas, 6 cases were low grade papillary urothelial carcinomas, 8 were high grade urothelial carcinomas and 7 cases were high grade urothelial carcinoma showing squamous differentiation and one case of high grade urothelial carcinoma of ureter. Of the 6 low grade papillary urothelial neoplasm's, 3 were non-invasive and 3 were invasive carcinomas. Out of 16 high grade Urothelial carcinomas 10 (62.5%) showed lamina propria invasion and muscular invasion [29].

A one year prospective study of the urothelial lesions was carried out in the Department of Pathology, Narayana Medical College, Nellore. A total of 48 lesions were evaluated. Out of the total cases, only 7 cases (14.58%) were radical cystectomy specimens and the remaining 41 cases (85.42%) were TURBT specimens. The peak age of incidence of the lesions was 61-70 years with male predominance. Hematuria was the most common presenting complaint. Benign condition includes, eosinophilic cystitis 1(6.25%), hemorrhagic cystitis 1(6.25%), non specific cystitis 7(43.75%), Granulomatous, fungal 5(31.25%), granulomatous Koch's 11(6.25%), Mesonephroid metaplasia 1(6.25%). Malignant lesion includes, HGPUC invasive 10(31.25%), HGPUC non-invasive 6(18.75%), LGPUC invasive 7(21.875%), LGPUC non-invasive 7(21.875%), PUNLMP 1(3.125%), Invasive with squamous differentiaton 1(3.125%). [30]

A study done on Urinary Bladder Tumors in Southern Pakistan: A Histopathological Perspective from December 1996 to December 2001. 500 patients were included in this study with male to female ratio of 5.3:1. The mean age was 57.5±8.6. The primary bladder tumors constituted the overwhelming majority (99%). 5 (1%) was the seat of metastatic tumors that originated mostly from the gut. One was a SCC primary from the cervix in a middle-aged female. Among the primary tumors of the bladder, TCC was the most common malignancy that accounted for 93.4%.A majority of these cases (62%) presented with superficial (muscle noninvasive) disease, while in 38%, the disease was muscle-invasive when first diagnosed. other primary tumor were Adenocarcinoma 13(2.6%), Squamous cell carcinoma 10 (2%), embryonal rhabdomyosarcoma 02(0.4%), Inverted papilloma 01(0.2%), Paraganglioma 01 (0.2%), Small cell carcinoma 01(0.2%).[31]

Descriptive study was performed on newly diagnosed primary bladder cancer patients at a urology unit of a tertiary care hospital (Colombo South Teaching Hospital, Sri Lanka) between 1 January 2011 and 31 December 2014. There were 148 patients with male to female ratio of 4.1:1. Haematuria was the most common clinical presentation encountered in 81% (120/148) of patients. Average age of the study was 65 years. There were 132 cases of urothelial tumors, 12 cases of SCC, 2 cases of adenocarcionma, 1 case of liomayosarcoma and 1 case of large B cell lymphoma. Among urothelial tumors, Infiltrating urothelial carcinoma accounts for 105 cases, infiltrating urothelial carcinoma With squamous differentiation 11 cases , infiltrating urothelial carcinoma With glandular differentiation 1 case, infiltrating Micropapillary carcinoma 1 case, Noninvasive urothelial neoplasm's accounts for 14 cases among which Urothelial carcinoma in situ accounts for 1 case, non invasive papillary urothelial carcinoma, low grade for 12 cases, Noninvasive papillary urothelial neoplasm of low malignant potential for 1 case. [32]

A research done on clinicopathological features of bladder tumors encountered over a five year Period in University Kebangsaan Malaysia Medical Centre from 2005 till 2009. Total of 83 cases were recorded. The main histopathology was transitional cell carcinoma (TCC) (90.4%), followed by adenocarcinoma (6%), squamous cell carcinoma (1.2%), leiomyoma (1.2%) and myeloid sarcoma (1.2%). For the TCCs, 58.6% were superficial while 41.4% were muscle invasive, and 13.3% had nodal metastasis with distant metastasis in 8%.Of the superficial tumors, 32.5% were high grade tumors. [33]

Retrospective study was conducted at the King Fahd Hospital, Madinah, Saudi Arabia, and comprised medical records related to bladder tumors, from January 2006 to October 2015. Of the 116 cases, 96(82.7%) were of men while 20(17.3%) were of women. The mean age was 62.4±15.62 years. Transitional cell carcinoma was the most common histological type, seen in 111(95.7%) cases, followed by adenocarcinoma 3(2.6%) and squamous cell carcinoma 2(1.7%). Of the transitional cell carcinoma cases, 78(70.5%) were superficial, while 33(29.5%) were muscle invasive. Most of the transitional cell carcinoma cases 72(65%) were of lower grade, while 39(35%) were of high grade. [34]

Retrospective study was done in department of pathology, faculty of Medicine, King Abdulah University Hospital between the years 1994 and 2000. 110 patients with histologically confirmed TCC of the urinary bladder were seen during the study period, 3 cases were adenocarcinoma and 2 cases were SCC. There were 99 males and 11 females. The mean age of the patients was 60.6 ± 13.7. Gross haematuria was the main symptom in 76 patients (69%).66 of the cases had low-grade and 44 had high-grade tumors. Pathological staging showed that 60 (54.5 percent) of the cases were stage PTa, 19 (17.3 percent) PTI, 22(20 percent) PT2, eight (7.3 percent) PT3 and one (0.9 percent) PT4. Most of the low-grade tumors (77.3%) were PTa, while most of the high-grade tumors 61.4%) were PT2. [35]

Study was carried out at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period of July 2006 to June 2007.a total of 150 cases of urinary bladder tumor were included in the study. The age range was from 25 years to 95 years with a mean age of 58.5 years. 143 (95.33%) cases were male and 7 (4.66%) cases were female. At the time of first consultation almost all 139 (92.66) patients had hematuria. Among 150 cases of urinary bladder tumor 145 (96.66%) TURBT and 5 (3.33%) were collected by cystectomy. muscularis propria was present in 93 (62%) cases and in 57 (38%) cases muscularis propria was absent. The microscopic type of 150 cases of urinary bladder tumor, 143 (95.33%) were papillary urothelial carcinoma, 4 (2.66%) were adenocarcinoma, 2(1.33%) were squamous cell carcinoma and 1(0.66) was carcinomasarcoma. Among 150 cases of urinary bladder tumor 27 (18%) had squamous differentiation and only 8 (5.33%) had glandular differentiation. A close association between smoking and bladder cancer was observed in this study. Among 150 cases 94 (62.66%) were smokers, 30 (20%) were non smoker and 26 (17.33%) had no information about it. [36]

A prospective study was done with the biopsy and resected specimen of the urinary bladder carcinoma during a period of two years (October 2012-June 2014) from Yenepoya Medical College hospital, Mangalore. The study was done on 43 cases of urinary bladder carcinomas. Peak incidence was seen in 6th decade of life, with a male to female ration of 3.1:1. Haematuria was the most common presenting symptom. Out of 43 cases 8 cases were of radical cystectomy of the bladder and 35 cases were transurethral resection of bladder tumor (TURBT).transitional cell carcinomas were the most common histological type found. 23 cases of non-invasive papillary urothelial carcinomas and 20 cases of invasive urothelial carcinomas were seen. Among non-invasive papillary urothelial carcinoma 15 cases were of low grade non-invasive carcinoma and 8 cases were of high grade non-invasive carcinoma. All 20 cases of invasive urothelial carcinomas were high grade. [37]

A retrospective study was done on surgical excision specimens of the bladder and cystoscopic bladder biopsies received over a 10-year period at the Department of Histopathology, University of Benin Teaching Hospital, Benin City: Nigeria. A total of 75 urothelial bladder lesions were received in the Pathology Department. Of these, 48 (64%) were from males and 27 (36%) were from females. The peak age incidence for all bladder lesions was in the 60–69 years age group. In all, 51 cases (68%) were malignant while 24 (32%) were nonmalignant. Among the nonmalignant lesions, inflammatory lesions constituted 18 (24%) of all cases while tumor like lesions accounted for six (8%) of all cases. Among inflammatory lesions, 10 were chronic nonspecific cystitis, 7 were Schistosomiasis and 1 case was Malakoplakia. Among benign or tumor like lesions, Inverted papilloma accounts for 4 cases, Angiofibroma and Inflammatory polyp accounts for one case each. In this study, TCC was the most commonly encountered class of carcinoma constituting 33 cases. This was followed by adenocarcinoma accounting for ten cases. SCC constituted only three cases. There were two cases of anaplastic carcinoma and embryonal carcinoma respectively and a single case of leiomyosarcoma. High grade papillary urothelial carcinoma was the most common tumor grade accounting for 51.4%. Only 40.6% cases were urothelial confined carcinoma (PTa) while 29.7% each accounted for lamina propria (PT1) and muscle (PT2) invasive carcinoma. [38]

A study was conducted in the period from January 2004 through December 2005 at three centers in Khartoum, Sudan. One hundred and six patients with urinary bladder neoplasm's were included in the study. The commonest affected age group was 60-80 years with male to female ratio 4.6:1.The common presenting was gross heamaturia in 75 (84.3%) cases. Histopathologically, TCC with its different grades was seen in 72 (67.9%), SCCs in 26 (24.5%), TCC with sqamous differentiation in three (2.8%) and others in five (4.7%) patients, the others include adenocarcinoma (2 patients), liposarcoma, leiomyosarcoma, and malignant fibrous histocytoma. There were 43.4% of TCC patients graded as papillary carcinoma of high grade, 52.6% papillary carcinoma of low grade, 1.3% papillary neoplasm of low malignant potential, one papilloma, and another was graded as a flat neoplasm at presentation. 28/76(36.8%) of TCCs showed histologically signs of muscle invasion at diagnosis. [39]

Another study was done in Nigeria, Lagos State University Teaching Hospital between 1st January, 2011 and 31st December, 2018. There were 87 cases of bladder tumor that presented at Pathology department with mean age of 56.9±13.9 years. Of all the bladder carcinomas, urothelial carcinoma was the most common. This accounted for 83.6%. SCC presented next representing 14.6%. Only one case of adenocarcinoma was observed. In this study, papillary urothelial neoplasms of low malignant potential (43.4%) were commoner than high grade urothelial carcinoma (39.6%).Low grade urothelial carcinoma accounts for 17% of cases. [40]

Eight years hospital based descriptive, retrospective study was conducted from 2006 to 2013 at Kilimanjaro Christian Medical Centre, Moshi-Tanzania. A total of 120 subjects were included in the study. Majority 90 (75%) had TCC followed by SCC (18%). Forty nine percent of subjects with TCC presented with non muscle invasive bladder cancer (NMIBC). Majority (87%) of subjects with non-muscle invasive TCC of bladder experienced recurrence within a period of one year after diagnosis. [41]

A hospital based retrospective cross sectional analysis was conducted in, Tikur Anbessa Hospital, department of surgery, Addis Ababa, Ethiopia. Patients' medical records and Operation Theater Registers of 97 patients operated upon for bladder tumors, between January2006 and December 2008 were analyzed. Sixty patients were male and 37 female (M: F of 1.6:1) with mean age of 49.73±1.5.The most common presenting symptoms were hematuria in 89(91.8%). Histopathologically, 87(89.7%) and 10(10.3%) patients had malignant and benign bladder tumors respectively. Of the patients with malignant bladder tumors, 78 (80.4%) had TCC, 5(5.2%)SCC, and 3 (3.1%) adenocarcinoma. Common patterns of bladder masses were papillary 77(79.7%), sessile or mixed 10(10.3%), and nodular 6(6.2%).Upon presentation, 66(74.7%) of patients had low grade, whilst 20(23.0%) had high-grade disease, 85.5% of bladder tumors were nonmuscle invasive, while 14.9% were muscle invasive, and 2.4% metastatic. The commonest surgical technique employed for bladder tumor removal was TURBT in 80 (82.5%) patients. [42]

3. Objective of the study

3.1. General objective

- To determine hisopathologic Patterns of bladder lesions diagnosed in Tikur Anbessa specialized Hospital from January 2016 to August 2020.

3.2. Specific objectives

- To describe the socio – demographic characteristics of patients with neoplastic and non-neoplastic bladder lesions.
- To assess type of bladder biopsy specimens.
- To show the prevalence and frequency of the neoplastic and non-neoplastic bladder lesions.
- To show distribution of various neoplastic and non-neoplastic bladder lesion cases by age and gender.
- To show distribution of neoplastic bladder lesions by histopathologic pattern.
- To determine patterns of grade and stage of neoplastic bladder lesions
- To show frequency of distribution of non-neoplastic bladder lesions by histopathologic pattern.
- To assess the presence or absence of muscle proper in TURBT specimens.
- To compare and contrast results from other similar studies done from different parts of the world with that of the result from the present study.

4. Methodology

4.1 Study Area

This study was conducted at Black Lion (Tikur Anbessa) specialized teaching Hospital. Tikur Anbessa (Black Lion) Specialized Hospital is located in Addis Ababa at Lideta sub-city opposite to Immigration office Ethiopia. It is the teaching hospital of the Addis Ababa University and the largest referral hospital in the country with over 700 beds, and serves as a training centre for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, radiology technologists, and others who shoulder the responsibilities to solve the health problem of the community and the country at.

4.2 Study Design and Period

The study was a cross-sectional retrospective descriptive study where data was retrieved from the archive of the department of pathology that was registered from January 01, 2016 up to August 30, 2020.

4.3 Source Population

All patients whose biopsy specimens were submitted to the department of pathology.

4.4 Study population

- All patients whose bladder biopsy specimens were submitted to the department in the study period from January 01, 2016 to August 30, 2020.

4.5. Inclusion and exclusion criteria

4.5.1 Inclusion Criteria

- All patients with bladder lesions who underwent cystoscopic bladder biopsies or cystectomy.

4.5.2 Exclusion criteria

- Bladder lesions with descriptive diagnosis.
- Bladder lesions without original biopsy request form.
- Recurrent bladder tumors.
- Those patients with two or more missing variables.

4.6 Sample size estimation

All patients fulfilling the criteria during the study were included

4.7 Sampling procedure

All the hard copy of bladder biopsy histopathology reports from January 01, 2016 to August 30, 2020 were reviewed from the archive of pathology department.

4.8 Data collection tools and procedures

Demographic data, clinical presentation of the patients and histopathology diagnoses were extracted from the hard copy using data extraction sheet.

4.9 Study variables

In this study, the variables included for analysis are depicted as the following.

- Age of patient at diagnosis.
- Sex of patient.
- Clinical presentation.
- Histopathologic type.
- Histologic grade of cancer.
- Stage of cancer at diagnosis.
- Type of bladder biopsy specimen.
- Presence or absence of muscle proper in TURBT specimens.

4.10 Data analysis

The data was processed and analysed by using IBM SPSS 26.0.

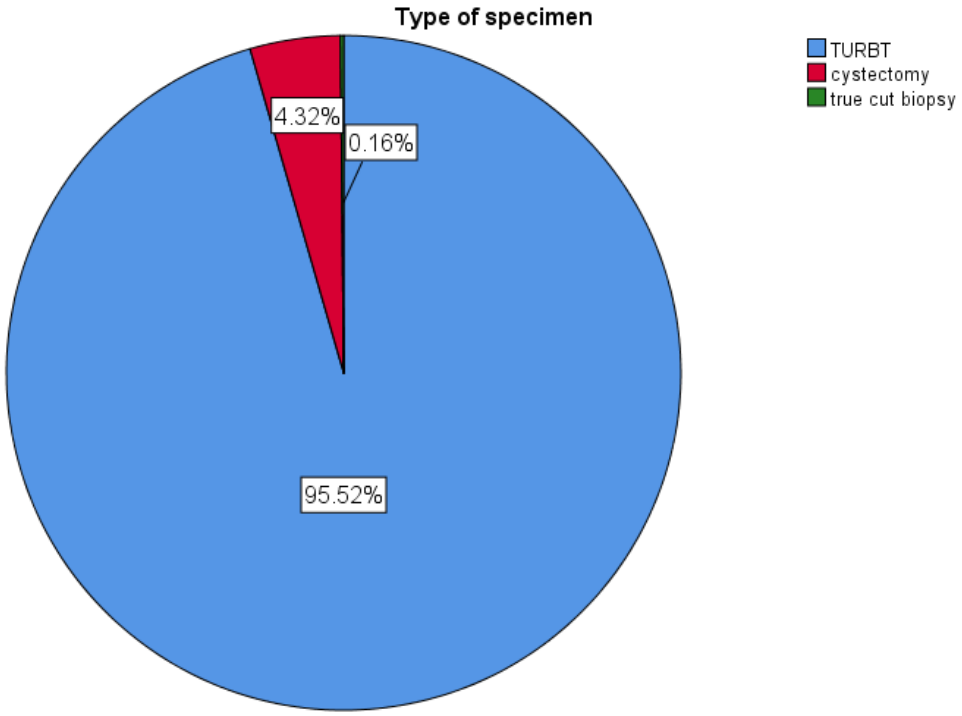
4.11 Ethical consideration

The study was approved by Addis Ababa University, School of medicine, Department of Research Ethics Review Committee (DRERC) and Department of pathology. An official letter was written to the respective health facilities and the study was conducted after obtaining their approval.

5. Results

From a total of 700 cases reviewed, 625 cases fulfilled the study criteria and included in this study. Out of 625 cases, 597 cases were of transurethral resection of bladder tumor (TURBT), 27 cases were cystectomy specimens (25 radical and 2 partial cystectomy specimens) and 1 case was true cut biopsy.

Figure 1.Graph showing the frequency of type of bladder biopsy specimens during the study period.



The age of the patients in this study ranged from 1-89 years. Mean age of cases was 53.81. The Majority of patients were in the age group between 51 and 60 years (Fig-2). Out of 625 patients, 480 were males (76.8%) and 145 were females (23.2%) with a male to female (M: F) ratio of 3.3:1.Hematuria was found to be the commonest clinical presentation, followed by LUTS. In 79 cases clinical presentation was not mentioned in the pathologic request paper. (Table-1).

Among 625 cases, 111(17.8%) were non- neoplastic lesions, 16(2.6%) were benign tumors and 498(79.6%) were malignant tumors.

Off 111(17.8) non- neoplastic lesions chronic non specific inflammation was the commonest accounting for 23(20.7%) cases.14 (12.6%) were cystitis glandularis, 12(10.8%) were cystitis cystica and polypoid cystitis each and 9(8.1%) were tuberculosis.non neoplastic lesions were common in males and more commonly occur with age range of 41-50(Table 2).

Figure 2.Distribution of age in decades .

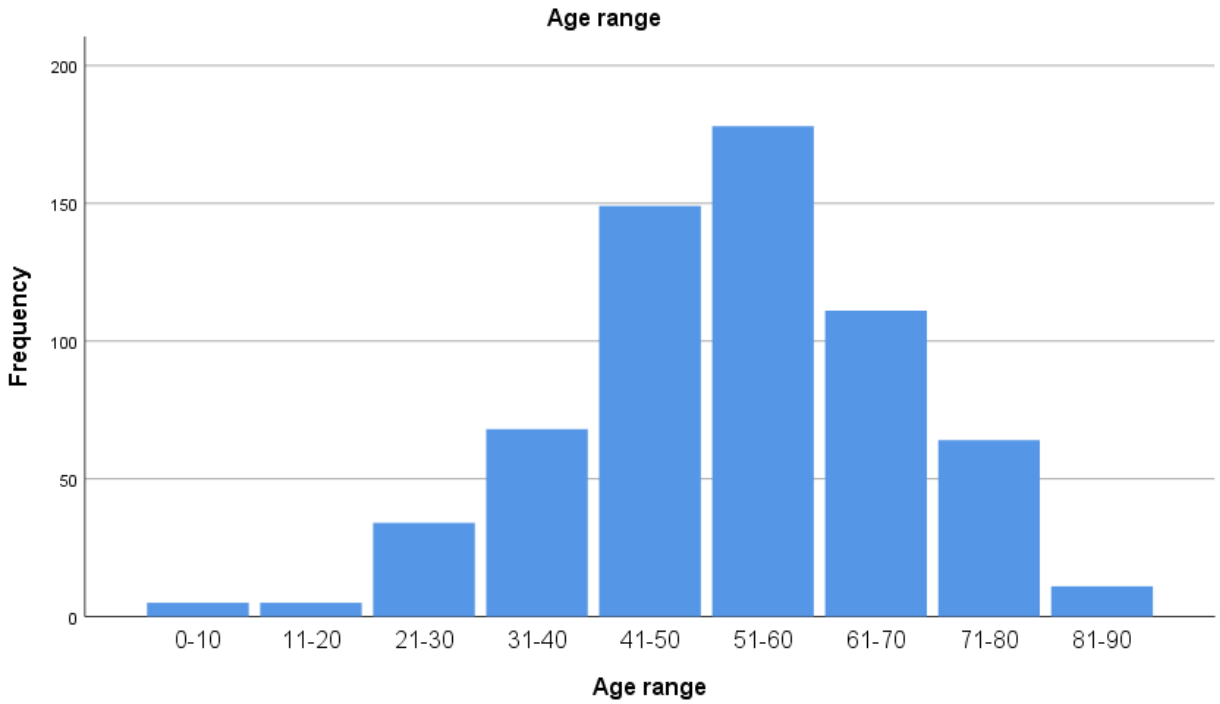


Table 1.Distrbution of clinical features of all cases.

	Clinical presentation	Frequency	Percent
	Hematuria	369	59.0
	LUTS	94	15.0
	both hematuria and LUTS	77	12.3
	not mentioned	79	12.6
	BOO	4	.6
	flank pain	1	.2
	Acute urinary retention	1	.2
	Total	625	100.0

Table 2.Frequence of non neoplastic lesions.

Non neoplastic lesions		Frequency	Percent
	Chronic non specific cystitis	23	20.7
	Cystitis glandularis	14	12.6
	Cystitis cystic	12	10.8
	Polypoid cystitis	12	10.8
	Tuberculosis	9	8.1
	Follicular cystitis	8	7.2
	Cystitis cystica et glandularis	7	6.3
	Eosinophilic cystitis	5	4.5
	Granulomatous cystitis	4	3.6
	Cystitis granularis with intestinal metaplasia	4	3.6
	Schistosomiasis	3	2.7
	Chronic cystitis with squamous metaplasia	3	2.7
	Acute cystitis	2	1.8
	Interstitial cystitis	1	0.9
	Radiation cystitis	1	0.9
	Xanthogranulomatous cystitis	1	0.9
	Detroser muscle hyperplasia	1	0.9
	Biopsy	1	0.9
	Total	111	100.0

From 16 benign cases, the most common tumor was urothelial papilloma accounting for 7 (43.8%) cases.3 (18.8%) were inverted urothelial papilloma and inflammatory myofibroblastic tumor each (Fig 3). There were 2(12.5%) cases of leiomyoma and 1(6.3%) case of benign vascular lesion. benign tumors were seen more commonly in males. mean age of presentation was 41 years. The minimum age identified was 2 years and maximum was 72 years (Table-3).

Malignant lesions were 498(79.6%) of the total cases.392 (78.7%) were males and 106(21.3%) were females with M: F ratio of 3.6:1. The age ranges from 2-88 years peak age being in the fifth and sixth decade. Among the malignant lesions urothelial carcinomas were by far the commonest neoplasm accounting for 480 (96.4%) cases.7 (1.4%) were metastatic carcinoma, 5(1%) were adenocarcinma and squamous carcinoma each and 1(0.2%) case was embroynal rhabdomyo-sarcom (Fig 4).

Figure 3.Frequency of histopathologic patters of benign bladder tumors.

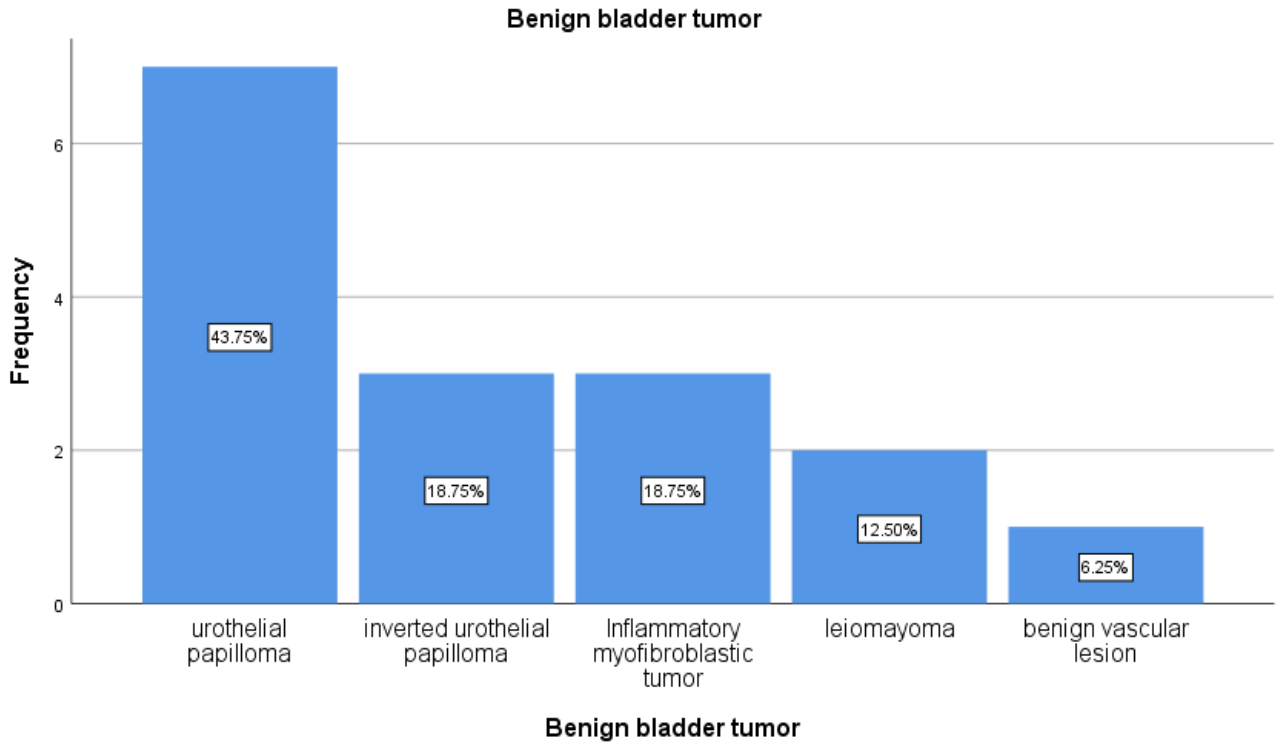
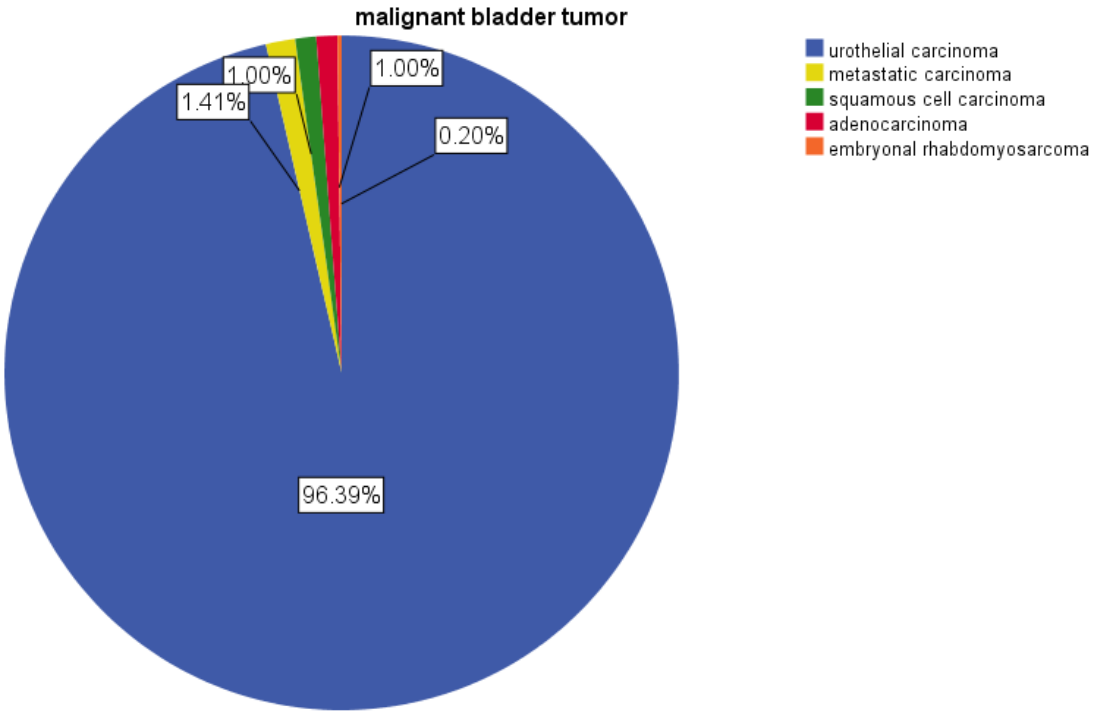


Table 3.Distribution of benign bladder lesions by age.

		Benign bladder tumor					Total
		urothelial papilloma	inverted urothelial papilloma	Inflammatory myofibroblastic tumor	leiomayoma	benign vascular lesion	
Age range	0-10	0	0	0	0	1	1
	11-20	1	0	0	0	0	1
	21-30	1	0	1	1	0	3
	31-40	0	1	2	0	0	3
	41-50	0	2	0	1	0	3
	51-60	3	0	0	0	0	3
	61-70	1	0	0	0	0	1
	71-80	1	0	0	0	0	1
Total		7	3	3	2	1	16

Figure 4.Distribution of malignant bladder tumors.



Majority of urothelial carcinoma cases were low grade papillary urothelial carcinomas 284(59.2%) followed by high grade papillary urothelial carcinomas 175(36.5%) and PUNLMP 15 (3.1%). 2(0.4%) cases were urothelial carcinoma in situ and nested urothelial carcinoma each.1 (0.2%) case was micropapillary urothelial carcinoma and 1 case (0.2) was diagnosed as suggestive of plasmacytoid urothelial carcinoma. urothelial carcinomas were common in male with M: F ratio 4:1. Peak age of presentation was in the fifth and sixth decade (Table-4).

Of the 284(59.2%) low grade papillary urothelial carcinomas, 249(87.7%) were non invasive and 35(12.3%) were invasive. Of the 175(36.5%) high grade papillary, 165(94.3%) were invasive and 10(5.7%) were non invasive (Table-5). 8 case of invasive high grade papillary urothelial carcinoma shows squamous differentiation, 1 case shows glandular differentiation and 1 case shows both glandular and squamous differentiation.

Of the 5 cases of adenocarcinoma one case was mucinous adenocarcinoma and there was one case of clear cell (mesonephroid) adenocarcinoma. Among 5 cases of squamous cell carcinoma 3 were keratinizing and 2 were non-keratinizing. Of the 7 case of metastatic carcinoma, 2 were prosatatic adenocarcinoma,2 were cervical squamous cell carcinoma(keratinizing and non keratinizing),2 were rectal signet ring and mucinous adenocarcinoma each and 1 case of mucinous adenocarcinoma in which primary site is not stated in the pathology request form(Table-6).

Among 597 TURBT specimens, 455 cases were urothelial carcinoma. In 280(61.6%) cases of urothelial carcinoma muscle proper was not represented and in 108(23.7%) cases muscle proper was represented. In 67(14.7%) cases, it was not reported in the pathology result whether muscle proper was represented or not (Table-7).

Of 108 cases in which muscle proper was represented, 37 case shows muscle invasion. Of 37 case of muscle invasive urothelial carcinoma seen in TURBT specimens, 35 cases were high grade invasive papillary urothelial carcinoma and 2 cases were low grade invasive papillary urothelial carcinoma.

There were 27 cystectomy specimens.19 cases were high grade papillary urothelial carcimona, 4 cases were low grade papillary urothelial carcinoma and 1 case was nested urothelial carcinoma and micropapillary urothelial carcinoma each. saquamous cell carcinoma and mucinous adenocarcinoma accounts for 1 case each. The most common tumor stages were PT2a and PT3a accounting for 6 case each.

Table 4.Distribution of urothelial carcinoma by age.

Urothelial carcinoma		Age range								Total
		11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	
	Low grade papillary urothelial carcinoma	1	7	32	69	88	52	29	6	284
	High grade papillary urothelial carcinoma	0	3	12	41	55	38	23	3	175
	PUNLMP	0	1	2	2	6	2	2	0	15
	Urothelial carcinoma in situ	0	0	0	0	1	0	1	0	2
	Nested urothelial carcinoma	0	0	0	2	0	0	0	0	2
	Micropapillary urothelial carcinoma	0	0	0	0	1	0	0	0	1
	Suggestive of plasmacytoid urothelial carcinoma	0	0	0	0	1	0	0	0	1
Total		1	11	46	114	152	92	55	9	480

Table 5.Shows the grade and invasiveness of urothelial carcinoma.

Urothelial carcinoma		Invasive		Total
		yes	no	
	Low grade papillary urothelial carcinoma	35	249	284
	High grade papillary urothelial carcinoma	165	10	175
	PUNLMP	0	15	15
	Urothelial carcinoma in situ	0	2	2
	Nested urothelial carcinoma	2	0	2
	Micropapillary urothelial carcinoma	1	0	1
	Suggestive of plasmacytoid urothelial carcinoma	1	0	1
Total		204	276	480

Table 6.Distribution of metastatic bladder carcinoma by age.

Metastatic bladder carcinoma		Age range				Total
		21-30	41-50	51-60	61-70	
	Prostatic adenocarcinoma	0	1	0	1	2
	Cervical keratinizing squamous cell carcinoma	0	0	0	1	1
	Cervical non keratinizing squamous cell carcinoma	0	0	1	0	1
	Rectal adenocarcinoma	0	1	0	0	1
	Rectal signet ring carcinoma	1	0	0	0	1
	Mucinous adenocarcinoma(primary not stated)	0	0	0	1	1
Total		1	2	1	3	7

Table 7.Shows cross tabulation of urothelial carcinoma and the presence or absence of muscle proper in TURBT specimen.

		Urothelial carcinoma						
		Low grade papillary urothelial carcinoma	High grade papillary urothelial carcinoma	PUNLMP	Urothelial carcinoma in situ	Nested urothelial carcinoma	Suggestive of plasmacytoid urothelial carcinoma	Total
muscle proper represented or not	yes	51	57	0	0	0	0	108
	no	188	80	9	2	1	0	280
	not reported	41	19	6	0	0	1	67
Total		280	156	15	2	1	1	455

6. Discussion

Bladder cancer is the 7th most common cancer worldwide, with an estimated 260,000 new cases occurring each year in men and 76,000 in women [17]. Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females (ratio worldwide is about 3.5:1) [18]. According to Globocan, there were 1455 newly diagnosed bladder cancer cases in Ethiopia in 2018 and accounts for 2.2% of cancer death in the same year [21].

In the present study, a total of 625 urinary bladder biopsy specimens were evaluated. Most cases were transurethral resection of bladder tumor (TURBT) specimens (95.52%), which was similar to a study done in India (96.66%) [36]. The Mean age of patients with bladder lesions was 53.81.this finding was similar with a study done in Nigeria (54.9) [38]. Bladder lesions were more common in males as compared to their female counterparts. Specifically male to female (M: F) ratio was 3.3:1, this result was similar to a study done in India (M: F 3.1:1) [37]. In our study, the commonest clinical presentation was hematuria followed by LUTS. This was similar to a study done in Ethiopia [42].

In the present study majority of the bladder lesions noted were neoplastic lesions accounting for 82.2 % of the cases, which was comparable to a study done in North Maharashtra, India (73.38%) [28]. However, this study is differing from study done in Lalitpur, Nepal in which the majority of bladder lesions were non non-neoplastic (61.11%) [27].in our study among the non-neoplatic lesions chronic non specific inflammation was the commonest accounting for 23(20.7%) cases, this was comparative to a study done in North Maharashtra, India (12.94%) [28].There were 3 cases of chronic cystitis with squamous metaplasia.

The second common non-neoplastic lesion was cystitis glandularis accounting for 14 (12.6%) cases, 4 cases showing intestinal metaplasia. This data shows relative higher incidence of this lesion compared to other studies [28, 29]. In the present study, tubercular cystitis was found in 8.1% of non-neoplatic lesion. Tuberculosis remains the most common cause of granulomatous inflammation of the bladder in many parts of the world. It invariably develops from secondary foci, most often located in kidney [43]

Urothelial papilloma was the most common benign bladder tumor in this study accounting for 7 (43.8%) cases of benign tumors. In this study Urothelial papilloma accounts for 2.47% of non invasive bladder tumors, this is similar to a data given by WHO classification of tumors of the urinary system and male genital organs, 4^{th} edition (<4%) [44]. among benign tumors 3 (18.8%) were inflammatory myofibroblastic tumor. Inflammatory myofibroblastic tumor was previously regarded as a reactive condition. Its distinction from ordinary sarcomas and carcinomas is certainly of importance because of its generally indolent nature [1].

In this study bladder cancers were seen mainly in men with male to female ratio of 3.6:1. This result was comparable to a study done in Sri Lanka (M: F ratio 4.1:1) [32] and Sudan (M: F ratio 4.6:1) [39]. The mean age of occurrence was 56 years which is comparable to a study done in Tanzania (58.45) [41]. Urothelial carcimoma was the most common urothelial bladder lesion constituting 96.4% of all bladder cancers. This finding was similar to reports documented in Saudi Arabia where urothelial carcinoma constituted 95.7% of all histologically confirmed bladder carcinomas [34]. Study done in Nigeria [40] urothelial carcinoma accounted for 83.6% of bladder cancers. Study in Ethiopia [42] also showed urothelial carcinoma to be the commonest malignant bladder tumor (80.4%).

Out of all urothelial carcinoma in the present study, low grade papillary urothelial carcinomas were the commonest accounting for 284(59.2%) cases followed by high grade papillary urothelial carcinomas 175(36.5%).this is comparable to a study done in Ethiopia in which 74.7% of patients had low grade, whilst 23.0% had high-grade disease [42].study in Sudan [39] also showed low grade papillary urothelial carcinomas to be the commonest urothelial carcinoma (52.6%). On the other hand, our findings are contrary to studies done in India [28] where there is high prevalence of high grade urothelial carcinoma (55.43%) followed by low grade urothelial carcinoma (22.82%). In this study most of low grade papillary urothelial carcinomas were non invasive (87.7%) which was comparable to a study done in Nigeria (81.1%) [38].most of high grade papillary urothelial carcinoma were invasive (94.3%) which was similar to a study done in India (95.4%) [25].

Beside urothelial carcinoma there were 5 cases of adenocarcinoma and squamous carcinoma each, which was comparable to a study done in Ethiopia [42] (5 SCC and 3 Adenocarcinoma) and India [36] (4 Adenocarcinoma and 2 SCC). There were also 7 cases of metastaic carcinoma in which 5 cases were secondary adenocarcinoma form various sites. This finding was comparable to a study done in Nigeria [38] in which there were 8 cases of metastatic adenocarcinoma.

Among 597 TURBT specimens, 455 cases were urothelial carcinoma. In 280(61.6%) cases of urothelial carcinoma muscle proper was not represented and in 108(23.7%) cases muscle proper was represented. this study is differing from a study done in India [36] in which muscle proper was present in 62% of cases and absent in 38% cases.

7. Limitation

There were missing request papers and incompletely filled clinical information affecting the completeness of the study.

8. Conclusion

This study revealed a wide spectrum of non- neoplastic and neoplastic urinary bladder lesions. The most common bladder biopsy specimen was TURBT. Hematuria was the most common presenting complaint. Majority of the cases were malignant bladder neoplasms of urothelial origin, large number of which was low grade non-invasive papillary urothelial carcinoma. urothelial carcinoma were common in males with mean age of 56 year. Urothelial carcinoma displays many forms and some of these variant morphologies were seen in this study and may pose diagnostic difficulties because of their similarity to other malignancies and / or benign lesions. The most common benign tumor was urothelial papilloma. Chronic nonspecific cystitis was the commonest non-neoplastic lesion encountered in routine practice. The clinicopathological characteristics, frequency and distribution of different types of bladder lesions in this study are, in general, comparable to those reported in other studies.

9. Recommendation

- In the majority of TURBT specimens done for urothelial carcinoma muscle proper was not represented. Improvements in the TURBP techniques would be of benefit as muscle invasion is an important predictor of prognosis.
- Uniform reporting of presence or absence of muscle proper should be practiced.
- Attempts should also be made to create awareness among the public regarding the bladder symptoms, so as to prevent mortality and morbidity faced by the people due to bladder tumors.
- Some of the data sent to the Pathologist are incomplete. So it would be helpful to have interdepartmental relations between the clinicians and Pathologists to minimize such problems.
- The majority of patient's medical records was incomplete and handled inappropriately. Therefore, the record archiving of the hospital needs to be improved, implementing a sustainable digital data archiving system, and providing continuous training and audit.

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