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PREVALENCE AND ASSOCIATION OF MICROALBUMINURIA IN HYPERTENSIVE PATIENTS WITH OR WITHOUT TYPE 2 DIABETES.

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ABSTRACT

Background: Microalbuminuria develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease. Microalbuminuria is typically defined as a 24-h urinary albumin excretion rate (UAE) of 30-300mg (20-200μg/min) or urinary albumin: creatinine ratio (UACR) of 2.5-30mg/mmol in men, 3.5-30mg/mmol in women. The aim of this study was to determine prevalence and association of urinary microalbuminuria (MAU) in patients with hypertension and/or type 2 diabetes mellitus (DM). **Methods:** The study was a prospective, cross sectional and observational study conducted on patients with hypertension with or without type 2 diabetes mellitus of KIMS Hospital and Research Centre, Bangalore. The main outcome measures were the prevalence of MAU as assessed by fully automated immune turbidometry method and blood pressure. Demographic variables, presence of co morbidities, use of cardiovascular and antidiabetic drugs and biochemical variables were also analyzed. **Results**: A total of 150 patients (50 with hypertension, 50 with both DM and hypertension and 50 controls), 66%woman, were included in the study. Overall prevalence of MAU was 86% in patients with DM and hypertension, 76% in patients with hypertension. In multivariate analysis, predictors for MAU were the presence of DM or hypertension, HbA1c, male, age, blood pressure, and total cholesterol and triglyceride TG. **Conclusion**: Hypertension and DM are the established risk factors for cardiovascular disease and renal disease. Routine MAU screening by turbidometry method would help identify individuals at risk and increase awareness of kidney disease and TOD.

KEYWORDS: Microalbuminuria – hypertensive – patients with T2DM – prevalence.

INTRODUCTION

Microalbuminuria develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease.[1,2] Microalbuminuria is typically defined as a 24-h urinary albumin excretion rate (UAE) of 30-300mg (20-200μg/min) or urinary albumin: creatinine ratio (UACR) of 2.5-30mg/mmol in men, 3.5-30mg/mmol in women.[3] The association between renal and cardiovascular (CV) pathologies in advanced kidney and heart disease is well characterised; however, in early disease, these associations are less clearly defined.[4] In addition to being an early sign of kidney damage, microalbuminuria is a marker of inflammatory process. It is often found in patients with essential hypertension or glucose intolerance. These latter observations suggest that it may be involved in early vascular damage and could be used to predict the onset and progression of CV disease.[1] In 1999, World Health Organization (WHO) identified microalbuminuria as a component of metabolic syndrome; an indication that microalbuminuria is recognised as a predictor of CV mortality.[5,6] The WHO definition of metabolic syndrome has been challenged, as microalbuminuria is usually seen in patients with diabetes and is a marker of diabetic rather than overt nephropathy.[7] Microalbuminuria, how ever, has now been demonstrated to be a sensitive and early predictor of CV risk in patients with essential hypertension regardless of their diabetic status or whether they have existing renal disease.[8,9] Even very low levels of microalbuminuria are strongly correlated with CV risk.[10-13] Early identification of a patient at risk of CV events provides an opportunity for early treatment, to slow the progression of disease. Screening for microalbuminuria is a sensitive, reliable and accessible test for renal disease and CV morbidity or mortality. Because microalbuminuria has been shown to predict CV events - both in patients with hypertension with or

without diabetes - the 2007 ESH/ESC (European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) guidelines recommend screening for microalbuminuria in all patients with hypertension.[14] The JNC-7 report states that 'the presence of albuminuria, including microalbuminuria, even in the setting of normal GFR, is also associated with an increase in CV risk' and recommends annual screening for microalbuminuria in high-risk groups, such as those with diabetes or renal disease and optional in other hypertensive.[15] The level of albumin protein produced by microalbuminuria can be detected by special albumin-specific urine dipsticks. A microalbumin urine test determines the presence of the albumin in urine. In a properly functioning body, albumin is not normally present in urine because it is retained in the bloodstream by the kidneys. An albumin level above the upper limit values is called "macroalbuminuria", or sometimes just albuminuria. Sometimes, the upper limit value is given as one less (such as 300 being given as 299) to mark that the higher value (here 300) is defined as macroalbuminuria.[16] To compensate for variations in urine concentration in spot-check samples, it is helpful to compare the amount of albumin in the sample against its concentration of creatinine. This is termed the albumin/creatinine ratio (ACR)[17] and microalbuminuria is defined as ACR ≥3.5 mg/mmol (female) or ≥2.5 mg/mmol (male),[18] or, with both substances measured by mass, as an ACR between 30 and 300 µg albumin/mg creatinine.[19] For the diagnosis of microalbuminuria, care must be taken when collecting sample for the urine ACR. An early morning sample is preferred. The patient should refrain from heavy exercises 24 hours before the test. A repeat test should be done 3 to 6 months after the first positive test for microalbuminuria. Lastly, the test is inaccurate in a person with too much or too little muscle mass. This is due to the variation in creatinine level, which is produced by the muscle.[20]

The objective of this study was to find out the prevalence and association of urinary microalbuminuria in patients with hypertension and/or type 2 diabetes mellitus (DM) at KIMS hospital Bangalore, to examine the differences in the distribution of MAU in the three groups (hypertensive, hypertensive diabetic and normotensive non-diabetic) studied and the association of different Clinical and epidemiological variables with MAU in each of the subgroups, to evaluate possible relationship among microalbuminuria and lipid parameters, to evaluate whether the use of different antihypertensive drug classes in general practice influences microalbuminuria level in non diabetic subjects.

METHODS

The study was a prospective, cross sectional and observational study conducted on patients with hypertension with or without type 2 diabetes mellitus of KIMS Hospital and Research Centre, Bangalore. The study was approved by the Institutional Ethical Committee. Participants who met the inclusion and exclusion criteria were divided into three groups (hypertensive, hypertensive diabetic and control group). The study participants included patients aged ≥18 years with hypertension, with or without type 2 DM. (Blood pressure [BP] ≥140/90 mmHg or under antihypertensive therapy) and/or diagnosed DM (fasting blood glucose ≥126 mg/dl, random blood sugar ≥200 mg/dl or under oral anti diabetics [OADs] and/or insulin). Pregnant, menstruating or breastfeeding women, patients with urinary tract infection, patients aged less than 18 years were excluded. Type 1 DM, autoimmune disease or receiving treatment with oxytetracycline, and those participating in physical activity in the previous 24 hours, all of which increase the likelihood of a false positive result for MAU (Microalbuminuria) were also excluded from the study. Inclusion criteria for the control group were: age ≥18 years, BP <140/90 mmHg, fasting blood glucose <110 mg/dl and not taking antihypertensive medication or OADs (Oral antidiabetic drugs) or insulin.

STUDY DESIGN AND PROCEDURES

Demographic details and medical history was collected from the patients and physical examination was performed by the physician. BMI was calculated. Biochemical profiles measured included parameters like total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglyceride (TG), creatinine, and albumin and Fasting blood sugar (FBS) and random blood sugar (RBS) from all participants. The urine sample was estimated for urinary microalbuminuria and creatinine and albumin. Laboratory standard operation procedures were maintained for all laboratory analysis. Urine sample microalbuminuria was measured by using a fully automated immune turbidometry method. The levels of MAU considered in the analysis should be ≥30 mg/l.

STATISTICAL ANALYSIS

Results were expressed as mean± SD or percentage where appropriate Statistical analyses were performed using the (SPSS version). Chi-square tests were used to determine the relationship between variables. Bivariate relationships were expressed as odd ratio.

RESULT

(Table 1, 2) show the group of hypertensive patients comprised of 50(33.33%) individuals, 31(62%) of whom were females and 19(38%) were males; the group of hypertensive diabetic patients included 50(33.33%) individuals of which 28(56%) were females and 22(44%) were males and the control group comprised of 50(33.33%) individuals 10(20%) males and 40(80%) females.

Table 1 Distribution of the sample among the three groups studied.

Subgroup	Number	Percentage%	95%Cl
Hypertensive	50	33.33	21.35925 ≤ x ≤ 29.64075
Hypertensive diabetic	50	33.33	21.35925 ≤ x ≤ 29.64075
Control	50	33.33	21.35925 ≤ x ≤ 29.64075

Cl: confidence interval.

Table 2 Distribution of the sample by gender for each of the groups studied.

subgroup	Gender	Number	Percentage
Hypertensive	female	31	62%
	male	19	38%
Hypertensive diabetic	female	28	56%
	male	22	44%
Control	female	40	80%
	male	10	20%

Chi-square test comparing distribution by gender.

Figure 1 A show the prevalence of MAU in the different subgroups. The highest prevalence (86%) was observed among hypertensive diabetic and the prevalence of MAU among nondiabetic hypertensive was 76% and MAU was absent in individuals of the control group. The difference between groups were significant (chi square: p<0.001).

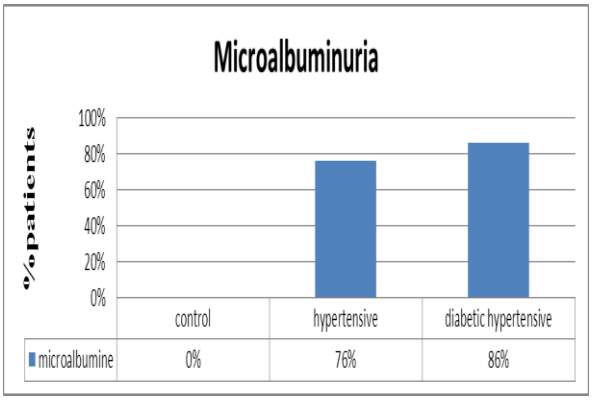

Fig 1A: Prevalence of microalbuminuria in the three groups.

Table 3 show the mean ages of the three subgroups. The hypertensive diabetic group with microalbumineuria was significantly present in older patients (mean age 68.21±10.1 years), followed by the hypertensive group with MAU (mean age 60.65±40.3 years) and the control group (mean age 43.10±21.8 years). Patients with microalbuminuria had higher BMI compared to normoalbiminuric subjects. BMI (Body mass index) in the hypertensive diabetic group with microalbuminuric Vs normoalbuminuric subjects were (28.76±40.09 Vs 25.23+-10.01), followed by the hypertensive group with microalbuminuric Vs normoalbuminuric subjects were (25.98±10.02 Vs 24.42±4.65) and BMI in the control group was (22.30+-1.09) (P<0.05). Patients with microalbuminuria had higher duration of diabetes or hypertension or both as compared to normoalbuminuric subjects (p<0.05). The prevalence of microalbuminuria significantly increased with diabetes or hypertensive duration or both. Table 3 show Glycated haemoglobin HbA1c was significantly higher in microalbuminuric subjects compared to normoalbuminuric subjects. Table 3 shows the microalbuminuria groups had a higher systolic and diastolic pressure compared to the normomicroalbuminuria groups (p<0.001). The microalbuminuria groups had a more deranged lipid profile with higher LDL, TG and lower HDL levels compared to the normomicroalbuminuria groups. The prevalence of microalbuminuria was high in microalbuminuria groups as compare to the normomicroalbuminuria groups.

Table 3: Characteristics of three subgroups (normoalbuminuric and microalbuminuric). (Mean +-SD)

Parameters	Control group	Hypertensive without MA	Hypertensive with MA	Hypertensive diabetic without MA	Hypertensive diabetic with MA
Number	50	12	38	7	43
Age	43.10±21.8	58.12±10.1	60.65±40.3	61.32±12.3	68.21±10.1
BMI	22.30±1.08	24.42±4.65	25.98±10.02	25.23±10.01	28.76±40.03
Duration of hypertensive	0	6.8±6.0	7.1±4.6	3.1±9.1	9.1±5.4
Duration of diabetic (year)	0	0	0	3.9±3.1	9.8±2.20
HbA1C (%)	5.6±3.01	5.7±2.01	5.8±1.04	6.4±3.20	8.9. ±2.0.26
LDL-C(mg/dl)	130.32±11.02	162.24±21.32	225.20±26.30	180.32±21.34	230.26±46.25
TG(mg/dl)	95.43±12.30	147.24±10.1	210.34±50.04	160.21±23.10	240.50±56.06

HDL(mg/dl)	52.87±7.68	45.89±6.23	45.54±1.12	45.70±7.01	45.62±1.12
Systolic BP	120.34+-14.4	149.32±21.30	157.10±24.4	145.13±24	150.13±14.3
Diastolic BP	80.1±12.2	90.01±10.1	95.60±12.1	85.12±10.1	90.01±20.3
Smoking					
Yes	5(10%)	2(16.66%)	33(86.84%)	0	37(86%)
No	45(90%)	10(83.33%)	5(13.15%)	7(100%)	6(13.95%)

Figure 2 shows co morbidities by subgroup. Previous stroke /TIA(Transient Ischemic Attack) were negative in the control group and highest (17%) in the hypertensive diabetic group, PVD(Peripheral vascular diseases) prevalence was (8%) in hypertensive diabetics, 3% in hypertensives, while CVD (Cardiovascular disease) prevalence was highest in hypertensive diabetics (18%), (17%) of hypertensive diabetics had LVH(left ventricular hypertrophy) and (12%) in hypertensive. A history of HF (Heart failure) was observed in 20% of hypertensive diabetics, with much lower percentage in hypertensive patients. The percentage of dyslipidemia was found to be 73%, 63%.18% in hypertensive diabetic, hypertensive and control patients respectively.

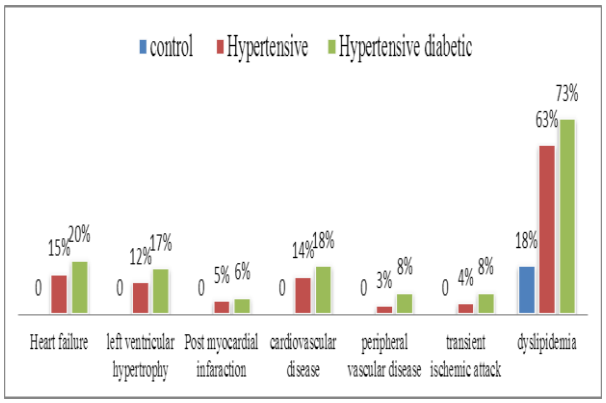

Fig 2 Co morbidities in the three subgroups

Figure 3 show most patients were taking cardiovascular medication. The percentages of lipid-lowering drugs were found to be 68%, 54%, 10% in hypertensive diabetic, hypertensive and control patients respectively. The percentages rennin angiotensin system inhibitors drugs were found to be 44%,43%,0% in hypertensive diabetic, hypertensive and control patients, ACEI (Angiotensin-converting-enzyme inhibitor) prescribed respectively in 35%, 33%, 0% in hypertensive diabetic, hypertensive and control patients, CCBs prescribed in 28%,24%,0% in hypertensive diabetic, hypertensive and control patients, Diuretics were prescribed in 65%, 52%, 0% in hypertensive diabetic, hypertensive and control patients. Beta blocker prescribed in 16%, 18%, 0% in hypertensive diabetic, hypertensive and control patients. Alpha blockers prescribed in 6% of hypertensive diabetic patients. Out of 184 antihypertensive drugs 50% of patients were taking one antihypertensive, 30% were taking two and 20% more than two. Use of OADs or insulin in hypertensive diabetic patient. The mean ±SD number of antihypertensive drugs taken was 2.3±0.4.

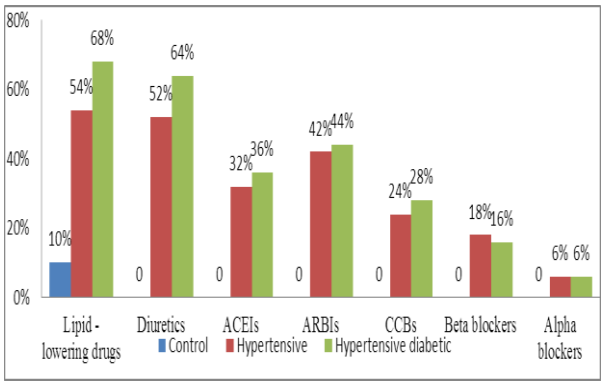

Fig 3 Percentage of patients medicated with lipid - lowering drugs and antihypertensive drugs

Table 4 show results show a clear relationship between MAU and male gender, diabetes, hypertension, HbA1c, total cholesterol, TG (Triglyceride) and use of CCBs (Calcium channel blockers), which are effective cardiovascular risk factors.

Table 4: Multivariate logistic regression analysis of risk factors associated with microalbuminuria

Variable	OR	95% CI	p
Age	1.011	1.002_1.021	0.005
Male	1.123	1.054-1.321	0.014
Famale	0.987	0.980-0.990	0.020
Total cholesterol mg/dl	1.002	1.001-1.004	0.005
TG mg/dl	1.003	1.002-1.005	0.004
HDL cholesterol mg/dl	0.981	0.976-0.989	0.023
Hypertension	2.032	2.015-2.040	<0.001
DM	3.043	3.012-3.044	<0.001
Hypertension+CCBs	1.212	1.209-1.219	0.0029
HbA1c	1.052	1.050-1.060	<0.001
Smoker	2.012	2.011-2.020	0.0032

OR: odds ratio; CI; confidence interval; DM: diabetes mellitus; HbA1C; glycated haemoglobin; CCBs: Calcium channel blockers

DISCUSSION

It was shown in this study that out of 150 patients the group of hypertensive patients was comprised of 50(33.33%) individuals, 31(62%) of whom were females and 19(38%) were males; the group of hypertensive diabetic patients included 50(33.33%) individuals 28(56%) were females and 22(44%) were males and the control group was comprised of 50(33.33%) individuals 10(20%) males and 40(80%) were females(Table 1,2). The prevalence of MAU in female population was higher than in male population in our study where as the reverse was found in other studies conducted in the south-east Asia by Joshi VD.[20] Increased prevalence of MAU in female than in male might be related to lower muscle mass (approximately 15%) hence low creatinuria in woman therefore some authors have suggested the use of sex –related cutoff points to define MAU(2.5-30mgalbumin/mmol creatinine for male and 3.5-30mg albumin/mmol creatinine for female).[21] Median age differed significantly in all subgroups ($p<0.001$): the hypertensive diabetic group with MAU was significantly older (mean age 68.21±10.1), the hypertensive diabetic group without MAU was (mean age 61.32±12.3), followed by the hypertensive group with MAU (mean age 60.65±40.3), the hypertensive group without MAU was (58.12±10.1) and the control group (mean age 43.10+-21.8). The Present study has shown the highest MAU prevalence (86%) was observed among hypertensive diabetic and the prevalence MAU among nondiabetic hypertensive was 76% and MAU was absent in individuals of the control group microalbuminuria, which is much higher when compared to the study by Pedro marques da silva and et al. where the MAU prevalence (58%) was observed among hypertensive diabetic and the prevalence MAU among hypertensive group was 43%.[22] Higher prevalence in the present study may be due to the fact that most of the patients were on irregular treatment with poor glycemic control and high blood pressure also may be due to the small sample size. Method of estimation of microalbuminuria as well as ethnical differences would have also played a role in giving higher prevalence in the present study.

The level of glycemic and blood pressure control seems to be the strongest factor influencing transition from normoalbuminuria to microalbuminuria.[23] Microalbuminuria may be useful in identifying persons at increased risk of coronary heart disease and subsequent death. Therefore, in addition to Framingham score,[24] developing new scores for prediction of absolute risk of primary coronary heart disease should include microalbuminuria.[25] It is important to include microalbuminuria in cardiovascular disease risk assessment because patients with microalbuminuria, especially diabetic patients, have much greater atherosclerotic burden than patients without it.[26] Accordingly, guidelines from the American College of Cardiology and American Heart Association now include microalbuminuria as a potent risk factor for the development of coronary heart disease, as well as a poor prognostic marker in patients with pre-existing coronary disease.[27] This study also showed that increased microalbuminuria level is associated with the higher risk of developing cardiovascular risk. Higher prevalence of MAU have been reported in patients with a longer duration of diabetic and hypertension. This was similar to the results of the studies conducted in Gujarat by Deepak Parchwani[28] it was found that the relevance of MAU significantly increased with duration of diabetes. In another study conducted in Thailand by P buranakit[29] it was found that the prevalence MAU increase with duration of hypertension.

According to American diabetes association (ADA) body mass index 19-25 is taken as normal, while 25-30 is considered as overweight and BMI >=30 is obesity. Weight gain was significantly associated with diabetes.[30] The present study had diabetic hypertensive patients with MAU with mean value of 28.76±40.03, patients with diabetic hypertensive without MAU had a mean value was 25.23±10.01, followed by hypertensive group with MAU with the mean value of 25.98±10.02. Hypertensive patients without MAU the mean value was 24.42±4.65 and the mean value in control group was 22.30±1.08. A study on type 2 diabetes mellitus patients by Mokdad et al reported a correlation between BMI and microalbuminuria.[31] The present study also found a significant correlation between microalbuminuria and BMI as shown in (table 3). However, a study from Africa showed no relation of MAU to BMI.

There is strong evidence that obesity is related to insulin resistance. Several studies have shown an association between microalbuminuria and insulin resistance. and the WHO definition of metabolic syndrome lists microalbuminuria as one of the important component of the syndrome.

The risk of MAU is higher in smokers, than in the nonsmokers.In our study, high occurrence of smokers were found in the MAU groups. This finding is in agreement with studies conducted in Italyan by Bruno G et al.[32]

Our study showed an association between poor glycemic controls with MAU, as there was a significant difference in the HbA1c values among cases of the MAU group in comparison with the NA (normoalbuminuric) group. Similarly, a study was conducted in india by Varghese A et al.[33] Showed the association of glycaemic control with MAU, however other studies conducted by HasslacherC etal. Have failed to confirm this association.[34]

According to Cirillo, the main correlation with microalbuminuria is blood pressure, whether systolic or diastolic. The relationship between blood pressure and microalbuminuria is continuous and gradual because the prevalence of microalbuminuria increases with severity of hypertension.[35] In our study The microalbuminuria

positive group had a higher systolic and diastolic blood pressure compared to the microalbuminuria negative group ($p<0.001$) (Table 3). This was also similar to the results of a study conducted by Hirano T et al.[36] The microalbuminuria positive group had a more deranged lipid profile with higher serum total cholesterol, triglyceride and lower HDL compared to the microalbuminuria negative group. In a prospective observational study by Gall et al. base – line cholesterol was found to be an independent risk factor for the development of microalbuminurria.[37]

The prevalence of MAU may also be affected by treatment. In our study the results show a clear relationship between MAU and CCBs (Calcium channel blockers) which is in agreement with other studies conducted by Bohm M, et al.[38] Although the BP levels of patients using CCBs and those using ACE – inhibitors/ARBs were similar in the present study, treatment to achieve the BP target with CCBs may occur earlier, resulting in effective BP control before target organ damage develops and may explain the lower occurrence of MAU in patients on CCBs.

CONCLUSIONS

The prevalence of MAU in KIMS Hospital is high in hypertensive patients with or without T2DM. According to the analysis of this study, duration of diabetes, poor glycemic control, history of hypertension, smoking and serum levels of cholesterol, HDL and TG are risk factors for MAU. Hypertension and DM are the established risk factor for cardiovascular disease and renal disease. Routine MAU screening by urine strip testing would help identify individuals at risk and increase awareness of kidney disease and TOD.

REFERENCES

1. Mogensen CE. Microalbuminuria in prediction and prevention of diabetic nephropathy in insulin-dependent diabetes mellitus patients. J Diabetes Complicat. 1995; 9: 337-49.
2. Newman DJ, Mattock MB, Dawnay AB et al. Systematic review on urine albumin testing for early detection of diabetic complications. Health Technol Assess. 2005; 9: iii-vi, xiii-163.
3. Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. Am J Hypertens. 2004; 17: 986-93.
4. Montalescot G, Collet JP. Preserving cardiac function in the hypertensive patient: why renal parameters hold the key. Eur Heart J., 2005; 26: 2616-22.
5. World Health Organization. The World Health Report: Reducing Risks, Promoting Healthy Life, 2002. http://www.who.int/whr/2002 (accessed April 2007).
6. Alberti KG. Impaired glucose tolerance: what are the clinical implications? Diabetes Res Clin Pract. 1998; 40(Suppl.): S3-8.
7. Shaw DI, Hall WL, Williams CM. Metabolic syndrome: what is it and what are the implications? Proc Nutr Soc., 2005; 64: 349-57.
8. Jensen JS, Feldt-Rasmussen B, Strandgaard S et al. Arterial hypertension, microalbuminuria and risk of ischemic heart disease. Hypertension., 2000; 35: 898-903.
9. Pedrinelli R, Dell'Omo G, Di Bello V et al. Microalbuminuria, an integrated marker of cardiovascular risk in essential hypertension. J Hum Hypertens., 2002; 16: 79-89.
10. Gerstein HC, Mann JF, Yi Q et al. Albuminuria and risk of cardiovascular events, death and heart failure in diabetic and nondiabetic individuals. JAMA., 2001; 286: 421-6.
11. Wachtell K, Ibsen H, Olsen MH et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE study. Ann Intern Med, 2003; 139: 901-6.
12. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B et al. Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. Circulation, 2004; 110: 32-5.
13. Schmieder RE, Schrader J, Zidek W et al. Low-grade albuminuria and cardiovascular risk: what is the evidence? Clin Res Cardiol, 2007; 96: 247-57.
14. Mancia G, De Backer G, Dominiczak A et al. Guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2007; 25: 1105-87.
15. Chobanian AV, Bakris GL, Black HR et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Hypertension, 2003; 42: 1206-52.
16. Lemley KV, Abdullah I, Myers BD, et al. "Evolution of incipient nephropathy in type 2 diabetes mellitus". Kidney Int. 2000; 58(3): 1228–37.
17. Lièvre M, Marre M, Chatellier G, et al. "The non-insulin-dependent diabetes, hypertension, microalbuminuria or proteinuria, cardiovascular events and ramipril (DIABHYCAR) study: design, organization and patient recruitment. DIABHYCAR Study Group". Controlled Clinical Trials, 2000; 21(4): 383–96.
18. Parving HH, Lehnert H, Bröchner-Mortensen J, Gomis R, Andersen S, Arner P "The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes". N. Engl. J. Med. 2001; 345(12): 870–8.
19. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter., Suppl. 2013; 3: 1-150.

20. Joshi VD, Nandkumar M, Lim J. Prevalence and risk factors of undetected proteinuria in an eldery South-East Asian population. Nephrology (Carlton), 2006; 11: 347–54.
21. Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. Am JHypertens, 2004; 17: 986–993.
22. Marques da Silva P, Carvalho D, Nazaré J et al. Prevalence of microalbuminuria in hypertensive patients with or without type 2 diabetes in a Portuguese primary care setting: The RACE (micRoAlbumin sCreening survEy) study. Rev port cardiol. 2015; 34(4): 237-246.
23. N. K. Chowta, P. Pant, M. N. Chowta. Microalbuminuria in diabetes mellitus: Association with age, sex, weight and creatinine clearance: Indian Journal of Nephrology: April 2009; 19(2).
24. Wilson PW, D'Agostino RB, Levy D, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories Circulation, 1998; 97: 1837–47.
25. Thomsen TF, Davidsen M, Ibsen H, Jørgensen T, Jensen G, Borch-Johnsen K. A new method for CHD prediction and prevention based on regional risk scores and randomized clinical trials: PRECARD and the Copenhagen Risk Score J Cardiovasc Risk., 2001; 8: 291–7.
26. Sukhija R, Aronow WS, Kakar P, et al. Relation of microalbuminuria and coronary artery disease in patients with and without diabetes mellitus Am J Cardiol., 2006; 98: 279–81.
27. Mogensen CE. Practice guidelines for chronic kidney disease Ann Intern Med, 2004; 140: 933–4.
28. Parchwani D, Singh S.P. microalbuminuria in diabetic patients: prevalence and putative risk factors: national journal of community medicine. 2011; 2(1).
29. P. buranakitjaroen, M. phoojaroenchanachai. microalbuminuria in thai essentialhypertensive patients: Journal of International Medical Research, 2007; 35: 836 – 847.
30. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2006; 29: S43–8.
31. Mokdad AH[1], Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes and obesity-related health risk factors. JAMA. 2003 Jan 1; 289(1): 76-9.
32. Bruno G, Cavallo-Perin P, Bargero G. Prevalence and risk factors for micro-and macroalbuminuria in an Italian population-based cohort of NIDDM subjects. Diabetes Care, 1996; 9: 3-7.
33. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes center in Southern India. Postgrad Med J, 2001; 77: 399-402.
34. Hasslacher C, Bostedt-Kiesel A, Kempe HP, Wahl P. Effect of metabolic factors and blood pressure on kidney function in proteinuric type 2 (non-insulin-dependent) diabetic patients. Diabetologia, 1993; 36: 1051-6.
35. Cirillo M, Lombardi C, Bilancio G, Chiricone D, Stellato D, De Santo NG. Urinary albumin and cardiovascular profile in the middle-aged population. Semin Nephrol. 2005; 25(6): 367-71.
36. Gall MA, Hougaarod P, Borch-Johnsen K, Parving HH. Risk factors for development of incipient and over diabetic nephropathy in patients with non-insulin dependent diabetes mellitus prospective observation study. BMJ. 1997; 314: 783-8.
37. Bohm M, Thoenes M, Danchin N, et al. Association of cardiovascular risk factors with microalbuminuria in hypertensive individuals: the i-SEARCH global study. J Hypertens. 2007; 25: 2317-24.