

## A histopathological and epidemiological study of urothelial carcinoma at a tertiary care centre in Peshawar, Pakistan

Saria Saeed<sup>1</sup>, Danyal Khan<sup>2</sup>, Shah Faisal<sup>3</sup>, Fozia Rauf<sup>4</sup>, Muhammad Owais Ali<sup>5</sup>, Asif Rehman<sup>6</sup>

### Abstract

Bladder cancer is the ninth leading cause of death worldwide and 14th leading cause of death in Pakistan. The objective of this study was to determine the frequency of urothelial carcinoma in various age groups, its gender distribution, and grades. A total of 131 cases of urothelial carcinoma, received at Department of Pathology, Peshawar Medical College, Peshawar, between January 2017 to December 2022, were included in the study; of them 107 (81.6%) were males while 24 (18.3%) were females with a mean age of 62±13 years. The most common histological subtype was papillary urothelial carcinoma in 117(89.3%) cases, followed by Squamous and Glandular in 5(3.8%) cases. Majority of the urothelial carcinoma with high grade showed a statistically significant relation with muscle invasion 38 (50.66%). Males were four times more likely to have urothelial carcinoma while older age groups were more likely to have high grade urothelial carcinoma.

**Keywords:** Carcinoma, Urinary bladder, Cancer, Neoplasm, Urothelial.

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### Introduction

Urothelial carcinoma (UCs) of lower urinary tract is the ninth leading cause of death worldwide and accounts for around 573,000 new cases annually and 213,000 deaths per year. It is the 14th leading cause of cancer-related deaths in Pakistan, accounting for approximately 4,671 new cases and 2,776 deaths every year.<sup>1</sup> Singapore has the highest prevalence of bladder cancer among Southeast Asian countries, followed by Indonesia, Thailand, and Malaysia.<sup>2</sup> Risk of UC varies between genders, geography, and age groups. The risk of UC is greatly impacted by exposure to a number of carcinogens, the most common of which is

<sup>1-4</sup>Department of Pathology, Peshawar Medical College, Riphah International University, Peshawar, Pakistan; <sup>5</sup>Department of Surgery, Peshawar Medical College, Riphah International University, Peshawar, Pakistan; <sup>6</sup>Department of Community Health Sciences, Peshawar Medical College, Riphah International University, Peshawar, Pakistan.

**Correspondence:** Asif Rehman. e-mail: [asifrehman173@gmail.com](mailto:asifrehman173@gmail.com)

ORCID ID. 0000-0002-6133-3349

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cigarette smoking.<sup>1</sup> Other risk factors include carcinogen exposure (those who work in chemical industries, e.g. paints or fabric dyes), inflammation, infection (*Schistosoma Haematobium*, chronic bacterial infections), cyclophosphamide chemotherapy, and radiotherapy.

Men are diagnosed three to four times more frequently than women. The reason can be exposure to risk factors, occupational hazards, and lifestyle factors. Although women are less frequently diagnosed with UC, they have worse cancer specific and overall survival which may be due to delay in diagnoses. Bladder carcinoma is considered the disease of old age as 90 percent of bladder carcinoma affected individuals are above the age of 55 years.

About 75% of UC cases present with non-muscle invasive bladder cancer and 25% with muscle-invasive or metastatic disease at the time of presentation. If the tumour is invasive but has not yet spread outside the bladder, the five-year relative survival rate is 70%.<sup>3</sup>

The purpose of this study was to determine the frequency of UC in various age groups, as well as its gender distribution and grades, at a tertiary care hospital in Khyber Pakhtunkhwa (KP), Pakistan.

### Methods, Results and Discussion

This was a retrospective observational cross-sectional study conducted in the Department of Pathology, Peshawar Medical College. Census sampling technique was used to select the cases of UC received between January 2017 to December 2022. The biopsy tissue was fixed in 10% buffered formalin and was processed routinely. The paraffin embedded tissue was cut on microtome up to 3-4 microns. The sections were then stained with haematoxylin and eosin and were examined under the microscope and the details were noted. Poor quality slides and biopsies with missing information were excluded. Variables included age, gender, histological subtype, tumour grade, detrusor muscle invasion, and vascular invasion. The data was entered in SPSS version 24.0 for statistical analysis. Mean and standard deviation were calculated for quantitative variables, whereas frequencies and percentages were calculated for categorical variables. Chi Square/Fisher Exact tests were used to compare categorical variables. P-value of ≤0.05 was considered statistically significant.

**Table-1:** Socio-demographic characteristics (n=131).

	n (%)
<b>Mean Age</b> (years)	62±13
<b>Age groups</b> (Years)	
<50	21 (16.03)
≥50	110 (83.96)
<b>Gender</b>	
Male	107 (81.67)
Female	24 (18.32)
<b>Histological Sub-types</b>	
Papillary UC	117 (89.31)
Squamous & Glandular	5 (3.80)
Poorly differentiated	5 (3.80)
Nested UC	1 (0.76)
Microcystic UC	1 (0.76)
Clear cell UC	1 (0.76)
Giant cell UC	1 (0.76)

**Table-2:** Relation of Grades of Urothelial Carcinoma with Gender.

Gender	Low Grade	High Grade	p-value
	(n=56) n (%)	(n=75) n (%)	
<b>Gender</b>			0.99
Male	47 (35.87%)	63 (48.09%)	
Female	9 (6.8%)	12 (9.1%)	
<b>Relation of Grades of Urothelial Carcinoma with Muscle and Vascular Invasion</b>			
<b>Muscle Invasion</b>			
Not present	49 (87.5%)	37 (49.3%)	< 0.01
Present	7 (12.5%)	38 (50.6%)	
<b>Vascular Invasion</b>			
Not present	53 (94.6%)	60 (80%)	< 0.05
Present	3 (5.3%)	15 (20%)	

The study included 131 cases of UC. Among them, 107 (81.6%) were males and 24 (18.3%) were females. The mean age of the study sample was 62±13 years. Majority of the cases 110(83.96%) were of age 50 years and above. The most common histological subtype was papillary UC 117 (89.3%) followed by Squamous and Glandular 5 (3.8%), poorly differentiated UC 5 (3.8%), while microcystic, nested, giant cell, and clear cell accounted for 1 (0.7%) each [Table 1].

Most i.e. 75 (57.2%) cases were identified as high grade UC compared to 56 (42.7%) as low grade. No statistically significant association was identified between high grade and low grade when compared with gender using chi-square test ( $p>0.05$ ) [Table 2].

When muscle invasion was compared with grades, highly statistical significant association was identified ( $p<0.01$ ) similarly significant association was also identified when vascular invasion was compared with different grades of UC ( $p<0.05$ ) [Table 2].

Bladder cancer is the most common malignancy. The five-

year survival rate is about 10-15%, especially in locally advanced and metastatic disease.<sup>4</sup> The age-standardised frequency rate (ASIR) varies greatly between geographical regions. Age-standardised mortality rates (ASMR) are beginning to decline in developed countries, while rising in low-income countries.<sup>5</sup>

The mean age in our study was 62±13 years. Majority of the patients, i.e. 110 (83.96%), were ≥50 years of age. Similar findings were reported in studies by F. Kamal et al. (2022)<sup>6</sup> and A. Chughtai et al. (2022)<sup>3</sup> from Pakistan. Contrary to our results, Anwar et al.<sup>7</sup> observed mean age of 72 years.

In the present study, UC was observed more in males, with male to female ratio of 4:1. This was in accordance with the study done by Anwar et al. from Faisalabad<sup>7</sup> and Mubarak et al. reported a higher frequency of UC in females and revealed a M:F ratio of 1:3.<sup>8</sup>

Papillary UC was the most prevalent histological subtype of bladder cancer in the current study, accounting for 117 (89.31%) out of the 131 cases followed by UC with divergent differentiation at 5 (3.8%).

Detrusor muscle invasion was observed in 38(50.6%) of the high grade UC and 7(12.5%) in low grade UC. This difference was statistically highly significant ( $p< 0.01$ ). A study by J. A. Al-Maghrabi<sup>9</sup> from Saudi Arabia noted similar results with 53.8% high grade UC and 46.2% low grade UC showing muscle invasion in 46.1% cases which was statistically significant with p value of 0.007. In the current study, 15 (20%) high grade UC cases showed vascular invasion. This was in accordance with the study by K. A. G. Tampubolon et al. (2022) from Indonesia,<sup>10</sup> who noted similar results with 17.3% vascular invasion in UC. The major limitation of the present study was that it was a single-centre study and the results cannot be generalised to other parts of the country; secondly, it was a cross-sectional study with a small sample size.

## Conclusion

In the present study it was observed that older age groups are more likely to have high grade UC. Males are more likely to have UC as compared to females. The detrusor muscle and vascular invasion are significantly related with high grade UC. The results of this study provide an insight into demographics of UC in a small cohort from Northern areas of Pakistan. Further studies regarding risk factors and survival of UC patients are needed to take national level measure for health awareness in our population.

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## Abbreviations

PMC – Peshawar medical college

UCs – Urothelial carcinoma

HGUC – High grade urothelial carcinoma

LGUC – Low grade urothelial carcinoma

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## Author Contribution:

SS: Concept, design, abstract, introduction, discussion, conclusion.

DK: Methodology.

SF: Discussion.

FR: Proofread, conclusion.

MOA: Referencing.

AR: Data analysis, results.