



ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2019; 2(1): 191-195
Received: 13-11-2018
Accepted: 17-12-2018

Dr. Dipti Gajjar
Tutor, Department of
Pathology, GMERS Medical
College, Vadnagar, Gujarat,
India

Dr. Mansi Faujdar
Honorary consultant,
Department of Pathology,
Santokba Durlabhji Memorial
Hospital, Jaipur, Rajasthan,
India

Dr. Rohit Jain
Honorary consultant,
Department of Pathology,
Santokba Durlabhji Memorial
Hospital, Jaipur, Rajasthan,
India

Dr. Shubha Gupta
Senior Honorary consultant,
Department of Pathology,
Santokba Durlabhji Memorial
Hospital, Jaipur, Rajasthan,
India

Correspondence
Dr. Dipti Gajjar
Tutor, Department of
Pathology, GMERS Medical
College, Vadnagar, Gujarat,
India

Histomorphological spectrum of urothelial tumors according to WHO/ISUP consensus classification (2016): Tertiary care center study

Dr. Dipti Gajjar, Dr. Mansi Faujdar, Dr. Rohit Jain and Dr. Shubha Gupta

DOI: <https://doi.org/10.33545/pathol.2019.v2.i1c.29>

Abstract

Background: Neoplastic urinary bladder lesions are responsible for significant morbidity and mortality throughout the world. The WHO/ISUP consensus classification (2016) for Urothelial tumors reflects an improved understanding and knowledge of the morphological types. The new diagnostic categories will increase the diagnostic reproducibility, clinicopathological correlation and prognostication. The most important criterion for optimal cancer treatment is a correct classification of the tumor.

Aim & Objectives: The aim is to study Histomorphological spectrum of urothelial tumors according to World Health Organization / International Society of Urological Pathology consensus classification (2016) and to determine age and sex distribution of urothelial tumors.

Material & Method: Study included 300 urothelial tumor specimens, conducted over a period 15 months, extending from March 2016 to May 2017. H & E stained sections were examined for morphologic diagnosis of urothelial neoplasm. An attempt was made to classify urothelial neoplasm according to WHO/ISUP consensus classification (2016) by two senior consultants of the department.

Results: Among 300 cases, 14.33% cases were diagnosed as Infiltrating urothelial carcinoma, 85.66% cases were of Non-invasive urothelial neoplasia. Amongst which Non-invasive papillary urothelial carcinoma, low grade were most common that is 55.33% cases. Maximum no. of cases was diagnosed (33%) in 61-70 years of age group and male Female ratio being 3:1.

Conclusion: This study documents a high frequency of non-invasive than infiltrating type of urothelial neoplasm. Non-invasive papillary urothelial carcinoma, low grade constitutes the commonest of urothelial tumors. Urothelial tumors are seen commonly in seventh decade with overall a male predominance.

Keywords: Urothelial tumors, histomorphological spectrum, WHO/ISUP consensus classification (2016)

Introduction

Neoplastic urinary bladder lesions are responsible for significant morbidity and mortality throughout the world ^[1]. Urinary 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 ^[2]. It 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) ^[3]. This differences is probably accounted by differences in smoking habits and occupational exposure in the two sexes. It is also suggested that social, occupational, environmental or dietary factors might promote the development of bladder cancer ^[4]. Various risk factors are associated development of urinary bladder carcinoma including tobacco smoking, occupational exposure such as radiation, aniline dye industry, aromatic amines benzidine, cyclophosphamide, schistosoma haematobium infestation and arsenic ^[5]. The most common presenting symptom of bladder cancer is painless gross hematuria which occurs in 85% of patients ^[6].

Spectrum of primary malignancies can vary from superficial, well differentiated to highly malignant tumors. The vast majority of primary bladder tumors are of transitional cell variety (90-95%) ^[7]. The classification & grading of papillary urothelial neoplasms has been a long standing subject of controversy. Previously, numerous diverse grading schemes for bladder tumor, including 1973 WHO classification, existed whereby one of the major limitations was poor inter-observer reproducibility among pathologists.

The WHO/ISUP consensus classification system of urothelial neoplasms of the urinary bladder was developed in 1998 & was revised most recently in 2003 (published in 2004). This system is designed to be a universally acceptable one for bladder tumors that not only could be effectively used by pathologists, urologists & oncologists but also stratifies the tumors into prognostically significant categories [8]. As further management & prognosis of patients is based on accurate diagnosis, therefore this categorization is of utmost significance.

12 years after the previous WHO classification, a new WHO classification was published in January 2016 [9]. The new 2016 WHO blue book continued to endorse the classification of urothelial flat and papillary lesions proposed initially by ISUP in 1997, and adopted by the WHO in 2004. In bladder and urothelial tract, within the spectrum of flat and non-invasive lesions, a newly introduced term “urothelial proliferation of uncertain malignant potential” replaced the term “urothelial hyperplasia” and the term “urothelial dysplasia” was better defined. A category of “invasive urothelial carcinoma with divergent differentiation” was introduced for tumors showing a component of “usual type” urothelial carcinoma combined with other morphologies [10].

The aim is to study Histomorphological spectrum of urothelial tumors according to World Health Organisation / International Society of Urological Pathology consensus classification (2016) and to determine age and sex distribution of urothelial tumors in a tertiary care centre, Jaipur.

Material and Method

An Observational Prospective Study was carried out in the Histopathology Department at, Santokba Durlabhji Memorial Hospital cum Medical Research Institute, Jaipur, Rajasthan. Study included 300 urothelial tumor specimens, which was conducted over a period 15 months, extending from March 2016 to May 2017. After receiving the specimen in the histopathology department, a detailed clinical history and type of specimen (endoscopic biopsy / TURBT / resected specimen) of the patients under study were recorded. Written consent was obtained after explaining the nature and purpose of study. Specimen was fixed in formalin for 12 to 24 hours. Grossing, processing, paraffin embedding, section cutting and staining were done by standardized methods routinely used in the department. H & E stained sections were examined for morphologic diagnosis of urothelial neoplasm. An attempt was made to classify urothelial neoplasm according to WHO/ISUP consensus classification (2016) by two senior consultants of the department.

Result

The study included 300 cases of Urothelial tumors for evaluation. In present study 75% cases were seen in males. 25% cases were seen in females. Male Female ratio being 3:1 (table-1).The mean age of the study group was 60.65 year. Minimum 27 years and maximum 88 years age was found in our study. Maximum no. of cases was diagnosed (33%) in 61-70 years of age group (Table-2). In present study, maximum no. of specimen received were TURBT type, 77% cases, followed by endoscopic biopsy in 18% cases and minimum no. of specimen received were Radical

cystectomy type in 5% cases (Table-3).

14.33% (n=43/300) cases were diagnosed as Infiltrating urothelial carcinomas, amongst which 10.33% (n=31/300) cases were infiltrating urothelial carcinoma, 03% (n=9/300) cases were diagnosed as with micropapillary differentiation and 01% (n=3/300) cases were diagnosed as sarcomatoid differentiation. 85.66% (n=257/300) cases were of Non-invasive urothelial neoplasias. Amongst which Non-invasive papillary urothelial carcinoma, low grade were most common that is 55.33% (n=166/300) cases, followed by Non-invasive papillary urothelial carcinoma, high grade comprising of 14% (n=42/300) cases, Urothelial papilloma comprising of 07% (n=21/300) cases, Inverted urothelial papilloma comprising of 06% (n=18/300) cases and Non-invasive papillary urothelial neoplasm of low malignant potential comprising of 3.34% (n=10/300) cases. (Table-4)

Table 1: Distribution of Urothelial tumors according to gender (N=300)

Gender	No of cases	%	M: F Ratio
Male	225	75	3:1
Female	75	25	
Total	300	100	

Table 2: Distribution of the cases according to age groups (N=300)

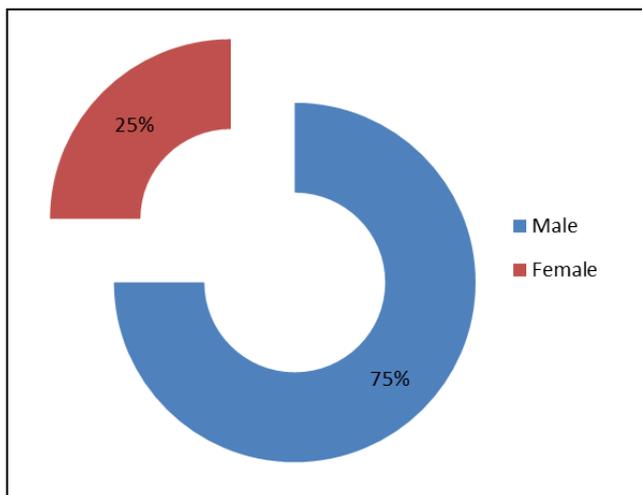
Age group	Number	Percentage
21 to 30	10	3.33
31 to 40	20	6.67
41 to 50	37	12.33
51 to 60	81	27
61 to 70	99	33
>70	53	17.67
Total	300	100

Table 3: Distribution of the cases according to Specimen Type (N=300)

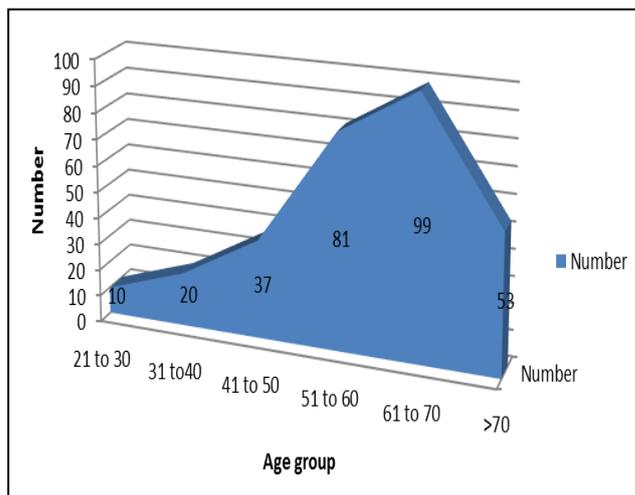
Specimen type	No.	%
Endoscopic biopsy	54	18.00
Radical cystectomy	15	5.00
TURBT	231	77.00
Grand Total	300	100.00

Table 4: Distribution of Urothelial tumors based on Histomorphology (N=300) (WHO / ISUP consensus classification – 2016)

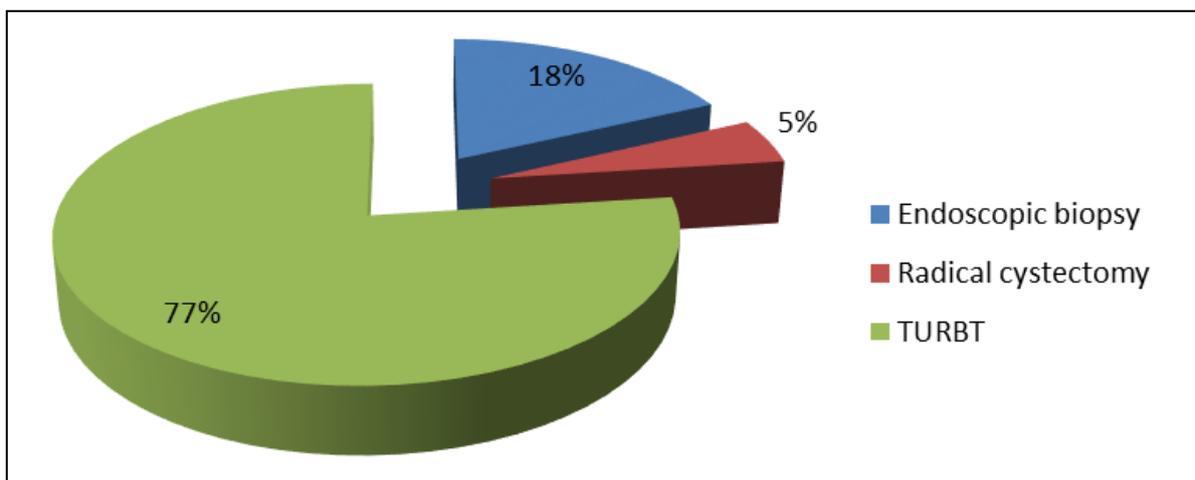
Urothelial tumors	No.	%
Infiltrating urothelial carcinoma	31	10.33
With micropapillary differentiation	09	03
With sarcomatoid differentiation	03	01
Total	43	14.33
Non-invasive urothelial neoplasia		
Non-invasive papillary urothelial carcinoma, high grade	42	14
Non-invasive papillary urothelial carcinoma, low grade	166	55.33
Non-invasive papillary urothelial neoplasm of low malignant potential	10	3.34
Urothelial papilloma	21	07
Inverted urothelial papilloma	18	06
Total	257	85.66
Grand Total	300	100



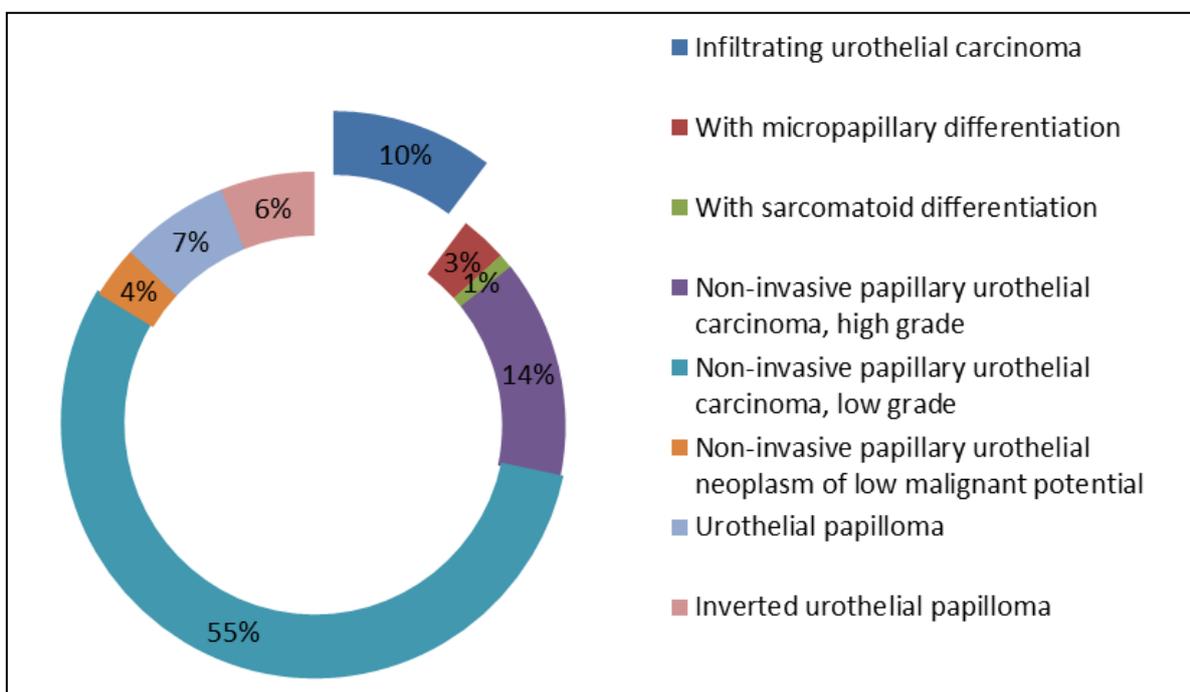
Graph 1: Distribution of Urothelial tumors according to gender



Graph 2: Distribution of the cases according to age groups (N=300)

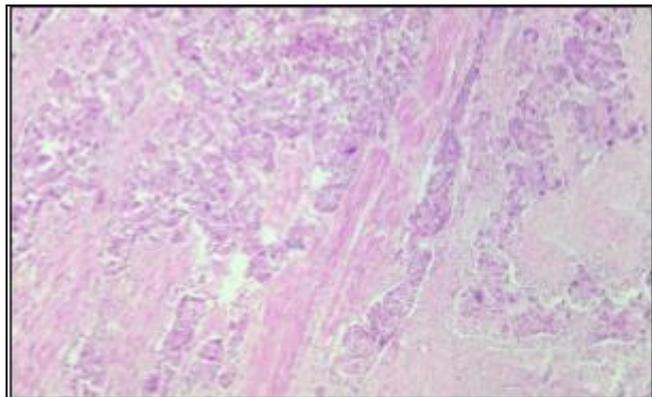


Graph 3: Distribution of the cases according to Specimen Type (N=300)

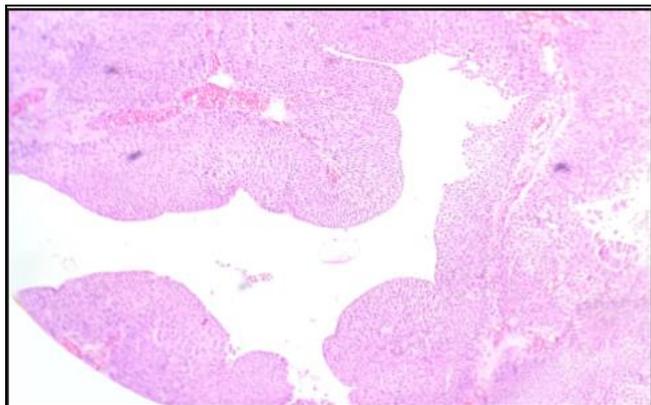


Graph 4: Distribution of Urothelial tumors based on Histomorphology (WHO/ISUP Consensus Classification-2016) (N=300)

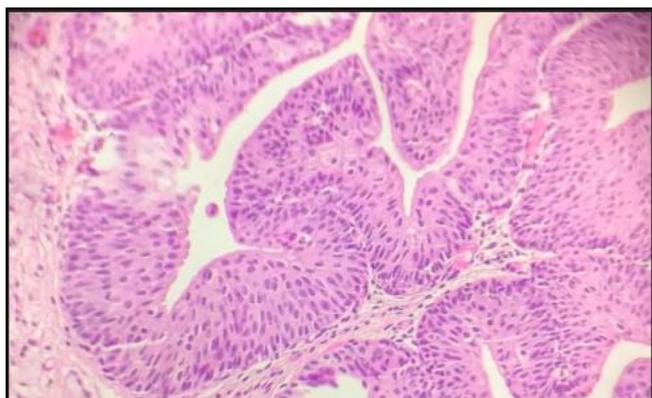
Photos:



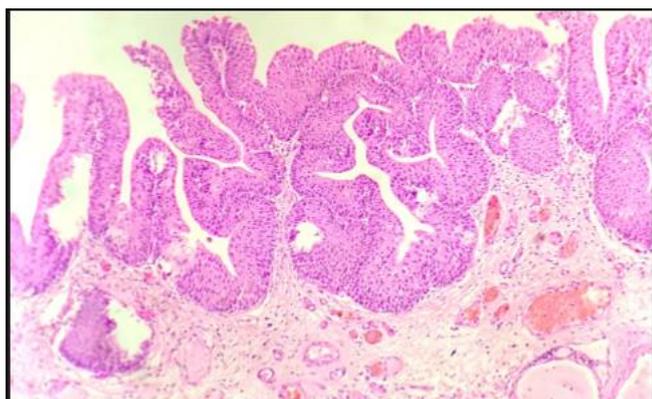
Infiltrating urothelial carcinoma (H&E; 40X)



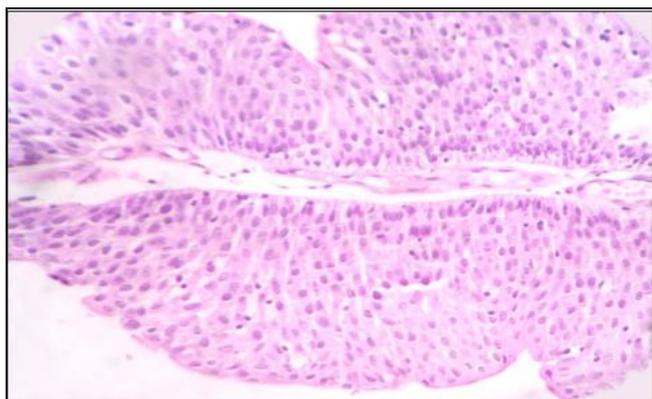
Papillary urothelial carcinoma, low grade (PUCLG) (H&E; 40X)



Urothelial papilloma (H&E; 40X)



Inverted urothelial papilloma (H&E; 40X)



Papillary urothelial neoplasm of low malignant potential (PUNLMP) (H&E; 40X)

Discussion

The new 2016 WHO blue book continued to endorse the classification of urothelial flat and papillary lesions proposed initially by ISUP in 1997, and adopted by the WHO in 2004 [10]. The classification underlines the interest of recognizing variant histology as a predictor of more aggressive tumor behavior [9]. One of the major problems of urothelial carcinoma is the extremely heterogenous genetic profile. The most important criterion for optimal cancer treatment is a correct classification of the tumor. During the last three years, several very important progresses have been made with a better definition of urothelial carcinoma, especially from a molecular point of view. It seems to be clear that in the very near future urothelial carcinoma will not only be treated according to histological grading and staging, but molecular and genetic profiles will play a major role. This will help to select only chemo sensitive patients but also to avoid heavy treatments to patients who will not benefit from chemotherapy. Nevertheless, histology will keep an important place as it permits quick and low cost diagnosis [11]

The present study includes 300 cases presenting as urothelial tumors and attempt has been made to study histomorphological spectrum of urothelial tumors according to WHO/ISUP classification 2016.

In our study, the most common age group was 61-70 years with 33% cases followed by 27% in age group of 51-60 years. Mean age of presentation was 60.65 years (range 27-88 years). Our study was in concordance with studies performed by Goyal *et al.* [12] and Vaidya *et al.* [13] (61-70 years with 33% cases and 61-70 years with 33.37% cases respectively). Our mean age of presentation also correlated well with Goyal *et al.* [12] and Matalka *et al.* [14]

Among 300 cases 75% (N=225) were males and 25% (N=75) were females. Male to female ratio was 3:1. Our study correlates with Cheng *et al.* [15], Hasan *et al.* [16] and Thapa *et al.* [17] which also had male to female ratio 3.3:1, 2.58:1 and 2.7:1 respectively while Vaidya *et al.* [13], Mumtaz *et al.* [18] and Goyal *et al.* [12] had male to female ratio 4.2:1, 4.5:1 and 5.25:1 respectively which was higher than our study.

In our study 85.66% cases were non-invasive urothelial neoplasia and 14.33% cases were of infiltrating type. C.Aparna *et al.* [19] observed that 69.3% of cases were non-invasive and 30.7% were invasive which was in concordance with our study. However other studies

performed by Gandhi B. *et al.* ^[20] (56.24% invasive) and Blaveri *et al.* ^[21] (83% invasive) observed higher percentage of invasive than non-invasive urothelial tumors.

In non-invasive papillary urothelial neoplasia, predominant type was PUCLG (55.33%) followed by PUCHG (14%), papillomas (13%) and PUNLMP (3.34%). This was in concordance with studies performed by Laishram RS *et al.* ^[22] who showed maximum number of PUCLG (53.9%) followed by PUCHG (37.6%), papillomas (7.7%) and PUNLMP (3.9%) and Thapa *et al.* ^[17] who observed high prevalence of PUCLG (50%) followed by PUCHG (30.36%), PUNLMP (10.71%) and papilloma (9%). Our study was also in concordance with Shah P *et al.* ^[23] who observed maximum no. of non-invasive PUCLG (47.36%) in prevalence of PUCLG (50%) followed by PUCHG (30.36%), PUNLMP (10.71%) and papilloma (9%). Our study was also in concordance with Shah P *et al.* ^[23] who observed maximum no. of non-invasive PUCLG (47.36%) in their study.

Conclusion

The WHO/ISUP consensus classification (2016) for Urothelial tumors reflects an improved understanding and knowledge of the morphological types and enables us to diagnose the urothelial tumors into clinically and prognostically relevant entities. This study documents a high frequency of non-invasive than infiltrating type of urothelial neoplasm. Non-invasive papillary urothelial carcinoma, low grade constitutes the commonest of urothelial tumors. Urothelial tumors are seen commonly in seventh decade with overall a male predominance.

Reference

1. Srikousthubha, Sukesh, Raghuvver CV, Hingle S. Profile of Lesions in Cystoscopic Bladder Biopsies -A Histopathological Study. *J Clin Diagn Res* 2013; 7:1609-12.
2. Ferlay J, Bray F, Pisani P, Parkin DM. *GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide*. IARC Press: Lyon, 2001.
3. Parkin DM, Pisani P, Ferly J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer* 1999; 80:827-41.
4. Wynder EL, Goldsmith R. The epidemiology of bladder cancer: a second look. *Cancer*. 1977; 40(3):1246-1268.
5. IARC IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Tobacco smoke and involuntary smoking. IARC Press: Lyon (in press), 2004.
6. Varkarakis MJ, Gaeta J, Moore RH, Murphy GP. Superficial bladder tumor. Aspects of clinical progression. *Urology* 1974; 4:414-20.
7. Mehta N, Rathore RS, Pillai BS *et al.* Intrinsic tumor factors affecting recurrence in non-muscle invasive bladder cancer: a hospital based study from India. *Asia Pac J Cancer Prev*. 2015; 16:2675-7.
8. Miyamoto H, Miller JS, Fajardo DA, Lee TK, Netto GJ, Epstein JI. Non-invasive papillary urothelial neoplasms: the 2004 WHO/ISUP classification system. *Pathol Int*. 2010; 60(2):147
9. 4th edition of WHO classification of Tumours of the Urinary System and Male Genital Organs. Enup, 2016.
10. Daniel AA, Trpkov K. What is new in Genitourinary

Pathology? Recent developments and highlights of the new 2016 World Health Organization classification of tumors of the urinary system and male genital organs. *Applied Cancer research*. 2016; 36:1

11. Comperat E. The WHO classification 2016 of tumors of the Urinary system and Male Genital Organs and Impact on the Bladder cancer. *Clin Oncol*. 2017; 2:1235.
12. Goyal VK, Vyas SP, Kothari DC. Spectrum of lesion in Urinary Bladder Biopsies: Histological study. *Int. J Dent Med Res*. 2015; 1(6):42-46
13. Viadya S, Lakhey M, KCS, Hirachand S. Urothelial tumors of the urinary bladder: a histopathological study of cystoscopicbiopsies. *J Nepal Med Assoc* 2013; 52:475-8.
14. Matalka I, Bani-Hani K, Shotar A, Bani-Hani O, Bani-Hani I. Transitional cell carcinoma of the urinary bladder: A clinicopathological study. *Singapore Med J*. 2008; 49(10):790-4.
15. Cheng L, Neumann RM, Bostwick DG. Papillary urothelial neoplasms of low malignant potential. Clinical and biological implication. *Cancer*. 1999; 86:2102-08
16. Hasan SM *et al.* Frequency of transitional cell carcinoma in local suburban population of Karachi. *JLUMHS* 2007; 83-85.
17. Thapa R, Lakhey M, Bhatta AD. Spectrum of histomorphological diagnosis in cystoscopic bladder biopsies. *Journal of Pathology of Nepal*. 2017; 7:1062-1065.
18. Mumtaz S, Hashmi AA, Hasan SH *et al.* Diagnostic utility of p53 and CK20 immunohistochemical expression grading urothelial malignancies. *Int Arch Med*. 2014; 7:36.
19. Aparana C, Reddy T, Padmavati C, Vanapalli J, Mounika T. Histological spectrum of urothelial lesion-experience of a single tertiary care institute. *International journal of Contemporary Medical Research*. 2016; 3(6):1731-1733
20. Gandhi B, Rao S, Shanthi V, Vydehi B, Rao M, Goel A. Histopathological Spectrum of Urothelial Lesions. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*. 2016; 15(6):04-07
21. Blaveri E, Brewer JL, Roydasgupta R *et al.* Bladder cancer stage and outcome by array-based comparative genomic hybridization. *Clin Cancer Res*. 2005; 11:7012-22.
22. Laishram RS, Kipgen P, Laishram S, Khuraijam S, Sharma DC. Urothelial tumors of the urinary bladder in Manipur: A histopathological perspective. *Asia Pacific Journal of Cancer Prevention*. 2012; 13:2477-9.
23. Shah P, Nanavati M, Patel R, Goswami H. Spectrum of lesions in urinary bladder -a histopathological study. *Int J Cur Res Rev*. 2016; 8(4):19-24.