Summary and Conclusions

Bladder cancer is considered the fourth highest new cancer diagnosis in men in the United States.

In Egypt, the urinary bladder malignancy represents a high incidence of 26.4% of total malignant tumors.

While transitional cell carcinoma is the predominating histopathologic type of cancer bladder in western countries, squamous cell carcinoma is the most common type in Egypt representing an incidence of 58.4% of all bladder tumors.

Bladder tumors are classically diagnosed by cystoscopy. The procedure represents the highest valuable standard for detection and monitoring; but it is invasive and expensive.

Urinary cytology is a long established non-invasive and very effective in diagnosing high grade lesions but it has a low sensitivity in detecting grade I tumors which are the most common type of UCC.

The limitations of cytology and cystoscopy, both for primary diagnosis and monitoring of patients after UCC has been removed led to the development of new urinary bound tests for the early detection of UCC.

Among these, there are NMP22 which has recently been approved by the Food and Drug Administration for bladder cancer evaluation and UBC antigen which measures urinary fragments of cytokeratins 8/18.

The aim of this work is to evaluate urinary bladder cancer (UBC) antigen and urinary nuclear matrix protein 22 (NMP22) as new non-invasive tumor markers in diagnosis of squamous cell carcinoma of the bladder.

This study included 60 patients diagnosed by histopathology following cystoscopic biopsy to have squamous cell carcinoma of the bladder (group I), 15 patients with other benign urological conditions (group II) and finally 15 apparently healthy controls (group III).

The patients and control persons were subjected to the following:

-Complete history taking including:

Age, sex and presence of hematuria.

-Clinical examination:

Patients of group I were subjected to PR examination and cystoscopy, and the cystoscopic findings with confirmatory biopsies were considered the gold standard for diagnosis.

-Laboratory assays:

Urine samples from the patients and control persons were subjected to the following:

1. Complete urine examination especially for pus cells and RBCs.
2. Urinary creatinine measurement.
3. Detection of NMP22.
4. Detection of urinary bladder cancer (UBC) antigen.

The results of this study were summarized as the following:

1- At a cutoff value of greater than 7 U/ml (determined from ROC curve) for NMP22; maximum sensitivity (76.67%), specificity (80%), positive predictive value (88.46%), negative predictive value (63.16%) and accuracy (77.78%) were observed.

2- Upon correction of NMP22 for creatinine concentration, the threshold from ROC analysis was 5 U/mg. creatinine. The sensitivity (83.33%) and specificity (83.33%) were slightly higher but not significantly different from the uncorrected estimate.

3- Group I showed highly significant increase in median NMP22 as compared to both group II and group III ($P < 0.001$).

4- At a cutoff value of greater than 7.5 µg/l (determined from ROC curve) for UBC, maximum sensitivity (85%), specificity (85%), positive predictive value (92.73%), negative predictive value (74.29%) and accuracy (85.56%) were observed.

5- Upon correction of UBC for creatinine concentration, the threshold from ROC analysis was 6 µg/gm. creatinine with no change in both sensitivity and specificity.

6- Group I showed highly significant increase in median UBC as compared to both group II and group III ($P < 0.001$).

7- UBC was found to be more sensitive (85% versus 76.67%) and more specific (86.67% versus 80%) than NMP22.

8- When calculating the combined measurement of UBC and NMP22, we found NMP22 to increase the sensitivity (88.3%), specificity (86.7%), positive predictive value (92.9%), negative predictive value (78.8%) and accuracy (87.8%) of UBC.

9- When correlating all parameters with each other we found that:

-There was positive significant correlation between NMP22 and UBC among patients in group I.

-There was positive non-significant correlation between NMP22 and UBC among patients in group II.

-There was negative non-significant correlation between NMP22 and UBC among healthy subjects in group III.

In conclusion:

The preliminary results of this study indicate that the urinary bladder cancer antigen and nuclear matrix protein 22 can potentially be

incorporated into a biomarker profile for the detection and monitoring of bladder cancer.

There was a statistical difference in UBC and NMP22 in patients with evidence of cancer bladder compared to those with no evidence of the disease. The higher sensitivity and specificity of UBC suggest that it performs better than NMP22 and it may replace cytology as an adjunct to cystoscopy n diagnosis and follow up of bladder cancer cases.