

PROTEINURIA

By Alpana Pasricha

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Qualitative testing - Dipstick, dye impregnated paper strip -1-4+

Quantitative testing

Urine protein to creatinine ratio - spot urine sample

Urine albumin to creatinine ratio

Urine PER - Protein excretion rate - timed urine sample

Urine Albumin excretion rate



Proteinuria and Nephrotic Syndrome

Covert - Microalbuminuria - (KDIGO 2012) Moderately increased albuminuria -
Urine ACR 30 - 300mg/gm

Overt - Macroalbuminuria - (Severely increased Albuminuria) Urine ACR
>300mg/gm, Urine PC >200mg/gm.

Nephrotic Range Proteinuria

Urine PC > 3000mg/gm, 3500gm/day

Nephritic Syndrome

Proteinuria with hematuria



Proteinuria Evaluation : Caveats

Dipstick - Semi Quantitative, Affected by Specific Gravity

Insensitive to light chains and globulins

False Positive : Alkaline Urine, contrast agents, cephalosporins

Myoglobin and hemoglobin

Gross Hematuria - Urinary tract Bleeding can give 1+ proteinuria on dipstick

Transient Proteinuria - Fever, Vigorous exercise, UTI



ALBUMINURIA:

New Definitions- KDIGO-2012

	<i>UACR**</i>	<i>Dipstick</i>
<i>Normal</i>	<10	Negative
<i>Mildly Increased</i>	10-<30	Neg-Trace
<i>Moderately Increased*</i> 30-300		Trace-1+
<i>Severely Increased</i>	>300	2+-4+
<i>(Nephrotic</i>	3000+	3-4+)

(* formerly micro-albuminuria; **UACR=mg albumin/gm creatinine in an spot early morning urine specimen)

Proteinuria vs Albuminuria ??



Proteinuria vs Albuminuria??

Proteinuria screening identifies an additional 16% of patients missed by ACR

Proteinuria screening would miss the mild - moderately increased albuminuria



Proteinuria vs Albuminuria??

Urinary albumin excretion above normal but below the dipstick detection (30 - 300mg/day)

Numerous studies show strong association of UACR with progressive CKD, CV events and all cause mortality

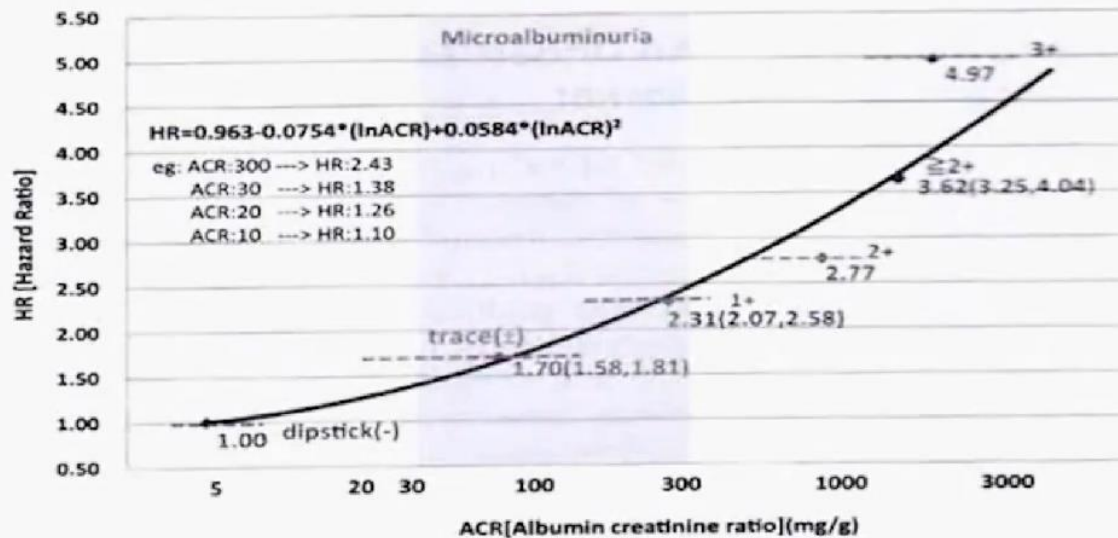
In Diabetics - predictive of eventual Diabetic Nephropathy.

In Cardiovascular disease - Microalbuminuria - strong and independent risk factor for CVD



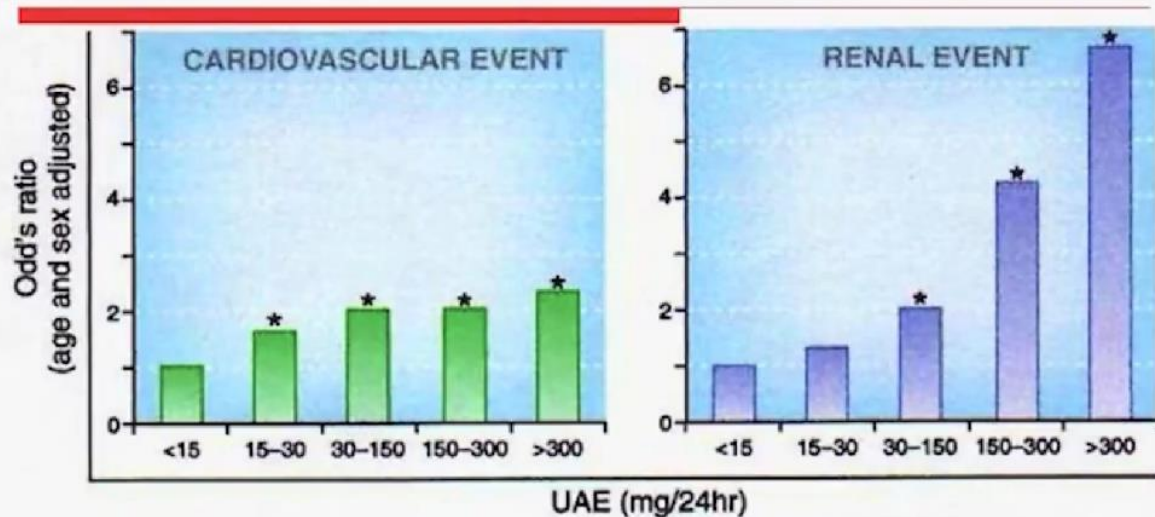
Albuminuria, Urinary Dipsticks and All-Cause Mortality

(Wen, et al AJKD 58:1-3, 2011)



Albuminuria and the Risk of CVD and ESRD: PREVEND Study

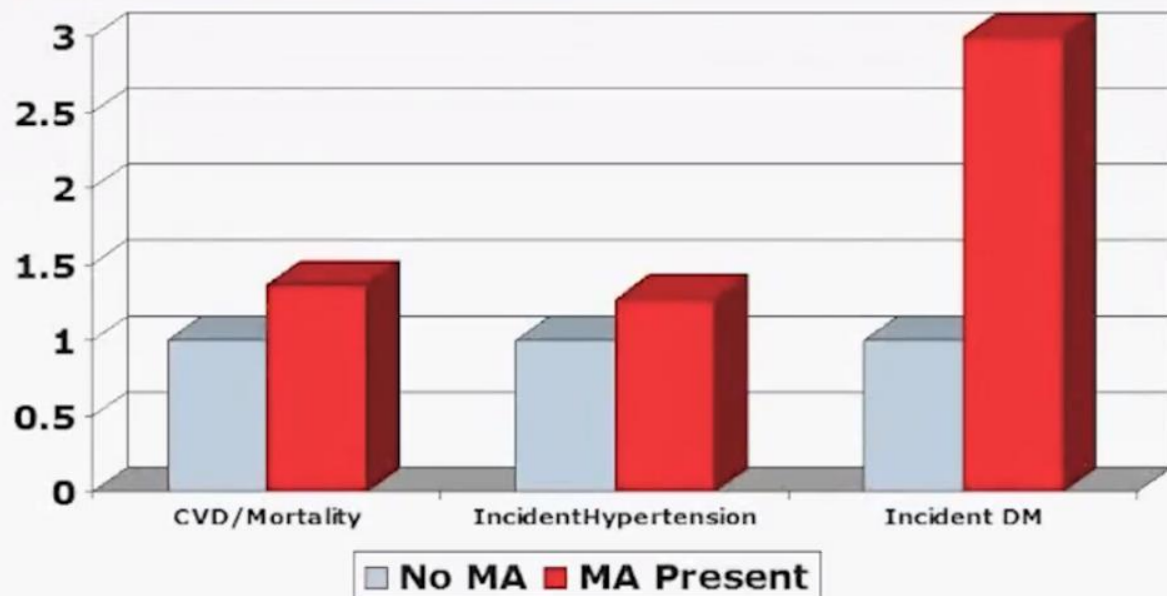
(Gansevoort RT, de Jong P JASN 20:465-468, 2009)



N	6,013	1,279	1,023	121	134
n	252	121	150	20	25

N	4,132	796	574	51	57
n	143	42	49	9	13

**Isolated Microalbuminuria:
Hazard Ratios for
CVD events/Mortality/Hypertension. DM
(Fully Adjusted)**



Percentage of US Population by eGFR and Albuminuria Category:
KDIGO 2012 and NHANES 1999-2006

				Persistent Albuminuria Categories, Description and Range			All
				A1	A2	A3	
				normal to mildly increased	moderately increased	severely increased	
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol	
GFR Categories, Description and Range (mL/min/1.73 m ²)	G1	normal or high	>90	55.6	1.9	0.4	57.9
	G2	mildly decreased	60-89	32.9	2.2	0.3	35.4
	G3a	mildly to moderately decreased	45-59	3.6	0.8	0.2	4.6
	G3b	moderately to severely decreased	30-44	1.0	0.4	0.2	1.6
	G4	severely decreased	15-29	0.2	0.1	0.1	0.4
	G5	kidney failure	<15	0.0	0.0	0.1	0.1
				93.2	5.4	1.3	100.0

Dipstick Proteinuria and RKFD

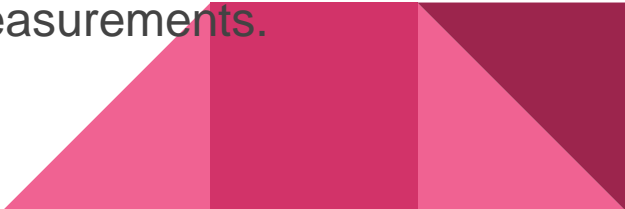
(Clark W, et al JASN 22:1729-1736, 2011)

Qualitative test showing the association of dipstick with rapid kidney function decline - loss of eGFR >5 per year (2754 community living adults with median follow up of 7 years)

1 out of 40, (2.5%) persons screened had dipstick urine of 2+. ($>100\text{mg/dl}$)

1 out 2.6 patients had rapid kidney function decline

Screening of pts with dipstick protein will detect 90% of those with rapid kidney function decline. Should be followed closely for eGFR measurements.



Screening

Recommend screening for microalbuminuria in all Type 2 diabetics at the time of diagnosis of diabetes, and annually thereafter

Recommend for Type 1 DM screening for microalbuminuria 5 years after the diagnosis of Type 1 DM and yearly thereafter

Advocated to screen for microalbuminuria in non diabetics with HTN to assess cardiovascular risk.

Global Proteinuria Guidelines : DM, HTN, obesity, current smoking, established CVD.



Proteinuria categories

Glomerular

Tubular

Overflow

Tissue



Proteinuria categories

Glomerular - Abnormal protein excretion due to abnormal glomerular permeability
(Diabetic Nephropathy vs other glomerular diseases)

Tubular - normally filtered but defective tubular reabsorption

Overflow - Immunoglobulin light chains (Multiple Myeloma), lysozyme (leukemia)

(Urine dipstick does not correlate with PCR - Light chains/ Globulins. Urine dipstick of 1+ with PCR 3000.)

Tissue - inflammation or infiltration



Evaluation

Isolated proteinuria vs urine sediment indicating glomerular disease - presence of hematuria, RBCs, RBC casts, WBCs, WBC casts.

Diabetes Mellitus - Diabetic Nephropathy.

Non Diabetic - persistent proteinuria $>500\text{mg/gm}$.

Systemic autoimmune disease, malignancy, Myeloma, Hepatitis, HIV.



Preventing Progressive Diabetic Nephropathy

- Glycemic control
- Lipid lowering
- Quit smoking/weight loss
- Blood pressure control
- Inhibition of renin angiotensin system



Management

Inhibition of renin angiotensin system

Persistent Proteinuria > 500 mg/day in the non Diabetic

Referral to Nephrology!!

