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Original Article

Pathology Section

Reproducibility of Histopathological Diagnosis of Urinary Bladder Neoplasms on Microphotographs

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ABSTRACT

Introduction: Diagnostic reproducibility and accuracy in pathology are the main issues in oncology screening of various malignancies. Urothelial carcinoma accounts for majority of bladder cancers in the industrialised nations. The reproducibility of histopathological features of different WHO grading systems has shown considerable variation.

Aim: To evaluate the reproducibility of histopathological features of urinary bladder neoplasms (categorised according to WHO 2016 classification) on microphotographs.

Materials and Methods: This was a retrospective observational study of urinary bladder neoplasms conducted at a rural tertiary care referral Institute, PES Institute of Medical Sciences (PESIMSR), Kuppam, Andhra Pradesh, India, from January 2017 to December 2019 for a period of three years. Histopathology slides of urinary bladder neoplasms were retrieved and reviewed. The urinary bladder neoplasms were categorised according to WHO 2016 classification. Representative images of the neoplasm were captured by 13 megapixels primary mobile camera and sent to two pathologists by e-mail. The histopathological characteristics of the lesions were evaluated. Concordance was calculated. The strength of agreement was analysed by Kappa statistics (Cohen).

Results: Concordance was highest in recognising deep muscle invasion {95.24% (Pathologist 1) and 100% (Pathologist 2)}, good for recognising the pattern {86.96% (Pathologist 1 and 2)} and grading the lesions {80.95% (Pathologist 1) and 68.42 (Pathologist 2)}, satisfactory for appreciation of lamina propria invasion {78.26% (Pathologist 1) and 69.57% (Pathologist 2)} and histopathological diagnosis {73.91% (Pathologist 1) and 56.52% (Pathologist 2)} and not satisfactory for identifying specific variants {50% (Pathologist 1) and 66.67% (Pathologist 2)}. Kappa value suggested almost perfect agreement for recognising deep muscle invasion (0.86), substantial agreement for both the pattern recognition (0.65) and grading (0.67), moderate agreement for lamina propria invasion (0.48), fair agreement for histopathological diagnosis (0.34)) and only slight agreement for recognising the specific variants (0.09).

Conclusion: The interpretation of bladder neoplasms has satisfactory reproducibility on microphotographs. The evaluation of representative microphotographic images is a prudent and pragmatic exercise. The pathologists must train themselves to interpret the microphotographs images. The study emphasises the importance of intra-disciplinary consultation. The concept can be extrapolated and employed to solve perplexing cases my means of effective communication technology.

Keywords: Carcinoma, Lamina propria, Muscle, Pathology

INTRODUCTION

The field of pathology is driven by the use of microscopic images [1]. Diagnostic reproducibility and accuracy in pathology are the main issues in oncology screening of various malignancies like cervical, breast and colorectal cancers. The chance of interpreting microscopic digital photographs provides an interesting alternative to read and analyse conventional microscopic slides [2]. Pathologists can quickly transmit the microscopic images photographed in a certain location to remote centers for the purpose of analysis, interpretation and diagnosis. The method of storing and analysing the images at a later time allows us to transmit the images captured by the digital camera as an electronic mail file and to analyse them at convenient time [3]. Worldwide, urinary bladder cancer is ranked seventh most common cancer [4]. Urothelial carcinoma accounts for about 90% of bladder cancers in the industrialised nations [4,5]. In the current diagnosis of urothelial carcinomas, histology is still considered as the gold standard [6]. Different World Health Organisation (WHO) grading systems showed considerable variations in the reproducibility of histopathological features [5].

WHO 2016 classification system of urothelial tumours has been recommended to be adopted worldwide because of its inherent advantages such as use of uniform terminology and definitions, elimination of ambiguity in diagnostic categories and inclusion of Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP) category of papillary neoplasm. However, controversy still remains mainly due to the fact that clinical risk of progression is determined not only by growth pattern but also by factors such as multifocality, size, time of recurrence and prior intravesical therapy. In addition, grading is subjective and may need ancillary studies to improve the reproducibility and better correlation with clinical outcome [7].

In most of the studies, evaluation was done on microscopic slides [5,8-11]. The current study was undertaken to evaluate the reproducibility of histopathological features of bladder neoplasms (categorised according to WHO 2016 classification) on microphotographs. The present study highlights the novel application of microphotographs for evaluating the reproducibility of histopathological findings of bladder neoplasms.

MATERIALS AND METHODS

The present retrospective observational study was conducted on archival cases of bladder neoplasms in the Department of Pathology at a rural tertiary care Institute, PES Institute of Medical Sciences (PESIMSR), Kuppam, Andhra Pradesh, India from January 2017 to December 2019. Ethical clearance was obtained from the Institutional Ethics Committee bearing number PESIMSR/IHEC/184.

Inclusion and Exclusion criteria: All cases of bladder neoplasms confirmed by histopathological examination were included in the study. Those cases in which biopsies performed were unsatisfactory for interpretation were excluded from the study.

In the present study, 23 cases were analysed.

Sample size calculation: The sample size was calculated by using following formula:

$$n=\frac{Z^2_{(1-\alpha/2)}\times=p\times(1-p)}{d^2}$$

"n" is the sample size

"$z^2_{(1-\alpha/2)}$" is the level of significance at 5% that is 95% confidence interval

"p" is the expected proportion of haemorrhagic cytology samples

"d" is the desired error of margin

[The calculation was done on the basis of data from the previous study Dravid NV et al (9) where p=73.38%, d=18%].

Histopathology slides of bladder neoplasm were retrieved. The histological characterisation of bladder neoplasms was reviewed from April 2020 to May 2020. Neoplasms were categorised according to the WHO 2016 classification [4]. All the representative images of the neoplasm were captured by using the same primary mobile camera (13 megapixels) and single microscope. This was done for the sake of standardisation. For each case, the images were captured at low power (X100) and high power (X400) for appreciating various histopathological parameters. The images were captured at low power for recognising the pattern and architectural details. The images were captured at high power for assessing tumour grade, tumour type, lamina propria invasion, mucularis propria invasion and specific variants. On an average, about nine images were captured for each case. The images were sent to two pathologists by e-mail. The interpretation, findings and the diagnosis were documented and analysed. The histopathological diagnosis, tumour type, tumour grade, lamina propria invasion, muscularis propria invasion and specific variants were evaluated (wherever applicable). Concordance was calculated and the strength of agreement was analysed by Kappa statistics (Cohen).

STATISTICAL ANALYSIS

The socio-demographic variables were represented using frequencies and percentages. The extent of reproducibility of histological diagnosis of bladder neoplasms on microphotograph was analysed by concordance and kappa statistics (Cohen). Jacob Cohen suggested the Kappa to be interpreted as follows: values ≤0 as indicating no agreement, 0.01-0.20 as none to slight agreement, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial and 0.81-1.00 as almost perfect agreement [12]. All statistical calculations were performed through statistic software STATA version 14.1.

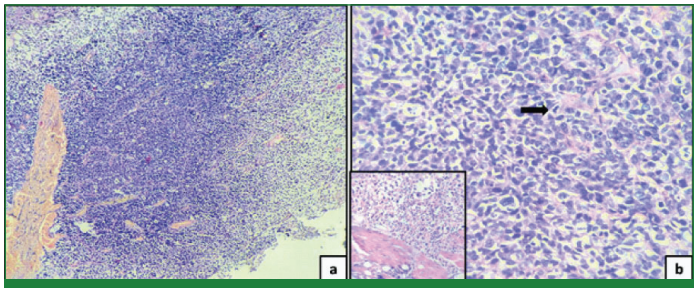
RESULTS

In the present study, 23 cases of bladder neoplasm were analysed. The lesions were seen in the range of 36-90 years. Clustering of cases were seen in the eighth decade (mean=62.35). The lesions were predominantly seen in males {17 cases (73.91%)} with M:F ratio of 2.8:1.

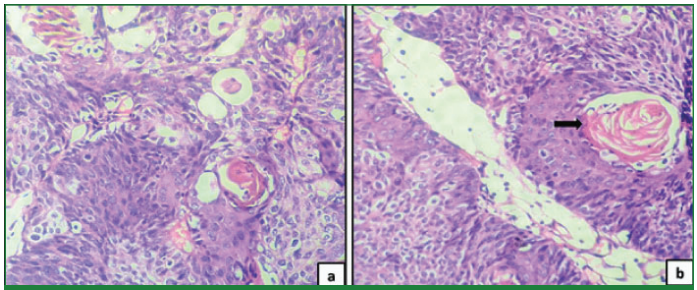
All the specimens were those of Trans Urethral Resection of Bladder Tumour (TURBT). Most of site of involvement was right lateral wall {6 cases (26.09%)}. Infiltrating urothelial carcinoma was the most common lesion constituting 17 cases (73.91%). Among infiltrating urothelial carcinoma, usual type (papillary pattern) was most common lesion constituting 11 cases (47.83%) [Table/Fig-1]. The infiltrating urothelial carcinoma showed infiltration of tumour cells into the lamina propria. Among the conventional type, high grade lesions {7 cases (30.43%)} were more common than low grade lesions {4 cases (17.39%)}. Tumour cells of high grade lesions showed marked cytological atypia, pleomorphism, marked loss of polarity and mitotic figures [Table/Fig-2]. The tumour cells of low grade lesions showed mild cytological atypia, pleomorphism and mild loss of polarity. Among infiltrating urothelial carcinoma of specific variant, poorly differentiated carcinoma was the most common type constituting 3 cases (13.04%). The other variants included infiltrating urothelial carcinoma with squamous differentiation {1 case (4.35%)}, infiltrating urothelial carcinoma with glandular differentiation {1 case (4.35%)} and infiltrating urothelial carcinoma with plasmacytoid differentiation {1 case (4.35%)}. Poorly differentiated carcinoma was characterised by tumour cells displaying marked nuclear pleomorphism, bizarre morphology, multinucleation and mitotic figures. Infiltrating urothelial carcinoma with squamous differentiation showed polygonal tumour cells displaying squamous differentiation. Also, seen were keratin pearls [Table/Fig-3]. Infiltrating urothelial carcinoma with glandular differentiation showed tumour cells arranged in glandular pattern. The columnar tumour cells showed significant nuclear pleomorphism [Table/Fig-4]. Infiltrating urothelial carcinoma with plasmacytoid differentiation showed tumour cells arranged in diffuse sheets. Individual tumour cells showed plasmacytoid morphology displaying eccentrically placed nucleus.

Sl. No.	Histopathology diagnosis	Cases (%)
1	Infiltrating urothelial carcinoma	17 (73.91%)
	Infiltrating urothelial carcinoma-Usual (papillary) type	11 (47.83%)
	Infiltrating urothelial carcinoma-Usual type (high-grade)	7 (30.43%)
	Infiltrating urothelial carcinoma-Usual type (low-grade)	4 (17.39%)
	Infiltrating urothelial carcinoma-Divergent differentiation/ Specific variant	6 (26.09%)
	Infiltrating urothelial carcinoma-Poorly differentiated carcinoma	3 (13.04%)
	Infiltrating urothelial carcinoma with squamous differentiation	1 (4.35%)
	Infiltrating urothelial carcinoma with glandular differentiation	1 (4.35%)
	Plasmacytoid urothelial carcinoma	1 (4.35%)
2	Non-invasive urothelial carcinoma	6 (26.09%)
	Non-invasive papillary urothelial carcinoma (low-grade)	4 (17.39%)
	Non-invasive papillary urothelial carcinoma (High-grade)	2 (8.7%)

[Table/Fig-1]: Distribution of urinary bladder neoplasms.

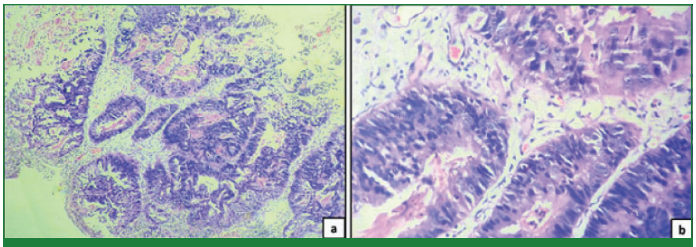


[Table/Fig-2]: Infiltrative urothelial carcinoma-usual type: (a) Tissue section of infiltrative urothelial carcinoma displaying tumour cells arranged in papillary pattern. (H&E, X100); (b) Tumour cells displaying marked cytological atypia and mitotic figure (arrow). Inset: muscle invasion (H&E, X400).

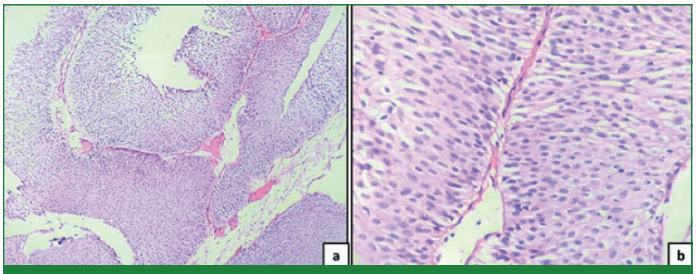


[Table/Fig-3]: Infiltrative urothelial carcinoma with squamous differentiation: (a) Tumour cells arranged in nests and sheets composed of tumour cells displaying squamous differentiation. (H&E, X400); (b) Tumour cells displaying squamous differentiation and keratin pearl (arrow). (H&E, X400).

Among non-invasive papillary urothelial carcinoma, low grade lesions {4 cases (17.39%)} were more common than high grade lesions {2 cases (8.7%)}. In the low grade lesions, the tumour cells were limited to the basement membrane and showed mild cytological atypia [Table/Fig-5]. In high grade lesions, the tumour cells were limited to the basement membrane and showed marked cytological atypia, pleomorphism and marked loss of polarity.



[Table/Fig-4]: Infiltrative urothelial carcinoma with glandular differentiation. (a) Tumour cells arranged in glandular pattern. (H&E, X100). (b) Tumour cells displaying nuclear pleomorphism. (H&E, X400).



[Table/Fig-5]: Noninvasive urothelial carcinoma-Low grade: (a) Tissue section of non-invasive urothelial carcinoma displaying tumour cells arranged in papillary pattern. (H&E, X100); (b) Tumour cells displaying mild cytological atypia. (H&E, X400).

High grade lesions {15 cases (65.22%)} were common than low grade lesions {8 cases (34.78%)}. Deep muscle tissue was sent for histopathological evaluation in 21 cases. Deep muscle invasion was seen in 5 cases (23.81%).

Concordance and agreement (by Cohen kappa statistics) were calculated for histological diagnosis, pattern {papillary (usual type)/ variant}, grade (high/low), lamina propria invasion (present/absent), deep muscle invasion (present/absent) and specific variants. Concordance and discordance were analysed with respect to reviewed histopathological evaluation of the slides. The values were calculated for both the pathologists who evaluated the microscopic images sent by e-mail. Kappa statistics was calculated to know the strength of agreement between the two pathologists. Concordance was highest in recognising deep muscle invasion. Kappa value suggested almost perfect agreement for recognising deep muscle invasion. The p-value was highly significant (p=0.0001). Concordance was good for recognising the pattern and grading the lesions. Pathologist 1 had not attempted to grade the lesion in two cases. Pathologist 2 had not attempted to grade the lesion in four cases. Hence, those cases were exempted from calculating the concordance. Kappa statistics suggested substantial agreement for both the pattern recognition and grading the lesions. The p-values were highly significant {Pattern recognition (p=0.0004), Grading (p=0.0013)}. Concordance was satisfactory for appreciation of lamina propria invasion and histological diagnosis. Kappa value suggested moderate agreement for lamina propria invasion. The p-value was statistically significant (p=0.011). Kappa value suggested fair agreement for histopathological diagnosis. The p-value was highly significant (p=0.0067). The concordance was not satisfactory for recognising the specific variants. Kappa statistics suggested only slight agreement for recognising the specific variants of the lesion. The p-value was not significant (p=0.1807). The performance of first pathologist with respect to most of the histopathological parameters was better than the second pathologist. However, the overall performance of both the pathologists was found to be satisfactory [Table/Fig-6,7].

DISCUSSION

In the history of pathology, photomicrographic representation of microscopic findings has been regarded as the central focus for the purpose of teaching, communication and practice of pathology [1]. Telepathology refers to practice of pathology at a distance through visualisation of microscopic images sent for consultation on a computer screen rather than direct analysis of the slides under the microscope [3]. Digital image capture technique has found a new application in slide sharing and has assisted in second opinion consultations of unusual or difficult cases in pathology [1]. Telepathology can be considered as a good alternative for a second opinion consultation [3]. Good quality images can be interpreted safely and utilised for patient care [13].

Urothelial carcinoma of bladder is a complex and heterogeneous disease having potentially lethal behavior [8]. The aim of the tumour classification is to identify the groups of the patients with different outcomes and manage them accordingly. An ideal classification system should be robust, reproducible and transparent. Different WHO grading systems showed considerable variations with respect to the reproducibility of histopathological features [5]. But the WHO 2004 classification showed better reproducibility than the WHO 1973 classification system. Strong points of the 2016 classifications are clear cut-offs between high-grade and low-grade tumours, along with clear precise description of each grade in order to obtain homogeneous groups of tumours [14]. Most of the studies have compared the reproducibility of histopathological features between WHO 1973 and WHO 2004/WHO 2016 classification. In most of the studies, evaluation was done on microscopic slides [5,8-11]. The current study was undertaken to evaluate the reproducibility of histopathological diagnosis, pattern recognition, grading, lamina propria invasion muscle invasion and specific variants diagnosed in bladder tumours on microphotographs, according to WHO 2016 classification.

Total number of cases was highest in the study conducted by Mangrud OM et al., [11]. In contrast to the other studies, the present study had less number of cases. Most of the studies, including the present study had a wide age range [5,8,11]. In the present study, median age was 65 yrs. Similar to the present study, Nabebina TI et al., documented median age of 64 years in their study [8]. Kvikstad V et al., and Mangrud OM et al., documented higher median age in their study [5,11]. Clustering of cases was seen in eighth decade in the present study. Dravid NV et al., observed that most of the cases were in seventh decade in their study [9]. Other studies had not specified clearly. Most of the studies, including the present study documented male predominance. In most of the studies,

S. No.	Parameters	Pathologist 1			Pathologist 2		
		Concordant cases n (%)	Discordant cases n (%)	No. of cases	Concordant cases n (%)	Discordant cases n (%)	No. of cases
1	Histopathological diagnosis	17 (73.91)	6 (26.09)	23	13 (56.52)	10 (43.48)	23
2	Pattern	20 (86.96)	3 (13.04)	23	20 (86.96)	3 (13.04)	23
	Infiltrative urothelial carcinoma	14 (82.35)	3 (17.65)	17	14 (82.35)	3 (17.65)	17
	Non-invasive urothelial carcinoma	6 (100)	0	6	6 (100)	0	6
3	Grade	17 (80.95)	4 (19.05)	21	13 (68.42)	6 (31.58)	19
4	Lamina propria invasion	18 (78.26)	5 (21.74)	23	16 (69.57)	7 (30.43)	23
5	Deep muscle invasion	20 (95.24)	1 (4.76)	21	21 (100)	0	21
6	Specific variants	3 (50)	3 (50)	6	4 (66.67)	2 (33.33)	6

[Table/Fig-6]: Distribution of concordant and discordant cases of urinary bladder neoplasms.
Kappa analysis

Parameters	Kappa value	p-value*
Histopathological diagnosis	0.34 (Fair)	0.0067 (Highly significant)
Pattern	0.65 (Substantial)	0.0004 (Highly significant)
Grading	0.67 (Substantial)	0.0013 (Highly significant)
Lamina propria invasion	0.48 (Moderate)	0.011 (Significant)
Deep muscle invasion	0.86 (Almost perfect)	<0.0001 (Highly significant)
Specific variants	0.09 (Slight)	0.1807 (Not significant)

[Table/Fig-7]: Kappa value and statistical significance of histopathological parameters of urinary bladder neoplasms.
*Kappa statistics (Cohen kappa coefficient) was the statistical tool used to perform statistical analysis

including the present study, TURBT specimen was the most common specimen type [5,8-11]. Right lateral wall was the most common site of involvement in the present study. Other studies had not specified the site of involvement of the lesion. Infiltrating urothelial carcinoma – usual type was the most common lesion was the common histological in the present study. High grade papillary urothelial carcinoma was the most common diagnostic entity in the studies conducted by Dravid NV et al., and Sharma P et al., [9,10]. Kvikstad V et al., conducted study on papillary urothelial carcinoma [5]. But the study had not further specified about the histological subtype. Similarly, other authors conducted studies on urothelial carcinoma, but had not specified the histological subtype. High grade tumours were common in the present study and in the study conducted by Kvikstad V et al., Dravid NV et al., and Sharma P et al., [5,9,10]. In contrast, low grade tumours were common in the studies conducted by Nabebina TI et al., and Mangrud OM et al., [8,11]. Most of the studies compared reproducibility of histopathological features between WHO 1973 classification and WHO 2004 classification [5,8-11]. In contrast, in the present study, the reproducibility of histopathological features was focused on WHO 2016 classification of bladder tumours. Most of the studies had not evaluated deep muscle invasion [5,8-11]. In contrast, deep muscle invasion was evaluated in the present study. Nabebina TI et al., and the present study used Cohen kappa coefficient to analyse the strength of agreement [8]. In contrast, Kvikstad V et al., used Gwet's AC agreement coefficient to analyse the strength of agreement [5]. Sharma P et al., employed Intraclass Correlation Coefficient (ICC) to analyse the strength of agreement [10]. Mangrud OM et al., had not specified the nature of agreement scale used to analyse the strength of agreement [11].

In a study conducted by Kvikstad V et al., histopathological features like papillary architecture, nuclear polarity, cellular maturation, nuclear enlargement and giant nuclei had Gwet's AC agreement coefficient of above 0.60 (good agreement) for both grading system (WHO 1974 and WHO 2004) [5]. Nabebina TI et al., documented kappa value suggesting slight agreement (0.15) for low-grade tumours and fair agreement (0.30) for high-grade tumours (according to WHO 2004 classification) [8]. Sharma P et al., had documented intraclass correlation coefficient value of 0.853 which suggested good agreement [10]. Mangrud OM et al., observed a kappa value of 0.70 for WHO 2004 classification of bladder tumours. However, the author had not specified the nature of agreement scale used in the study [11]. Dravid NV et al., had not analysed reproducibility in their study [9]. In the present study, Kappa value (for WHO 2016 classification) suggested fair agreement for histopathological diagnosis (0.34), substantial agreement for pattern recognition (0.65) and grading (0.67), moderate agreement for lamina propria invasion, almost perfect agreement for deep muscle invasion (0.86) and slight agreement for recognising specific variants (0.09) [Table/Fig-8].

Parameters	Present study	Kvikstad V et al., [5] (Norway, 2019)	Nabebina TI et al., [8] (Republic of Belarus, 2016)	Dravid NV et al., [9] (India, 2016)	Sharma P., [10] (India, 2015)	Mangrud OM et al., [11] (Norway, 2014)
Total number of cases	23	38	158	139	50	193
Age (years)	Range=36-90 y Mean=62.35 Median=65 y Eighth decade	Range=56-87 y Median=72 y	Range=29-92 y Median=64	Seventh decade	-	Range=39-95 y Median=74
Gender	Males	Males	Males	Males	-	Males
Specimen type	TURBT*	TURBT*	TURBT*	TURBT*	TURBT*	TURBT*
Site	Right lateral wall	-	-	-	-	-
Histopathology diagnosis	Infiltrating urothelial carcinoma- usual type (papillary)	Papillary Urothelial carcinoma	Urothelial carcinoma	Urothelial carcinoma	Urothelial carcinoma	Urothelial carcinoma
Pattern	Papillary	Papillary	-	Papillary	Papillary	-
Grade	High-grade	High-grade	Low-grade	High grade	High grade	Low-grade
Classification	WHO 2016	WHO 1973 WHO 2004	WHO 1973 WHO 2004	WHO 2004	WHO 2004	WHO 1973 WHO 2004
Deep muscle invasion	Evaluated	Not evaluated	Not evaluated	Not evaluated	Not evaluated	Not evaluated
Agreement scale used	Cohen Kappa coefficient	Gwet's AC agreement coefficient	Cohen Kappa coefficient	-	Intraclass Correlation Coefficient (ICC)	-
Inference	Kappa suggested fair agreement for histopathological diagnosis (0.34), Substantial agreement for pattern recognition (0.65) and Grading (0.67), moderate agreement for lamina propria invasion, Almost perfect agreement for deep muscle invasion (0.86) and slight agreement for recognising specific variants (0.09)	Papillary architecture, nuclear polarity, cellular maturation, nuclear enlargement and giant nuclei had Gwet's AC agreement coefficient of above 0.60 (good agreement) for both grading system	Slight agreement (0.15) for low-grade Fair agreement (0.30) for high-grade	-	ICC = 0.853 (Good)	Kappa = 0.70 (Substantial agreement)

[Table/Fig-8]: Comparison of clinico-pathological parameters of urinary bladder neoplasms in various studies.
* TURBT: Trans urethral resection of bladder tumour

The most common cause of discordance in histopathological diagnosis was failure to identify small foci of tumour invasion into the lamina propria associated with breach in the basement membrane on microphotographs. The causes of discordance in pattern recognition included fusion of papillary structures and poorly differentiated tumours. Under-grading was the more common cause of discordance than the over-grading in the present study. The reason for under-grading was mainly due to failure to identify the small foci of high-grade features on microphotographs. Tumour grade is considered as the most important prognostic factor in bladder cancer. It has an impact on the treatment and patient follow-up [5]. It is stated that not all urothelial lesions are homogeneous and heterogeneity of the lesion is common. A mixture of two grades in the same tumour has been reported in the 3-43% of tumours [14]. The tumour heterogeneity may also contribute to the inter-observer variability. The most common cause of discordance in lamina propria invasion was failure to identify small foci of tumour invasion into the lamina propria associated with breach in the basement membrane. The discordance in recognising specific variants was mainly due to poorly differentiated tumours. The muscle invasion was well appreciated by both the pathologists. It is important to identify detrusor muscle invasion as it signifies higher stage (pT2) [4,6]. However, the other studies had not focused on muscle invasion.

In the present study, concordance between the reviewed histopathological findings and the findings appreciated by each pathologist was assessed. The performance of first pathologist was better than the second pathologist. The accuracy of interpretation depends on many factors like experience and enthusiasm of the interpreting pathologist, the quality of images sent by the pathologist and the field chosen to take the microphotographs. However, the overall performance of both the pathologists was satisfactory.

It may be suggested the accuracy of diagnosis and reproducibility may be improved in future studies by providing arrow marks on the microphotographs to mark the area of interest. Thereby, the chances of missing the important microscopic feature may be minimised.

Limitation(s)

The number of cases analysed in the present study was relatively less in comparison with other studies.

CONCLUSION(S)

The histopathological interpretation of bladder neoplasms has satisfactory reproducibility on microphotographs. The evaluation of representative microphotographic images happens to be a prudent and pragmatic exercise. It may be suggested that the accuracy of diagnosis and reproducibility may be improved in future studies by providing arrow marks on the microphotographs to mark the area of interest. The pathologists must train themselves to interpret the microphotographs images. The study emphasises the importance of intradisciplinary consultation. The concept can be extrapolated and employed to solve perplexing cases my means of effective communication technology.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
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- Manual Googling: Dec 26, 2020
- iThenticate Software: Feb 22, 2021 (12%)

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- Was informed consent obtained from the subjects involved in the study? NA
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