Original Article

AGE AND GENDER RELATED COMPARISON OF HISTOLOGICAL GRADES OF PAPILLARY UROTHELIAL CARCINOMA

Syed Muhammad Ishaque[1], Shaista Gul[1], Abdullah Jan[2], Shahnaz Imdad Kehar[3], Sanaullah Gazozai[1], Nazish Jaffer[4]

[1]Bolan Medical College, Quetta Pakistan
[2]Loralai Medical College Loralai Pakistan
[3]Jinnah Postgraduate Medical Center (JPMC) Karachi, Pakistan
[4]Sindh Medical College, Jinnah Sindh University of Medical and Health Science Karachi Pakistan

ABSTRACT

Objective: To study the histological grades of papillary urothelial carcinoma in various age groups and gender.

Material & Methods: This cross-sectional study was conducted in the department of pathology BMSI, JPMC Karachi from Jan 2009 to Dec 2016. Total numbers of 247 cases of urothelial carcinoma were reviewed and morphological diagnosis done on H&E. Histological grades of papillary urothelial carcinoma were categorized, the data analyzed by SPSS version 21 and excel 2007 version.

Results: In total 247 cases, 41% cases were high grade, 38% were low grade and 21% were invasive variant of papillary urothelial carcinoma. In male gender 90%, 85% & 77% cases were noted in high, low grade and invasive PUC, while in female sex 23%, 15% &10% cases were in invasive, low and high grade respectively. Majority of the lesion were seen in 5th & 6th decades i-e 59% cases as compare to other age groups and only 02% cases was seen in less than 30 years of age and mean & median age was 57.62 & 65 years for this carcinoma.

Conclusion: Out of 247 cases, 101, 93 & 53 cases were high grade, low grade and invasive variants of papillary urothelial carcinoma. Majority were noted in high grade, followed by low grade and invasive type of PUC. Gender wise were in high grade 91, 10, in low grade 79, 14 and in invasive PUC 41, 12 cases were noted in male and female sex respectively. While 85, 60, 57, 24, 17 & 04 cases were in 5th, 6th, 4th, more than 7th, 3rd and less than 3rd decades respectively, minimum and maximum age was 22 and 90 years noted.

Key Words: Age, Gender, Histological grades, Papillary urothelial carcinoma (PUC), Transurethral resection of bladder tumor (TURBT), World health organization (WHO).

INTRODUCTION

Papillary urothelial carcinoma is very complicate, heterogeneous and varied histopathological pattern in neoplasm [1-2]. In USA urinary bladder neoplastic lesions considered the 5th commonest diagnosed cancer [3].

Worldwide 90% of cancer development is due to environmental factors and somatic mutations, on other hand germline mutations are rare causes. Epidermal growth factor receptor (EGFR) its sub-family human epidermal growth factor receptors (HER2/neu), P53 and fibroblast growth factor receptor 3 (FGFR3) have role in the growth of the cell, its differentiation and proliferation which are located in chromosome 17q21. Over expression of EGFR and HER2/neu are associated with high grade and advanced stage of transitional cell malignancy [4].

Large amount of animal fat consumption, smoking, benzidine 2 nephthylamine, analgesic abuse and ionizing radiation increase risk of urinary bladder malignancy [5]. Secretions from normal urothelial epithelial cells are inhibitory while from the cancer cells it stimulates new vascular regeneration (angiogenesis) [6].

Urinary bladder tumors can be classified into histopathological and clinical basis, at the time of presentation 80% cases are non-muscle invasive and 20% have muscle invasion which shows poor prognosis and rapid progression to fatal outcome [7,8].

Malignant transformations of urinary bladder lesions are multi step phenomena i-e urothelial hyperplasia > urothelial atypia > low grade papillary transitional cell carcinoma > dysplasia > carcinoma in situ (CIS) > invasive transitional cell carcinoma [9,10]. Histologically urinary bladder cancer can have papillary form (exophytic) i-e papilloma, low malignant potential and papillary carcinoma, while non-papillary solid form (endophytic) i-e urothelial carcinoma in situ and invasive carcinoma [11, 12].

According to World Health Organization (WHO) classification 1973 & WHO/ISUP system 2004 urinary bladder cancer have following variants [3,11,13,14,15,16].

Correspondence: Dr Syed Muhammad Ishaque; Assistant Professor, Department of Pathology, Bolan Medical College, Consultant Pathologist Sandeman Civil (Prov) Hospital Quetta.

Email: **ishaqsyed784@gmail.com**

WHO 1973	WHO/ISUP 2004
Urothelial papilloma	Urothelial papilloma
Well differentiated (G1)	Papillary urothelial neoplasm of low malignant potential
Moderately differentiated (G2)	Low grade Papillary Urothelial Carcinoma
Poorly differentiated (G3)	High Grade Papillary Urothelial Carcinoma

Low grade papillary urothelial neoplasm has better prognosis instead of that 50-80% of recurrence rate, while non-papillary urothelial cell carcinoma has poor prognosis and up to 90% were presented as local to regional invasion at the time of diagnosis [17].

Hinosu *et al* reported two different type of recurrence after TURBT. Early recurrence which are true presented within 500 days (16.5 months) after the procedure may treated or delayed by local vesicle therapy and late recurrence which are presented after the above mention period and are not prevented by any local therapy [15].

MATERIAL AND METHODS

This cross-sectional study was carried out at the department of Pathology Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Center (JPMC) Karachi from 1st January 2009 to 31st December 2016. The 247 cases of PUC from both male and female sex who approached this tertiary care government institute were included. These patients were operated at Urology department of JPMC Karachi. All specimens in the form of transurethral resection of bladder tumor (TURBT) and cystectomy were included, whereas poorly fixed, inadequate tissue, bladder tumor other than PUC and metastatic tumors were excluded.

Formalin fixed, paraffin embedded blocks, surgical pathology & clinical records and Hematoxylin & Eosin (H&E) stained slides were used. The relevant clinical information and others data were collected. Section were taken and stained with H&E. All slides were studied under light microscope using scanner (4x), low power (10x) followed by high power (40x) by different consultant histopathologists.

The data was analyzed by using Statistical Package for Social Science (SPSS) software version 21 and excel 2007 version.

RESULTS

This Figure-I shows the distribution of various morphological grades of PUC. Out of 247 cases highest encountered figures i-e 101 (41%) cases were in high grade (noninvasive) followed by 93

(38%) in low grade and 53 (21%) cases were observed in invasive variants of PUC.
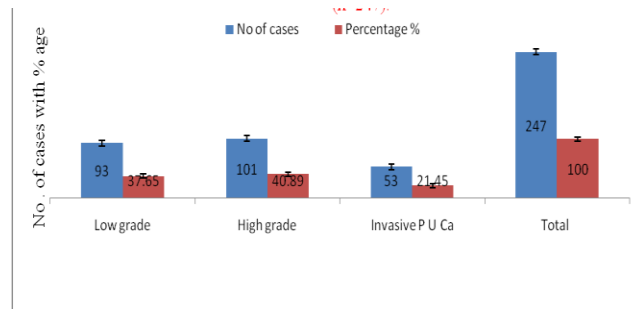
Figure-I: Distribution of histological grades of papillary urothelial carcinoma (n=247).

This Figure-II shows the various morphological grades of PUC according to gender. In male the most common i-e 90% cases were found in high grade (noninvasive), compared to low grade and invasive variants of PUC, i-e 85 % & 77 % cases respectively. While in female gender the majority of cases were found in invasive PUC, i-e 23%, followed by 15% & 10% cases in low and high grades respectively. In gender the Chi-Square = 4.559 and p-value = 0.102 noted.
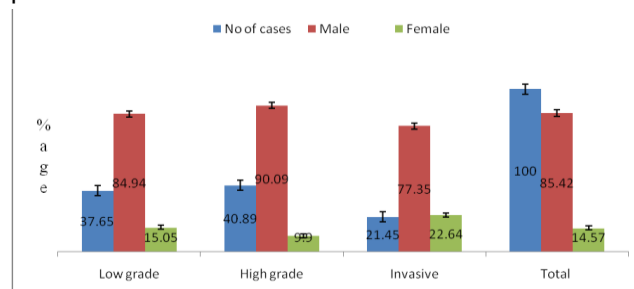

Figure-II: Gender wise distribution of various histopathological grades of papillary urothelial carcinoma (n=247).

This Table-I showed the distribution of various morphological grades of PUC according to different age groups. The most frequently involves age group were 5th decades in all three histological grades of PUC i-e 29 (31%), 38 (38%) & 18 (34%) cases low grade, high grade and invasive PUC, followed by 6th decades i-e 25 (27%), 23 (23%) & 12 (23%) cases were observed in low, high grade and invasive PUC. The mean age was 57.62, median was 65, minimum was 22 while maximum age was 90 years and standard deviation (S-D) ± 11.48 were noted.

Table-I: Showing the distribution of various morphological grades of PUC according to different age groups.

Morphological type of PUC	Total	20-30 years	31-40 years	41-50 years	51-60 years	61-70 years	>71 years
Low grade	93 (37.65%)	00	06 06.45%	26 27.95%	29 31.18%	25 26.88%	07 07.52%
High grade	101 (40.89%)	02 01.98%	07 06.93%	19 18.81%	38 37.62%	23 22.77%	12 11.88%
Invasive Variants	53 (21.45%)	02 03.77%	04 07.54%	12 22.64%	18 33.96%	12 22.64%	05 09.43%
Total	247	04 01.61%	17 06.88%	57 23.07%	85 34.41%	60 24.29%	24 09.71%

Our result showed that most of low grade lesion was seen in 51 to 60 & 41 to 50 years age groups, while high grade tumors were seen in age group between 51 to 60 years followed by 61 to 70 years and in invasive morphological type of PUC cases were mostly seen in 51 to 60 followed by equal in both 41 to 50 & 61 to 70 years of age groups. According to age presentation the Chi-Square = 6.876 and p-value = 0.737 noted.
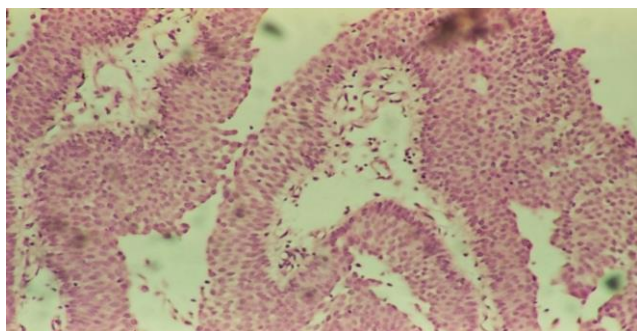
Figure-III: Low grade Papillary Urothelial Carcinoma H&E stain (40X)
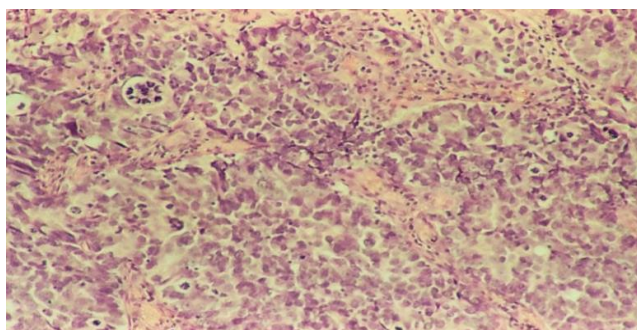
Figure-IV: High grade Papillary Urothelial Carcinoma H&E stain (40x).
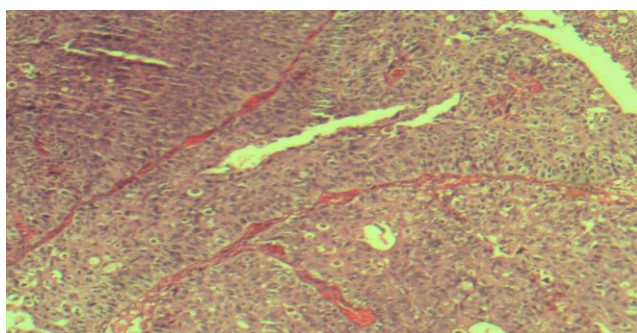
Figure-V: Invasive Papillary Urothelial Carcinoma with muscular invasion H&E stain (10x).
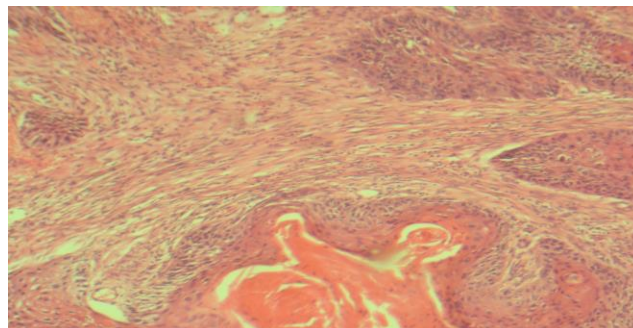
Figure-VI: Invasive Papillary Urothelial Carcinoma with muscular invasion H&E stain (10x).

DISCUSSION

The aim of this study was to correlate the gender and age with different histological grades of PUC in tertiary care government hospital Karachi.

In present study of PUC 41% cases were observed in high grade, 38% in low grade and 21% cases in invasive variant of PUC. These are in correspondence with the study by Enache et al (2013) [1] reporting 49%, 33% & 18% cases in low grade, high grade and invasive PUC, Kumar et al (2012) [18] who reported 54% cases in high grade and 43% in low grade papillary urothelial carcinoma. Iranian study by Salehi et al (2011) [19] reported 60% cases in high grade and 40% in low grade, some studies reported variable results. A Japanese study by Liu et al (2013) [16] noted 23% & 77% cases in low grade and high grade while no invasive type was observed, Ahmad et al (2002) [20] reported 44% in low grade and 12.5% cases in invasive type, Al-Bazzaz (2009) [21] showed 19% in invasive variant and Hassan (2007) [22] also noted 11% cases in invasive urothelial carcinoma.

In our observation male and female gender distribution was 85.5% & 14.5% cases of PUC respectively. Almost similar finding were noted by Biswas et al (2013) [2] i-e 86%, 14% cases, Choi et al (2007) [9] reported 87%, 13% cases, Zhang et al (2012) [11] and Salehi et al (2011) [19] both of them were showed 83% & 17% of cases in male and female gender respectively, Ayub medical college study by Ahmad et al (2010) [23] noted 78% in male, 22% cases in female sex.

In our study gender presentation showed that in male 90% cases were high grade, 85% low grade

and 77% invasive variant of PUC. Whereas in female gender 23% cases were invasive, 15% low grade and 10% high grade. We also noted that in male mostly cases were seen in high grade, while in female sex majority of cases were found in invasive PUC. Similar finding was reported in Iranian study by Salehi *et al* (2011) [19] and Indian study by Biswas *et al*(2013) [2] who reported that survival of papillary urothelial carcinoma had bad prognosis in female gender than male, which showed that aggressive pattern were seen in female as compared to male.

Our observation also showed that the incidence of PUC was decreased with advancing age and in younger age group's i-e in 5th decade 34.5%, in 6th decade 24.3%, in above 71 years of age group 9.7% cases, while in less than 40 years only 8.5% cases were observed respectively. These finding were comparable with the study by Altimari (2011) [24] who showed that in 6th decade 89.5% and in 7th decade 86% cases. United State SEER [25] study by Lynch (1998-2000) showed that in 4th decade 2.3% cases, in 5th decade 5.8% cases, in 6th decade 26.8% and in 7th decade 32.6% cases. These dissimilarities could be due to sample size difference and environmental factors.

CONCLUSION AND RECOMMONDATION

During eight years period in 247 cases of PUC, the most common lesion in male sex was high grade followed by low grade and invasive variant of PUC. Although majority of female gender showed low grade, but a considerable number of cases were noted in invasive variant of PUC. Identification of various histological grades of PUC in biopsy specimens of non-invasive and easy procedure TURBT in initial stage may be helpful for early diagnosis, further managements and treatment of these patients.

AUTHOR CONTRIBUTIONS
Syed Muhammad Ishaque: Conceived/ design, analysis and editing of manuscript.

Abdullah Jan and Nazish Jaffer: Help in data collection, drafting the manuscript and statistical analysis.

Shahnaz Imdad Kaher, Shaista Gul and Sana Ullah Gazozai: Did review, final approval of manuscript.

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