

MICROALBUMINURIA AND HYPOALBUMINEMIA AS PREDICTORS OF OUTCOME IN CRITICALLY ILL PATIENTS

Thesis submitted for fulfillment of MD

by

Abd El halim Mohamed Abd El halim A. Hegazy

MBBCh., MSc

SUPERVISORS

Prof. Dr. Ahmad Abd El aziz Mohamed

Professor of Critical Care Medicine
Faculty of Medicine
Cairo University

Prof. Dr. Abeer Mosbah Abd El hameed

Professor of Clinical Pathology
Faculty of Medicine
Mansoura University

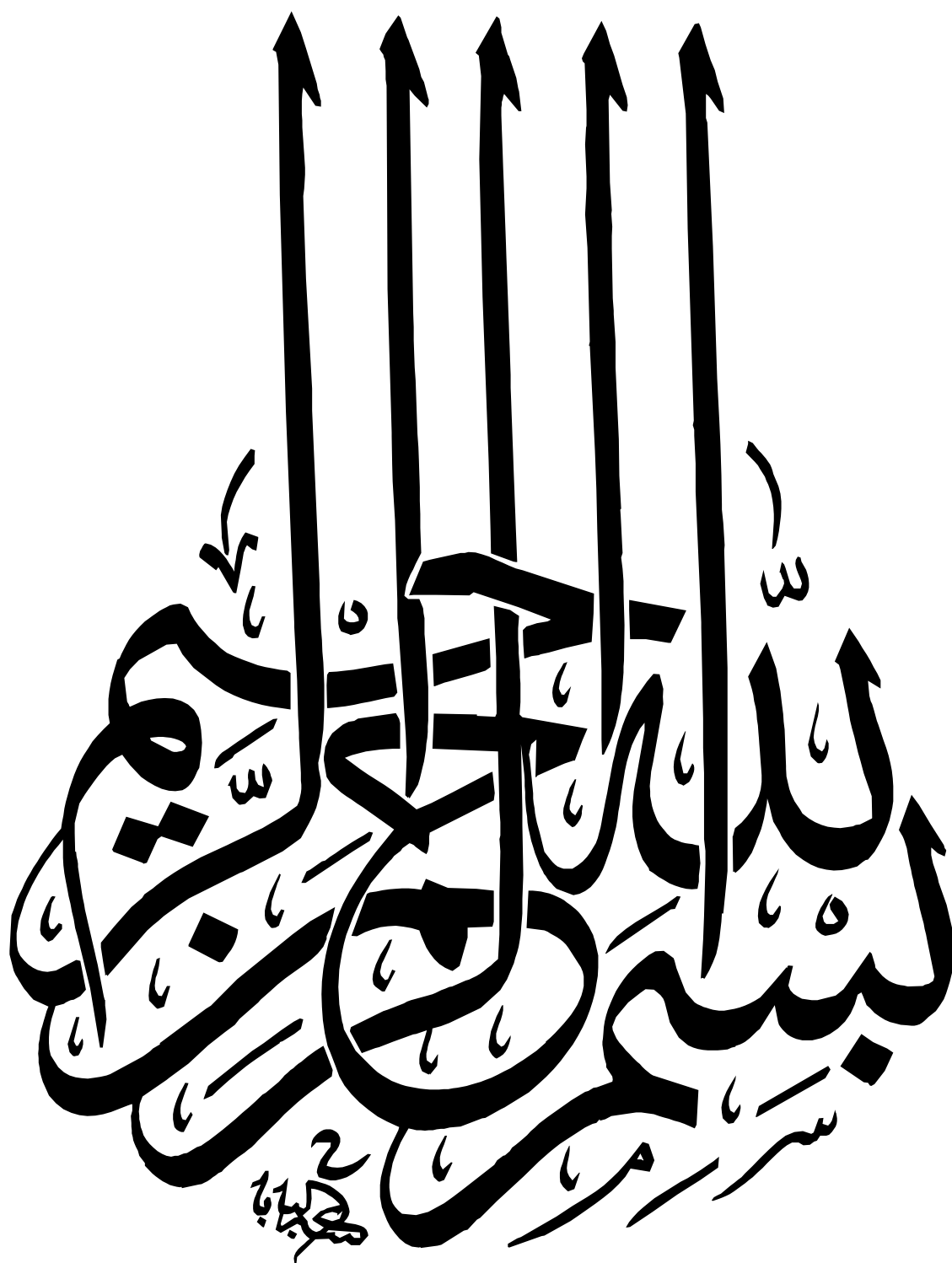
Dr. Mohamed Fawzy Abd El aleem

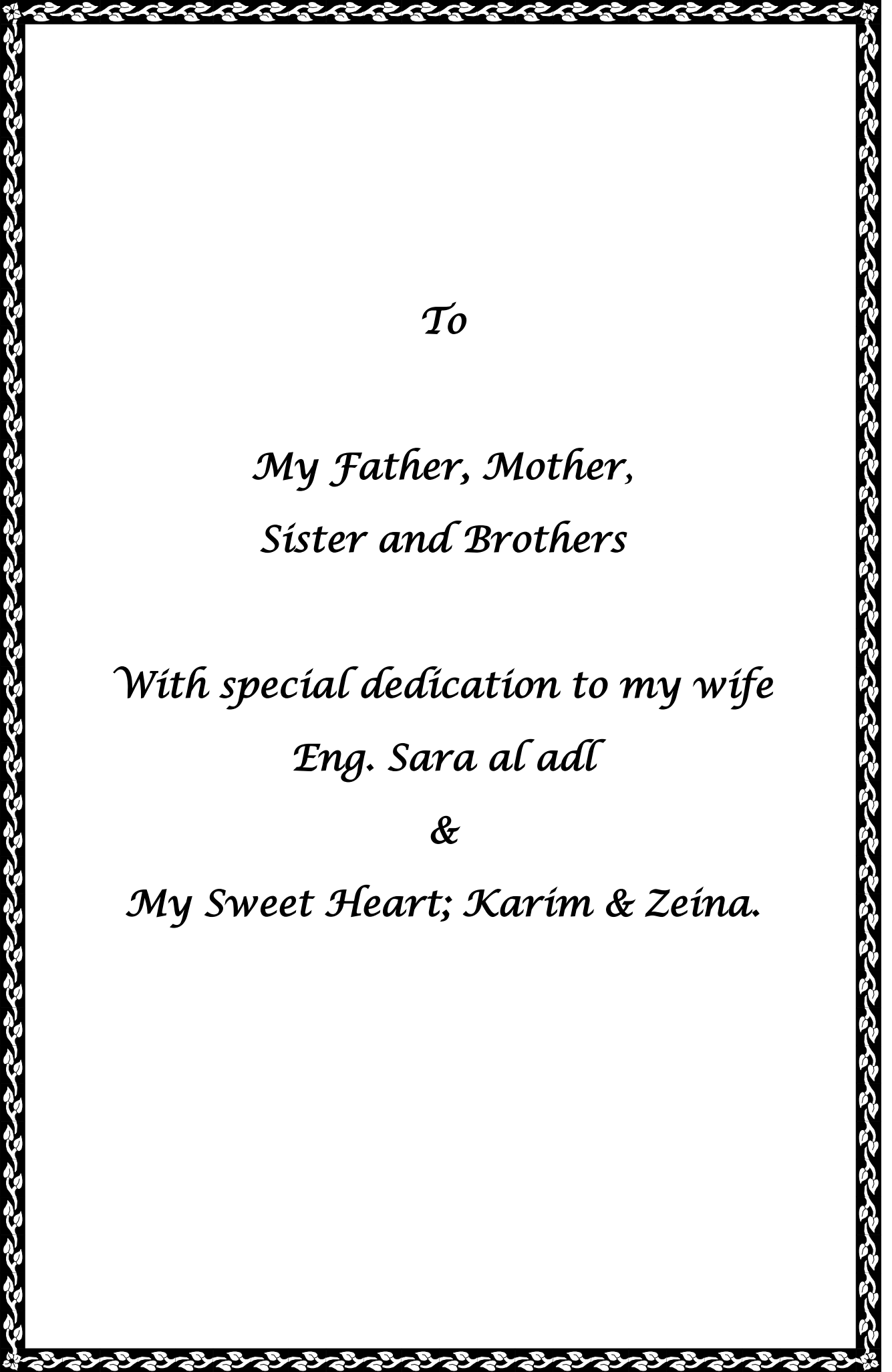
Lecturer of Critical Care Medicine
Faculty of Medicine
Cairo University

Dr. Mahmoud Khaled Mahmoud

Lecturer of Critical Care Medicine
Faculty of Medicine
Cairo University

Cairo University
2016





To

*My Father, Mother,
Sister and Brothers*

With special dedication to my wife

Eng. Sara al adl

&

My Sweet Heart; Karim & Zeina.

Acknowledgement

For **ALLAH** the merciful, the compassionate, I kneel to express my gratitude for all the countless gifts I have been offered, including those who gave their hands to enable me to fulfill this work.

No words are sufficient to express my deep appreciation and profound gratitude to **Prof. Dr. Sherif Mokhtar** and **Prof. Dr. Hossam Mowafi**, Professors of Critical Care Medicine, for offering all their students an inspirational role model, for showing us the excitement and joy of critical care medicine, for their dedication to education and for their encouraging attitude and invaluable advice made it possible for any one to overcome even the most difficult obstacles in preparing the research. I am really honored to belong to the school of these scientists.

No words are sufficient to express my deep appreciation and profound gratitude to, **Prof. Dr. Ahmed abd el aziz** Professor of critical care medicine, Cairo University for his abundant encouragement, continuous support and endless giving.

My true appreciation is to **Dr. Abeer mosbah**, Professor of clinical pathology for her meticulous supervision, for his kind guidance, valuable instructions and generous help.

I am deeply thankful to **Dr. Mohamed fawzy**, lecturer of Critical Care Medicine for his great help, outstanding support and active participation, for his sympathy, kindness and constructive advice and for treating me in a brotherly way.

I wish to thank **Dr. Mahmoud khaled**, lecturer of Critical Care Medicine, for his great efforts and important contributions. The time I worked under his supervision consolidated my knowledge, refined my experience and made me feel confident as a research student, because of the freedom he gives his students to express themselves no matter how inexperienced they might be. Thus, I really acknowledge that I consider myself lucky for ingoing the advantage of being supervised by such a great supervisor.

Finally I am so thankful and honored to belong to the critical care medicine department, the land of imagination, innovation and fruitful research.

Abd el halim hegazy

Abstract

Microalbuminuria and Hypoalbuminemia as predictors of outcome in critically ill patients

Background: assessment of the Microalbuminuria and Hypoalbuminemia can be good tools for prediction of intensive care unit outcome in critically ill patients
Purpose: to evaluate and compare the prognostic significance of microalbuminuria (albumin creatinine ratio {ACR}) and serum albumin level on admission and after twenty four hours in (ICU) patients. **Methodology:** sixty patients admitted to ICU were involved in a prospective randomized clinical study (mean age were 44.4 ± 16.7 /years, 78.3 % male) were divided into 2 groups according to mortality and were subjected to laboratory measurement of the mentioned biomarkers at admission and after twenty four hours. **Results:** there were 34 patients (56.67 %) survived in group A and 26 patients (43.33 %) died in group B. Albumin creatinine ratio on admission (ACR1), albumin creatinine ratio after 24 hours (ACR2) were significantly lower in survivors than non-survivors P value were < 0.001 for both, serum albumin level after 24 hours of admission (s. alb. 2) was significantly higher in survivors than non-survivors P value 0.02 while admission serum albumin(sr. alb. 1) was not significantly different between both groups P value was 0.1. There was a positive correlation between ACR2 and ICU stay and mechanical ventilator support with strong positive correlation to using of vasopressor support treatment (0.35,0.58 and 0.73 respectively), p values were (0.005, < 0.0001 and < 0.0001) respectively. There was a positive correlation between ACR2 with APACHE II and SOFA scores (0.46 and 0.43 respectively), p values were (0.001 and < 0.0001). There was a moderate negative correlation between serum albumin 1,2 and duration of mechanical ventilation (- 0.4 and - 0.39 respectively), P value were 0.001, and 0.002) respectively. By cox regression analysis 2 parameters were found to be independent predictors of mortality in ICU patients which were: age and using vasopressor treatment as P values= (0.01 and < 0.001), while the other parameters were not independent predictors of mortality, p values were more than 0.05. **Conclusions:** age and using vasopressor treatment both offer independent prognostic prediction of ICU outcome and bigger studies need for microalbuminuria and serum albumin.

Key words: Microalbuminuria, Hypoalbuminemia, mortality, ICU.

List of Abbreviations

ACEI	Angiotensin converting enzyme inhibitors
ACR	Albumin creatinine ratio
AKI	Acute kidney injury
APACHE	Acute physiology and chronic health evaluation
ARB	Angiotensin receptor blocker
AUC	Area under the curve.
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular system
CVP	Central venous pressure
DIC	Disseminated intravascular coagulopathy
EGDT	Early goal directed therapy
ERJ	European respiratory journal
ESICM	European Society of Intensive Care Medicine
FiO ₂	Fraction of inspired oxygen
GCS	Glasgow Coma Scale
HR	Heart rate
ICU	Intensive care medicine
IL	Interleukin
IUGR	Intra uterine growth restriction

LOD	logistic organ dysfunction
LOS	Length of stay
MA	Microalbuminuria
MAP	Mean arterial blood pressure
mg/dL	Milligram per decilitre
mL/kg	Milliliter per kilogram
mm Hg	Millimeter mercury
mmol/L	Millimole per litre
MODS	Multiple organ dysfunction syndrome
MPM	Mortality Probability Models
MSOF	Multiple System Organ Failure
ODIN	Organ dysfunction and infection system
PPROM	Preterm premature rupture of membranes
PSS	Poisoning severity score
RAS	Renin-angiotensin system
RCT	Randomized controlled trials
SAPS	Simplified acute physiology score
SBP	Systolic blood pressure
SCCM	Society of Critical Care Medicine
SIRS	Systemic inflammatory response syndrome

SOFA	Sequential organ failure assessment
TNF	Tumor necrosis factor
TRIOS	Three-day recalibrating ICU outcomes
WBC	White blood cell

List of Tables

Item	Page
Table (1): American Diabetic Association Classification of Microalbuminuria.	12
Table (2): Key points in the albumin story so far.	37
Table (3) The acute physiology and chronic health evaluation II.	56
Table (4): The Sequential Organ Failure Assessment Score.	61
Table (5): sex and co-morbidities in the studied population.	72
Table (6): Age, height, weight, & BSI of the studied patients.	73
Table (7): causes of admission among the studied patients.	74
Table (8): comparative demographic & clinical data in the two study groups.	76
Table (9): APACHE II & SOFA scores in the two study groups.	76
Table (10): laboratory data in the two study groups.	77
Table (11): outcome data in the two study groups.	78
Table (12): correlation between ACR1, ACR2& duration of mechanical ventilation.	79
Table (13): correlation between ACR1, ACR2& duration of ICU stay.	79
Table (14): Correlation between, ACR1,ACR2, APACHE II&SOFA in all studied patients	80
Table (15): correlation between serum albumin 1, serum albumin 2 and duration of mechanical ventilatory support.	83
Table (16): correlation between DM, serum albumin and microalbuminuria survivors in ICU.	84
Table (17): correlation between hypertension, serum albumin and microalbuminuria survivors in ICU.	85
Table (18): correlation between age, serum albumin and microalbuminuria survivors in ICU.	86
Table (19): Performance of ACR1& ACR2 as predictors for the mortality in ICU patients.	87

Item	Page
Table (20): Mean survival duration in days of ICU patients.	88
Table (21): Mean survival time of studied group classified according to ACR1 cutoff point 125 mg/g.	89
Table (22): Mean survival time of studied group classified according to ACR2 cutoff point 125 mg/g.	90
Table (23): Mean survival time of studied group classified according to serum albumin 2 cutoff point 2.5 g/dl.	91
Table (24): Mean survival time of studied group classified according to serum albumin 2 cutoff point 2.5 g/dl.	93
Table (25): Performance of serum albumin 1 & serum albumin 2 as predictors for the mortality in ICU patients.	94
Table (26): Performance of SOFA & APACHE II scores as predictors for the mortality in ICU patients.	
Table (27): cox regression analysis of the study markers.	
Table (28): Logistic regression analysis for significant predictors of mortality among ICU studied patients.	

List of Figures

Item	Page
Fig. (1): Schematic illustration of metabolism of albumin in healthy adults. GI, gastrointestinal.	31
Fig (2): Schematic illustration of the current understanding of vascular barrier function within the high-pressure segment of the vascular system.	32
Fig. (3): function of albumin.	34
Fig. (4): Mortality in the studied patients.	74
Fig. (5): correlation between ACR1 and APACHE II score.	81
Fig. (6): correlation between ACR2 and APACHE II score.	81
Fig. (7): correlation between serum albumin on admission (s. alb. 1) and SOFA score.	82
Fig. (8): correlation between serum albumin after 24 hours of ICU admission (s. alb.2) and SOFA score.	83
Fig. (9): ROC curve analysis of ACR1 and ACR2 as prognostic markers of ICU mortality.	85
Figure (10): Kaplan- Meier survival function curve of the studied patients (60 patients).	86
Fig (11): Kaplan Meier plot of association between ACR1 125 mg/g & ICU stay.	87
Fig (12): Kaplan Meier plot of association between ACR2 & ICU stay.	88
Fig (13): Kaplan Meier plot of association between serum albumin 1 & ICU stay.	89

Item	Page
Fig (14): Kaplan Meier plot of association between serum albumin 2 & ICU stay.	90
Fig (15): ROC curve analysis of serum albumin 1 and serum albumin 2 as prognostic markers of ICU mortality.	91
Fig (16): ROC curve analysis of SOFA and APACHE II scores as prognostic markers of ICU mortality.	92

Table of Content

Item	Page
Introduction	1
Aim of Work	5
Review: ○ <i>Chapter I: Microalbuminuria in critically ill patients</i> ○ <i>Chapter II: Albumin and Hypoalbuminemia</i> ○ <i>Chapter III: Different scoring system used in assessment of critically ill patients.</i>	6 27 51
Patients & Methods	64
Results	72
Discussion	98
Summary	111
Conclusion	114
References	115
Arabic Summary	4-1

Introduction

Introduction

The predictive power of microalbuminuria for renal and cardiovascular disease morbidity and mortality was subsequently confirmed in type 2 diabetes, arterial hypertension and in the general population.^(1,2) Publications on microalbuminuria soared to the level of more than one every other day. Both the term and the significance of microalbuminuria have been criticized. It has been argued that microalbuminuria is a misnomer.

Micro is Greek for small in size and, etymologically, microalbuminuria would indicate a smaller albumin molecule in the urine. It has been suggested that the correct term should be oligoalbuminuria to mean small amounts of albumin in the urine. More recently, moderate albuminuria has been proposed as a term to replace microalbuminuria. Levels of microalbuminuria are variable and their relation with the severity of histological lesions, though significant, is weak. Isolated spot measurements of microalbuminuria may be misleading and less reliable than the rate of change of microalbuminuria, specifically a rise in albumin excretion rate, as indicators of progressive renal disease. Moreover some patients apparently can develop renal impairment without developing microalbuminuria.⁽³⁻⁶⁾

Despite these critiques (some of which are criticizable themselves; for instance, there is no proven early histological marker of progressive renal disease in diabetes), an overwhelming body of evidence indicates that a small increase of albumin in the urine above the normal range (and this is what microalbuminuria means) is one of the strongest predictive biomarkers of cardio-renal disease.⁽⁷⁻⁹⁾ The concept that raised albumin excretion rate flags early risk is here to stay. Of course the level of risk increases further as the albuminuria gets heavier, but this