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A SYSTEMIC REVIEW OF MICROALBUMINURIA AND ITS SIGNIFICANCE IN CRITICALLY ILL PATIENTS

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ABSTRACT

Microalbuminuria is associated with increased risk of renal and cardiovascular morbidity and mortality in diabetes and hypertensive patients. The aim of this study was to review the level of urinary albumin excretion (microalbuminuria) which is associated with increased risk of coronary heart disease and death worldwide. Search strategy and selection criteria: Pubmed and citation lists of published articles were used to identify risk of microalbuminuria in CHD, diabetes, hypertension, trauma, acute inflammation and burns patients. Our review resulted out relationship between microalbuminuria, and risk factors, microalbuminuria and different ethnic groups. Our article suggests that effective treatment and appropriate life-style changes may prevent morbidity and mortality of the critically ill patient.

INTRODUCTION

A healthy person does not excrete proteins in the urine or the excretion of proteins is less than 150 mg per day. Microalbuminuria is defined as the excretion of 30 to 300mg of albumin per day in urine. It is not a different form or fraction of albumin but just a very small amount of albumin.

PREVALENCE OF MICROALBUMINURIA WORLDWIDE

Microalbuminuria is a common condition particularly associated with diabetes and hypertension. Nonetheless, it is frequently encountered in non-diabetic, non-hypertensive individuals and shows some differences in prevalence according to age, gender and ethnic group.

- Prevalence of microalbuminuria in the general population: 7-8% [2, 3].
- Prevalence of microalbuminuria in the general elderly population (60–79 years): 13.7%[2].
- Prevalence of microalbuminuria in the general elderly population without diabetes and hypertension: 5.2%[2].
- Prevalence of microalbuminuria in the elderly diabetic population: 30.7%[2].
- Prevalence of microalbuminuria in the elderly hypertensive population: 18.5%[2].
- Prevalence of microalbuminuria in the general population without diabetes and hypertension: 5-7%[2, 3, 4].
- Prevalence of microalbuminuria in the diabetic population: 15-40%[2, 3, 5, 6].
- Prevalence of microalbuminuria in people with hypertension: 11-16%[2, 3].
- Prevalence of microalbuminuria in hypertensives with left ventricular hypertrophy: up to 23%[7].
- Prevalence of microalbuminuria in hypertensives with diabetes: 12-36%[8].

Table 1 shows the values which constitute microalbuminuria[1]

Category	24 hr. collection (mg / 24 hr)	Timed collection		Albumin Creatinine Ratio	
		(µg/min)	(mg/L)	µg / mg	mg/mmol
Normal	< 30	<20	<20	< 30	<3.4
Microalbuminuria	30 – 300	20 – 200	20-200	30 – 300	3.4 – 33.9
Macroalbuminuria	>300	>200	>200	>300	>33.9

TYPES AND CAUSES OF PROTEINURIA

Albuminuria could be organi**c** (due to involvement of kidneys or other organs) or functional (due to physiological or biological stress on kidneys).

Functional albuminuria: It is usually intermittent and not accompanied by any symptoms or evidence of kidney disease. Renal function tests and urinary deposits are found to be normal during the functional albuminuria. It may be connected with:

1) Posture
2) Growth and development of kidneys
3) Severe stress (transient albuminuria)
4) Severe cold and excessive exercise or physical activity (functional or transient proteinuria)
5) Pregnancy

Organic albuminuria is of three types:

1. Renal Albuminuria: It is found in all forms of kidney disease. The cause of renal disorder or kidney disease may be inflammatory (infectious), degenerative (immunological) or destructive (toxic or malignant). The urine would be smoky in color if macroscopic hematuria (blood in urine) is also associated with proteinuria. The cases of acute glomerulonephritis may excrete 0.5-2.0% (0.5g-2.0g/dl) protein in the urine, whereas the cases affected by chronic glomerulonephritis generally excrete less than 0.5% (0.5 g/dl) protein in the urine. The amount of protein excreted daily would vary depending on the volume of urine voided daily. The ratio of albumin to globulin excreted in the urine may vary from 10:1 to 5:1. A routine and quantitative urine analysis is required to evaluate the extent of excretion of proteins in the urine.

2. Pre-renal Albuminuria: It is found in a variety of conditions exerting stress on the kidneys. The pre-renal albuminuria usually disappears when the primary disease is cured. Impairment of renal circulation due to dehydration, diarrhea or vomiting, blood loss due to accidental injuries or anemia is the most common conditions, which could lead to pre-renal albuminuria.

3. Post-renal Albuminuria: The proteinuria or albuminuria is termed as post-renal albuminuria if protein is possibly added to the urine as it passes along the urinary tract after leaving the urinary tubules of the kidneys. The major causes of the post-renal albuminuria are the lesions of the renal pelvis or urinary bladder. Lesions of the prostate (in male patients) and urethra also lead to post-renal albuminuria. Admixture of discharges from the vagina (in female patients) and semen (in male patients) may also give positive tests for protein.

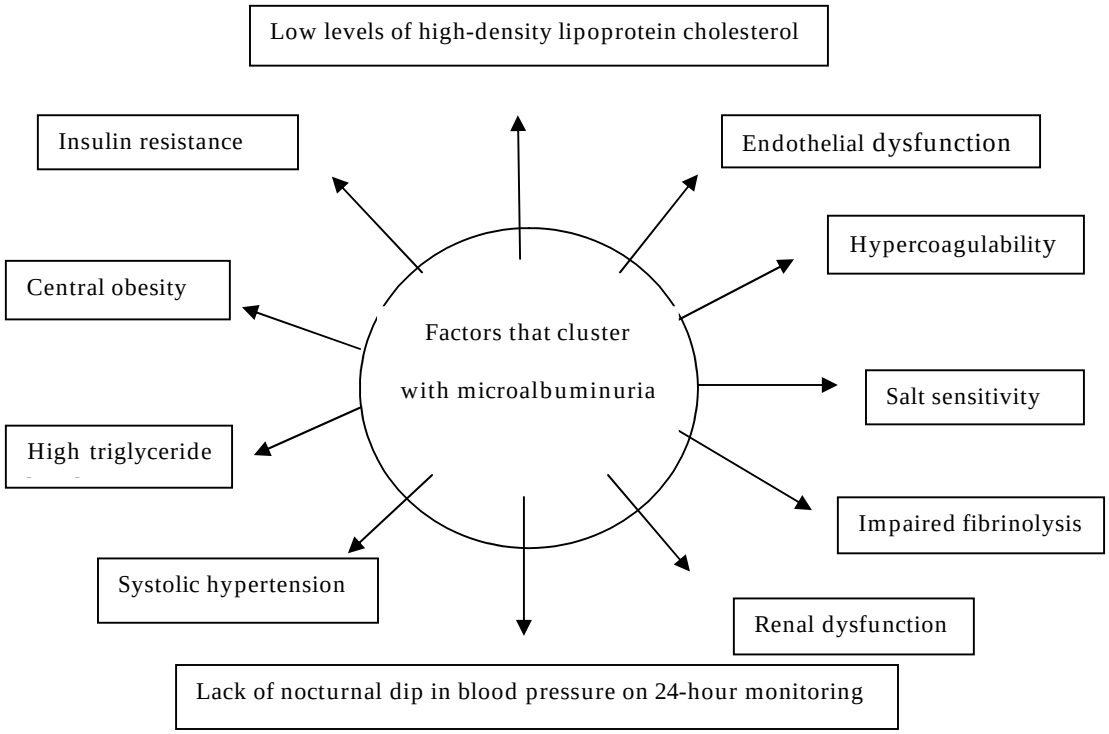
POSSIBLE MECHANISMS OF DAMAGE

Microalbuminuria may be related to cardiovascular damage by several biological pathways (Figure 1).

Renal dysfunction The amount of albumin in the urine depends on the electrochemical characteristics of the glomerular membrane barrier, the intraglomerular pressure, and tubular reabsorption. In this view, changes in any of these may translate into an excess of urinary albumin excretion.
However, nondiabetic people with hypertension and microalbuminuria were found to have normal urinary excretion of β-2 microglobulin, a marker of tubular protein transport[9]. This suggests that microalbuminuria results from an increased filtered albumin load rather from decreased tubular reabsorption.

Systemic blood pressure correlates with intraglomerular pressure and microalbuminuria[10]. Moreover, systolic blood pressure is one of the most relevant determinants of microalbuminuria[11]. However, microalbuminuria continues to be an independent risk factor for cardiovascular disease even after adjustment for blood pressure. In hypertensive patients, microalbuminuria is related to salt sensitivity, absence of a nocturnal dip in blood pressure, and higher mean 24-hour blood pressure measurements. All of these factors have been related to a high prevalence of cardiovascular disease in hypertensive populations.

Figure 1



Metabolic syndrome (MS): Microalbuminuria is also associated with the MS (includes insulin resistance, low HDL-C levels, high triglyceride levels, and truncal obesity). Current evidence strongly suggests that hyperinsulinemia is associated with a greater risk for cardiovascular disease[10]. Patients with type 1 and type 2 diabetes mellitus with microalbuminuria are more insulin-resistant than those without microalbuminuria. Insulin itself could lead to arteriosclerosis, renal damage, and microalbuminuria, either directly by its trophic actions, or indirectly by its effects on blood pressure and lipid metabolism[11].

Endothelial dysfunction: Microalbuminuria has also been proposed as a marker of endothelial dysfunction, as microalbuminuria has been related to elevated concentrations of accepted markers of endothelial dysfunction such as von Willebrand factor, thrombomodulin, and activated factor VII. Whether endothelial dysfunction detected by vasodilatation techniques is an earlier marker of subclinical atherosclerotic disease than microalbuminuria warrants further consideration.

Inflammation: Microalbuminuria could also be considered a marker of inflammation in multiple inflammatory processes such as sepsis, trauma, acute pancreatitis, and acute respiratory distress syndrome[12]. Two recent studies reported on the association of microalbuminuria with markers of chronic inflammation[13].

Transvascular escape of albumin: There is some evidence that microalbuminuria reflects a generalized increase in transvascular escape of albumin[11]. In animals, increased transvascular albumin transport is associated with increased transport of lipoproteins into the arterial wall. Whether this induces or enhances the development of atherosclerotic plaque in the vessel wall, and therefore could be the link between microalbuminuria and atherosclerotic disease, is unknown. In this regard, microalbuminuria correlates with the thickness of the intima of the common carotid artery, quantitative surrogate measurement of systemic atherosclerosis[14].

Blood lipids: Some studies, particularly in hypertensives, imply that microalbuminuria is accompanied by higher levels of blood lipids. UAE has been significantly correlated with serum triglyceride levels[15], and VLDL, triglycerides and lipoprotein (a) [16]. Non-diabetic hypertensives also reported that the microalbuminuric subgroup had a higher prevalence of hyperlipidaemia in comparison to normoalbuminurics (57.4 vs. 52.2%) [17]. Another study with salt-sensitive hypertension found higher levels of UAE, HDL, LDL and lipoprotein (a) when compared with patients with salt-resistant hypertension[18]. By contrast, another study of hypertensives found no relationship between various lipid components and microalbuminuria[19].

Obesity: Obesity is considered to be a well-recognized risk factor for increased morbidity and mortality, usually from cardiovascular complications[18]. It has been postulated that high intake of food (including protein) can lead to renal hyperfiltration and renal impairment[17]. Consistent with this hypothesis, proteinuria and focal glomerulosclerosis have been reported in obese patients,

with strong correlations between BMI and UAE, and between BMI and kidney volume. A correlation of UAE with waist-to-hip ratio and insulin levels has also been noted in hypertensive men and in obese healthy subjects[17]. These findings imply that microalbuminuria may be one of the metabolic abnormalities that accompany central-type obesity; these have been included together as part of the insulin resistance syndrome ('syndrome X').

Retinopathy: In hypertensive subjects, an increased prevalence of hypertensive retinopathy has been reported in microalbuminuric patients[17]. The significantly higher prevalence of retinopathy in patients with irreversible (after short intensive therapy) microalbuminuria was considered to be compatible with the hypothesis that microalbuminuria is a marker of widespread diabetic microangiopathy.

Smoking: Smoking correlates positively with UAE in patients with IDDM on univariate analysis, but not on multivariate analysis[17]. This suggests that smoking probably plays a minor role in the evolution of diabetic nephropathy.
Smoking appears to be an important link between microalbuminuria and endothelial damage or dysfunction in diabetics. Increased von Willebrand factor levels, an index of endothelial damage, have been demonstrated in smokers irrespective of their blood pressure.

MICROALBUMINURIA IN DIFFERENT CLINICAL SETTINGS

Microalbuminuria in the Diabetic

Microalbuminuria arises from the increased passage of albumin through the glomerular filtration barrier. This requires ultrastructural changes rather than alterations in glomerular pressure or filtration rate alone. Compromise of selective glomerular permeability can be confirmed in early diabetic nephropathy but does not correlate well with reported glomerular structural changes. The loss of systemic endothelial glycocalyx—a protein-rich surface layer on the endothelium in diabetes suggests that damage to this layer represents this missing link[21]. The epidemiology of microalbuminuria reveals a close association with systemic endothelial dysfunction and with vascular disease, also implicating glomerular endothelial dysfunction in microalbuminuria.

Microalbuminuria in the hypertensive

Urinary albumin excretion is increased in benign essential hypertension. Microalbuminuria is considered as worth screening in the early morning urine samples in hypertension apart from diabetes mellitus and the elderly[21].

Microalbuminuria and acute myocardial infarction

Microalbuminuria being an early marker of incipient diabetic nephropathy is closely linked to vascular endothelial function by mechanisms which might represent common pathways for the

development of both large and small vessel disease. This makes microalbuminuria a possible marker of vascular disease activity rather than simply a marker of cardiovascular risk. Even small ischemic episodes can produce microalbuminuria. It is also noticed in patients with intermittent claudication after exercise and in these patients it is proportional to the severity of the vascular disease. It is interesting to note that it is even altered by revascularization[22].

Small increases in filtered albumin due to changes in systemic vascular permeability are amplified by renal concentrating mechanisms producing relatively large changes in microalbumin excretion. One more possible mechanism relating microalbuminuria in vascular diseases could be loss of glomerular charge selectivity.

Whatever may be the cause of microalbuminuria in myocardial infarction, it has already been proved that microalbuminuria is associated with vascular diseases independent of renal damage. Microalbuminuria was found to occur early in the course of myocardial infarction (within 7 days), proportionate to the area of infarct and predicted mortality significantly.

Microalbuminuria in acute inflammation

Microalbuminuria occurs in acute inflammatory conditions such as ischemia. Microalbuminuria reflects vascular endothelial permeability and has been associated with many inflammatory processes such as bacterial meningitis, rheumatoid arthritis, inflammatory bowel disease, acute pancreatitis, trauma and surgery. Surgical operations are associated with a rapid increase in urinary protein excretion reflecting changes in vascular permeability.

In all these conditions the degree of microalbuminuria is proportional to the severity of the inflammatory insult, is predictive of outcome and not associated with any other feature of renal disease.

Microalbuminuria in surgical illness

Surgical stress usually cause a diffuse inflammatory response associated with important changes of endothelial cells properties due to the action of pro-inflammatory cytokines. In the kidneys, these physiopathologic changes affect glomerular permeability resulting in transient proteinuria. There is evidence of transient microalbuminuria in the first 6–24 hr of even uncomplicated postsurgical period[23]. The amount and the duration of the postoperative increase in microalbuminuria depends on the extent of the surgical stress. This phenomenon is found also in children. During surgery, there was a direct relationship between glomerular permeability and the severity of the surgical insult[23].

If microalbuminuria decreases and normalizes in the first 6–24 hr after surgery it is probable the postoperative period will be uneventfull, while a persistent postoperative microalbuminuria may warn that important complications are imminent.

Microalbuminuria in trauma

Major trauma, is also associated with a diffuse inflammatory response and increased endothelial permeability seen as microalbuminuria[24]. Microalbumin creatinine ratio (MACR) has also been used to predict acute respiratory distress syndrome (ARDS) after trauma. These results suggest that a persistent increase in microalbuminuria after trauma is associated with important complications. In septic patients with trauma MACR was measured and the impact of polymyxin B immobilized fiber treatment evaluated[25]. MACR after sepsis was significantly greater than that before sepsis, and there was a correlation between plasma endotoxin levels and MACR. MACR decreased significantly with polymyxin B immobilized fiber treatment.

In burns thermal stress produces a florid systemic inflammatory reaction. These patients lose albumin through the skin and the mucosae. MACR is often increased in the early period after injury and seems to be correlated with the level of microvascular permeability in burn patients. It is a potential indicator of the time to administer albumin to a burn patient[24].

An increased MACR and persistent or increasing abnormal values are probably correlated with high severity of illness, high likelihood of complications and high mortality risk.

Microalbuminuria in the nondiabetic

In nondiabetic patients it can still be a predictor of cardiovascular disease. Microalbuminuria occurs in acute myocardial infarction even in the absence of diabetes mellitus [23].

The review interprets the available evidence-direct, inferential or circumstantial- about non-diabetic, diabetic, hypertensive subjects available cross sectional and prospective epidemiological studies (see table 2) focusing on the independent effect of microalbuminuria as a marker and/or predictor of clinical events.

No.	Author/Year	Subjects	Design	Population	End-point
1	Yudkin[40] 1988	187	C/P	Diabetic, glucose-intolerant and non-diabetic subjects	Major, minor ECG changes, history of MI & angina, peripheral vascular disease
2	Haffner [40] 1990	316	C	Non-diabetic subjects	Self-reported MI
3	Damsgaard [40]1990	216	P	Non-diabetic subjects	Total mortality
4	P. Gosling et al [23]1991	112	P	Subjects with suspected acute MI	Increased urinary protein excretion is an early & proportional response to acute MI
5	Winocour [40]1992	447	C	Diabetic and non-diabetic subjects	ECG abnormalities
6	Damsgaard [40]1992	216	P	Non-diabetic subjects	Total abnormality
7	Damsgaard [40]1993	216	P	Non-diabetic subjects	Total mortality
8	Gould [40]1994	959	C	Non-diabetic subjects	MI, angina, peripheral vascular disease
9	Howard [40]1995	4549	C	Diabetic and non-diabetic American Indians	Definite MI and ischemic heart disease
10	Kuusisto [40]1995	1069	P	Non-diabetic subjects	Fatal and non-fatal coronary heart disease
11	Gorgels [40]1995	233	P	Diabetic and non-diabetic women	MI and angina
12	Agewall [40]1995	119	C	94 essential hypertensive and 25 NIDDM diabetic	Subclinical carotid atherosclerosis
13	Bigazzi [40]1995	90	C	Hyper- and normotensive subjects	Subclinical carotid Atherosclerosis

14	Ljungman [40]1996	120	P	Hyper- and normotensives	MI, angina, stroke, peripheral vascular disease
15	Agrawal [40]1996	11343	C	Hypertensive subjects	Previous MI, angina, stroke, peripheral vascular disease
16	Jensen [40]1997	2613	C	Hyper- and normotensives	History of MI
17	Agewall [40]1997	439	P	94 diabetic and 345 non-diabetic	Total and cardiovascular mortality (MI, sudden death, hypertensive subjects fatal stroke, cardiac failure, aortic aneurysm)
18	Jensen [40]1997	1254	C	Hypertensive subjects	Previous MI
19	Mykkanen [40]1997	1441	C	991 non-diabetic, 450 diabetic	Subclinical carotid atherosclerosis
20	Bigazzi [40]1998	141	R	Hypertensive subjects	Fatal and non-fatal MI, angina, TIA, intermittent claudication
21	Pontremoli [40]1998	53	C	Hyper- and normotensive subjects	Subclinical carotid atherosclerosis
22	Fabsitz [40]1999	4276	C	Diabetic and non-diabetic American Indians	Ankle/brachial index <0.9
23	Howard [40]1999	4549	P	Diabetic and non-diabetic American Indians	Fatal and non-fatal coronary and cerebrovascular events
24	Borch-Johnsen [40]1999	2085	P	Subjects healthy at baseline	Fatal and non-fatal MI, angina pectoris, ischemic heart disease
25	Jager [40]1999	631	P	Diabetic and non-diabetic Subjects	Total and cardiovascular mortality
26	Beamer [40]1999	121	P	Diabetic and non-diabetic patients with ischemic stroke	Stroke, MI, vascular death
27	Diercks [40]2000	7579	C	Non-diabetic subjects	ECG changes
28	Gerstein [40]2000	5708	C	Non-diabetic with cardiovascular Disease	Peripheral vascular disease
29	Jensen [40]2000	204	P	Uncomplicated hypertensive subjects	Fatal and non-fatal MI, angina, ischemic heart disease
30	Pedrinelli [40]2000	136	C	Uncomplicated hypertensive men	Subclinical carotid atherosclerosis
31	Roest [40]2001	1118	P	Postmenopausal women	Cardiovascular mortality
32	Gerstein [40]2001	5545	P	Non-diabetic with cardiovascular disease	MI, stroke, CV death, all-cause mortality, VHF hospitalization
33	G. Berton [25]2001	432	P	Unselected, consecutively enrolled subjects with acute MI	Urinary albumin assessed in the first week after acute MI is a strong prognostic factor for 1year mortality
34	Kristian Wachtell 2003	8206	P	Diabetic and non-diabetic subjects	Cardiovascular death, fatal or non-fatal stroke, MI, all-cause mortality
35	George Ioannidis [26]2004	76	P	CAD, diabetic subjects	Predictive microalbuminuria for presence of asymptomatic CAD
36	Matthew F. Yuyun [27]2004	23,964	P	Individuals who completed health and lifestyle questionnaire	Microalbuminuria is independently associated with cardiovascular risk factors and prevalent CVD
37	Holly Kramer [35] 2005	6814	P	Subjects without clinical CVD	Subclinical CVD among adults without established CVD
38	Spyridon Koulouris[28] 2006	223	P	Non-diabetic with acute MI	Fatal & non-fatal events was significantly higher in patients with microalbuminuria
39	S. Rinaldi [24]2006	1181	Retrospective cohort study	Surgical, trauma, cardiac and medical ICU subjects	The significance of microalbuminuria in critical illness
40	K. P. Klausen et al[29] 2006	491	P	Diabetic subjects	Very low level of microalbuminuria(above 5µg min^{-1}) is associated with increased risk(100%) of death in cardiovascular or cerebrovascular disease
41	P.Jordanova-Laleva[30] 2007	73	P	Acute MI subjects	Unclear problem regarding role of microalbuminuria in infarction patients

42	Erik Ingelsson[31] 2007	1106	P	Non-diabetic with without MI	Low grade albuminuria and incidence of heart failure
43	Surupa Basu[32] 2010	525	P	Diabetic, hypertensive subjects	Mortality in critically ill patients
44	Mustafa Taskiran[33] 2010	151	P	Acute MI subjects	Microalbuminuria in hospitalized patients with acute MI is prognostic for increased long term mortality
45	Rowl Henrene 2010	3779	P	Youth population of Cuba	Microalbuminuria is a marker for risk and for early renal, cardio-cerebral vascular damage
46	Hertzel C Gerstein [34] 2011	9043	P	Diabetic and non-diabetic subjects with CVD	Screening for albuminuria identifies people at high risk for cardiovascular events

Microalbuminuria in the nondiabetic, nonhypertensive population

Microalbuminuria may occur even in the absence of diabetes mellitus and hypertension. It has also been suggested that microalbuminuria is by itself an independent risk factor of cardiovascular disease and cardiovascular morbidity. Its prevalence in such patients was found to be 6.6% and has been considered to be useful in early risk profiling and prevention of cardiovascular disease [36].

SCREENING METHODS

(i) Qualitative: Various qualitative tests are shown in table 3.

Test	Reaction	Observation	End point
Boiling Test	Sample + Acetic acid or Nitric acid	Turbidity	Presence of albumin
Heller's Nitricacid Test	Sample + Nitric acid	White ring at point of contact	
Johnson's Picricacid Test	Sample + Saturated Picric Acid	Turbidity or White ring	
Ferrocyanide-of-Potassium and Aceticacid Test	Sample + Potassium –ferrocyanide + Acetic acid	Cloudiness	
Magnesium Nitric Test	5volumes of Saturated magnesium sulphate + 1volume of Nitricacid	Cloudy ring	

(ii) Semiquantitative [38]: This includes test strips most of which are optimized to read "positive" at a predetermined albumin concentration: examples are shown in table 4.

Test	Principle	Measuring conc.	Sensitivity	Specificity
Albu screen test	Latex agglutination inhibition test	>20 mg/L	90-95 %	90-95 %
Albu sure test		>30 mg/L	90-95 %	90-95%
Microbumin test	Detection of albumin using bromophenol blue in alkaline matrix	>40 mg/ml	95%	80 %
Micral test	Monoclonal antialbumin IgG complexed to β galactosidase	---	100 %	90 %

(iii) Quantitative[37]

a) **Immunoturbidimetry**

In this process turbidity is produced by an immune complex reaction. This causes a reduction in the intensity of light as it passes through the solution. Turbidimetry is the measurement of this loss in intensity because of scattering, absorption or reflection of the incident light in the angle/direction of the incident light.

Most colorimeters and spectrophotometers can measure turbidity with good precision and accuracy. This is the most widely used test as it can be done on most semi auto chemistry analyzers. It can even be done on automated chemistry analyzers.

Manual procedure: Mix 60 µL of standard, control(s) and samples with 900 µL of MAL buffer. Read optical density (OD1) of standards, control(s) and samples at 340 nm. Add 150 µL of antiserum. Mix and incubate for 5 minutes at room temperature. Read optical density (OD2) of standards, control(s) and samples at 340 nm.

Calculate OD's, plot a standard curve and read the concentration of control(s) and samples.

b) **Nephelometry**

This assay is also based on scatter detection but unlike turbidimetry It measures scattered light at 90° C to the incident light. The instrument is called a nephelometer. It is more sensitive than turbidimetry.

c) **Radioimmunoassay (RIA)**

This assay procedure involves competitive binding between radio labelled and unlabelled molecules of antigen to high affinity, specific antibody. The amount of unlabelled antigen

present in the specimen is measured by its competitive effect on the labelled antigen for limited antibody sites. It involves the use of radio isotopes like tritium (^{3}H), ^{131}I or ^{125}I as labels. It has high sensitivity and specificity.

d) **Chemiluminescent immunoassay (CLIA)**

Chemiluminescence is a chemical reaction that emits energy in the form of light. When used with immunoassay technology, the light produced by the reaction indicates the amount of analyte in a sample. This again is of two types: -

1. Luminescent Immunoassay (LIA):- Here the labelled and unlabelled antigen competes for the limited binding sites on the labelled antibody. An inverse relationship exists between concentration of labelled antibody bound to the antigen and the unlabelled antigen.
2. Immuno Chemiluminometric assay (ICMA):- This is a sandwich assay in which unlabelled antigen is sandwiched between antibody bound to paramagnetic particles and antibody labelled Acridinium ester (AE). A direct relationship exists between the concentration of antigen in the patient sample and the amount of light emitted during oxidation of the AE.

Both RIA and CLIA are preferred globally for their sensitivity, specificity and reproducibility but unavailability, cost factor, big infrastructure, government permission for use of radioactive materials is the limiting factors.

e) **Radioimmunodiffusion**

This method requires long incubation and cannot be automated so it is not widely accepted. Monospecific antiserum to human albumin is incorporated into an agar gel. Samples and calibrators are added to the wells and allowed to diffuse into the agar at equilibrium, the antigen-antibody complexes precipitated and after staining the distance of migration is being measured[41].

f) **ELISA method**

ELISA can be semiautomated with the use of a microplate reader. In all ‘sandwich’ techniques the primary antibody (antialbumin antiserum) is fixed on the plastic plate. Then the samples, calibrators and controls are added. The antibody-antigen complexes are detected and quantified by second antibody conjugated to the enzyme level[41].

g) **Esbach's albuminometer method**

This tube bears two marks: U, indicating the point to which the urine must be added; and R, the point to which the reagent is added. The lower portion of the tube upto U bears a scale reading from one to seven. The tube is filled upto U with filtered albuminous urine, and the reagent added till the point R is reached. The tube is then closed with a stopper, inverted twelve times, and set aside for twenty-four hours. At the expiration of this time serum-albumin, serum-

globulin, and albuminose, as well as uric acid and creatinin, will have settled down, when the amount per milli, in grams, may be directly read off from the scale. The solution used is composed of ten grams of picric acid and twenty grams of citric acid dissolved in 1,000 c. c. of distilled water.

TREATMENT MODALITIES FOR MICROALBUMINURIA

Microalbuminuria can thus be reduced by glycaemic control, control of hypertension and by the use of ACE inhibitors even in the normotensives. ACE inhibitors have been recommended routinely in acute myocardial infarction especially when failure sets in. They reduce mortality after acute myocardial infarction and this effect is additive to those achieved by aspirin and β blockers. Maximum benefit is seen in high-risk patients. A short-term benefit also occurs in haemodynamically stable patients owing to the following: -

(i) ACE inhibitors reduce ventricular remodeling after infarction.

(ii) Reduces risk of congestive cardiac failure.

It is also observed that patients treated chronically with ACE inhibitors have a reduced risk of recurrent infarction [48].

RECOMMENDATIONS FOR PATIENTS WITH MICROALBUMINURIA

- Renoprotection with ACE inhibitors or angiotensin receptor blockers for patients with diabetes
- BP control
  <140/90 mmHg for the general population
  <130/80 mmHg for patients with diabetes
- Glycemic control: hemoglobin A1c <7%
- Consider screening in patients with diabetes
- LDL cholesterol control for diabetes in the general population
  <100 mg/dl (<2.6 mmol/L) for patients with or without diabetes
  <70 mg/dl (<1.8 mmol/L) for patients with CVD
- Correct disturbances in triglyceride, HDL, and non- HDL levels
- Smoking cessation
- Dietary limitation of salt (<3 g/d) and saturated fat
- Regular exercise and weight control
- Antiplatelet therapy

CONCLUSION

Our article suggests that effective treatment and appropriate life-style changes may prevent morbidity and mortality of the critically ill patient. Whereas, albuminuria is an important marker for both cardiovascular and non-cardiovascular mortality. Strong associations with blood pressure levels, metabolic status, lipids and smoking habits make microalbuminuria an integrated marker of cardiovascular risk in hypertensive, non-diabetic individuals. Microalbuminuria is a good predictor of severity of illness in ICU patients. The interindividual variability in microalbuminuria is high and already present just after birth indicating that microalbumnuria is not only a consequence of vascular damage but also the result of the ordinary interindividual variability in endothelial function.

Most of the researchers suggest that microalbuminuria is mostly found in individuals with diabetes and hypertension. Monitoring of microalbuminuria is very much essential to prevent cardiovascular complications in future.

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