

# Expression of HER2/NEU in Different Grades of Urothelial Carcinoma of Urinary Bladder

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## ABSTRACT

**Aim:** To demonstrate HER2/neu expression in various grades of urothelial carcinoma of urinary bladder.

**Methodology:** This descriptive study was done in four tertiary care hospitals of Lahore and Faisalabad during period of one year. HER2/neu expression was examined in specimens from 90 patients of urothelial carcinomas of urinary bladder by IHC (Immunohistochemistry). Frequency and percentage were calculated for histological grade of the tumor and expression of HER2/neu.

**Results:** Mostly the patients were >66 years of age and male to female ratio was 5:1. +2 and +3 scores of HER2/neu expression were 20%(n=18) and 18.9%(n=17) respectively i.e. maximum in high grade cancer when comparing with low grade tumors i.e. +2 and +3 scores (8.9%,n=08 and 3.3%,03) respectively.

**Conclusion:** There is positive association between grades of urothelial cancer & HER2/neu expression scores.

**Keywords:** Expression, Urothelial carcinoma, HER2/neu

## INTRODUCTION

Urothelial tumors are the most common type of cancer worldwide. There are about 549,000 cases/ year and 200,000 deaths every year from urothelial cancer throughout the world<sup>1</sup>. The incidence rises with advancing age, more in the 6<sup>th</sup> decade and maximum in the 8<sup>th</sup> decade. Urothelial cancer have a natural progress from superficial non-invasive tumors to deep muscle invasive cancers<sup>2</sup>. Usually these tumors are invasive at diagnosis; appropriate diagnosis and management is most important<sup>3</sup>. Even with treatment, spread rates are high and affect the survival rate with a five year survival around 40-50%<sup>4</sup>. Urothelial tumors are divided on the basis of 2004 WHO/ISUP classification into papillary urothelial tumors of high and low grade urothelial malignancy<sup>5</sup>.

## METHODOLOGY

**Study Design:** Descriptive study

**Settings:** Samples were collected from LGH, Mayo Hospital, Jinnah Hospital Lahore and Allied Hospital Faisalabad.

**Duration Of Study:** 7-12-2016 to 7-11-2018

**Sampling Technique:** Non-probability purposive sampling.

**Inclusion Criteria:** All ages and both genders with diagnosis of urothelial carcinoma were included.

**Exclusion Criteria:** Patients receiving chemotherapy and recurrent cases of urothelial carcinoma were excluded.

Data was entered in SPSS 20 version. For age, mean± SD were calculated. For Qualitative data e.g. expression of HER2/neu and grades of TCC, frequencies and percentages were determined. Association between HER2/neu and grade of urothelial carcinoma was determined by "Chi square test".

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## RESULTS

The detail of results is given in tables 1, 2, 3, 4, 5, The study included 90 subjects with urothelial cancer of bladder. All the subjects fulfilled the inclusion criteria of study. In this study, 23(25.6%) patients were with zero Her2/neu expression score while 21 (23.3%) patients were with +1 score. 26(28.9%) patients had +2 Her2/neu expression score and 20(22.2%) patients were with +3 Her2/neu expression score. Her2/neu expression scores +2 and +3 were maximum in patients of high grade tumors as compared to that of low grade tumors and difference was highly significant statistically (p<0.01).

Table 1:Age distribution.

Age (yrs.)	n	%age
20-35	01	1.1
36-50	12	13.3
51-65	34	37.8
>66	43	47.8
Total	90	100

Mean age: 61.4±10.9 years

Gender distribution.

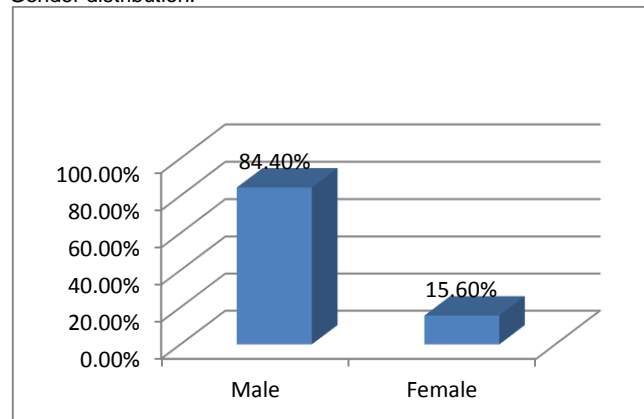


Table 2: Her2/neu expression score urothelial carcinoma.

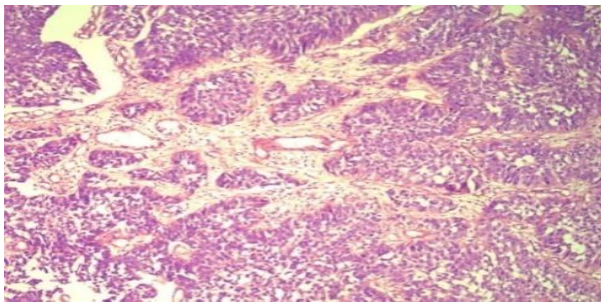
Her2/neu Score	n	%age
Zero	23	25.6
+1	21	23.3
+2	26	28.9
+3	20	22.2
Total	90	100

Table 5: Association of grades with Her2/neu expression score

Her2/neu score	Grades		Total	%age
	High	Low		
Zero	---	23 (25.6%)	23	25.6
+1	7(7.8%)	14 (15.5%)	21	23.3
+2	18(20%)	08 (8.9%)	26	28.9
+3	17 (18.9%)	03 (3.3%)	20	22.2
Total	42(46.7%)	48 (53.3%)	90	100

P < 0.01 (Highly significant)

Fig 1: UC-High grade, H&E staining



**DISCUSSION:**

In this study, mean age of the patient was 61.4±10.9 years. This is consistent with the study of Hashmi *et al.*, (2018)<sup>4</sup> at Karachi. A study at Rawalpindi by Zeb *et al.*, (2018)<sup>3</sup> stated the mean age of 56.4 years. Another study in Africa states the mean age ranges from 36.8 to 61 years<sup>8</sup>. According to a study by Hussain *et al.*, (2018)<sup>1</sup> the mean age of bladder cancer patients was 63.6±14.5 years. In this study, 76 (84.4%) patients were males and 14 (15.6%) were females. M: F ratio was 5:1.

In this study, specimen of 23(25.6%) patients were with zero Her2/neu expression score while 21 (23.3%) patients were with +1 score. 26(28.9%) patients had +2 Her2/neu expression score and 20(22.2%) patients were with +3 Her2/neu expression score. These results are consistent with study by Krüger *et al.*, (2002)<sup>6</sup>, who shows HER2 expression i.e. zero in 22 (15.9%) tumors, +1 in 28 tumors (20.3%), +2 in 31 tumors (22.5%) and +3 in 57 of 138 tumors (41.3%).

In a study by Jimenez *et al.*, (2001)<sup>7</sup>, 41 (51.25%) cases had zero score, 17 (21.25%) cases had +1 score, 8 (10%) cases had +2 score and 14 (17.5%) cases had +3 score.

As far as low grade malignancy is concerned, 23(25.6%) cases are with zero Her2/neu expression score, 14(15.4%) cases had +1 Her2/neu score while 07(7.8%) had +1 Her2/neu score. 18(20%) cases of high grades had +2 Her2/neu expression score while 08(8.9%) cases of low grade had +2 Her2/neu expression score as well. 17(18.9%) cases of high grade malignancy had +3 Her2/neu score while 03(3.3%) cases of low grade had also +3 Her2/neu expression in this study. This study is in favor of a study by Krüger *et al.*, (2002)<sup>10</sup>. A study in Saudi Arabia by Nedjadi *et al* in 2016 showed 60% bladder carcinoma with 2+ and 3+ score of Her2/neu protein expression<sup>8</sup>.

**Conclusion:** HER2/neu overexpression is high in high grade urothelial carcinoma and that may be related with the disease progression in such patients.

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