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Application of SEM model in identifying the interrelationship of risk factors of microalbuminuria among type II diabetes mellitus

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Abstract

Background: *Diabetes is one of the largest health emergencies of the 21st century. In future there will not only be increase in the incidence and prevalence of diabetes but also there will be an increase in economic burden, disability and life years lost due to disease. Microalbuminuria is used as predictor for early micro and macrovascular changes in diabetes.*

Objectives: *The objectives wereto find the interrelationship between the known risk factors of microalbuminuria among diabetic patients.*

Methodology: *A descriptive cross sectional study was carried out in the urban field practice area of urban health centre between October 2015 and July 2016, among 200 study participants who had type II diabetes mellitus.*

Results: *The prevalence of microalbuminuria among the study participants was 41.5%. According to Structural equation modelling, Age, duration of diabetes, duration of hypertension, systolic blood pressure and diastolic blood pressure were found to influence the occurrence of microalbuminuria in type II diabetes mellitus patients.*

Conclusion: *An intensive education of patients as well as general practitioners on microalbuminuria, risk factors and their interactions were mandatory to prevent various complications.*

Keywords: *Microalbuminuria, Type II diabetes mellitus, duration of diabetes, duration of hypertension.*

Introduction

Global prevalence of diabetes mellitus (DM) has increased dramatically over the past 2 decades (from 177 million in 2000 and 285 million in 2010) and if this situation continues, by 2030 more than 360 million people will have DM.[(1)]

expecting that DM remains among the main causes of human mortality and morbidity [1,4]. Diabetes mellitus is known for its microvascular and macrovascular complications that contribute to high rates of mortality and morbidity associated with this disease[4] As the number of persons with diabetes increases, the development of microvascular complications like retinopathy, nephropathy and neuropathy also rises.[2] The magnitude of damage caused by these microvascular complications of diabetes stresses the need for sensitive markers of screening for retinopathy and nephropathy [2].

Kidney disease in type 2 DM is more complex for several reasons, mainly because the onset of DM is almost unknown and may be many years before diagnosis.[1] Diabetic nephropathy (DN) is a progressive kidney disease and, at present, in many countries, is the most common cause of end-stage renal disease (ESRD).[5,8] The risk of developing DN starts with albuminuria, progressing from micro- to macroalbuminuria.[8] Microalbuminuria associated with diabetes is an independent risk factor for developing diabetic nephropathy[3] also as one of the initial markers of this condition which indicates an increased risk of deteriorating renal function and mortality [5,6,8]. With no therapeutic intervention is in place, about 20% to 40% of type 2 diabetic patients with microalbuminuria, progress to overt nephropathy and finally approximately 20% develop end-stage renal failure [1]

Microalbuminuria is defined as subclinical urinary excretion of albumin and it has been shown to predict the progression of renal disease in patients with diabetes[6] Microalbuminuria, defined as a urinary albumin excretion rate of 30 to 300 mg/d, or 20 to 200 mg/min, is the earliest clinical sign of nephropathy[9] In diabetics, increased glucose levels leads indirectly, through various metabolic pathways cause endothelial damage including glycocalyx disruption[11] In the capillaries of the renal glomeruli, albumin binds to the glycated basement membrane which leads to increased basement membrane thickening and is a characteristic of diabetic microangiopathy [10]

This endothelial damage is reflected by microalbuminuria[11]. microalbuminuria is also a marker of greatly increased cardiovascular morbidity and mortality in patients with type I or type II DM. [9] Microalbuminuria represents the simplest and most sensitive prognostic factor to evaluate the risk of overt nephropathy in diabetes, representing the first stage of progressive diabetic renal disease [11] It is at this stage that one can hope to reverse diabetic nephropathy or prevent its progression.[13]

Early recognition and treatment of microalbuminuria can prevent irreversible complications such as kidney problems, which ultimately leads to kidney failure and cardiovascular events [1]. Though renal biopsy that is the gold standard diagnostic investigation for diabetic nephropathy [1]. Microalbuminuria is the most sensitive marker widely used as diagnostic investigation [11]. A diagnosis of microalbuminuria can be made by measuring its excretion rate during 24 hours or in an overnight urine collection, or by measuring albumin/creatinine ratio or albumin concentration in the morning or a random urine sample.[13]

The Developing Education on Microalbuminuria for Awareness of Renal and Cardiovascular risk in Diabetes (DEMAND), a multinational cross-sectional clinic/center-based study, revealed that approximately 50% of type 2 diabetic patients had micro- or macroalbuminuria, and Asians had a higher prevalence of albuminuria compared with Caucasian patients[8] Patients with type 2 diabetes often have a clustering of risk factors [5] leading to the microvascular complications which are the duration of diabetes mellitus, poor glycaemic control and systolic hypertension [2] The main risk factors identified in DEMAND were HbA1c, systolic blood pressure (BP), ethnicity, retinopathy, duration of diabetes, kidney function, body height, and smoking.[8] Because of the ageing population and an increase in obesity and sedentary lifestyle, the prevalence of diabetes is growing, particularly in Asia. The prevalence of hypertension is even greater in patients with type 2 diabetes and elevated urinary albumin excretion (UAE).[5] systolic blood pressure (BP) is found to

be an independent risk factor for albuminuria in type 2 diabetes mellitus (T2DM). Based on these studies, the prevalence of albuminuria is expected to be higher in T2DM with hypertension relative to T2DM without hypertension, but it has been largely unexplored.[17]

Thus the present study was carried out with objectives of finding the interrelationship between the known risk factors of microalbuminuria among diabetic patients.

Methodology

The study was a descriptive cross-sectional type conducted in carried out in the field practice area of Urban Health centre (UHC) under division of community medicine, Rajah Muthiah Medical Collge and Hospital, Chidambaram, Tamilnadu. The study was carried out for a period of 10 months from October 2015 to July 2016. People living in field practice area of urban health centre, aged more than 30 years and had type II diabetes mellitus had been included in the study. The study was ethically approved by the ethical committee of the same institute. Also informed consent was obtained from participants prior to interview.

Sample Size Calculation

With absolute prevalence fixed as 7% and prevalence as 0.4 the sample size was calculated to be 188 which was then rounded upto 200 thus taken as the sample size. Convenient sampling was applied by house to house visit in the study area till the required sample size was achieved. Persons aged >30, non diabetic, sick, pregnant and rheumatic heart diseases were excluded.

Study tool and data collection

Study tool used in the study was a pretested semi structured questionnaire including details on socio-demographic details, anthropometry, clinical examination and biochemical examination. Proforma was prepared in English and local dialect, was used during interview to make it convenient for the participants.

In the study tool, Socio-demographic details included age, sex, marital status, educational status and income. The information regarding diabetes and hypertension were collected which included details on the duration of diabetes and hypertension, whether they were taking their anti-diabetic and anti-hypertensive medications regularly and the drugs that they were taking to treat the conditions. Further information was collected on lifestyle habits- smoking and alcohol consumption.

Following the data collection, height and weight of the study participants were measured. body Mass Index (BMI) was calculated by using the formula weight (kg)/height (m) 2. Blood Pressure was measured by sphygmomanometer and Stethoscope in sitting position. Urine samples of the participants were collected in sterile containers and were sent to the laboratory within 20 minutes for the estimation of urine albumin and urine creatinine values.

Data Analysis

Data collected was entered in Microsoft 2013 excel spread sheet, compiled and analysed using IBM SPSS Version 21 statistical package. Descriptive statistics, Pearson chi-square test and logistic regression analysis were performed to find out association between microalbuminuria and selected risk factors, co-morbid conditions.

Results

Out of the 200 study participants with type II diabetes mellitus, 59.5% belonged to the age group of 51-70 years. The mean age of the study participants was 57.34 ± 10.87 years. (Table 1)

42.5% of the study participants had systolic blood pressure of more than 140 mmHg and 34% had their systolic blood pressure between 140 and 159 mmHg. Diastolic blood pressure was recorded to be more than 90 mmHg in 47% of the study participants and between 80 to 89 mmHg in 29% of the study participants (Table: 2). The duration of diabetes mellitus among 50.5% of the study participants was 2 to 5 years. Among the study participants, 43% had hypertension for 2 to 5 years. (Table: 3)

According to Structural equation modelling, Age, duration of diabetes, duration of hypertension, systolic blood pressure and diastolic blood pressure were found to influence the occurrence of microalbuminuria in type II diabetes mellitus patients. All these factors were also found to be influencing one another, age was found to influencing duration of diabetes mellitus. Both age and duration of diabetes were found to be influencing systolic blood pressure and all the three were found to be influencing microalbuminuria. This interaction extents to almost all the selected risk factors. (fig 1)

Table: 1 Distribution of study participants according to age.

Age	N	%
31-40	19	9.5
41-50	38	19
51-60	67	33.5
61-70	52	26
>70	24	12
Total	200	100

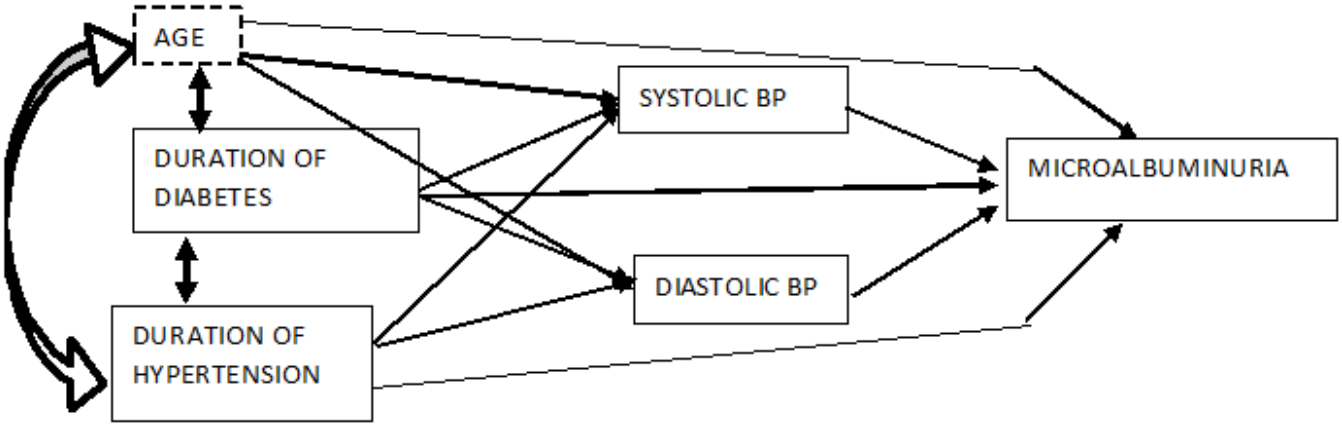
Table: 2 Distribution of study participants according to systolic and diastolic blood pressure.

Systolic blood pressure (mm/Hg)	N	%
< 120	47	23.5
120-139	68	34
140-159	77	38.5
≥160	8	4
Diastolic blood pressure (mm/Hg)	N	%
< 80	48	24
80-89	58	29
90-99	74	37
≥ 100	20	10
Total	200	100

Table: 3 Distribution of study participants according to the duration of diabetes mellitus and hypertension.

Duration of diabetes mellitus. (years)	N	%
≤ 1	33	16.5
2-5	101	50.5
6-10	32	16
11-20	17	8.5
>20	17	8.5
Duration of hypertension (years)	N	%
≤ 1	19	19
2-5	43	43
5-10	19	19
10-20	17	17
>20	2	2
Total	100	100

Fig: 1 Relationship between selected risk factors and microalbuminuria using structural equation modelling.



Discussion

Microalbuminuria is not only the earliest manifestation of diabetic nephropathy but is also a significant risk factor for the progression of nephropathy in diabetic patients [17] As one of the first clinical symptoms of diabetic nephropathy it may progress to macroalbuminuria and the progressive loss of glomerular filtration rate (GFR) and finally the end stage renal disease. Elder patients often suffer from other diseases,

including hypertension and atherosclerosis, which can also damage the renal parenchyma. [1,5]
Microalbuminuria is thus an indicator of possible vascular disease requiring aggressive intervention to reduce cardiovascular risk. Various epidemiological and cross-sectional studies have reported marked variation in the prevalence of microalbuminuria, ranging from less than 10% in the United Kingdom8,9 to 18% in Singapore10 and more than 30% in southern India. [9]
Microalbuminuria is likely to be found in one-third or more of diabetic patients [1]

Prevalence

In the present study the prevalence of microalbuminuria among the type 2 diabetes mellitus patients in urban Chidambaram was found to be 41%. This is similar to the result of studies conducted in neighbouring Asian countries reported different prevalence rates of microalbuminuria ranging from 14.2% in Iran to 36.3% in India. While in other European countries, the total prevalence was observed as 47%. [1] Also similar findings were reported by Aldani et al and Chota et al [8,13]
According to a report by the World Health Organization (WHO), the prevalence rates of nephropathy after 15 years of diabetes ranged between 17.7 and 56.6% in men and between 11.9 and 71% in women[2] supporting the outcome of our result. It was also observed that the prevalence of microalbuminuria was found to be 52.04% among all diabetic patients [10].
The MAPS is the first large multicentre epidemiological study conducted in Asia to determine the prevalence of microalbuminuria and macroalbuminuria in patients with type 2 diabetes and hypertension. The prevalence of microalbuminuria was slightly higher than the rates of 17% to 21% reported from western population–based studies in patients with diabetes.[5] which is contrast to our study results.
In Zakerkish et al study done in Iran the prevalence rates of microalbuminuria in diabetic patients vary from 16.7% to 35.2%. In another study carried out by this group in 2008, they showed 33% microalbuminuria which is much lesser than our results[1] though it shows the increase in the prevalence still lesser than the present study result. In rani et al the prevalence of microalbuminuria was 191 out of1166, 16.4% in individuals with known diabetes, It means that every 6th individual in the population ofindividuals with diabetes had albuminuria. [2]

Age and microalbuminuria

Age is found to influence occurrence of microalbuminuria. Rani PK et al stated that microalbuminuria occurrence is influenced by age, raised blood pressure and poor glycaemic control [2]. Chowta NK et al reported a similar relationship between age and microalbuminuria occurrence in type II diabetes mellitus patients.[13]. Similar association with age were also recorded byParving et al [16], Tam TKW et al., in 2004 [9].

Duration of diabetesand microalbuminuria

As the duration of diabetes mellitus increased so do the probability being microalbuminuric. Similar association was also reported by Rani PK et al [2]. Zakkerkrish M et al also stated that similar association in their univariate analysis [1]. Chowta et al in their study has stated a similar correlation between microalbuminuria and type II diabetes mellitus. Nakhjavani and colleagues showed that only the duration of DM, HDLC, and Hb A1c were the independent risk factors [1]. Tam TKW et al, Agarwal J et al and Baig et al also stated a similar increase in probability [9,10,12].

Duration of hypertensionand microalbuminuria

As the duration of hypertension increased so did the occurrence of microalbuminuria. Similar significant association between duration of hypertension and microalbuminuria in type II diabtes mellitus individuals were reported by Al-Rubeaan K et al [4]. Microalbuminuria is also characterized by increased prevalence of arterial hypertension [13]. Rani Pk et al also reported similar association.

Systolic blood pressure and microalbuminuria

Increase in systolic blood pressure was associated with increase in microalbuminuria incidence. Yang C et al also reported similar associations between systolic blood pressure and microalbuminuria. Elevated blood pressure is documented as the most significant contributing factor in the pathogenesis and the progressionof abnormal AER and eventually development of diabetic nephropathy in both Type 1 and Type 2 diabetic patients. Type 2 patients with abnormal AER had statistically significant higher SBP and DBP than those with normal AER, ($p < 0.0001$) [(15)]. Al-Adsani A reported hypertension as independent risk factor associated with albuminuria [(8)].

Diastolic blood pressure and microalbuminuria

Increase in diastolic blood pressure was associated with increased occurrence of microalbuminuria. Rani PK et al reported that the diastolic blood pressures were higher in those individualswith macro - or microalbuminuria compared to those with normoalbuminuric (83.8 ± 12.9 vs. 84.0 ± 11.5 vs.81.5 ± 11.2, p = 005) For microalbum-inuria, the significant variables included increase in age per year Odds Ratio (OR) 1.01 (95% CI: 1.00-1.04), increase in systolic blood pressure per mm of Hg OR 1.01 (95% CI: 1.00-1.02) [(2)]. Similar findings were also reported by Unni Krishnan et al [(2)].

Conclusion

The selected risk factors were found to interact with each other and also with microalbuminuria. An intensive education of patients as well as general practitioners on microalbuminuria, risk factors and their interactions were mandatory to prevent various complications.

Limitations

The definition of albuminuria and diabetic nephropathy is another source of discrepancy, as well as the methods of measurement of albuminuria and urine collection.The results of the study cannot be generalized because the study was confined to urban population of the field practice area. Recall bias can be present in association with certain variables of the study, where the study participants had to remember past dates. Microalbuminuria has a high biological variability. Though albumin creatinine ratio was used to estimate microalbuminuria in order to overcome this variability, it will not account to the variation fully.

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