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Histopathological spectrum of renal Neoplasms and tumor like lesion in a tertiary care center

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Abstract

Introduction: Renal neoplasms are tumors that arise in renal tubular epithelium. These tumors account for about 2% of all cancer deaths. Benign renal neoplasm and tumor like conditions overlap with the malignant tumors. Accurate diagnosis is important for the treatment and prognosis of the patients.

Aim: To study histopathology of renal neoplasms and tumor like lesions. To differentiate malignant renal neoplasms from benign and tumor like conditions.

Materials and Methods: This retrospective study includes 31 cases admitted in our hospital. Patients who underwent nephrectomy for renal masses were enrolled in the study. Clinical data was obtained, grossing of the nephrectomy specimens and histological examination was done. Immunohistochemistry markers were used wherever necessary.

Results: Out of 31 cases studied, 21 were malignant, 3 were benign and 7 were categorized into tumor like conditions. The Panel of IHC markers used in this study were (CD 10, CK 7, CD 117).

Keywords: Renal Cell Carcinoma, Chromophobe RCC, Oncocytoma, Xanthogranulomatous pyelonephritis

Introduction

Renal neoplasms are heterogeneous group of neoplasm arising from the renal tubular epithelial cells. Most of the renal neoplasms are malignant. Renal cell carcinoma accounts for about 2% of all cancer. It mostly occurs in men in fifth and sixth decades of life. Most of the renal neoplasms are sporadic with few exceptions (VHL syndrome associated with clear cell RCC) [1, 2].

Accurate histological classification is very important in order to distinguish it from tumor like conditions and determine the treatment and the prognosis of the patients. Although histological diagnosis is straightforward in many cases, some cases require IHC to classify the subtype of RCC and to differentiate renal cell carcinoma from benign mimics [3].

Materials and methods

This study includes 31 cases during the time period of September 2016 to August 2018 admitted in SRM Medical College and Hospital. Patient who underwent nephrectomy for renal neoplasms and tumor like lesions were enrolled in the study. Relevant clinical data was obtained, grossing of the nephrectomy specimens and histological diagnosis were carried out on Haematoxylin and Eosin stained sections. The cases were reported according to CAP protocol. Finally Immunohistochemistry markers were used to confirm the diagnosis in certain cases.

Results

- The age of patients ranged from 29 to 70 years with a mean age of 53 years. In our study, the most common age group affected by renal neoplasm were 41 to 60 years seen in 19 cases (61%).
- Out of 31 cases studied, 19 cases were males constituting about 61% and 12 were females constituting about 39%.
- Flank pain was the most common clinical presentation found in 17 cases (55%), followed by abdominal mass in 6 cases (19%), haematuria in 2 cases (6.4%), flank pain with mass in one case (3.2%), flank pain with haematuria in one case (3.2%). Weight loss was observed in one case (3.2%) and three patients were found to be asymptomatic

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(10%).

- In our study out of 21 cases of malignant renal neoplasms analysed, majority of the tumour were found in the upper pole in about 43% of the cases, following which the most common site of location was lower pole which is accounting for about 33% of the cases.
- Among 24 cases of renal neoplasm, a tumor size ranging from 4cm to 7cm was noted predominantly in 15 cases (62%) followed by tumor size of more than 10 cm in 5 cases (21%).
- Out of 31 renal lesions, 7(23%) were found to be non-neoplastic (Xanthogranulomatous pyelonephritis) and 24(77%) were found to be neoplastic.
- Among 24 renal neoplasms, 21 cases (70%) were malignant and 3 cases (30%) were benign.
- Among 21 malignant renal neoplasms, the most common variant is clear cell renal cell carcinoma accounting for about 90% in 19 cases, followed by chromophobe RCC in 2 cases (10%).

Fig 4.1: Age distribution of patients

Age in years	Number of cases	Percentage
Less than or equal to 40	6	19.5
41-60	19	61
> 60	6	19.5
Total	31	100

Fig 4.2: Clinical presentation

Symptoms	No. of cases	Percentage
Flank pain	17	55%
Abdominal mass	6	19%
Haematuria	2	6.4%
Flank pain and haematuria	1	3.2%
Flank pain and mass	1	3.2%
Weight loss	1	3.2%
Asymptomatic	3	10%

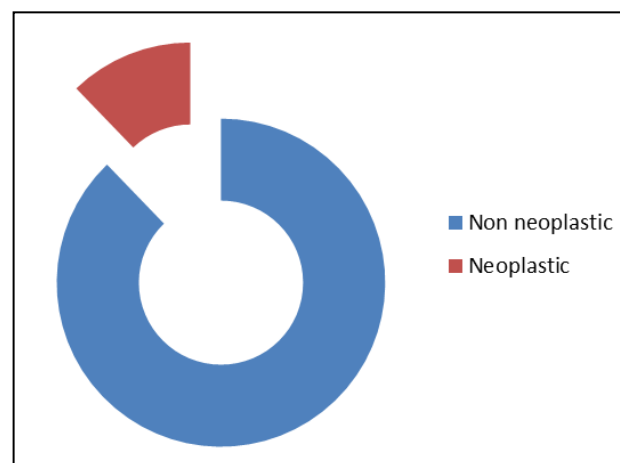


Fig 4.3: Distribution of neoplastic and non-neoplastic lesion

Grading	Clear cell RCC	Percentage
I	12	63%
II	2	11%
III	4	21%
IV	1	5%

Fig 4.3: Grading of clear cell RCC:

Among 19 cases of clear cell RCC, grade I was frequently found in 12 cases (63%) followed by grade III in 4 cases (21%).

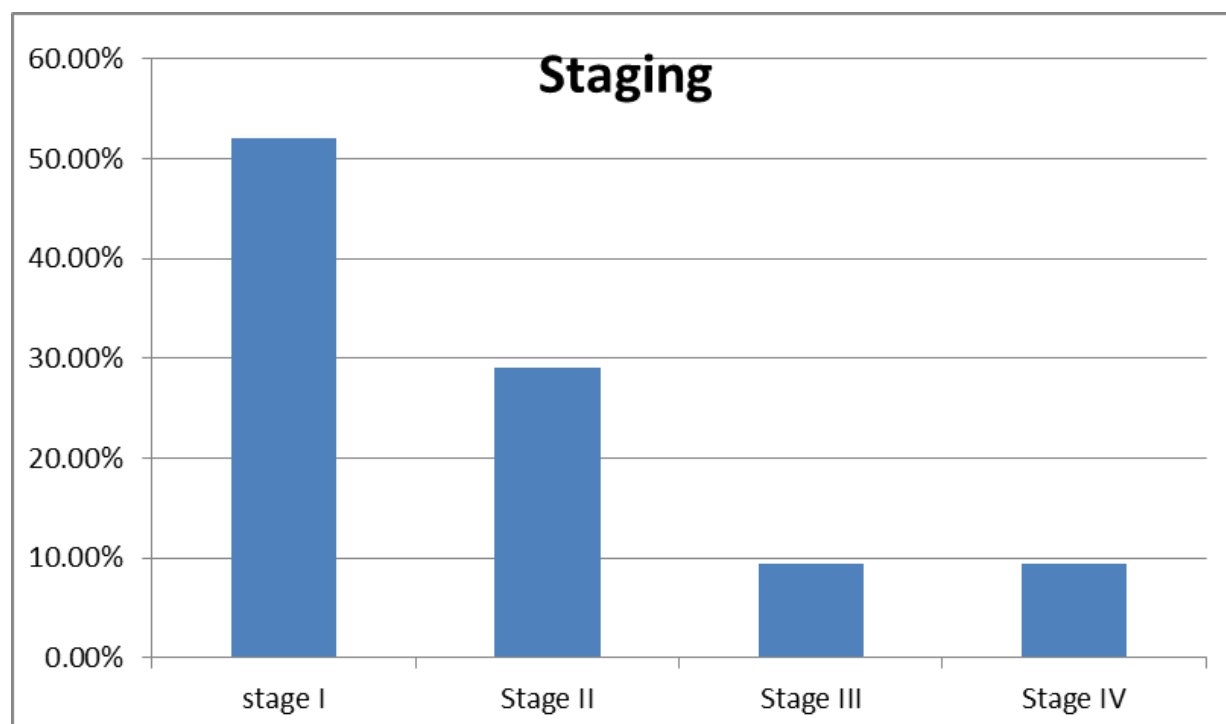


Fig 4.4: Staging of renal carcinoma Stage 1 accounts for about 11 cases (52%) followed by stage II in 6 cases (29%)

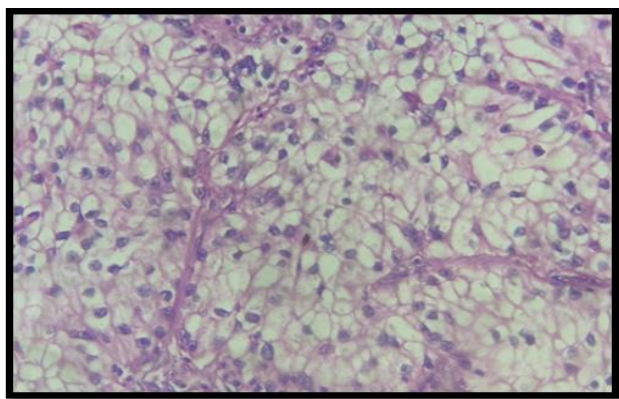


Fig 4.5: Clear cell renal cell carcinoma–Microphotograph shows tumor cells arranged in sheets traversed by fibrovascular septae. The cells are polygonal with clear to pale eosinophilic cytoplasm and mild to moderate pleomorphic central to peripherally placed nuclei. H & E (x400)

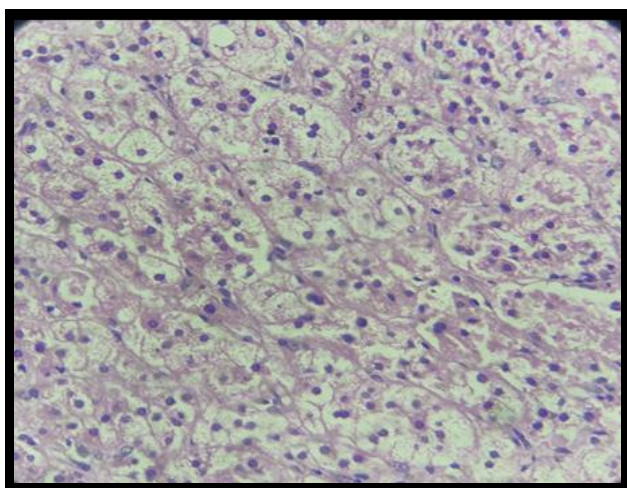


Fig 4.6: Chromophobe renal cell carcinoma. Microphotograph shows tumor arrangement in sheets. Tumor cells are large with well-defined borders with abundant pale to eosinophilic cytoplasm and round to oval hyperchromatic nuclei. H & E (x400)

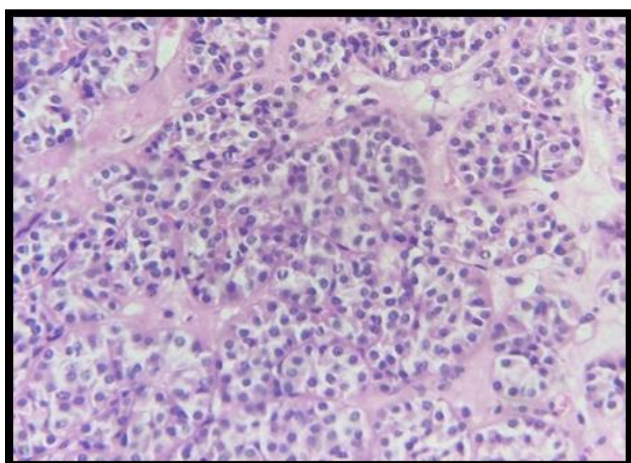


Fig 4.7: Oncocytoma. Microphotograph shows tumor arrangement in nests and alveolar pattern. The tumor cells are large with round, regular monomorphic nuclei with abundant granular eosinophilic cytoplasm. H & E (x400)

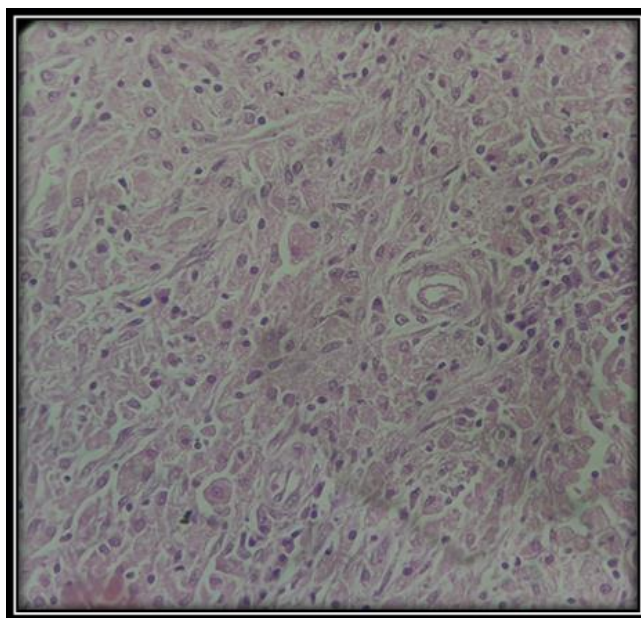


Fig 4.8: Xanthogranulomatous pyelonephritis. Microphotograph shows sheets of foamy macrophages, lymphocytes and plasma cells. H & E (x400)

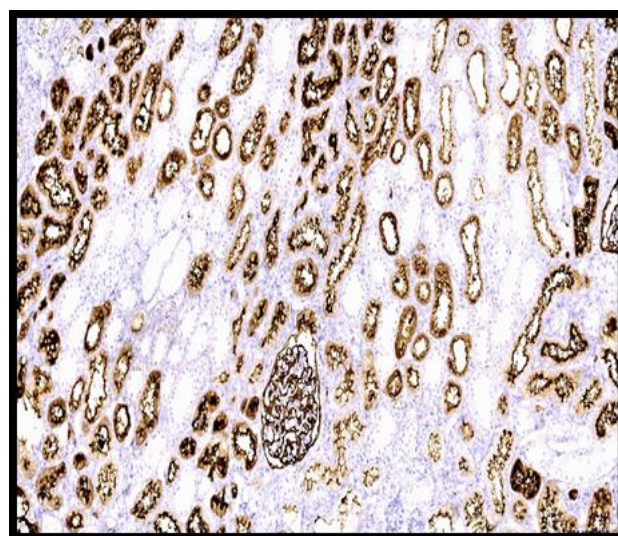


Fig 4.9: CD 10 positivity in clear cell RCC

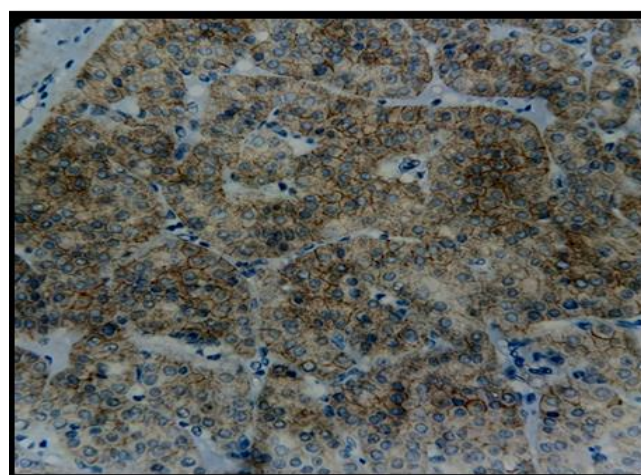


Fig 4.10: CD 117 positivity in Oncocytoma

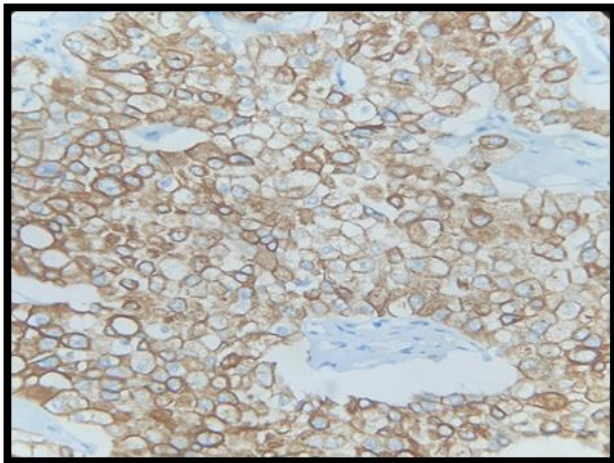


Fig 4.11: CK 7 Positivity in chromophobe RCC

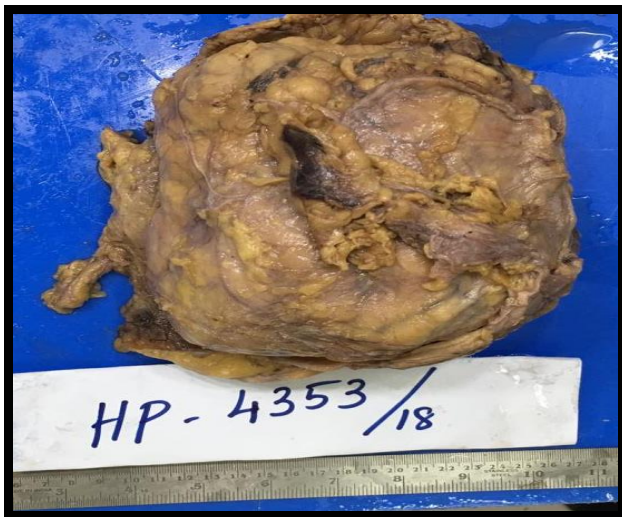


Fig 4.12: External surface of Oncocytoma- The kidney is enlarged and bosselated



Fig 4.13: Cut surface of oncocytoma shows tumor nodule which is mahogany brown in color with capsular invasion

Discussion

Renal neoplasms are heterogeneous group of cancers consisting of several subtypes of which clear cell renal cell carcinoma, papillary RCC and chromophobe RCC are the most common among the malignant. A wide variety of both

benign and malignant tumours arise from different components of the renal parenchyma, notably tubular epithelium. Renal cell carcinomas of different histologic subtypes differ in their prognosis and therapeutic response; therefore, it is important to classify malignant epithelial tumors of the kidney correctly, as well as to differentiate them from benign ones [3].

This study included 31 cases who underwent partial/radical nephrectomy in a tertiary care hospital. The mean age of the patients in our study was 53years (range 29-70yrs). In a study done by Yamakanamardi B *et al.* (n=32), mean age of the patients was 43.4 years (range 1 to 77years) similar to our study. In another study done by Bashir N *et al.* (n=184), the mean age of the patients was approximately 50 years, similar to our study [4, 5].

Males were commonly affected than females in about 19 cases (61%) and the M: F ratio was 1.5:1. This is similar to the studies reported by, Bashir N *et al.* (n=184) which is 1.7:1 [5].

The commonest clinical presentation observed in our study was flank pain in 17 cases (55%) followed by abdominal mass in 6 cases (19%), haematuria in 2 cases (6.4%) and 3 cases (6.6%) were asymptomatic. Least common clinical presentation noted was weight loss, flank pain with haematuria and flank pain with mass, one case each (3.2%). None of the patients were presented with the clinical trial of haematuria, flank pain and flank mass. Yamakanamardi B *et al.* (n=32) in his study showed flank pain as the commonest clinical presentation in 17 cases (53.1%) which is similar to our study [4].

Most of the renal tumors in our study arose from the upper pole of the kidney in 9 cases (43%). Study done by Yamakanamardi B *et al.* (n=32) observed tumors were located mostly in the upper pole in about 9 cases (28.1%). The tumor size in our study ranged from 4cm to 7cm in 15 cases (62%). In the study of Bashir *et al.* (n=184), there were similar findings with respect to tumor size [4, 5].

Out of 31 renal lesions, 7 cases (23%) were found to be non-neoplastic (Xanthogranulomatous pyelonephritis) whereas 24 cases turned out to be renal neoplasms (77%). Xanthogranulomatous pyelonephritis is a form of chronic pyelonephritis, classified as diffuse and focal forms and is characterized by the destruction of renal parenchyma and replacement with a chronic inflammatory infiltrate, foamy macrophages, Hemosiderin-laden macrophages. The exact etiology remains unknown. It occurs mostly in association with nephrolithiasis, urinary tract obstruction and chronic urinary infection. This disease mimics malignancy because the clinical and radiological findings are similar. The preoperative distinction between Xanthogranulomatous pyelonephritis and malignant renal tumors is often difficult [6].

The histological features of clear cell RCC and Xanthogranulomatous pyelonephritis often pose a diagnostic problem. This is because on microscopy clear cells may be confused with foamy macrophages. The differential diagnosis of Xanthogranulomatous pyelonephritis includes Malakoplakia, Clear cell RCC and Papillary RCC. Therefore we have utilized the IHC marker (CD 10) to distinguish the entities. Out of 19 cases of Clear cell RCC, CD 10 was expressed in all cases whereas it was found to be negative in Xanthogranulomatous pyelonephritis. In a study done by Avery AK *et al.* (n=62), 58 cases (94%) of clear cell RCC

were positive for CD 10 [7, 8].

The histological findings in our study revealed that out of 24 renal neoplasms, 21 cases (70%) were malignant neoplasms and 3 cases (30%) were benign. Similar observations were made by Madhu K *et al.* (n=14), observed malignant tumors in 10 cases (71.4%) [9].

Among the 21 malignant cases (70%), majority of the tumors were clear cell RCC in 19 cases (90%) followed by chromophobe RCC in 2 cases (10%). The findings were similar to study done by Reddy KD *et al.* in his subgroup analysis of (n=15) cases of which 13 cases (86.4%) were malignant and 2 cases (13.3%) were benign. In the malignant group 71.4% comprises clear cell RCC, one case (14.2%) each of Chromophobe RCC and sarcomatoid RCC [10].

One case in our study showed features of both chromophobe RCC with oncocytoma like areas on histopathological examination. Hales colloidal iron was performed and found to be negative in the same case. Immunohistochemistry was done and showed strong positivity for CD 117 and faint positivity for CK 7. This case was finally diagnosed as Oncocytoma based on both special stain (Hales colloidal iron) and IHC (CK 7). In the study by Ivan G *et al.* (n=38), 18 cases of oncocytoma and 20 cases of chromophobe RCC on histopathological examination were evaluated using special stain and immunohistochemistry. On this basis, he reclassified one case of chromophobe RCC as granular variant of clear cell RCC, two cases of atypical oncocytoma as chromophobe RCC and 2 cases of oncocytoma were reclassified as chromophobe RCC [11].

Chromophobe RCC especially with eosinophilia variant can also be confused with oncocytoma. Eosinophilia variant of chromophobe RCC is composed of tumor cells arranged in sheets with well-defined cell border and nuclei having wrinkled or raisinoid appearance. The ISUP grading system is not applicable for this type of RCC. It has a favorable prognosis and is associated with Birt-Hogg- Dube syndrome [11].

Out of 24 renal neoplasms, 3 cases (33.3%) were Oncocytoma. A Vinay KS *et al.* in his subgroup analysis of neoplastic cases (n=8) he reported one case of each (1.4%) oncocytoma, angiomyolipoma and another study done by Madhu Kumar *et al.* (n=14) found Angiomyolipoma in 2 cases (14.2%) [12].

Oncocytoma is considered as a benign mimic of RCC. These are the tumors with abundant granular eosinophilic cytoplasm with hyperchromatic round nuclei arranged in either tubular or in nested pattern and often difficult to differentiate from chromophobe RCC. The unusual features of oncocytoma includes microscopic vascular invasion and perinephric fat invasion. In some cases, it is difficult to diagnose oncocytoma accurately only with the help of histological findings. Hales colloidal iron is always not reliable since it is not specific. Therefore IHC plays a vital role in differentiating oncocytoma from chromophobe RCC [13, 14].

In our study, chromophobe RCC and Oncocytoma were evaluated using CK 7 and CD 117. Chromophobe RCC showed positivity for CK7 while CD 117 was negative. This finding was similar to the study done by Leroy *et al.* (n=17), where he reported strong positivity of CK 7 stain in chromophobe RCC.

In oncocytoma, CD 117 was positive in all 2 cases (100%).

This is comparable to the study done by Alshenawy HA, El-Shorbagy SH (n=55), CD 117 was positive in 91.7%. One case on IHC expressed both CD 117 (strong positive) and CK 7 (faint positive) [15].

In our study pathological grading using ISUP (International Society of Urologic Pathologists) grading system were carried out in 18 cases of clear cell RCC. Majority of the cases in our study, 12 (63%) were grade I, followed by grade III in 4 cases (21%). Grade II in two cases (11%) and grade IV in 1 case (5%). A study done by Aiman AN *et al.* found grade I neoplasms in 44.4% of the cases followed by grade III in 33.3% of the cases [16].

Staging was done for all malignant cases in our study. Most of the cases were predominantly detected at stage I in 11 cases (52%) followed by stage II in 6 cases (29%). In a study done by Agnihotri S *et al.*, majority of the tumors were stage I followed by stage II, similar to our study [17].

CD 10, a cell surface glycoprotein is strongly expressed in podocytes and proximal tubule brush border cells in a normal healthy kidney. Apart from its strong and diffuse expression in clear cell carcinoma, it is also expressed in various other cancers including ovarian cancer, pancreatic adenocarcinoma and hepatocellular cancers, indicating its importance in detecting metastatic cancers. However, it is essential to evaluate the possibility of using CD 10 in predicting the prognosis in metastatic cancers. High expression of CD 10 is noted in the proximal tubule cells in the apical section and occasionally in parietal and visceral epithelial cells. There is a need for molecular studies to evaluate this component, so as to evolve molecular targeted therapy in metastatic RCC [3, 18, 19].

Conclusion

The histological diagnosis of RCC is of utmost importance to distinguish neoplastic and non-neoplastic tumors of the kidney. Histological diagnosis helps in evaluating the prognosis and also aids in classification of the tumor based on their grades and stages. However, when the morphological features overlap, differential diagnosis becomes challenging and immunohistochemistry helps in deriving at accurate diagnosis. Overall, CD10, PAX8, CK-7 and CD117 are the most important biomarkers for RCC. Although each subtype of RCC shows positivity with more than one biomarker, the magnitude of expression and predominant site of expression help in differentiating one subtype from other. Moreover, certain biomarkers like CD10 and vimentin are useful in evaluating the metastatic RCC, and also aid in screening and assessing the prognosis of each subtype of RCC.

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