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Original Article

Expression and Subcellular Distribution of Membrane-Organizing Extension Spike Protein (Moesin/ MSN) are Associated with Epithelial-Mesenchymal Transition in Clear Cell Renal Cell Carcinoma

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Abstract:

Background: Clear cell renal cell carcinoma (ccRCC) is an aggressive urological malignancy. The aggressive potential of ccRCC is attributed to epithelial-mesechymal transition (EMT), which acquire the neoplastic cells more invasive properties. Membrane-Organizing Extension Spike Protein (Moesin/ MSN) plays an important role in controlling cellular morphology and motility. **Aim:** Evaluation of moesin expression in ccRCC and determining its cellular distribution, and then correlate its expression with certain clinico-pathological variables. **Methods:** Archived formalin-fixed, paraffin-embedded ccRCC tissue blocks from 55 patients were obtained and sectioned. Two tissue sections from each block were stained with anti-moesin immunohistochemical (IHC) antibody. **Results:** Moesin showed membranous localization in all enrolled cases which was associated with high tumor grades (p= 0.004), advanced stages (p< 0.001), capsular and perirenal fat invasion (p= 0.001& p< 0.001) and presence of lymph nodes invasion (p< 0.001). Less differentiated cases of ccRCC with high WHO/ISUP grades were significantly associated with male sex (p= 0.023), presence of perirenal fat invasion (p< 0.001) and advanced tumor stages (p= 0.003). Cytoplasmic redistribution of moesin was detected in 30 cases. Cytoplasmic moesin was correlated with capsular and perirenal fat invasion (p= 0.033 & p= 0.001), high tumor grades (p< 0.001), advanced tumor stages (p< 0.001) and presence of nodal metastasis (p= 0.002). **Conclusion:** Membranous overexpression of moesin and its cytoplasmic redistribution were detected in aggressive and less differentiated cases of ccRC

Keywords: Clear cell renal cell carcinoma, Epithelial-mesenchymal transition, Moesin, immunohistochemistry.

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Lists of abbreviations:

ccRCC: clear cell renal cell carcinoma, **EMT:** Epithelial-mesenchymal transition, **Moesin/MSN:** Membrane-Organizing Extension Spike Protein, **IHC:** immunohistochemical and/or immunohistochemically, **RCC:** Renal cell carcinoma, **ERM**: ezerin, radixin and moesin, **APCs:** antigen presenting cells, **H&E:** Hematoxylin and Eosin, **WHO/ISUP:** World Health Organization/International Society of Urological Pathology. **TNM:** Tumor-Node-Metastasis, **AJCC:** American Joint Committee on Cancer, **DAB:** diaminobenzidine, **PBS:** Phosphate Buffered Saline.

Introduction

Renal cell carcinoma (RCC) is a broad term that includes a heterogenous group of malignant neoplasms which arise from renal tubular epithelial cells. RCC represents about 85% of all primary renal neoplasms. It is associated with high mortality rates that reach about 40%, so it represents the most lethal urological malignancy .(1)

RCC represents about 2% of all worldwide human malignant neoplasms. However, the incidence of RCC varies widely in different parts of the world; RCC is the 7th most prevalent cancer in Western countries and there is a recent increase in the annual incidence of RCC, there. In Egypt; RCC is ranked for the 14th in terms of its incidence. (2)

RCC is classified into different subtypes, based on tumor histological and biological features. This classification is of utmost therapeutic and prognostic significance. The most common variants of RCC are clear cell RCC, papillary RCC and chromophobe RCC .(3)

Clear cell renal cell carcinoma (ccRCC) is the most common variant of RCC; it represents about 85% of all cases of RCC and it originates from proximal convoluted tubular epithelium. Most cases of ccRCC arise sporadically (about 95% of cases), while in about 5% of cases of ccRCC; there is a hereditary background where ccRCC occurs as a part of hereditary syndromes as von Hipple-Lindau disease and tuberous sclerosis .(2)

The most common genetic alteration detected in more than 90% of cases of ccRCC is loss of the short arm of chromosome 3. Other less frequent genetic aberrations include loss of short arm of chromosome 8 or gain of long arms of chromo somes 5 and 7. (1)

Metastatic potential of any malignant epithelial neoplasm is initiated by interactions between the neoplastic epithelial cells and the surrounding mesenchyme. These interactions result in degeneration of the mesenchymal tissue and its subsequent permeation by neoplastic epithelial cells. An epithelial- mesenchymal interaction necessitates changes in the morphology of the neoplastic epithelial cells and development of cellular spikes that allow mesenchymal permeation. (4, 5)

Epithelial-mesenchymal transition (EMT) is a biological process in which the epithelial cells lose their morphological features as cell-cell junctions and cell polarity. Instead, they become spindle and acquire invasive and migratory potentials.

EMT is classified into 3 distinct types; each type has specific functions and is triggered by certain signals. Type 1 EMT is met in embryogenesis and organogenesis, in this type the cells don't have the capacity to induce fibrosis or tissue invasion. Type2 EMT is responsible for tissue regeneration and wound healing, herein the cells can produce fibrosis, but can't produce tissue invasion. Type 3 EMT is found in malignant neoplasms, this type is responsible for both invasive and metastatic potentials seen in malignant tumors. (5, 6)

Normally; intracellular actin filaments are arranged in thin contractile fibrils, while in EMT; these actin filaments are reorganized as thick contractile bundles at the leading migratory surface. However, Linkers between cell membranes and intracellular actin assembly are needed to effectively induce changes in cell morphology. (7)

Membrane-Organizing Extension Spike Protein (Moesin/ MSN) is a 75 KDa protein; encoded by *MSN* gene located on chromosome Xq12. Moesin is a member of ezerin, radixin and moesin (ERM) family of proteins. Moesin and its related ERM proteins act as bridges between cell membranes and intracellular actin assembly, so moesin and its related ERM proteins control cell morphology, cell polarity, intercellular adhesions and cell motility. (8,9)

Physiologically; moesin is necessary for integration between T lymphocytes and antigen presenting cells (APCs), moesin is also involved in diabedesis of leukocytes and endothelial cell migration which is seen in tissue repair. (10)

It has been found that increased moesin expression is necessary for remodeling of actin assembly .[7] Overexpression of moesin has been detected in different human malignancies and such overexpression was found to be associated with unfavorable prognosis. [11-14]

Aim of the study:

The aim of this study is to evaluate moesin expression in ccRCC and determine its cellular distribution, then correlate levels of moesin expression with certain clinical and pathological features as patients' ages, sexes, tumor grades, pathological tumor stages, capsular, perirenal fat and regional lymph nodes invasion.

Materials and Methods:

Clinical data and specimen collection:

The present work was applied on archived formalin-fixed, paraffin embedded tissue blocks of renal cell carcinoma that were belonged to 55 patients who were admitted to Sohag University Hospital because of loin/ back pain, from January 1st, 2017 to December 31st, 2021. Radiological evaluation revealed renal neoplasms and patients underwent radical nephrectomies. Tissue blocks and clinical data were obtained from the archive at Pathology Laboratory, Sohag University Hospital.

Inclusion criteria included all cases of ccRCC, tissue blocks with material adequate for IHC evaluation and all cases with accessible clinical data. Exclusion criteria included all cases of renal neoplasms other than ccRCC, tissue blocks with destroyed or inadequate material, cases with poor clinical data, or cases who received pre-operative chemotherapy.

The study was confirmed by the Ethical Committee of Sohag University (approval **ID: Soh-Med-23-09-5PD**), then it was registered in Clinical Trials.gov PRS (Clinical Trials.gov **ID: NCT06055660**). From each ccRCC-laden tissue block, two tissue sections were obtained; one tissue section was stained by Hematoxylin and Eosin (H&E) stain to confirm the diagnosis of ccRCC and determine tumor grade according to World Health Organization/International Society of Urological Pathology (WHO/ISUP) grading of clear cell and papillary renal cell carcinoma .[15]

Data concerning capsular, perirenal fat and/or nodal invasion was obtained from archived pathology reports. The studied cases of ccRCCs were staged according to the Tumor-Node-Metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC), 8th edition). [16]

The other tissue section was stained IHC by anti-human moesin antibody.

Immunohistochemical staining of moesin

Avidin-Biotin complex approach was applied. Tissue sections were mounted on Silane-coated slides, and then they were de-paraffininzed and re-hydrated. Endogenous peroxidase activity was blocked by covering sections with hydrogen peroxide (H2O2) for 15 minutes. Tissue sections were then boiled in sodium citrate buffer solution, pH 6, for 20 minutes at 92°C in order to expose cell surface epitopes. Sections were incubated overnight with anti-moesin antibody; a mouse monoclonal primary antibody, in a dilution of 1:100, (Catalog# MSN/492, Concentrated form, NOVUS Biologicals, USA). The reaction results were visualized by immersing the sections in diaminobenzidine (DAB) for 10 minutes at room temperature (ScyTek, P.O. Box 3286- Logan, Utah 84323, USA). Nuclear counterstaining was achieved through Harris' Hematoxylin. Sections were dehydrated and cleared in ascending grades of ethyl alcohol followed by xylene. Each staining run harbored positive and negative control sections to ensure that staining procedures were working properly and the positive signals were specific. The positive control was obtained from human splenic tissues as recommended in data sheet. Negative control was achieved by replacement of anti-Moesin antibody by Phosphate Buffered Saline (PBS).

Evaluation of moesin immunostaining

Moesin expression was detected as brownish, granular membranous with or without cytoplasmic staining. Membranous expression of moesin was scored according to moesin intensity and percentage of its expression in tumor cells. The intensity of moesin staining was scored as: 0 (negative staining), 1 (weak expression), 2 (moderate expression) and 3 (high expression). The percentage of moesin-positive cells was calculated as: 0 (0%), 1 (<10%), 2 (10-50%), 3 (51-80%) and 4 (>80%positive cells). The ultimate score was obtained by multiplying the intensity score with the percentage of positive cells. The resulting score was classified into: negative (0), low (1-4), moderate (6, 8) and high

staining [9, 12). 17] Cytoplasmic moesin was evaluated as either positive or negative. [18]

Statistical analysis

Data was analyzed by SPSS Statistical Software version 25 (SPSS Inc., Chicago, IL, USA). Descriptive analysis was performed. Quantitative data was represented as mean ± standard deviation (SD), median and range. Qualitative data was reported as frequencies and percentages. Categorical data was analyzed using Chi-square (X^2) test. P value was considered significant if it was < 0.05.

Results

Patients' characteristics

The current study included 55 patients with ccRCC. Their ages ranged from 49 to 75 years old. They were 32 men and 23 women. On applying tumor grading system according to WHO/ISUP; Grade 1 was detected in 22 cases, Grade 2 in 20 cases, Grades 3 & 4 in 5 and 8 cases, respectively. Capsular invasion was found in 46 cases, while perirenal fat invasion was confirmed in 30 cases **(Figure.1)**. According to the Tumor-Node-Metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC), 8th edition; 14 cases showed pathological tumor stage 1 (pT1), pT2 and pT3 were found in 11 and 30 cases respectively. Positive regional nodal involvement by tumor cells was detected in 38/55 ccRCC cases **(Table. 1)**.

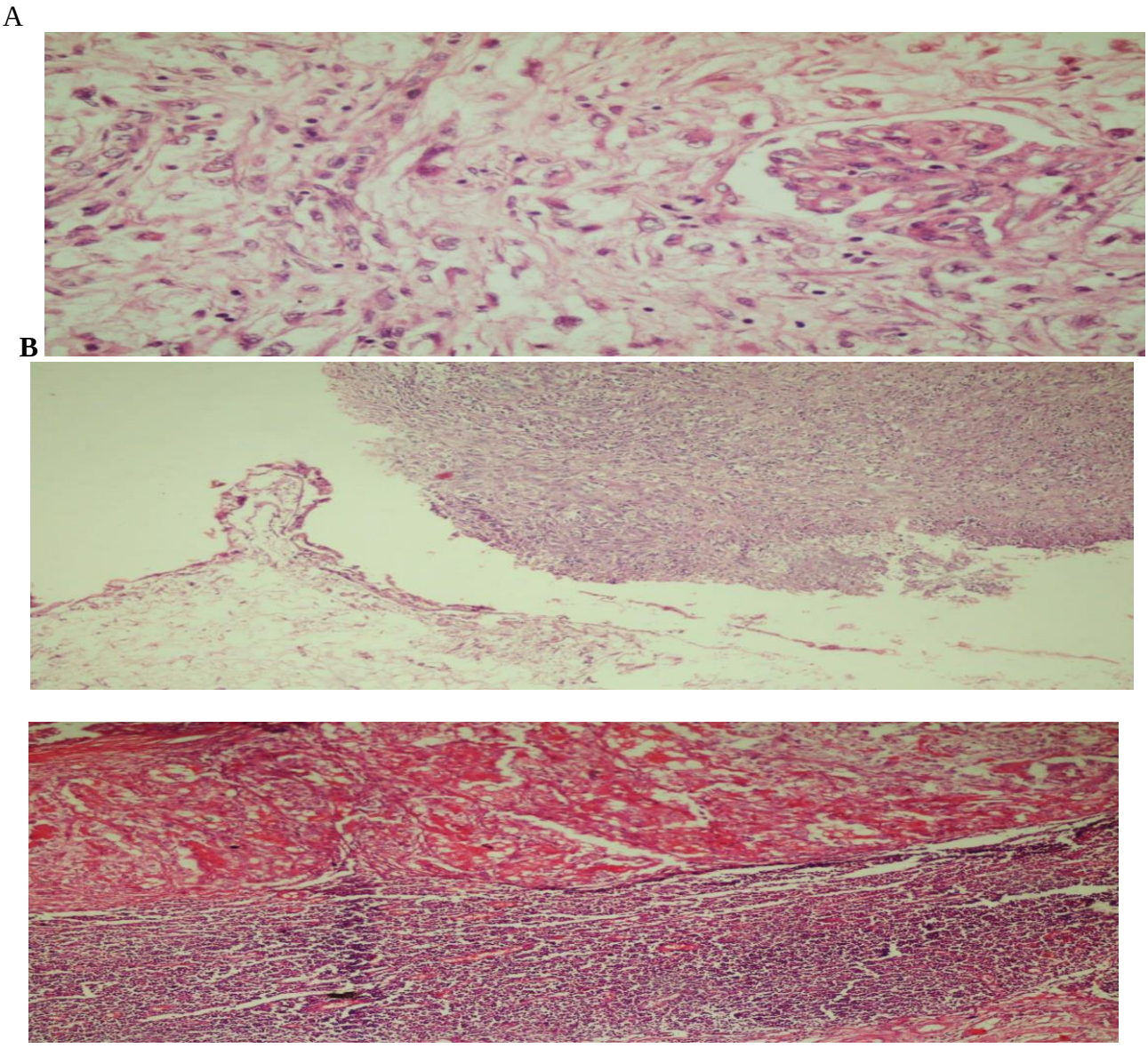

Fig 1: a) ccRCC, WHO/ISUP Grade IV infiltrating the renal tissue with entrapped renal glomeruli, X;200, **b)** perirenal fat invasion, X;100, **c)** metastatic deposits of ccRCC in a lymph node, (H&E-stain, x200).

Table.1: Clinicopathological criteria of the studied ccRCC cases.

Clinicopathological parameter	Number of cases (N)	Percentage (%)
Age		
<60	30	54.5%
≥60	25	45.5%
Sex		
Male	32	58.2%
Female	23	41.8%
Capsular invasion		
Positive	46	83.6%
Negative	9	16.4%
Peri-renal fat invasion		
Positive	30	54.5%
Negative	25	45.5%
WHO/ISUP Grade		
Grade 1	22	40%
Grade 2	20	36.4%
Grade 3	5	9.1%
Grade 4	8	14.5%
pT stage		
I	14	25.5%
II	11	20%
III	30	54.5%
Nodal status		
Positive	38	69.1%
Negative	17	30.9%

On correlating WHO/ISUP grades of the studied cases of ccRCC with their clinicopathological parameters, there was a statistically-significant relationship between WHO/ISUP grades and sex of the studied cases; 76.9% of WHO/ISUP grades 3&4 were found in men, while women represent about 23.1% of WHO/ISUP grades 3&4 (p= 0.023).

Invasion of the peri-renal fat seemed to be statistically associated with high WHO/ISUP grades; 72.7% of WHO/ISUP Grade 1 tumors didn't show perirenal fat invasion, while 75% of cases of Grade 4 tumors showed peri-renal fat invasion (p< 0.001).

High tumor grades of the studied ccRCC cases were associated with advanced pathological tumor stages; 78.6% of cases of pT1 had Grades 1&2 tumors, while 69.2% of Grades 3&4 ccRCC cases were staged as pT3 (p= 0.003), **(Table. 2)**.

Table 2: Correlation between the WHO/ISUP grading system and other clinicopathological parameters of studied cases.

Clinicopathological parameter	WHO/ISUP grades				*P* value
	Grade 1 N= 22	**Grade 2 N= 20**	**Grade 3 N= 5**	**Grade 4 N= 8**	
Age					
<60	14 (63.6%)	11(55.0%)	0 (0.0%)	5 (62.5%)	0.074
≥60	8 (36.4%)	9 (45.0%)	5 (100.0%)	3 (37.5%)	NS
Sex					
Men	9 (40.9%)	13 (65.0%)	2 (40.0%)	8 (100.0%)	0.023*
Women	13 (59.1%)	7 (35.0%)	3 (60.0%)	0 (0.0%)	
Capsular invasion					
Positive	15 (68.2%)	19 (95.0%)	5 (100.0%)	7 (87.5%)	0.079 NS
Negative	7 (31.8%)	1(5.0%)	0 (0.0%)	1 (12.5%)	
Perirenal fat invasion					
Positive	6 (27.3%)	18 (90.0%)	3 (60.0%)	6 (75.0%)	
Negative	16 (72.7%)	2 (10.0%)	2(40.0%)	2 (25.0%)	<0.001**
pT stage					
I	9 (40.9%)	2 (10.0%)	2 (40.0%)	1 (12.5%)	
II	8 (36.4%)	2 (10.0%)	0 (0.0%)	1(12.5%)	0.003**
III	5 (22.7%)	16 (80.0%)	3 (60.0%)	6 (75.0%)	
Nodal status					
Positive	11 (50.0%)	17 (85.0%)	3 (60.0%)	7 (87.5%)	0.055 NS
Negative	11 (50.0%)	3 (5.0%)	2 (40.0%)	1 (12.5%)	

p value was calculated by Chi-square test; *= significant, **= highly significant, and NS= non-significant.

Immunohistochemical detection of of Moesin:

All examined cases of ccRCC showed membranous moesin expression, with variable staining intensities. Low membranous moesin expression was detected in 6 cases, while moderate and high moesin membranous immunostaining were found in 16 & 33 cases, respectively **(Figure.2)**.

Intensity of moesin membranous expression was statistically associated with capsular invasion; 95.7% of ccRCC cases that showed capsular invasion in their H&E- stained sections, revealed moderate to high moesin membranous expression in their immunostained sections (p= 0.001).

As regards to peri-renal fat invasion; all ccRCC cases that showed low moesin membranous expression, didn't show peri-renal fat invasion (p< 0.001).

Intense moesin membranous expression was correlated with high tumor grades; all cases with WHO/ISUP Grades 3&4 ccRCC showed moderate to high moesin membranous expression, while all ccRCC cases that showed low moesin membranous expression were belonged to WHO/ISUP grades I&II (p= 0.004).

All of the studied cases of ccRCC that showed positive involvement of their regional lymph nodes, showed moderate to high moesin membranous expression (p< 0.001).

Advanced pathological tumor stages seemed to be statistically-associated with enhanced moesin expression; all cases of ccRCC with low moesin membranous expression, were staged as pT1, while all cases of pT2 and pT3 showed moderate to high moesin membranous expression (p< 0.001) **(Table. 3)**.

Cytoplasmic redistribution of moesin immunoostaining was detected in 30 cases of ccRCC **(Figure.3)**. Cytoplasmic moesin expression was correlated with the presence of capsular invasion (p= 0.033), perirenal fat invasion (p= 0.001), high WHO/ISUP grades (p< 0.001), advanced pathological tumor stages (p< 0.001) and the presence of lymph nodes metastasis (p= 0.002), **(Table. 4)**.

Table 3: Correlation between membranous expression of moesin and the studied clinicopathological parameters.

Clinicopathological parameter	Moesin membranous expression			*P* value
	Low N= 6	Moderate N= 16	High N= 33	
Age				
<60	4 (66.7%)	6 (37.5%)	20 (60.6%)	0.257
≥60	2 (33.3%)	10 (62.5%)	13 (39.4%)	
Sex				0.168
Men	2(33.3%)	12 (75.0%)	18 (54.5%)	
Women	4 (66.7%)	4 (25.0%)	15 (45.5%)	
Capsular invasion				
Positive	2 (33.3%)	13 (81.3%)	31 (93.9%)	0.001**
Negative	4 (66.7%)	3 (18.7%)	2 (6.1%)	
Peri-renal fat invasion				
Positive				
Negative	0 (0.0%)	5 (31.3%)	28 (84.8%)	<0.001**
	6 (100.0%)	11 (68.7%)	5 (15.2%)	
WHO/ISUP grades				
Grade 1	6 (100.0%)	10 (62.5%)	6 (18.2%)	0.004**
Grade 2	0 (0.0%)	4 (25.0%)	16 (48.5%)	
Grade 3	0 (0.0%)	1 (6.25%)	4 (12.1%)	
Grade 4	0 (0.0%)	1 (6.25%)	7 (21.2%)	
pT stage				
I	6 (100.0%)	7 (43.75%)	1 (3.1%)	<0.001**
II	0 (0.0%)	7 (43.75%)	4 (12.1%)	
III	0 (0.0%)	2 (12.50%)	28 (84.8%)	
Nodal status				
Positive	0 (0.0%)	4 (25.0%)	26 (78.8%)	<0.001**
Negative	6 (100.0%)	12 (75.0%)	7 (21.2%)	

p value was calculated by Chi-square test; *= significant, **= highly significant, and NS= non-significant.

Table 4: Correlation between cytoplasmic expression of moesin and the studied clinicopathological parameters.

Clinicopathological parameter	Moesin cytoplasmic expression		*P* value
	Positive N= 30	Negative N= 25	
Age			
<60	16 (53.3%)	14 (56.0%)	0.843.
≥60	14 (46.7%)	11 (44.0%)	
Sex			
Men	20 (66.7%)	12 (48.0%)	0.162.
Women	10 (33.3%)	13 (52.0%)	
Capsular invasion			
Positive	28 (93.3%)	18 (72.0%)	0.033 *
Negative	2 (6.7%)	7 (28.0%)	
Peri-renal fat invasion			
Positive			0.001**
Negative	24 (80.0%)	9 (36.0%)	
	6 (20.0%)	16 (64.0%)	
WHO/ISUP Grade			
Grade 1	0 (0.0%)	22 (88.0%)	< 0.001**
Grade 2	17 (56.7%)	3 (12.0%)	
Grade 3	5 (16.7%)	0 (0.0%)	
Grade 4	8 (26.7%)	0 (0.0%)	
pT stage			
I	3 (10.0%)	11 (44.0%)	<0.001 **
II	3 (10.0%)	8 (32.0%)	
III	24 (80.0%)	6 (24.0%)	
Nodal status			
Positive	26 (86.7%)	12 (48.0%)	0.002**
Negative	4 ((13.3%)	13 (52.0%)	

p value was calculated by Chi-square test; *= significant, **= highly significant, and NS= non-significant.

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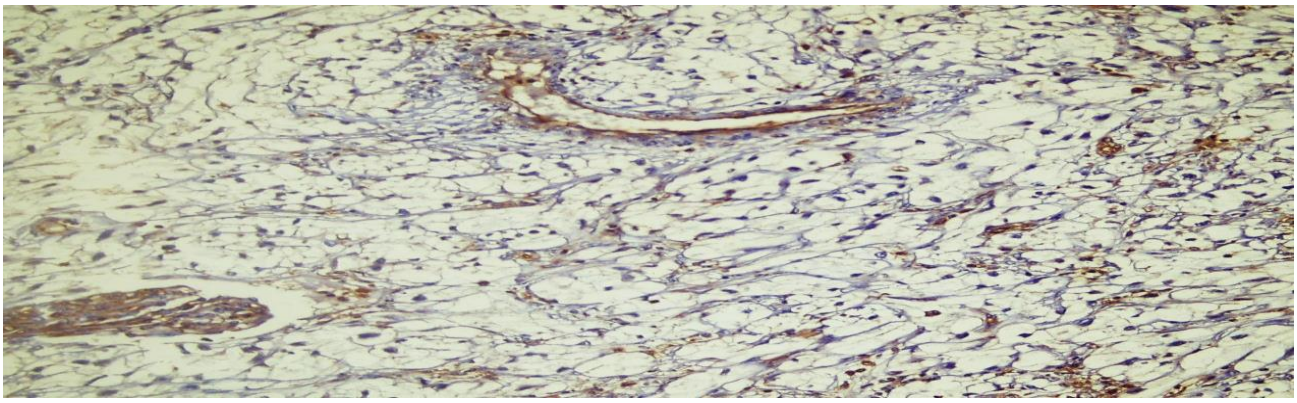

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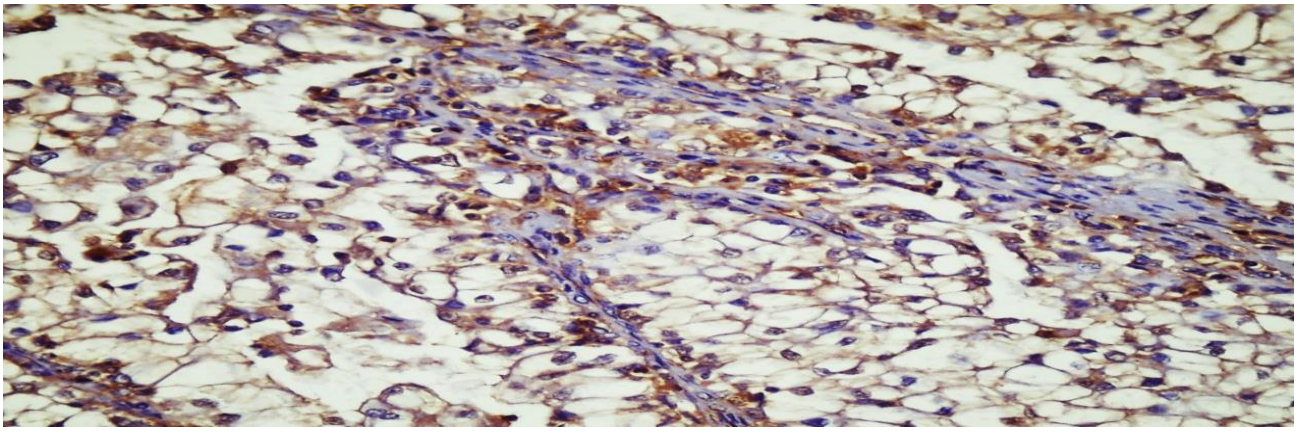

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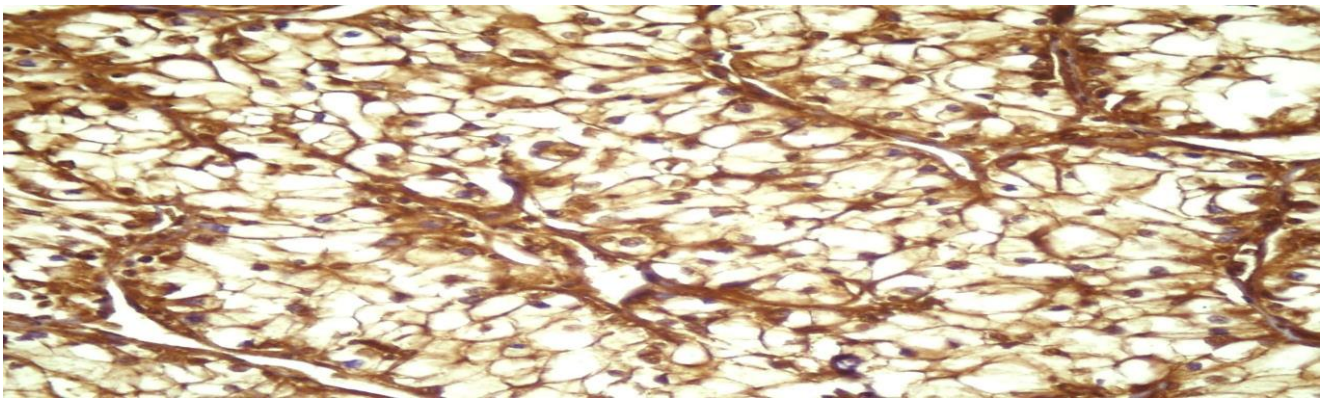

Fig 2: a) ccRCC shows normal/physiological expression of moesin in vascular endothelial cells and glomerular corpuscles, **b)** low and **c)** high moesin expression in ccRCC, (moesin immunostaining, x200).

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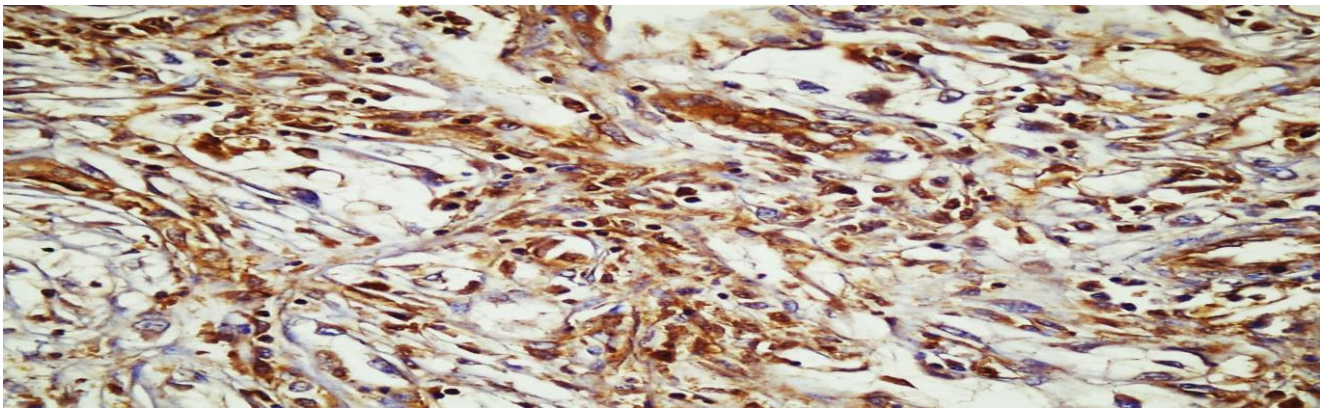

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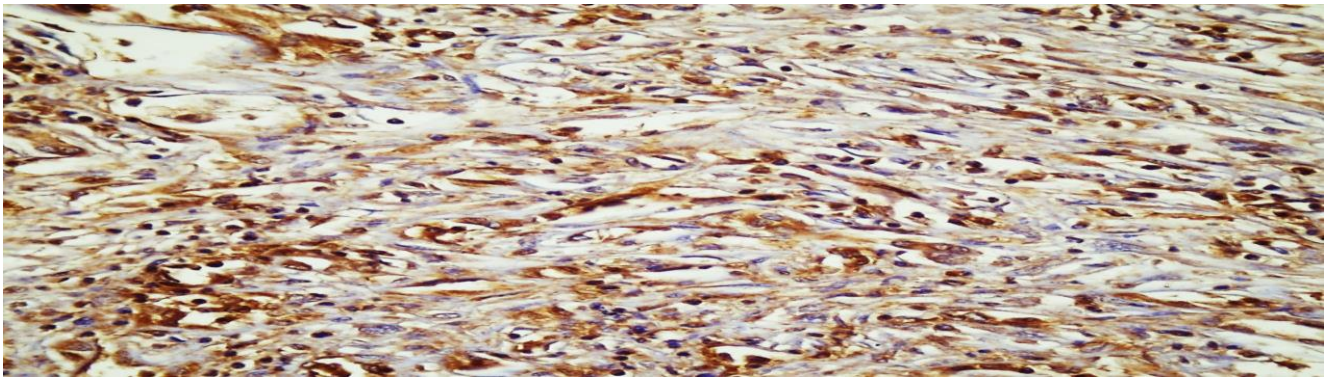

Fig 3: a) & **b)** Cytoplasmic redistribution of moesin in advanced grades of ccRCC, (moesin immunostaining, x200).

Discussion:

Adult renal cell carcinoma is a primary renal malignant epithelial neoplasm that showed an obvious increase in its incidence in recent years. There are many subtypes of RCC. However, ccRCC is the most prevalent subtype, accounting for about 85% of all cases of adult RCC. [1-3]

In the current study, we detected a slight predominance of ccRCC in men compared with women. Sex differences in RCC have been attributed to several genetic, lifestyle and environmental factors; smoking and hypertension, which are two important risk factors for RCC, are more prevalent in men than women [19]. Obesity is a lifestyle risk factor for RCC in both men and women. However, the association between visceral obesity and RCC is stronger in men than in women .[20] ***You et al***. have studied expression of androgen receptors (ARs) in 51 cases of ccRCC, including 36 men and 15 women; they

found high expression of ARs in aggressive and metastatic ccRCC. They concluded that ARs are associated with vasculogenic mimicry (VM); a condition in which the tumor cells form their own vascular channels without endothelial lining, such VM is helpful for tumor cells to invade extracellular matrix and metastasize to distant sites .[21]

Grading of any carcinoma has an important prognostic significance. There have been many grading systems for RCC. However, Fuhrman grading system has been adopted as the most frequently used grading system in clinical practice. Despite its popularity, the original Fuhrman grading system didn't have any prognostic value. Fuhrman grading system may show a prognostic significance only when grades are grouped into 2 tier system. Another obstacle met in applying Fuhrman grading system is that it depends on 3 distinct parameters; assessment of nuclear size, evaluation of nuclear shape and determination of nucleolar prominence, any of these parameters is subjected to interobserver variability. The World Health Organization/International Society of Urological Pathology Conference held in Vancover in 2012 has adopted a new prognostically-significant grading system for ccRCC and papillary RCC. It is a 4 tier grading system that depends only on nucleolar prominence for the first three grades, and presence of rhabdoid/sarcomatoid features for the 4^{th} grade. This WHO/ISUP grading system seemed to be easier with less interobserver variations. [15&19]

In the current study, we correlated different WHO/ISUP grads with different clinical and pathological parameters. High WHO/ISUP grads were detected more in men than in women, this could be attributed to role of sex hormones. ***Yu et al.*** have evaluated the role of estrogen in RCC cell lines, they found that estrogen receptor β (ERβ) inhibits tumor cells proliferation and migration through stimulation of apoptotic genes; they considered that ERβ acts as a potential tumor suppressor gene. [22]

Furthermore, less differentiated cases of ccRCC were associated with advanced pathological stages and presence of perirenal fat invasion, this could be explained on the basis that less differentiated tumors have more aberrant genes acquire the neoplastic cells more invasive properties.

RCC is an aggressive neoplasm with high incidence of metastasis and relapse. The ideal therapy for localized RCC is surgical resection. Treatment of metastatic RCC is dependent mainly on several targeted therapeutic modalities. [19]

ERM proteins act as bridges between cortical actin assembly and cell membranes. ERM proteins are concentrated at certain cell surface structures as microvilli, filopodia and cell-adhesion sites. Normal expression of ERM proteins is organ and tissue specific. Moesin is normally expressed in pulmonary and splenic tissues; it is also detected in vascular endothelial cells .[23, 24]

Moesin plays a pivotal role in controlling cell morphology and motility. However, dysregulated moesin expression is involved in proliferation, dissemination and metastasis in many malignant neoplasms. [11-14]

In the current study, moesin expression was increased in cases of ccRCC with high WHO/ISUP grades, advanced tumor stages, positive regional nodal metastasis, capsular and perirenal fat invasion. Moesin expression has been evaluated in 91 patients with hepatocellular carcinoma; enhanced moesin expression was positively associated with metastasis and poor prognosis in those patients. [25]

Two additional studies have evaluated the role of moesin in oral squamous cell carcinoma; they detected that high moesin expression was associated with marked decrease in overall survival. [9, 12]

In the present study, redistribution of moesin from membranous to cytoplasmic regions has been noticed in less differentiated and metastatic cases of ccRCC. This was keeping with **Wang et al.** they tested expression of moesin in 322 cases of breast carcinoma, included 23 cases with metaplastic breast cancer (MBC), they found overexpression of moesin in most cases of MBC compared with non-MBC cases. Furthermore, in non-MBC cases; moesin expression was positively associated with cases of breast cancer with higher tumor grades and poor overall survival. [14]

This could be explained on basis that moesin localization to the cell membranes ensures integrity of intercellular junctions and maintains cellular polarity, while its redistribution from membranous to cytoplasmic regions may weaken intercellular adhesions and may augment invasive potential. [7]

Conclusion:

Clear cell renal cell carcinoma is an aggressive neoplasm with high metastatic potential. Membranous overexpression of moesin and its cytoplasmic redistribution were detected in aggressive, invasive and less differentiated cases of clear cell renal cell carcinoma, this shows role of moesin in epithelial-mesenchymal transition. Targeting of moesin by novel anticancer therapeutic medicateons may improve tumor progression and overall survival.

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