UROTHELIAL CARCINOMA AND ITS ASSOCIATION WITH AGE AND GENDER.

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ABSTRACT… Objectives: To determine the histological grading of urothelial carcinoma and its association with age and gender. **Study Design:** Retrospective study. **Setting:** Pathology department of Liaquat university of Medical and Health Science. **Period:** One year from January 2016 to December 2016. **Material and Methods:** Four micrometer thick paraffin-embedded and formalin-fixed sections were prepared from transurethral resection of bladder tumor (TURBT) samples of urothelial carcinoma patients and were examined. Histological grading was categorized as low and high grades. All the data was collected by self-made proforma. Data was analyzed by SPSS version 20. **Results:** Total 83 cases were enrolled in current study; their mean age was 49.19 ± 12.33 years. Males were found in the majority 51(61.4%) and females were 32(38.6%). Most common age group was 46-60 years 36(43.4%). According to the histological grading high grade was most common as 65.10%, and low grade urothelial carcinoma was 34.90%. There was no significant difference according to age of histological grading. Male gender was most common, while progression of disease was higher among females in contrast to males; as high grade carcinoma was significantly higher among females, p-value 0.014. **Conclusion:** It was concluded that male gender is the contributing factor of urothelial carcinoma, but disease progression is significantly high among females. No significant association has been found according to age.

Key words: Age, Gender, Urothelial Carcinoma, Transitional cell carcinoma.

INTRODUCTION

Urothelial carcinoma (or transitional cell carcinoma(TCC)) of the urinary bladder, the 4th commonest carcinoma among males and the 9th commonest in females in the United states of America, brings about significant mortality and morbidity.[1] According to AFIP data TCC of bladder is the seventh most frequent malignancy among both males and females and constitutes 93.4% of all bladder cancers.[2] In around 75.0% – 85.0% bladder cancer cases, the disease remains restricted to mucosa and has a prolonged clinical course with multiple recurrences after local resection without tumor progression.[2,3] Hence prevalence of bladder malignancy is low in Sri Lanka than other South Asian nations like India (32/1,000,000) and Karachi, Pakistan (89/1,000,000), in Delhi, India, the age adjusted bladder malignancy prevalence reaches 58 per 1,000,000.[4-6] The significant

risk factors for urinary bladder carcinoma reported by epidemiologic studies are smoking (cigarette) and work-related exposure to musky amines.[7] Further risk factors include genetic/ biomarker susceptibility, water pollutants and fluid intake, gender (male), urinary tract infection (inflammation, stone), environmental toxic waste (arsenic), coffee consumption, socioeconomic status, urinary blood fluke infection, disclosure to ionizing radiations, cyclophosphamide, and further medicinal agents.[7,8] Sex disparities in epidemiology of bladder malignancy have been an attention of current research.[9] Female subjects seem to have poorer survival and further unfavorable pathology than male patients. Sex variances in mortality associated to bladder malignancy have frequently been reported, which can possibly be somewhat explained by the greater ratio of unfavorable pathology among female cases.[9,10] Sex variances in bladder

malignancy epidemiology can possibly be made clear by past-historical, biological, and lifestyle perspectives. First, sex variances in major hormones and in vascularity nearby the bladder can possibly be a related factor. As of a hormonal standpoint, the prevalence of bladder malignancy was exhibited to be greater among postmenopausal as compared to premenopausal females, and aggressive bladder malignances expressed elevated levels of some androgen receptors and estrogen receptor-β .[1,9] Patient's gender and age are vital factors in clinical selection for treating urothelial cancer of the bladder, there are no recommendations based on evidence to guide health care experts.[1] Additionally, the correlation and effect of gender on bladder TCC prevalence, prognosis, staging, and survival are incompetently understood,[11] and by recent studies, it is recommended that further research should be done to the better understanding for epidemiological risk-factors and differences according to gender.[12] Therefore this study has been conducted to determine the urothelial carcinoma and its association with age and gender.

MATERIAL AND METHODS
This retrospective study has been performed at pathology department of Liaquat university of Medical and Health Science. Study duration was one year from January 2016 to December 2016. Four micrometer thick paraffin-embedded and formalin-fixed sections were prepared from transurethral resection of bladder tumor (TURBT) samples of urothelial carcinoma patients and were examined. All the samples were stained with hematoxylin eosin. Non-invasive papillary urothelial neoplasm of low malignant potential, small cell carcinoma, adenocarcinoma, squamous cell carcinoma, and other neoplasms were excluded. Histological grading was categorized as low and high grades.[20] All the data regarding age, gender and histological grading was collected by self-made proforma. Data analysis was done by SPSS version 20.0. Frequency and percentage were computed for categorical variables like gender site of carcinoma age groups and histological grading. Mean and standard deviation were calculated for numerical

variables like age. Chi-square test was applied and a p-value less than 0.05 was considered as significant.

RESULTS
In this study total 83 cases were enrolled, their mean age was 49.19+12.33 years. Males were found in the majority 51(61.4%) and females were 32(38.6%). Most common age group was 46-60 years among 36(43.4%) patients, followed by 24(28.9%) patients were more than 60 years and 23(27.7%) were within age group of 30-45 years. Table-I.

According to the histological grading high grade urothelial carcinoma was most common as 65.10%, and low grade and low grade urothelial carcinoma was 34.90%. Figure-1

Urothelial carcinoma was most common in age group of 46-60 years, as out of 36 patients, 24 had low grade and 12 had high grade, out of 23 cases of 30-45 years age group; 13 had low grade and 10 had high grade, while among 24 patients of >60 years 17 had low grade and 7 had high grade urothelial malignancy. No significant variance was found according to age of histological grading; p-value 0.568. Males were most common in urothelial malignancy and out of total 51 males 28 had high grade and 23 had low grade urothelial malignancy, while high grade malignancy was significantly higher among females; as out of total 32 females 26 had high grade and only 6 had low grade carcinoma. Table-II

Basic Characteristics	Numbers/ Percentage
Gender	
Male	**51(61.4%)**
Female	**32(38.6%)**
Total	**83(100.0%)**
Age groups	
30-45 years	23(27.7%)
46-60 years	36(43.4%)
>60 years	24(28.9%)
Total	83(100.0%)
Age (mean+SD)	49.19+12.33 years

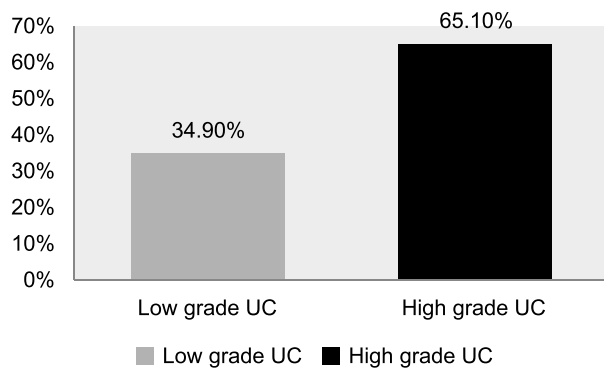Table-I. Patients according to age and gender distribution n=83

Figure-1. Grading of urothelial carcinoma n=83

| Variables | Urothelial carcinoma | | Total | P-Value |
	High Grade	Low Grade		
Age Groups				
30-45 years	13	10	23	
46-60 years	24	12	36	0.568
>60 years	17	7	24	
Total	54	29	**83**	
Gender				
Male	28	23	51	
Female	26	6	32	0.014
Total	54	29	83	

Table-II. Urothelial carcinoma according to age and gender n=83

DISCUSSION

Urothelial carcinoma is a classic pattern of a cancer, emerging from environmental carcinogenic influences. Bladder malignancy is further frequently noted among males, while prognosis is generally worse among females.[13] In this study males were found in the majority 51(61.4%) and females were 32(38.6%), which is similar to the study of Türk H et al,[13] which reported that out of five hundred sixty-nine patients, 497 (87.30%) cases were males and 72 (12.70%) were females. In recent times, many reviews have summarized and interpreted outcomes from published investigations on the gender disparity in prognosis of bladder malignancy.[12-16] Multiple factors are suspected to influence the gender specific prognostic outcome.[12,16] Distinctive anatomy, deferrals from the earliest symptoms to diagnosis among women, changes in hormone receptors in addition to tumor biology and less ideal treatment for females were proposed

to contribute in the observed disparities.[17-19] Though, even following adjustment for a few of these factors, the gender disparity in survival remained there.[12] We had suspected another factor for males, as smoking habits are frequent among males in contrast to females, this was also found among many studies that smoking is the commonest factor for urothelial carcinoma.[12,14,17] It is worth to note in all those studies that the males are most common as compared to females and it is also mentioned that smoking is commonest factor.[12,14,17] Similarly in this study mostly males had smoking habits.

In this study according to the histological grading high grade urothelial carcinoma was most common as 65.10%. Gupta et al[20] also found similar findings as high grade urothelial carcinoma was most common among 55.3% of the cases. While these findings were inconsistent to the results of Koyuncuer A et al[8], as low grade urothelial carcinoma was observed among 85 (68%) of the patients. In many studies these findings were controversial, and this may be because of difference in sample size of the studies or ethnicity. In this series no significant variance was found in age groups in terms of grading of malignancy, while other studies reported that old age is significantly correlated with high grade urothelial malignancy.[13,20,21] This difference may be because age range was lower in our study in contrast to other studies.

In this study, female ratio was lower involved in urothelial carcinoma, but the progression of disease was significantly higher among females in contrast to males, because high grade urothelial carcinoma was significantly higher among females; as out of 32 women, 26 had high grade malignancy. Similar findings were documented by Sikic D et al.[21] Among other factors, the expression of estrogen and androgen receptors has been discussed as a possible reason for gender-related differences.[21] Shen et al.[22] observed that the estrogen receptor-ß is the prevailing receptor expressed in UC of the bladder, and its level of expression raises with progressing tumor grade and stage. With this evidence in mind for the importance of hormone receptors in the formation

and advancement of UC of the bladder, in mind, one can hypothesize that the hormonal changes that occur after menopause also have an effect on the carcinogenesis of UC. McGrath et al.[11] showed in a cohort study, that post-menopausal women had a greater risk of acquiring bladder malignancy, moreover, early age at menopause (50 years). While inconsistently Türk H et al[17] reported that there was no significant difference among both genders in terms of tumor stages. According to these controversial ideas of the literature studies, further studies should be done with exclusion of other suspected risk factors for urothelial carcinoma to know the clear association of this malignancy and its progression with gender and age.

CONCLUSION

It was concluded that male gender is the contributing factor of urothelial carcinoma, but disease progression was significantly high among females. No significant association has been found according to age. Further research is required with exclusion of other risk factors such as smoking and menopausal histories to assess the pure association of gender and age.
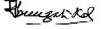**Copyright© 30 July, 2019.**

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