

## Research Article

# Value of urinary microalbumin test in cancer patients with borderline serum creatinine level

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## ABSTRACT

**Background:** Microalbuminuria (MA) is an early sign of incipient renal damage and cancer patients are at the risk of developing kidney diseases due to the use of nephrotoxic chemotherapeutic agents.

**Methods:** A pilot study of urinary microalbumin on 41 patients with borderline serum creatinine was carried out at regional cancer centre of North-East India during the period from June to August 2014. The patients whose serum creatinine levels were between 1.2 mg/dl to 1.3 mg/dl were considered as borderline for the present study. The assays were performed with a dimension Rxl max random access biochemistry analyzer.

**Results:** Out of 41 cases, 22 (53.6%) had MA, M:F = 1.75, <45 years 3 (13.6%) patients, in 45 years - 65 years 17 (77.2%) patients, and >65 years 2 (9.0%) patients were detected with urinary microalbumin. Chi square test showed P = 0.695 (Fisher's exact P value).

**Conclusion:** Testing of urinary microalbumin can be done in cancer patients with borderline serum creatinine level in order to identify patients at risk of developing kidney disease.

**Keywords:** Borderline creatinine, Cancer patients, Microalbumin, Urine

## INTRODUCTION

Microalbuminuria (Albumin in urine) is defined as a condition where the kidneys leak small amount of albumin in the urine due to high permeability for albumin in the kidneys. A microalbumin urine test determines the presence of albumin in urine and it is a traditional standard measure for evaluating glomerular filtration.<sup>1</sup> Recently the detection and determination of microalbumin in urine have gained momentum in various fields of medicine. Microalbumin in urine is an early sign of incipient renal disease especially in diabetic patients,

can identify patients who are susceptible to develop nephropathy, and is a good biochemical marker of progression of kidney disease.<sup>2</sup> Detection of microalbumin in urine specifies the need for intensive treatment in various diseases like diabetes mellitus, hypertension or any type of nephropathy and is a good predictor of cardiovascular diseases as well. Apart from its use in monitoring renal function in diabetes mellitus, hypertension and cardiovascular diseases, microalbumin in urine can also be used in monitoring patients receiving nephrotoxic drugs, like the use as a urinary renal biomarker in clinical trials.<sup>3</sup> Thus, screening of

microalbumin in urine can be used in identifying patients receiving nephrotoxic drugs who would be benefitted from renal protective therapy. One such group of patients is the cancer patients who receive chemotherapy or radiotherapy as a form of treatment which are very nephrotoxic. Generally the patients receiving chemotherapy or radiotherapy are screened for any renal function loss by tests like serum creatinine and blood urea but its main disadvantage is that serum creatinine and blood urea levels remains within normal limits until a large number of renal glomerular cells are damaged. Thus, in these patients testing of microalbumin in urine can be very useful in detecting incipient renal disease. Thus, proper measures can be taken to reduce the load on kidneys if microalbumin in urine is detected at an early stage in cancer patients receiving nephrotoxic chemotherapeutic agents.

The aim of the present study was to investigate microalbumin in urine in cancer patients whose serum creatinine level was normal but at the borderline limit i.e. between 1.2 mg/dl to 1.3 mg/dl.

## METHODS

A pilot study was carried out at regional cancer centre of North-East India during the period from June 2014 to August 2014. This study was approved by the institutional review board. Patients that were sent for the laboratory test for serum creatinine along with other tests and the patients whose serum creatinine levels were between 1.2 mg/dl to 1.3 mg/dl (patients with normal serum creatinine values but borderline levels) were sorted out for the study. The assays were performed with a Dimension Rxl max random access biochemistry analyzer which quantitatively measures albumin in human urine. The selection of patients was irrespective of stage at diagnosis, grade and site of the disease, duration of treatment and diabetic status.

### Principles of the procedure

The microalbumin test method is based on a particle-enhanced turbidimetric inhibition immunoassay adapted to the dimension clinical chemistry system which allows direct quantitation of albumin in urine sample. The microalbumin reagent contains a particle reagent consisting of synthetic particles with human albumin bound to the surface. Aggregates to these particles are formed when a monoclonal antibody (Ab) to human albumin is introduced. Albumin present in the sample competes with the particles for the antibody, thereby decreasing the rate of aggregation. Hence, the rate of aggregation is inversely proportional to the concentration of albumin in the sample. The rate of aggregation is measured using bichromatic turbidimetric reading at 340 and 700 nm. The reagents used were liquid and ready to use. Sampling, reagent delivery, mixing, processing are automatically performed by the dimension Rxl max system. The expected value of microalbumin in urine is

less than 20 mg/L (when tests were done with a dimension Rxl Max analyzer with ready to use reagents from the same company). For the calibration of the microalbumin method on the dimension Rxl max system, microalbumin calibrator of the same company was used as buffered aqueous solution containing weighed in quantities of human serum albumin.

## RESULTS

The study was carried out among 41 patients with various cancers who were sent to the central laboratory for doing serum creatinine test along with other tests. Age range was 30-91 years. 29 (70%) patients were male and 12 (30%) were females. Majority of the cases in this study that have normal creatinine value but in the borderline area were in the age group of 45 - 65 years of age (70.7%) as shown on Table 1. It was seen that out of 41 cases, 22 cases (53.6%) of the cases that underwent treatment of any form was detected with urinary microalbumin. Of the patients who were detected with urinary microalbumin 14 (64%) were males and 8 (36%) were females. All the cases were categorized into 3 age groups: 1) less than 45 years, 2) between 45 and 65 years, and 3) above 65 yrs. In the age group of less than 45 years 3 (13.6%) patients were detected with urinary microalbumin, between the age group of 45 years - 65 years, 17 (77.2%) patients were detected with microalbumin, and in the age group above 65 years 2 (9.0%) patients were detected with urinary microalbumin (Table 1). Chi square test showed  $P = 0.695$  (Fisher's exact p value) as shown in Table 1.

**Table 1: Age group and distribution of patients detected with urinary microalbumin.**

Age group	Number of cases (n1=41) # (%)	Cases (n2=22) detected with urinary microalbumin		P value
		Yes # (%)	No # (%)	
<45	7 (17.1)	3 (13.6)	4 (18.1)	0.695
45-65	29 (70.7)	17 (77.3)	12 (54.4)	
>65	5 (12.2)	2 (9.1)	3 (13.6)	

n1 = total cases, n2 = cases with urinary microalbumin, #numbers, %percentages

## DISCUSSION

The detection of urinary microalbumin is being increasingly accepted as an important clinical outcome predictor in case of diabetes mellitus and it improves the prediction of the future outcome in diabetes.<sup>4</sup> Microalbuminuria is also associated with an increased risk of cardiovascular and renal disease with diabetes mellitus and hypertension.<sup>5</sup> Also, urinary albumin excretion is associated with a worse cardiovascular risk profile and is a concomitant indicator of early target organ damage.<sup>6</sup> Microalbuminuria also represents a state of inflammation, both systemic and local.<sup>7,8</sup> This state of

inflammation may affect the kidneys due to the administration of nephrotoxic drugs in patients receiving cancer treatment, especially in patients who had a borderline creatinine level. Thus, doing a urinary microalbumin test in those patients can be very beneficial in detecting patients who are at a higher risk of developing future renal disease. Microalbuminuria is a significant risk marker for mortality in NIDDM, independent to other risk factors examined and its presence can be regarded as an index of increased cardiovascular vulnerability and a signal for vigorous efforts at correction of known risk factors.<sup>9</sup> Microalbumin is a marker of cardiovascular disease risk and should be monitored per guidelines once or twice a year for progression to macroalbuminuria and kidney disease development, especially if plasma glucose, lipids and blood pressure are at guideline goals.<sup>10</sup> There is also a relationship between insulin resistance and microalbuminuria in non-diabetic subjects that is partially dependent on blood pressure, glucose level and obesity.<sup>11</sup>

Thus any cancer patients specially elderly and obese, irrespective of stage, grade and duration of treatment, if detected with urinary microalbumin can have precautionary measures, so as to decrease the risk of developing kidney disease. In microalbuminuria due to diabetes mellitus there was no role of gender in its prevalence.<sup>12</sup> Though, the sample size was very small in the present study, but it showed a slight male preponderance in the occurrence of microalbuminuria (M:F = 1.75). In our present study 54% of patients had urinary microalbumin and associated borderline serum creatinine levels. Majority of patients in this study that were positive for urinary microalbumin were in 45-65 years of age. However, in the present study there was no association of microalbuminuria across three age groups ( $P < 0.05$ ). Microalbuminuria and metabolic syndrome are associated in a large, nationally representative cohort, possibly due to early renal effects of hypertension, and it may be useful to consider microalbuminuria as a component of the metabolic syndrome.<sup>13</sup> Metabolic syndrome is a disorder of energy utilization and storage diagnosed by a co-occurrence of three out of five of the following medical condition i.e. abdominal (central) obesity, elevated BP, Elevated fasting plasma glucose, high serum triglyceride and low high density lipoprotein. As some elderly cancer patients may also suffer from metabolic syndrome, testing of urinary microalbumin in such patients can be found to be helpful in preventing further kidney damage. In a multivariate model, which adjusted for age, sex, performance states, histological type and TNM stage, microalbuminuria continued to be a significant predictor of survival and an increased prevalence of microalbuminuria has been demonstrated in patients with lung cancer.<sup>14</sup> It is seen from this study that the percentage of patients detected with urinary microalbumin in cancer patients with borderline serum creatinine level receiving cancer treatment of any form ranges between 40-60%. A recent study has shown the use of tumor biomarkers in cancer patients with impaired

renal function should be done with precaution.<sup>15</sup> This highlights the importance of detecting early kidney damage by testing urinary MA in cancer patients for interpreting the results of tumor biomarkers.

A major limitation of the present study is the sample size. Further large scale studies are desired in this regard to know the exact beneficial effect of doing microalbumin test in cancer patients receiving nephrotoxic drugs, so as to prevent future kidney disease.

## CONCLUSION

Testing of urinary microalbumin can be done in cancer patients with borderline serum creatinine level who are receiving treatment. This shall help in identifying patients who are at a higher risk of developing kidney disease.

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