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A TERTIARY CARE HOSPITAL EXPERIENCE OF NON CLEAR CELL RENAL CELL CARCINOMA

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Abstract :
Renal cell carcinomas are a heterogenous group of tumours with varying prognosis. Most common histological type is clear cell variant constituting about 60 70 of all cases. The rest comprises a mixture of tumors of different histological types. Hence in this study we aimed to evaluate the clinical and histomorphological features of non -clear cell renal cell carcinomas. Among renal cell carcinomas diagnosed over a period of 6 years and two months, 40 cases (28.5) fell into the category of non-clear cell type. They included papillary, chromophobe, sarcomatoid, unclassified and collecting duct carcinomas, each constituting 16.4 , 3.5 , 5, 2.2 and 0.7 percentage respectively. Clinically most of them presented in Stage III and histologically most of them belonged to Fuhrman nuclear grade 2. Histological subtype, tumour staging, nuclear grading and microvascular invasion are useful for determining the prognosis, adjuvant therapy and for follow-up.

Keyword :
Renal cell carcinoma - non clear cell RCC papillary RCC chromophobe RCC - collecting duct carcinoma sarcomatoid carcinoma.

INTRODUCTION:

Cancer of kidney accounts to 2 % of total human cancer burden [1]. Around 2,08,500 new cases of kidney cancer are diagnosed in the world each year [2]. They are heterogenous tumours with different histological types, genetic characters with varying prognosis [2].

Malignant epithelial renal neoplasms in Heidelberg classification (1997) include clear cell, papillary, chromophobe, collecting duct and medullary variants of renal cell carcinoma [3,4]. The sarcomatoid carcinoma is a form of differentiation of each of the preceeding five primary histological variants of renal cell carcinoma and not a separate entity as previously thought. Final category of unclassified type includes those carcinomas whose

histological types. WHO -2004- updated classification include other variants such as multilocular cystic, mucinous tubular, spindle cell types, Xp11.2 translocation/TFE3 gene fusion tumor, t(6;11) translocation/ TFEB gene fusion tumor, carcinoma following neuroblastoma and lymphoepithelial carcinoma.

In this study we aimed to evaluvate the clinical and histomorphological features of subtypes of renal cell carcinoma other than the clear cell variant.

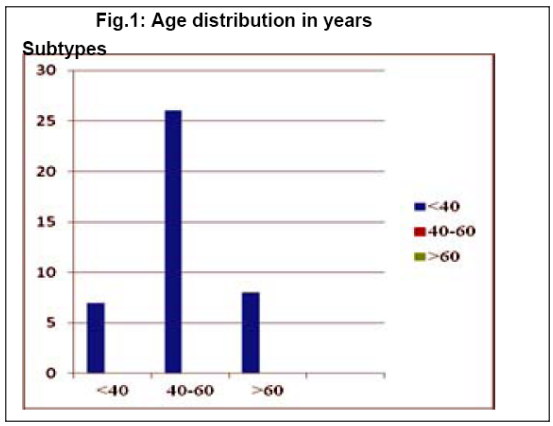
MATERIALS AND METHODS:

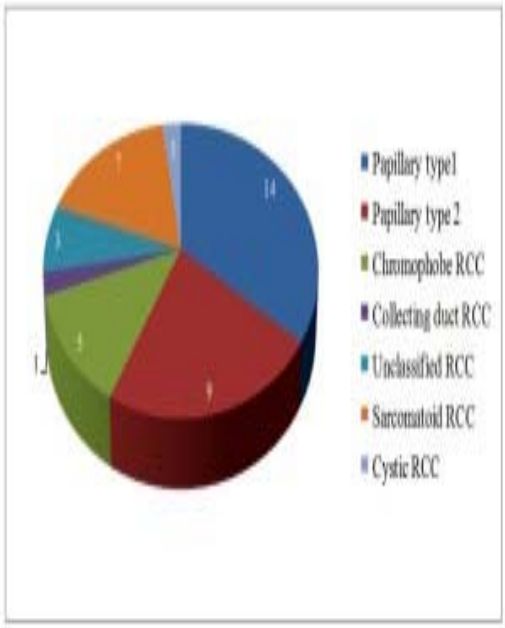
This is a retrospective study conducted on non-clear cell renal cell carcinomas diagnosed in the Institute of Pathology, Madras Medical College, during the year 2007 – February 2013. Surgical specimens received in the Institute of Pathology from patients who underwent radical nephrectomy were fixed in 10%formalin, subjected to paraffin embedding followed by 5 sections and staining by Hematoxylin & Eosin.

Clinicopathological features like age, sex, growth pattern, tumour stage, nuclear grade and invasion were evaluated from medical records and histopathological slides. Nuclear grading was based on Fuhrman system. Tumour staging was based on 2002 AJCC staging system.

Our study detected 141 cases of renal cell carcinoma for a period of 6years & two months. Non-clear cell RCC constituted 28.6 % (40 cases) of all cases. It was twice more common in males than in females as there were 27 males (67.5%) and 13 (32.5%) females in our study. Peak incidence was seen in the age group of 40-60 years (Fig.1).

Fig.1: Age distribution in years Fig.2. Histological Subtypes





In our study, clear cell RCC constituted 71.2%

Papillary RCC was the second most common type of RCC, constituting 16.4% (Fig.2).

5% of cases had sarcomatoid differentiation .

Chromophobe RCC constituted 3.5% and the Unclassified RCC 2.2%.

Collecting duct and cystic RCC each constituting 0.7%

Two cases of papillary RCC had sarcomatoid differentiation.

Two cases of Papillary RCC had . psammoma bodies.

25% of cases had necrosis.

One case of papillary RCC had osseous metaplasia.

Two cases of Sarcomatoid RCC had rhabdoid differentiation

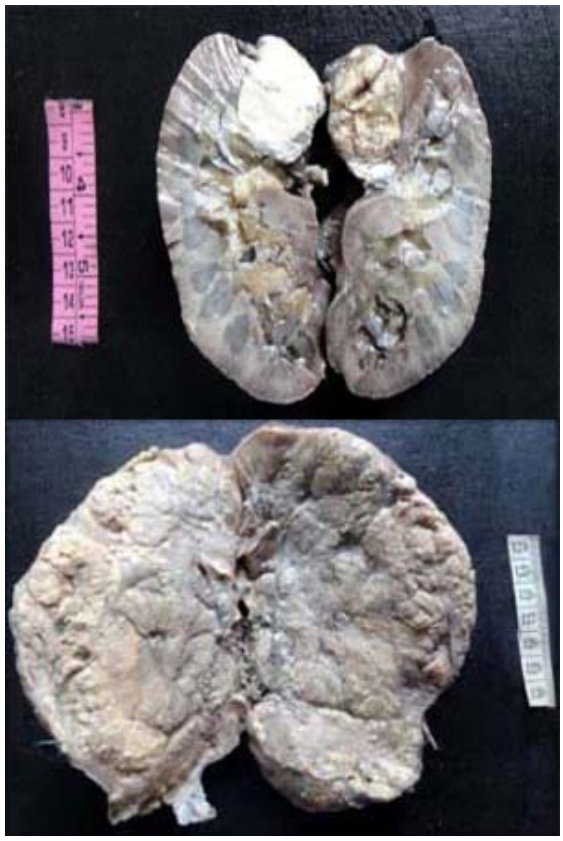


Figure 3 Figure 4 Figure 5 Figure 6 Figure 7 Figure 8 Figure 9 Figure 1o

Fuhrman Nuclear Grading:

GRADE I	II	III	IV
2 Cases	17 Cases	14 Cases	7 Cases

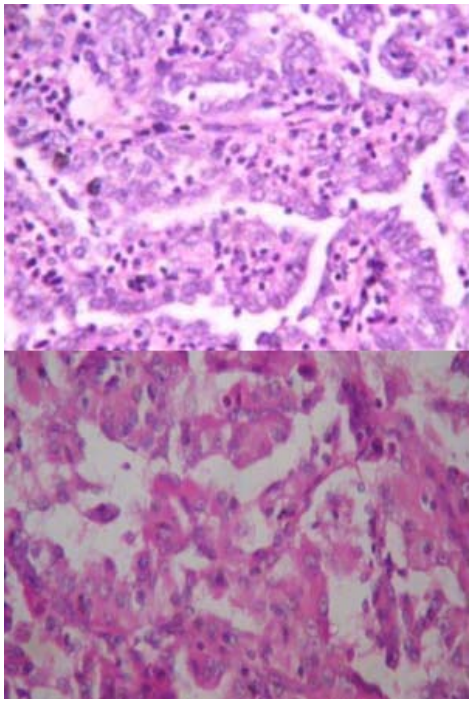
Capsular invasion	Vascular invasion	Renal pelvis involvement	Ureter invasion	Pericapsular, hilar fatty tissue infiltration	Lymphatic Invasion
23 cases (57.5%)	18 cases (45%)	5 cases (12.5%)	3 cases (7.5%)	8 cases (20%)	4 cases (10%)

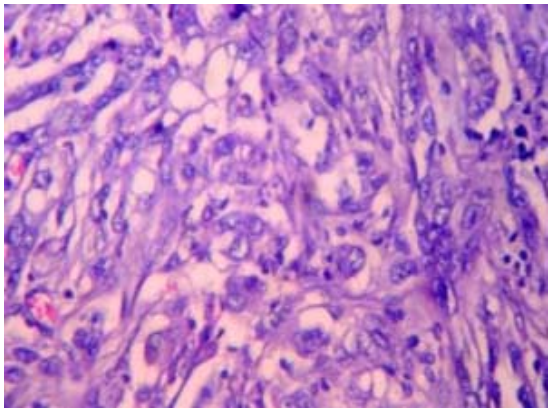
One case had adrenal invasion.

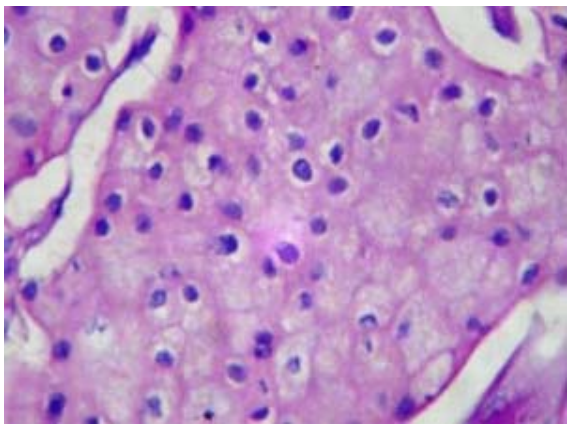
One case showed infiltration into adjacent colonic serosa.

Three cases were associated with chronic tubulo-interstitial disease.

STAGE I	STAGE II	STAGE III	STAGE IV
3 cases (7.5 %)	14 cases (35%)	22 cases (55%)	1 case (2.5%)







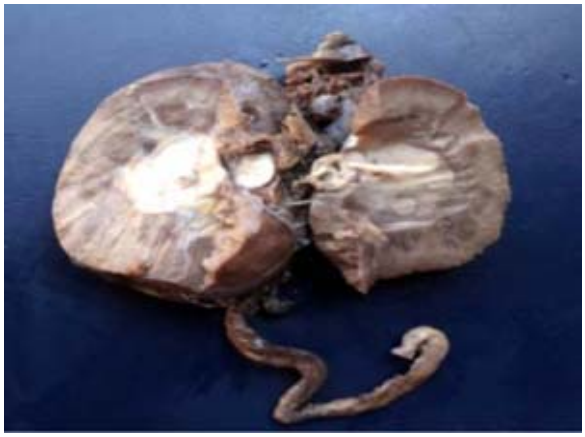


Figure 13

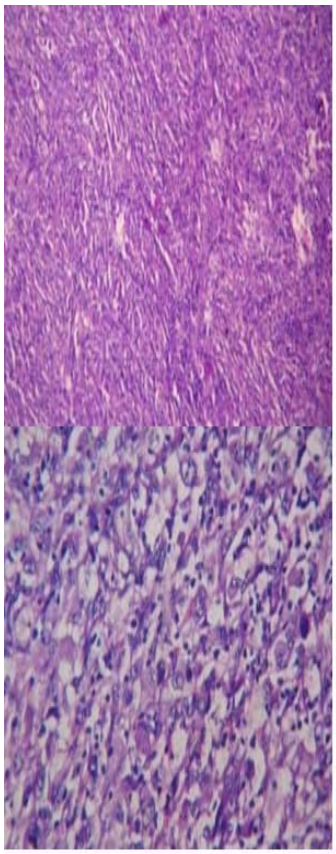


Figure 14

DISCUSSION:

Renal cell carcinomas are a family of carcinomas arising from renal tubular epithlium.These carcinomas have distinct morphologic features and arise through different constellation of genetic lesions [3]. Non clear cell RCC accounts for 20 % of all renal neoplasms [5].Papillary RCC is the most common of them and they are usually well circumscribed tumors with solid pale tan cut surface (Fig.3). A gray white friable necrotic growth occupying the entire renal parenchyma was found to be Type II papillary RCC (Fig.4). Type I papillary RCC is characterised by small cuboidal cells with scant cytoplasm covering thin papillae with a single line of round uniform nuclei & small nucleoli (Fig.5). Type II has papillae covered by large eosinophilic cells with pleomorphic nuclei and prominent nucleoli and nuclear pseudostratification (Fig.6). Type II was found associated with higher Fuhrman grade. Papillary RCC shows better prognosis than clear cell RCC [6,7].

Chromophobe RCC, the least aggressive of common renal cell carcinomas are well circumscribed globular solid brown tumors [7].We had a case with poorly circumscribed tumour with slightly lobulated surface occupying the lower and middle portions of kidney (Fig.7). Typical & Eosinophilic are the two variants. In the classical variant, the tumour cells have well defined thick cytoplasmic membrane, pale staining flocculant cytoplasm and thick walled blood vessels. Abundant eosinophilic granular cytoplasm, round nuclei, wrinkled nuclear membrane, perinuclear halo are characteristic of eosinophilic variant (Fig.8). Hales colloidal iron stains the cytoplasm blue thus helping to differentiate from oncocytoma (Fig.9).Collecting duct carcinomas arise from ducts of Bellini from inner medulla.They are solid tan white firm tumors occupying the renal pelvis and renal sinus (Fig.10).

They have mixed features of adenocarcinoma & transitional cell carcinoma. Microscopically they have tubules with branching lumens embedded in an abundant stroma (Fig11). Tubules are lined by cells with small amounts of cytoplasm and lining by hobnail cells is characteristic of collecting duct carcinoma (Fig.12).

Sarcomatoid component can occur in all histologic subtypes of RCC and it indicates an aggressive behaviour [8]. Diagnostic criterion requires a distinct malignant spindle cell component occupying a minimum of one low power field (Fig.13).

Unclassified tumours comprise a highly heterogenous group of tumours constituted by sarcomatoid carcinoma without recognisable epithelial elements, tumours with mucin production, mixtures of epithelial and stromal elements and unrecognisable cell type. Microscopically, they may show round to spindle cells with scant cytoplasm and hyperchromatic nuclei and some show vesicular nuclei with small basophilic nucleoli (fig.14).

CONCLUSION:

Non-clear cell renal cell carcinomas encompass a variety of tumour types of different histology and behaviour. Chromophobe and papillary RCC have less propensity for vascular invasion and have good prognosis than clear cell RCC. Sarcomatoid differentiation is a poor prognostic factor. Collecting duct carcinoma also has poor prognosis. Since the histologic subtypes have variable prognosis – the importance of subclassification is highlighted in our study. It is worthwhile to remember that accurate histological diagnosis is necessary for correct treatment and to assess

prognosis & follow-up especially in this era of molecular classification of tumours with availability of targeted therapies, for some of these tumours.

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