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DIAGNOSTIC UTILITY OF P53, CK20 AND CD10 IMMUNOHISTOCHEMICAL EXPRESSION IN GRADING AND STAGING UROTHELIAL MALIGNANCIES AT A TERTIARY CARE CENTER.

Pathology

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ABSTRACT

BACK GROUND: Cancer of the bladder represents the ninth most common cause of cancer worldwide and the 13th most numerous cause of death from cancer. Most patients (70-80%) with newly diagnosed urothelial carcinoma of the bladder present with well-differentiated superficial papillary tumors. Prolonged survival in most patients with superficial cancers is achieved by transurethral resection (TUR) with or without intravesical chemotherapy. Nonetheless, these patients still have a high risk of recurrence following initial resection. The major prognostic factors in carcinoma of the bladder are the depth of invasion into the bladder wall and the degree of differentiation of the tumor.

AIMS & OBJECTIVES: To evaluate and analyze the diagnostic utility of immunochemical expression of p53,CK20,CD10 in urothelial malignancies as per 2016 WHO/ISUP classification with reference to histopathological grading and TNM staging, age, sex preponderance and clinical presentation.

RESULTS: The age of the patients ranged from 24 to 90, Among 76 cases, 65 cases were male and 11 cases were female with an average male to female ratio of 8.5:1. All bladder lesions were classified according to 2016 WHO/ISUP. No flat lesions were detected, 3 cases of PUNLMP, 17 cases of low grade papillary urothelial carcinoma, 42 cases of high grade papillary urothelial carcinoma, 7 cases of high grade papillary urothelial carcinoma with squamous differentiation, 7 cases of invasive urothelial carcinoma (6 cases- T2N0M0 & 1 case - T1N0M0). CD10,p53 and CK20 immunohistochemical markers were run on selected slides of 56 cases out of 76 cases due to unavailability of the rest of the paraffin blocks of 20 cases. Out of 5 cases of invasive urothelial carcinoma with squamous differentiation (4 cases with T2N0M0 and 1 case of T1N0M0) high expression of p53 and CD10 with negative expression of CK20 was noted and 5 cases of noninvasive urothelial carcinoma showing squamous differentiation which showed high expression of CD10 and p53 with variable expression of CK20 (negative/1+)

CONCLUSION: Our findings indicate that CD10 expression is strongly correlated with high tumor grade and stage in urothelial carcinoma of the bladder, and that CD10 may be associated with tumor progression in bladder cancer pathogenesis. The p53 and cytokerain 20 expression is diffuse and strong positive in cases of higher grade urothelial carcinoma as compared to low grade urothelial carcinoma which in majority of cases show focal and weak positive expression. These markers should be used in assigning grade to urothelial malignancies in cases of borderline histologic features.

KEYWORDS

urothelial carcinoma, CD10, CK20, p53, 2016 WHO/ISUP

INTRODUCTION:

Urinary bladder tumors make up approximately 4% of all urological lesions. A study of the incidence of urinary lesions in the metropolitan areas throughout the United States was completed by the public health service by 1954. The Incidence rate for cancer of the bladder per 10000 populations in 1947 was 6 for male and 8 for female subjects. In Individuals over the age of forty years, the urinary bladder lesions afflict 17 persons per 1, 00,000 populations.

Cancer of bladder is the most important of the malignant tumors of the urinary tract. In 1950 the public health services reported that 1,77,464 persons in the united states died of malignant diseases during 1945. Of these 8546 men and 1864 women died of cancer of the bladder. The death rate from this disease, therefore was 3% of total, per 1,00,000 population in 1945. The death rate from bladder cancer among persons 55 to 64 years of age was 10.5% among those 65 to 74, it was 26.2% and among persons 75 to 84, it had risen to 49.4%. In 1964 the total age adjusted mortality rate from cancer of bladder per 1,00,000 population was found to be 5.8% among males & 2.5% among females.

The mammalian bladder is of complex embryologic derivation. In the earliest stages of embryonal development the primordium of the bladder is a part of the cloaca, a vesicular space derived from the primitive gut. In to this space the lower intestine opens posterior. The wolffian ducts laterally and the omphalo-allontoic duct anteriorly. When the embryo reaches the length of 5mm, a membrane called urorectal septum begins to separate the future rectum from the ventrally located future bladder and urogenital sinus. The proximal position of the anterior chamber of the former cloaca becomes the urinary bladder and a portion of the urethra. The distal part, the urogenital sinus participates in the formation of the genital organs. The obliterated omphalo- allantoic duct becomes the urachus.

In some cases of extrophy of the bladder, this complex embryonal origin is reflected in the variety of epithelial types, such as mucus producing glandular epithelium, squamous epithelium, and the urothelium that may be seen side by side lining the bladder. Bladder epithelium retains the potential for producing these various epithelial types in the normal adult. This may be reflected in benign histologic variants of bladder epithelium and in bladder cancer.

AIMS

To evaluate and analyse the diagnostic utility of immunochemical expression of p53,CK20,CD10 in urothelial malignancies as per 2016 WHO/ISUP classification with reference to histopathological grading and TNM staging, age, sex preponderance, etiology and clinical presentation.

MATERIALS & METHODS

The present study was a 3 years prospective & retrospective study carried at The Upgraded Department Of Pathology, Osmania medical college, Hyderabad, Telangana state from june 2014 to May 2017, included all the patients with urinary bladder carcinoma diagnosed on biopsy from transurethral resection of bladder Tissue (TURBT).

Inclusion Criteria: All the Transurethral resection of bladder tissue (TURBT) biopsies diagnosed as urothelial carcinoma on histopathological examination received in the Upgraded department of pathology, Osmania Medical College, Hyderabad.

Exclusion Criteria:

- Autolysed specimen
- Benign bladder lesions
- Inadequate Biopsies

Formalin-fixed, paraffin embedded sectionsof TURBT biopsy bits were stained with haematoxylin and eosin and classified according to 2016 WHO/ISUP classification as papillary urothelial neoplasm of low malignant potential, low-grade papillary carcinoma, high-grade papillary carcinoma or invasive.

The TNM system was used for pathologic staging:

Ta, noninvasive papillary urothelial carcinoma;
T1, tumor invades subepithelial connective tissue;
T2, tumor invades muscularis propria, and
T3, tumor invades perivesical tissue.

IHC was performed using a streptavidin-biotin-peroxidase technique, 5-µm sections from paraffin-embedded samples were cut on poly-L-lysine coated slides, deparaffinized in xylene, and then dehydrated. For antigen retrieval, the slides were treated by microwave heating in citrate buffer (pH 6.0) for 10 minutes. 3% hydrogen peroxide was used for blocking endogenous peroxidase activity. The sections were incubated with primary antibody for one hour at room temperature. After washing in phosphate buffered saline, the samples were incubated with a biotin conjugated secondary antibody and then incubated using streptavidin-biotin system for 30 minutes at room temperature. The reactions became visible after immersion of the specimens in diaminobenzidine tetrahydrochloride. The sections were counterstained with hematoxylin, then rinsed and mounted. CD10 is a single-chain, 90-110-kDa cell surface zinc-dependent metalloprotease that inactivates various bioactive neuropeptides. Terms synonymous with CD10 include common acute lymphocytic leukemia antigen (CALLA), enkephalinase, membrane metalloendopeptidase (MME), membrane-associated neutral endopeptidase, and neprilysin[1,2,3]. Initially it was discovered on the surface of acute lymphoblastic leukemia cells, and considered to be a tumor-specific antigen[4].

It was then found that a variety of normal cells including cells of nonhematopoietic origin such as glomerular and proximal tubular epithelium of the kidney, liver, breast myoepithelium, and lung, as well as fibroblasts and cells of the central nervous system are able to express CD10[2,3,4,5]. CD10 is expressed by a number of hematopoietic cells such as immature T and B cells, B cells of the germinal centers of lymphoid follicles, and granulocytes as well as lymphoid malignancies including the majority of acute lymphoblastic leukemia, and also follicular center lymphoma, lymphoblastic, Burkitt's, and nodular poorly differentiated lymphocytic lymphomas, and chronic myelogenous leukemias in lymphoid blast crisis. CD10 expression has also been reported in several nonhematopoietic neoplasms including renal cell carcinoma, endometrial stromal tumor, solid and pseudopapillary tumor of the pancreas, melanoma, carcinoma of the prostate, breast, stomach, and colon. Staining of the cell membrane and/or cytoplasm was considered positive expression. A semiquantitative scoring based on the percentage of CD10 positive cells was performed according to the following staining criteria: negative (<5%); 1+ (5-50%); and 2+ (>50%).

P53, is a nuclear phosphoprotein which acts as tumor suppressor and plays a role in apoptosis, genetic stability, and inhibition of angiogensis. Wild-type p53 protein has a short half-life; however, the protein encoded by mutated p53 remains active for a long period. Therefore, mutation of p53 gene results in p53 accumulation in cells nuclei. This accumulation is detectable with immunohistochemical methods and correlates with p53 gene mutation, thus, detection of p53 protein in the nuclei of cells by immunohistochemical methods. Nuclear staining for p53 was interpreted as positive. p53 was evaluated according to the ratio derived from the number of p53-positive cells and staining intensity and scored as: 0 (no staining), 1+ (<15% cells, weak), 2+ (15-50% cells, moderate), 3+ (>50% cells, strong) by semi-quantitative reassortment.

ck20 : The cytokeratins are the intermediate filament proteins characteristic of epithelial cells. Some 20 different cytokeratin isotypes have been identified. Epithelial cells express between two and ten cytokeratin isotypes and the consequent profile which reflects both epithelial type and differentiation status may be useful in tumour diagnosis. The transitional epithelium or urothelium of the urinary tract shows alterations in the expression and configuration of cytokeratin isotypes related to stratification and differentiation. The most important recent finding is the demonstration that a normal CK20 expression pattern is predictive of tumor non-recurrence and can be used to make an objective differential diagnosis between transitional cell papilloma and carcinoma. Its expression beyond superficial layers of urothelium is considered positive.[6,7,8]

CK20 cytoplasmic stain was also semiquantitatively evaluated: 0 (no staining), 1+ (patchy, weak), 2+ (<50% cells, moderate), 3+ (>50% cells, strong).

The available information regarding patients age, gender, symptoms and mode of presentation, history of tobacco smoking and use of smokeless tobacco in various forms such as pan masala, tobacco leaves with betel nuts, chewing rolled dried leaves of tobacco, occupation of the patients were all collected and analyzed.

The material for the study was comprised of biopsy from transurethral resection of bladder tissue (TURBT). The specimens were received in 10% formalin and subjected to macroscopic description and appropriate relevant clinical details were noted.

Biopsy specimens were processed as per routine histopathological techniques and paraffin embedded blocks were prepared and cut as per standard tissue section and stained by Hematoxylin and Eosin, followed by immunohistochemistry panel of p53, CK20, CD10. The slides studied and classified according to WHO histological classification of tumors of urinary tract 2016
The WHO/ISUP Classification was used to grade the tumors into urothelial papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), low and high grade urothelial (Transitional cell) Carcinomas (TCC). Pathological staging of the urothelial cancers was done according to the TNM system and data recorded as pT0 tumor limited to the mucosa, pT1: invasion of Lamina propria and pT2 as invasion of muscle.

RESULTS:

The present study was carried out in the upgraded department of pathology, Osmania Medical college, General Hospital, Hyderabad. The Period of the study was 3 years from August 2014 to July 2017. During this three years, total number of 76 subjects with the diagnosis of urinary bladder carcinoma, attending in the department of urosurgery, Osmania medical college hospital were taken for the study. They were diagnosed by histopathological examination (HPE) of tissue, obtained from the urology department by transurethral resection of the bladder tumor (TURBT) method. Each case of clinical details, investigations of all patients was recorded in a case record proforma (CRP) and it was a retrospective & prospective study done on all the patients treated in this institute.

Table 1: Spectrum of Different pathological lesions

S.NO	Type of Bladder Lesions	No. Of Cases	Percentage
1	**Non-Neoplastic Lesions**	**12 cases**	**13.63%**
	• Non Specific Cystitis	7 cases	7.95%
	• Specific Cystitis	3 cases	3.4%
	• Urothelial Papilloma	2 cases	2.27%
2	**Neoplastic Lesions**	**76 cases**	**66.88%**
	• PUNLMP	2 cases	2.27%
	• Lowgrade Papillary Urothelial CA	25 cases	28.4%
	• Highgrade Papillary urothelial CA	34 cases	38.63%
	• Papillary urothelial carcinoma with squamous differentiation	6 cases	6.81%
	• Squamous Cell CA	7 cases	7.95%
	• Adeno CA	2 cases	2.27%
	Total	**88 cases**	**100%**

The present study intends to explore the diagnostic utility of immunohistochemical expression of p53, CK20, CD10 in urothelial carcinomas with reference to age, sex, presenting complaint and enlist variable risk factors like smoking history and occupations of the patients are important and responsible for development of the bladder tumors, also included. Histomorphological features and grading of tumors were studied in detail and findings were analysed according to World Health Organization (WHO) and International Society of Urological Pathologists (ISUP). The urinary bladder lesions were classified as Non-Neoplastic lesions (Sub- classified as Non- Specific or Specific) and Neoplastic Lesions. Total of 88 TURBT biopsies were analyzed. A Spectrum of different pathological lesions was observed in the study. Out of the 88 cases , 76 cases (66.88%) were neoplastic lesions, while 12 cases (13.63%) were Non-Neoplastic Lesions.

Table 2 : Age and Sex Distribution of Urinary Bladder Lesions

	Non-Neoplastic Lesions						Neoplastic Lesions										Total		
Age Group	Non Specific Cystitis		Specific Cystitis		Urothelial Papilloma		PUNLMP		Low Grade		High Grade		PUC - Squamous Differentiation		SCC		Adeno CA				%
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
21-30	1	0	1	0	1	0	0	0	0	1	1	1	0	2	0	0	0	0	0	7	1	9.09
31-40	1	0	0	0	1	0	0	0	0	1	2	3	0	0	0	0	0	0	0	4	4	9.09
41-60	1	3	1	1	0	0	0	0	2	1	3	4	2	1	1	1	1	1	0	3	1	47.72
>61	1	0	0	0	0	0	2	0	7	0	9	3	1	1	5	0	0	1	5	2	5	34.09
Total	4	3	2	1	2	0	2	0	9	2	15	11	3	4	6	1	1	1	5	6	1	100

The youngest patient in this study was 25 years old and the oldest patient was 85 years. The mean age being 55.6 years. Of these 88 cases, the majority of the patients i.e, 42 cases (47.72%) were in the age group of 51-70 years. Out of 88 patients , 67 were males (76.13%) , 21 were females (23.86%) with a male to female ratio of 3:1. Among these 67 male patients , majority of the patients shows Neoplastic. Lesions accounting for 59 cases (88.05%), 8 cases (11.94%) were Non-Neoplastic Lesions. Among the 21 female patients, 17 (80.95%) were neoplastic, 4 (19.04%) were Non-Neoplastic Lesions. All the types of Neoplastic lesions predominated in the age group of 51-70 years. The Primary Neoplastic lesions of the urinary bladder were predominantly seen in the patients aged more than 40 years and it was found to be statistically significant (P<0.01).

Table 3 : Age Distribution in Neoplastic Lesions

Age Group	PUNLMP	Low Grade TCC	High grade TCC	PUC Squamous Differentiation	SCC	Adeno CA	Total	%
21-30	0	2	1	2	0	0	5	6.57%
31-40	0	1	5	0	0	0	6	7.89%
41-60	0	15	16	2	2	1	36	47.36%
>60 yrs	2	7	12	2	5	1	29	38.15%
Total	2	25	34	6	7	2	76	100%

Of the 34 cases of High grade PUC, 26 (76.47%) were males, 8 cases (28.52%) were female, while among the 25 cases of low grade PUC, 20 cases (80%) were males and 5 cases (20%) were females. In 7 cases of SCC, 6 cases (85.71%) were males only 1 case (14.28%) was female respectively. In 2 cases of Adeno CA, 1 case (50%) was male and 1 case (50%) was female.

Table 4 : Sex Distribution in Neoplastic Lesions

TYPE	No Of cases				TOTAL
	M	%	F	%	
PUNLMP	2	100.00	0	0.00	2
Low Grade PUC	20	80.00	5	20.00	25
High Grade PUC	26	76.47	8	23.53	34
PUC-Squamous Differentiation	4	66.67	2	33.33	6
SCC	6	85.71	1	14.29	7
Adeno CA	1	50.00	1	50.00	2
Total	59	77.63	17	22.37	76

But all 2 PUNLMP patients were males in this study. The Primary urinary bladder lesions were predominant in the males than the females. In this study, 52 (59.10%) cases were smokers and 36 (40.90%) were Non- Smokers. Majority of the cases among the smokers were having Neoplastic Lesions accounting for 47 cases (90.39%), while 5 cases (9.61%) were having Non Neoplastic Lesions. Among the 36 (40.9%) Non-Smokers, 7 cases (19.4%) were Non-Neoplastic Lesions, 29 cases (80.6%) were Neoplastic Lesions. 47 Patients (61.84%) of primary Neoplastic bladder lesions were smokers and 29 patients (28.15%) were Non-Smokers.

Table 5: Smoking and Distribution of Bladder Lesions

Lesions	Smokers		Non-Smokers	
	No	Percentage	No	Percentage
Non-Neoplastic Lesions	5	9.61%	7	19.40%
Neoplastic	47	90.39%	29	80.60%
Total	52	59.10%	36	100%

Among 34 cases of High grade PUC, 22 cases (64.7%) were smokers and remaining 12 cases (35.29%) were Non-Smokers. Among 25 cases of Lowgrade PUC, 16 cases (64%) were smokers and remaining 9 cases (36%) were Non-Smokers. So Most of the Neoplastic lesions seen in smokers than non-smokers. The relative risk for smokers to develop Neoplastic lesions was doubled. Agriculture and labor was the major occupations in 25 cases (28.4%) and 24 cases (27.27%) respectively. Others included employees in 14 cases, Business class in 11 cases, housewives in 14 cases, and drivers in 14 cases.

Table 6: Distribution of Neoplastic Bladder Lesions among smokers and Non-Smokers

Type Of Lesions	Smokers		Non-Smokers		Total
	Number	Percentage	Number	Percentage	
PUNLMP	1	50%	1	50%	2
Lowgrade PUC	16	64%	9	36%	25
Highgrade PUC	22	64.70%	12	35.29%	34
PUC-Squamous Difference	2	33.33%	4	66.66%	6
SCC	5	71.42%	2	28.57%	7
Adeno CA	1	50%	1	50%	2
Total	47	61.84%	29	38.15%	76

The most common presenting symptom of the patients was haematuria in 70 cases (79.54%) followed by abdominal pain in 58 cases (65.9%) increased frequently of urine in 42 cases (47.72%), urinary urgency in 38 cases (43.18%), 4 others symptoms like mass per abdomen, dysuria, polyuria, Dribbling of urine seen less frequently in 24 cases (23.14%). Out of 88 cases, Majority of the cases were Neoplastic lesions seen in 76 cases (66.88%) and remaining 12 cases (13.63%) were Non-Neoplastic Lesions. Among 12 Non-Neoplastic Lesions, 7 cases (58.33%) were Non-Specific Cystitis, 3 cases (25%) were specific cystitis and remaining 2 cases (16.66%) were urothelial Papilloma. High grade papillary urothelial carcinoma was the most common Neoplastic lesion seen in 34 cases (44.73%), low grade papillary urothelial carcinoma seen in 25 cases (32.89%), papillary urothelial carcinoma with squamous differentiation seen in 6 cases (7.89%), squamous cell carcinoma seen in 7 cases (9.2%) and remaining adeno carcinoma and papillary urothelial Neoplasm with low malignant potential seen in cases (2.63%) and 2 cases (2.63%)

Table 7 : Distribution of Non Neoplastic bladder Lesions

Type of Lesion	No of cases	Percentage
Non-Specific Cystitis	7	58.33
Specific Cystitis	3	25
Urothelial Papilloma	2	16.66
Total	12	100

In this study, WHO/ISUP Grading of urothelial tumors reveal a higher Incidence of high grade papillary urothelial carcinoma (50.74%) compared to low grade papillary urothelial carcinoma(37.31%). High grade papillary urothelial carcinoma was seen in 34 cases, while 25 cases were low grade papillary urothelial carcinoma. Papillary urothelial carcinoma with squamous differentiation was seen in cases (8.95%) and 2 cases (2.98%) were papillary urothelial Neoplasm with Low malignant potential (PUN-LMP). In this study, papillary urothelial carcinoma was seen in 59 cases. Of these, Muscle Invasion was seen in 2 cases (3.38%) of low grade and 3 cases (5.05%) of high grade papillary urothelial carcinoma.

Table 8 : Distribution of Neoplastic bladder Lesions

Type	No of cases	Percentage
PUNLMP	2	2.63
Low grade PUC	25	32.89
High grade PUC	34	44.73
PUC Squamous Differentiation	6	7.89
Squamous Cell CA	7	9.21

DISCUSSION:

Histopathological diagnosis is gold standard for all urinary bladder tumors. Though Ultrasonography, computed tomography, Magnetic resonance Imaging modalities has created a lot better understanding of urinary bladder lesions, still histopathological diagnosis has remained importance for the classification and Management of urinary bladder Lesions. (As noted in various studies, the Incidence of bladder carcinoma have marked geographic and clinicopathological variation worldwide). Bladder cancer is the 7th most common cancer worldwide, with an estimated 2,60,000 new cases occurring each year in Men[9]. The Incidence of bladder carcinomas rises progressively with a peak incidence of 6th and 7th decade which is similar to other studies. This study consists of 88 cases of Urinary bladder lesions among these 12 cases were inflammatory lesions and remaining 76 cases were neoplastic lesions. It is considerably more common in males than females[10]. These findings are also confirmed in our study. The age of patients with bladder lesions ranged from 25-85 years in this study with a peak Incidence between 51-70 years. In both sex, the Incidence of bladder cancers increased with increase in age after 50 years. The age of presentation of bladder cancers were predominantly in the age group of 50-80 years with a mean age of 62 years.

Males were predominant in this study (67 cases) when compared to females (21 cases) with a male to female ratio of 3.5:1. This sex incidence in our study which is lower than the most of studies, similar to jaimin et al [11] study, but higher than the study done by Laishram et al[12].

Cigarette smoking has been a major Independent risk factor for bladder cancers. Smokers have four fold increased incidence of developing bladder carcinoma compared to Non-smokers. The risk increases as the frequency and duration of smoking levels increases and typically decreases in former smokers compared to current smokers. In our study, overall 52 patients (59.1%) were smokers. The majority of female patients being Non-Smokers but many of the Non- Smoking women actually revealed the history of Tobacco chewing. In the studies by chinnaswamy et al and Biswas et al, 71.15% and 75% of patients with bladder lesions were smokers respectively which are higher than one study, show 52 cases (59.10%) of the smokers.

Occupation and Distribution of Bladder Lesions:

In the present study, Majority of patients were farmers 25 cases (28.4%) and laborers 24 cases (27.2%). Others were employees, businessmen, housewives and drivers etc, who are in organized Sectors. Casual relationship between bladder cancer and occupational exposure is well established and concurrent smoking increases the risk to 90 fold. There are limited studies on occupation and bladder cancers in India. Study done by Biswas et al showed increase risk among laborers (50%) and industrial workers, including the man power of leather and textile Industries, hair dye handlers (Barbers) and shoe makers. Study done by chinnaswamy et al showed increased risk among Agricultural laborers (66.6%).

Clinical Presentation:

In the present study, we found that Hematuria was the most common presenting symptoms. Other symptoms are Abdominal pain , Abdominal Mass, Suprapubic Pain, Increased frequency of urine, urinary urgency and urinary Incontinence. In our study, Bladder tumors were the most common type of Lesion and was seen in 76 cases. All 76 cases of bladder tumors were of epithelial origin, of which 67 cases (88.15%) were urothelial (Transitional Cell) Tumors. Papillary urothelial carcinoma (PUC or TCC) was the most common bladder neoplasm in our study and was diagnosed in 67 cases (88.15%) cases. Similar data (82.60%) was published by shah et al from India, Mahesh et al (81.81%) also shows similar data. In the western literature and Vaidya et al study, these tumors account for 90% of bladder cancers. In our study there were 7 cases (9.21%) of squamous cell carcinoma which is similar to shah et al study showed 2 cases (8.69%) of squamous cell carcinoma.

In contrast to the studies done in south East Asian countries and western countries, Nigeria has squamous cell carcinoma as the most common type of urinary bladder tumors. This is because of high frequency of association of squamous cell carcinoma with schistosomiasis. However this pattern has been changing in Egypt in the last few year. There is decline in squamous cell carcinoma and increase in urothelial carcinoma. In India, there is only a focus of population infected by schistosomia hematobium as compared to other studies which explains lower incidence of squamous cell carcinoma of bladder. Adenocarcinoma and small cell carcinomas are uncommon tumors of the bladder and account for about 2% and 0.5% of all bladder cancers respectively. In our study only 2 (2.63%) cases of adenocarcinoma of bladder were noted, which is nearly similar to (1.23%) vaidya t al study. In our study, WHO/ISUP grading of urothelial tumors reveal a higher Incidence of high grade TCC compared to Low grade TCC. High-grade TCC was seen in 34 (50.74%) Cases, while 25 cases (37.31%) were low-grade TCC. This may be due to late presentation of the patient.

Adenocarcinoma and small cell carcinomas are uncommon tumors of the bladder and account for about 2% and 0.5% of all bladder cancers respectively. In our study only 2 (2.63%) cases of adenocarcinoma of bladder were noted, which is nearly similar to (1.23%) vaidya t al study. In our study, WHO/ISUP grading of urothelial tumors reveal a higher Incidence of high grade TCC compared to Low grade TCC. High-grade TCC was seen in 34 (50.74%) Cases, while 25 cases (37.31%) were low-grade TCC. This may be due to late presentation of the patient.

CONCLUSION:

In our study, Urinary bladder tumors were commonest lesions and peak Incidence was seen in 5th, 6th and 7th decade. Urothelial carcinomas show male predominance. Smoking revealed a strong relationship with bladder cancer and that was quantity and duration dependent. Subjects came from the different occupations, the highest being farmers and laborers. Most of the patients can presented with variety of symptoms, where hematuria was the most common presenting symptom. Non specific symptoms like increased frequency of urine and urinary urgency can also be seen as an alarming symptom. Transitional cell carcinoma (TCC) was the most common bladder tumor in our study most of these tumors were high grade. A large percentage of high grade transitional cell carcinomas presented with muscle invasion. Pathological grading and muscle invasion of Urothelial carcinomas is important for optimizing the prognosis, predictor of survival and the treatment of urinary bladder carcinomas. Therefore Therapeutic strategies should be based on histopathological grading of the tumor. This study represents a series of urothelial carcinoma of the bladder examined for CD10,CK20,P53 immunoexpression in relation to histologic grade and pathologic stage. We found that CD10, CK20, P53 expression is strongly correlated with tumor grade and stage in urothelial carcinoma of the bladder, and that CD10 may be associated with tumor progression in bladder cancer pathogenesis.

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