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Original Research Article

Association of Microalbuminuria with Glucose Levels, Microvascular and Macrovascular Complications in Relation with Blood Pressure in Diabetes Mellitus Type 2

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Abstract: ***Objectives***: Determine the association of Microalbuminuria (MAU) with glucose markers, micro vascular and macrovascular complications in relation with blood pressure in patients with type 2 diabetes mellitus. ***Material and Method***: This study was cross sectional study and data collected in Chemical laboratory of pathology department of Dr Akbar Niazi Teaching Hospital. It carried out during the time period of December 2021 to January 2022. Patients were divided into 2 groups which fulfill the inclusion and exclusion criteria patients having diabetes mellitustype 2 with good glucose control, HbA1c < 7% (n=33) patients having diabetes mellitus type 2 with bad control HbA1c ≥7% (n=33) each group were further dividedinto 2 sub-groups Patients with Pre-hypertension (n) and patients with HTN (n). The sampling technique of this study was non-probability convenience sampling was done. Data/Documentation was collected by Performa and laboratory investigation. Spss version 21 used to analyze the data. Normality of data was assessed by KS test. Quantitative test was measured as mean and standard deviation. Qualitative variables were calculated as number percentage. ANCOVA test and chi square test were used for comparison of quantitative and qualitative variables respectively. Pearson correlation was applied to determine the association of MAU with glucose levels and diabetes related complications. ***Result***: Among total 66 patients, the sample of patients were included 47 males (71.2%) and 19 females (28.8%). Patients of type 2 diabetes mellitus in HbAlc ≥7% group showed higher levels of Blood Glucose level, MAU, Systolic BP and Diastolic BP as compared to HbA1c < 7% group. The comparison of the variables between 2 groups showed statistical differences in nephropathy and cardiovascular complications. In HbA1c ≥ 7% group, correlation of MAU with Systolic BP, Diastolic BP, Fasting Blood Glucose (FBG), HbA1c, Nephropathy, and Cardiovascular events were statistically significant. In Pre-HTN group, MAU was significantly correlated with Fasting blood glucose level, HbA1c, Nephropathy and cardiovascular complications. Patients of HTN showed more significant association with blood pressure (BP), BloodGlucose, HbA1c, Cardiovascular events with MAU as evident by higher r-values as compared to pre-HTN group. Regarding nephropathy, r-value was slightly higher in Prehypertensive group. ***Conclusion***: Patients with uncontrolled diabetes mellitus have increased risk of developing HTN, MAU as well as diabetes related complication including nephropathy and cardiovascular events. More over MAU showed significant positive association with BP, blood glucose levels, nephropathy and cardiovascular events. Both pre- hypertensive and hypertensive patients showed significant positive association of MAU with blood glucose levels and diabetes related complication including nephropathy and cardiovascular events. This study suggested that Prehypertensive andhypertensive patients with altered blood glucose levels have increased risk of MAU, that why proper evaluation and treatment of MAU may lead to early diagnosis and decrease progression of HTN, diabetes mellitus type 2 and its related complications.

Keywords: Microalbuminuria, macrovascular complications, glucose markers, diabetes mellitus, Nephropathy, Cardiovascular.

INTRODUCTION

Diabetes Mellitus

Diabetes mellitus (DM) is the most common disease in humans and spreads worldwide. Diabetes is an ailment characterized by chronic hyperglycemia, carbohydrate and lipid disturbance and protein metabolism associated with absolute or relative insulin deficiency secretion (action of insulin). Long-term complications affecting the retina, kidneys and the nervous system as micro-vascular complications [1].

Pathogenesis

Type 1 Diabetes

Type 1 diabetes mellitus (T1DM) is usually diagnosed in children and young adults. It develops when the body's immune system destroys pancreatic beta cells, the only cells in the body that make the hormone insulin, which regulates blood glucose.

Type 2 Diabetes

T2DM is the most common form of diabetes. The causes of T2DM are multi-factorial and include both genetic and environmental elements that affect beta-cell function and tissue (muscle, liver, adipose tissue, and pancreas) insulin sensitivity. In type 2 diabetes, either the body does not produce enough insulin or the cells ignore the insulin. It usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce it.

When glucose builds up in the blood instead of going into cells, it can cause far- reaching health implications like heart disease, nerve damage and kidney damage.

Global Problem

T2DM is recognized as a serious public health problem that affects life and human health. Due to the rapid development and urbanization of industry, diabetes mellitus is increasing in many parts of the world [2]. Diabetes mellitus affects an individual's functional capacity and quality of life, leading to significant morbidity and premature mortality [3]. Recently, concerns have been raised that more than one-third of diabetes-related deaths occur in people under the age of 60 [4]. The fact that different proportions of people with T2DM have not been diagnosed or treated is a major public health problem. T2DM is distinguished by abnormal regulation of lipid, carbohydrate, and protein metabolism, leading to impaired insulin resistance or hyperglycemia. T2DM is more common than other gestational diabetes mellitus and T1DM.

Local Problem

The international diabetes mellitus federation diabetes mellitus atlas 2017 ranks Pakistan at number 2 out of 21 countries for the prevalence of diabetes mellitus in the Middle East and North Africa (MENA) region, with 7.5 million cases of diabetes mellitus (20–79 years), and at number 18 out of 21 countries for its 6.9% prevalence of diabetes mellitus (20–79 years) [5].

Overall weighted prevalence of diabetes mellitus was 26.3%, of which 19.2% had known diabetes, and 7.1% were newly diagnosed people with diabetes. Prevalence of diabetes mellitus in urban and rural areas was 28.3% and 25.3%, respectively. Prevalence of pre-diabetes mellitus was 14.4% (15.5% in urban areas and 13.9% in rural areas). Age greater than or equal to 43 years, family history of diabetes, HTN, obesity and dyslipidaemia were significant associated risk factors for diabetes [6].

The prevalence is higher in males than females and more common in urban areas compared to the rural areas. Pakistan must include diabetes mellitus preventive measures in their national health policy to minimize the burden of the disease. [7].

Microalbuminuria

Microalbumin in HTN shown to be the first sign of renal damage and predictor of end stage kidney disease and heart disease Studies also revealed the association of MAU with development of cardiovascular diseases [8].

MAU is defined as excretion of albuminuria in urine, which cannot be detected by normal routine dipstick method [9].

Hypertension: Hypertension (HTN) is classified according to the JNC-VII definition of blood pressure (BP) readings.

Normal: Normal (systolic <120 mmHg and diastolic <80 mmHg).

Pre-Hypertensive: Prehypertensive (systolic 120 to 139 mmHg or diastolic 80 to 89mmHg).

Hypertension: HTN stage I (systolic 140 to 159 mm Hg. Or diastolic 90 to 99 mm Hg) And HTN stage II (systolic ≥160 or diastolic 00-100 mm Hg) [10].

Microvascular

People with diabetes mellitus are at increased risk of developing micro-vascular complications of small blood vessels or macro-vascular complications that affect large blood vessels [11]. Arterial narrowing reduces blood flow to the heart, brain, or legs, leading to a variety of Macro-vascular diseases. The effects of micro-vascular problems such as kidney, retinal and organ neuropathy increase with the duration of diabetes. Macro-vascular problems associated with diabetes, i.e., coronary heart disease, cerebrovascular disease and vascular disease are the result of an increase in atherosclerosis.

Diabetic Retinopathy

Diabetic retinopathy is probably the most common problem of diabetes. In the United States alone, it is responsible for about 10,000 new blind patients each year [12]. The risk of developing diabetic retinopathy or other microcardiovascular complications of diabetes mellitus depends on the duration and severity of hyperglycemia.

Diabetic Nephropathy

Diabetic nephropathy is the leading cause of kidney failure in the United States. It is defined by proteinuria of more than 500 mg per 24 hours in a diabetic situation, but a low level of proteinuria preceding it, "microalbuminuria". MAU is defined as 30-299 mg/24 h of albumin excretion.

Diabetic Neuropathy

The American Diabetes Association (ADA) has identified Diabetic neuropathy as "the presence of symptoms or signs of peripheral nerve dysfunction in diabetic patients after excluding other causes [13].

Macrovascular Disease

Central macrovascular disease is the process of atherosclerosis that leads to narrowing of the arterial wall throughout the body. Atherosclerosis is thought to be caused by chronic inflammation and damage to the walls of the limbs and coronary arteries [14].

The purpose of this study is to determine the association of albuminuria with glucose markers, micro vascular and macrovascular complications in relation with BP in patients with diabetes mellitus type 2. Currently, in Pakistan the data is still limited that's why this study was planned.

Diabetes, Hypertension and Microalbuminuria

Diabetes mellitus and HTN are more common diseases that co-exist in great numbers. The risk of heart disease, peripheral vascular disease, and renal disease in diabetic patients is high [15]. T2DM patients may have HTN for several years before the appearance of diabetes. In the diagnosis of type 2 diabetes, HTN is present in approximately 70-80% of patients. BP is higher in diabetic nephropathy patients [16].

Diabetic nephropathy is the main reason of End-stage renal disease (ESRD) which is also called ESRD worldwide [17]. The development of diabetic nephropathy is characterized by excretion of great amount of proteins more especially albumin. Early and prolonged increase in systolic BP and delayed decrease in glomerular filtration rate, which ultimately leads to end-stage renal failure High BP and MAU are often associated with each other. MAU is a risk factor for the development of heart and cerebrovascular diseases. In addition, MAU is an early marker of renal damage and has been identified as the leading cause of ESRD and coronary heart disease. Even high BP is associated with an increased risk of MAU and may be a biomarker of increased cardiac output. MAU can also be described as an indicator of the significant increase in kidney disease and heart disease associated with insulin resistance and metabolic disorders.

Risk Factor

Kidney disease associated with coronary heart disease and MAU (i.e. urinary albumin release of 30 - 300 mg / day, or 20-200 µg/min) [18]. Predicts adverse effects in patients with kidney and heart disease. In the United States, about 6% of men and 9.7% of women have MAU [19]. MAU does not directly cause cardiac events; it serves as a signal to alert those who may be at increased risk. High BP is thought to increase MAU in association with changes in blood sugar levels. Therefore, the detection of MAU in HTN, where blood glucose levels are mild to moderate, especially in the initial stages of the disease, may help to reduce the development and progression of complications associated with diabetes.

There is ample evidence to suggest that people with T2DM (T2D) may be at risk for epidemiological and mechanical microvascular and macrovascular diseases. For example, results from prospective diabetes mellitus study in the UK show that the risk of T2-DM-related macrovascular and micro vascular complications was associated with hypoglycemia [20].

MATERIALS AND METHODS

Ethical Clearance

Ethical clearance of the study was obtained from Institutional review board (IRB) of Islamabad Medical and Dental College (IMDC) (IRB letter No. 50/IMDC/IRB-2021) prior to study conductance. Permission was obtained from Director, Dr. Akbar Niazi Teaching hospital for collection of data from Pathology and Nephrology department. Confidentiality of the data was maintained throughout the study.

Study Setting

This was a cross-sectional study conducted in the department of pathology and nephrology of Dr. Akbar Niazi Teaching Hospital (ANTH) in Islamabad from December 2021.

Subjects

Inclusion Criteria:

Both male and female age 30-75 years with FBG≥ 110 mg/dl and hba1c ≥ 5.7% with or without history of HTN.

Exclusion Criteria:

Patients with gout, acute renal failure, liver disorders, urinary tract infection, systemic infections, major cardiovascular events, neoplastic disease, thyroid disorders, parathyroid disorders, adrenal disorders, as well as people, who could not cooperate, were excluded from the study.

Data Collection

Clinical Data

Patients were divided into 2 groups which fulfill the inclusion and exclusion criteria Patients having diabetes mellitus type 2 with good glucose control, hba1c <7% (n=33). Patients having diabetes mellitus type 2 with bad control hba1c ≥7% (n=33). Each group was further divided into 2 subgroups Patients with PreHTN (n) and patients with HTN (n)

Laboratory Investigation

Data Analysis

Spss version 21 used to analyze the data. Normality of data was assessed by KS test. Quantitative test measured as mean and standard deviation. Qualitative variables calculated as number percentage. ANCOVA test and chi square test were used for comparison of quantitative and qualitative variables respectively. Pearson correlation was applied to determine the association of MAU with glucose levels and diabetes mellitus related complications. P-value<0.05 was considered statistically significant.

RESULTS

Demographic Data

Among total 66 patients, there were 47 males (71.2%) and 19 females (28.8%) (Table4.1). baseline demographic and biochemical characteristics of participants had been provided in Table 4.1. The mean and standard deviation result of age of the participant 53.09±10.48.

The mean and standard deviation result of HbA1c test of patients was 7.68 ± 1.38%. Mean and standard deviation of urinary albumin level in patients is 3.69 ± 1.51 mg/mmol. Out of 66 patients 4 (6%) were affected by retinopathy, 11(16.6%) have nephropathy. Total 4 (6%) were affected by neuropathy, and 19 (28.7%) patients showed cardiovascular events out of 66 patients.

Comparison of Demographic and Biochemical Variables between Two Groups

Comparison of BMI (kg/m2), Systolic BP (mmHg), Diastolic BP (mmHg), FBG (mmol), HbA1c, Retinopathy, Nephropathy, Neuropathy, Cardiovascular within two groups of HbA1c (<7, ≥7) shown in (Table 4.2). Patients of T2DM in HbAlc ≥7% group showed significantly higher levels of Systolic BP (mmHg),Diastolic BP (mmHg) and MAU as compared to HbA1c < 7% group.

Comparison of Macrovascular and Microvascular Complications

The comparison of the variables between 2 groups showed statistically increased number of nephropathy and cardiovascular complications in HbA1c ≥7% group. Comparison of retinopathy and neuropathy was non-significant (Table 4.3).

Correlation of Microalbuminuria with Variables

In patients having HbA1c < 7%, correlation of MAU with all biochemical variables (BMI (kg/m2), Systolic BP (mmHg), Diastolic BP (mmHg), FBG (mmol), HbA1c, Retinopathy, Nephropathy, Neuropathy, Cardiovascular) was non-significant (Table 4.4).

In HbA1c ≥ 7% group, correlation of MAU with Systolic BP (mmHg), Diastolic BP (mmHg), FBG (mmol), HbA1c, Nephropathy, and Cardiovascular events were statistically significant. Moreover BMI (kg/m2) Neuropathy and Retinopathy showed no significant correlation with MAU (Table 4.4).

Correlation of Microalbuminuria with Biochemical Variables in Blood Pressure Group

In PreHTN group, MAU was significantly correlated with FBG level, HbA1c, Nephropathy and cardiovascular complications. Retinopathy, Neuropathy, BMI, Systolic BP, diastolic BP and duration of diabetes mellitus showed no significant association with MAU in PreHTN patients (Table 4.5).

Patients of HTN showed more significant association with BP, Diastolic BP, Blood Glucose, HbA1c, Nephropathy and Cardiovascular events with MAU as evident by higher r-values as compared to PreHTN group. BMI, duration of diabetes, Retinopathy and neuropathy showed no significance correlation with MAU in hypertensive patients (table 4.5).

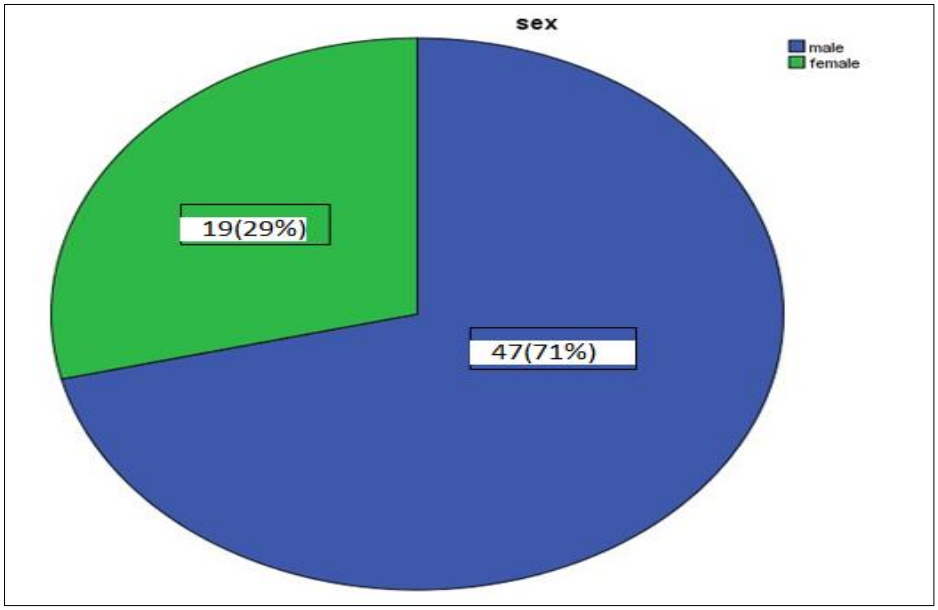

Figure 4.1: Frequency of male and female patients in study population.

Table 4.1: Demographic & biochemical characteristics of study participants.

Sr no	Variables	Mean ± Std. Deviation
1	BMI (kg/m2)	26.24 ± 1.987
2	Systolic BP (mmHg)	137.04 ± 11.86
3	Diastolic BP(mmHg)	89.24 ± 8.378
4	Duration of diabetes mellitus	12.33 ± 4.818
5	FBG (mmol)	9.62 ± 2.17
6	HbaA1c (%)	7.68 ± 1.377
7	Urinary Albumin (mg/mmol)	3.69 ± 1.512

BMI: BODY MASS INDEX

FBG: FASTING BLOOD GLUCOSE HBA1C: GLYCOSYLATED HEMOGLOBIN BP: BLOOD PRESSURE

Table 4.2: Comparison of variables between two groups (n=66).

Variables	HbA1c <7	HbA1c ≥7	
	Mean ±SD	Mean ±SD	P-value
BMI (kg/m2)	25.31 ± 1.45	27.17 ± 2.025	0.001
Systolic BP (mmHg)	130.75 ± 9.11	143.33 ± 11.01	0.001
Diastolic BP (mmHg)	84.70 ± 6.60	93.79 ± 7.503	0.001
Duration of diabetes mellitus	11.21 ±4.82	12.97 ± 4.061	0.108
FBG (mmol)	7.69± .55	11.54 ± 1.28	0.001
HbA1c (%)	6.46 ± 35	8.89 ± 82	0.001
Urinary Albumin (mg/mmol)	2.60 ± .89	4.77 ± 1.18	0.001

BMI: BODY MASS INDEX

FBG: FASTING BLOOD GLUCOSE HBA1C: GLYCOSYLATED HEMOGLOBIN BP: BLOOD PRESSURE

Table 4.3: Comparison of macrovascular and microvascular complications between two groups (n=66)

Complications	HbA1c <7			HbA1c ≥ 7			p- value
	No, n(%)	Yes, n(%)	Total, n(%)	No, n(%)	Yes, n(%)	Total, n(%)	
Retinopathy	31 (93.9)	2(6)	33	31 (93.9)	2 (6)	33	1.000
Nephropathy	31 (93.9)	2(6)	33	24 (72.72)	9 (27)	33	0.044
Neuropathy	32 (96.96)	1(3)	33	31 (93.9)	2 (6)	33	1.000
Cardiovascular	32 (96.96)	1(3)	33	15 (45.45)	18 (54)	33	0.001

Table 4.4: Correlation of microalbuminuria with biochemical variables (n=66).

Variables	HbA1c <7		HbA1c ≥7	
	r-value	P-value	r value	P-value
BMI (kg/m2)	0.103	0.57	0.128	0.33
Systolic BP (mmHg)	0.33	0.061	0.857	0.001
Diastolic BP (mmHg)	0.126	0.48	0.849	0.001
FBG (mmol)	0.202	0.259	0.639	0.001
HbA1c (%)	0.179	0.319	0.629	0.001
Retinopathy	0.073	0.68	-0.212	0.236
Nephropathy	0.024	0.894	0.520	0.002
Neuropathy	-0.165	0.358	0.246	0.167
Cardiovascular	-0.027	0.881	0.620	0.001

BMI: BODY MASS INDEX
FBG: FASTING BLOOD GLUCOSE HBA1C: GLYCOSYLATED HEMOGLOBIN BP: BLOOD PRESSURE

Table 4.5: Correlation of microalbuminuria with biochemical variables in blood pressure group (n=66).

Variables	Pre hypertension		Hypertension	
	r value	P value	r value	P value
BMI (kg/m2)	0.236	0.210	0.381	0.22
Systolic BP (mmHg)	0.184	0.330	0.413	0.012
Diastolic BP(mmHg)	-0.031	0.872	0.535	0.001
Duration of Diabetes mellitus	-0.059	0.758	0.238	0.161
FBS (mmol)	0.587	0.001	0.680	0.001
HbaA1c (%)	0.593	0.001	0.671	0.001
Retinopathy	-0.015	0.938	-0.302	0.073
Nephropathy	0.567	0.001	0.535	0.001
Neuropathy	-0.158	0.405	0.246	0.148
Cardiovascular	0.563	0.001	0.593	0.001

BMI: BODY MASS INDEX
FBG: FASTING BLOOD GLUCOSE HBA1C: GLYCOSYLATED HEMOGLOBIN BP: BLOOD PRESSURE

DISSCUSSION

This study included total 66 patients having T2DM which were enrolled from Dr. Akbar Niazi Teaching hospital, among them there were 47 males (71.2%) and 19 females (28.8%). Males were significantly higher as compared to females. The average age of the patient was 56 in years. Pakistan ranks at 10 of 221 countries of the world, in having number diabetic patients according to International Diabetes mellitus Federation (IDF) diabetes atlas 2017, having 7.5 million cases of diabetes [21]. Diabetes mellitus and HTN are both common diseases that coexist at a greater frequency [22].

This study patients of T2DM in ≥7% HbA1c showed higher systolic and diastolic BP as compared to <7% HbA1c patients. Previously a study conducted that showed that BP increases in ≥7% HbA1c patients [23].

Our study showed that MAU is significantly associated in those patients who has ≥7% HbA1c. A study was conducted which showed the patients of ≥7% HbA1c significantly associated with MAU [24].

MAU in <7% HbA1c patients showed no significant association with BMI, duration of diabetes, Systolic BP (mmHg), Diastolic BP (mmHg), Retinopathy, Nephropathy, Neuropathy and Cardiovascular. There was a study conducted in 2000 which showed chemical and demographic variables as independent variables which means it showed no significant association of MAU with variables [25].

On the other hand fasting blood glucose, Systolic BP (mmHg), Diastolic BP (mmHg), and Nephropathy and cardiovascular events has shown relation of MAU in ≥7% HbA1c patients, but retinopathy and neuropathy shown no relation with MAU in this group. Another study conducted in which statistical significant correlation showed between systolic BP, diastolic BP, nephropathy and cardiovascular disease in≥7% HbA1c patients [26].

Nephropathy show high significance in ≥7% HbA1c patients (P value: 0.002) in this study, in another study Increasing HbA1c categories above 7.0% showed with increased prevalence of nephropathy. HbA1c categories ≥7.0% is an important risk factor for the development of nephropathy **[**27]**.** Diabetic Nephropathy is said to be a common consequences of long standing DM. Elevated glucose levels in blood lead to binding of glucose to protein resulting in excessive protein glycosylation which in turn leads to elevated glycated end products. Increase deposition of these glycated end products on the glomerular resulting in renal & glomerular-hypertrophy and thickening of glomerular basement membrane. This allows leakage of low molecular weight protein [Albumin]. This condition is turned as incipient nephropathy [28].

MAU is not only a risk factor for end stage renal failure in diabetes mellitus but also an important marker of mortality in diabetic populations. American diabetes association (ADA) has stressed for early detection of MAU in diabetes mellitus patients as early treatment of MAU retard the progression of diabetic nephropathy. There are multiple risk factors for MAU and studies have shown poor glycemic control and increased duration of diabetes, male gender and increased creatinine as important risk factors. HTN is not only a risk factor but also has very strong relationship with MAU

Our study shows that if person has high urinary albuminuria level that person has nephropathy and cardiovascular diseases in diabetic patients. While a study shows patients having albuminuria show more nephropathy and cardiovascular events [29].

Cardiovascular disease (CVD) is the major cause of morbidity and mortality in people with impaired renal function and ESRD [30]. Individuals with diabetes-associated nephropathy typically have long periods of excessive albuminuria with gradual reductions in creatinine clearance as they approach end stage [31].

Patients with <7% HbA1c show no significance in cardiovascular events but cardiovascular disease is more significance in ≥7% HbA1c patients.

In both PreHTN and HTN cardiovascular is significant. In previous study shows that MAU was associated with cardiovascular risk factors such as obesity, HTN, and diabetes [32]. In other study the population of hypertensive patients of the IBERICAN study has a prevalence of MAU of 11%. This prevalence is higher, statistically significantly, in the presence of cardiovascular disease: ischemic heart disease, stroke, heart failure, peripheral arterial disease and atrial fibrillation [33].

Retinopathy showed no significant association with MAU in HTN patients. A study showed that retinopathy is significantly associated with MAU [34], this study showed slightly association with MAU in retinopathy. Another study showed the association of retinopathy with MAU in which statistically significant association between grade of MAU and severity of diabetic retinopathy was observed ($p < 0.001$) [35]. Diabetic retinopathy is probably the most common problem of diabetes. In the United States alone, it is responsible for about 10,000 new blind patients each year**.** The risk of developing diabetic retinopathy or other microvascular complications of diabetes mellitus depends on both the duration and the severity of hyperglycemia. Development of diabetic retinopathy in patients with T2DM was found to be related to both the severity of hyperglycemia and the presence of HTN in the U.K. Prospective Diabetes mellitus Study (UKPDS), and most patients develop evidence of retinopathy within 20 years of diagnosis [36].

Our study doesn't show the significance to neuropathy, there is a study conducted which shows that neuropathy is independently associated with MAU [37], there is another study which shows significant association of neuropathy with MAU. MAU is significantly associated with presence of neuropathy. The most common type of neuropathy observed in this study was distal symmetrical sensory motor neuropathy. Hence, MAU has an important role in their study as a biochemical marker for risk factor evaluation of microvascular complications in T2DM. Neuropathy is nerve injury that starts with the longest nerves that innervate the toes and progresses proximally. Common symptoms are numbness, tingling, pain and/or weakness starting in the distal lower extremities. Diabetes mellitus is well established as the most important metabolic risk factor for neuropathy, but treatment of hyperglycemia is not enough to prevent neuropathy in those with type 2 diabetes.

CONCLUSION

Patients with uncontrolled diabetes mellitus have increased risk of developing HTN. MAU as well as diabetes mellitus related complication including nephropathy and cardiovascular events.

More over MAU showed significant positive association with BP blood glucose levels, nephropathy and cardiovascular events. Both pre-hypertensive and hypertensive patients showed significant positive association of MAU with blood glucose levels and diabetes mellitus related complication including nephropathy and cardiovascular events.

This study suggested that Prehypertensive and hypertensive patients with altered blood glucose levels have increased risk of MAU, that why proper evaluation and treatment of MAU may lead to early diagnosis and decrease progression of HTN, diabetes mellitus type 2 and its related complication.

REFERENCES

1. Kahr, C. R., & Weire, G. C. (1994). Lea and Febiger. Joslin's diabetes mellitus, 13th ed. Philadelphia, 193-4.
2. Onyango, E. M., & Onyango, B. M. (2018). The rise of noncommunicable diseases in Kenya: an examination of the time trends and contribution of the changes in diet and physical inactivity. *Journal of epidemiology and global health*, *8*(1-2), 1.
3. Ramtahal, R., Khan, C., Maharaj-Khan, K., Nallamothu, S., Hinds, A., Dhanoo, A., ... & Lazo, M. (2015). Prevalence of self-reported sleep duration and sleep habits in type 2 diabetes patients in South Trinidad. *Journal of epidemiology and global health*, *5*(4), S35-S43.
4. Alotaibi, A., Perry, L., Gholizadeh, L., & Al-Ganmi, A. (2017). Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: An overview. *Journal of epidemiology and global health*, *7*(4), 211-218.
5. Adnan, M., & Aasim, M. (2020). Prevalence of type 2 diabetes mellitus in adult population of Pakistan: a meta-analysis of prospective cross-sectional surveys. *Annals of global health*, *86*(1).
6. Basit, A., Fawwad, A., Qureshi, H., & Shera, A. S. (2018). Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. *BMJ open*, *8*(8), e020961.
7. Meo, S. A., Zia, I., Bukhari, I. A., & Arain, S. A. (2016). Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. *JPMA. The Journal of the Pakistan Medical Association*, *66*(12), 1637-1642.
8. Meccariello, A., Buono, F., Verrengia, E., Orefice, G., Grieco, F., Romeo, F., ... & Morisco, C. (2016). Microalbuminuria predicts the recurrence of cardiovascular events in patients with essential hypertension. *Journal of hypertension*, *34*(4), 646-653.
9. Poudel, B., Yadav, B. K., Nepal, A. K., Jha, B., & Raut, K. B. (2012). Prevalence and association of microalbuminuria in essential hypertensive patients. *North American journal of medical sciences*, *4*(8), 331.
10. Lenfant, C., Chobanian, A. V., Jones, D. W., & Roccella, E. J. (2003). Seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) resetting the hypertension sails. *Hypertension*, *41*(6), 1178-1179.
11. Dormandy, J. A., Charbonnel, B., Eckland, D. J., Erdmann, E., Massi-Benedetti, M., Moules, I. K., ... & Tatoň, J. (2005). Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. *The Lancet*, *366*(9493), 1279-1289.
12. Fong, D. S., Aiello, L., Gardner, T. W., King, G. L., Blankenship, G., Cavallerano, J. D., Ferris, F. L., Klein, R. (2004). Retinopathy in diabetes. *Diabetes care*, *27*(suppl 1), s84-7.
13. Tan, A., & Leone, J. (2007). Naturopathic approaches to diabetic kidney disease. *Townsend Letter: The Examiner of Alternative Medicine*, (286), 76-83.
14. Fowler, M. J. (2011). Microvascular and macrovascular complications of diabetes. *Clinical diabetes*, *29*(3), 116-22.
15. Epstein, M., & Sowers, J. R. (1992). Diabetes mellitus and hypertension. *Hypertension*, *19*(5), 403-418.
16. Christensen, C. K., & Mogensen, C. E. (1985). The course of incipient diabetic nephropathy: studies of albumin excretion and blood pressure. *Diabetic Medicine*, *2*(2), 97-102.
17. Cordonnier, D., Bayle, F., Benhamou, P. Y., Milongo, R., Zaoui, P., Maynard, C., & Halimi, S. (1993). Future trends of management of renal failure in diabetics. *Kidney international. Supplement*, *41*, S8-S13.
18. Ruggenenti, P., Fassi, A., Ilieva, A. P., Bruno, S., Iliev, I. P., Brusegan, V., ... & Remuzzi, G. (2004). Preventing microalbuminuria in type 2 diabetes. *New England Journal of Medicine*, *351*(19), 1941-1951.
19. Wrone, E. M., Carnethon, M. R., Palaniappan, L., & Fortmann, S. P. (2003). Association of dietary protein intake and microalbuminuria in healthy adults: Third National Health and Nutrition Examination Survey. *American journal of kidney diseases*, *41*(3), 580-587.
20. Hayfron-Benjamin, C. F., Amoah, A. G., Maitland-van der Zee, A. H., van Charante, E. P. M., Galenkamp, H., van den Born, B. J., & Agyemang, C. (2021). Associations between macrovascular and renal microvascular dysfunction in type 2 diabetes and non-diabetes: the HELIUS study. *Microvascular Research*, *136*, 104162.
21. Patterson, C. C., Karuranga, S., Salpea, P., Saeedi, P., Dahlquist, G., Soltesz, G., & Ogle, G. D. (2019). Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas. *Diabetes research and clinical practice*, *157*, 107842.
22. Talukdar, A., & Dey, B. K. (2017). Coexistence of diabetes mellitus and hypertension—a review. *Am J PharmTech Res*, *7*(2), 33-44.
23. Eeg-Olofsson, K., Zethelius, B., Gudbjörnsdottir, S., Eliasson, B., Svensson, A. M., & Cederholm, J. (2016).

Considerably decreased risk of cardiovascular disease with combined reductions in HbA1c, blood pressure and blood lipids in type 2 diabetes: report from the Swedish National Diabetes Register. *Diabetes and Vascular Disease Research*, *13*(4), 268-277.

24. Goyal, B., Goyal, J., Sinha, M., Fiza, B., Sharma, P., Bandhari, S., & Sharma, P. (2017). Association of glycosylated hemoglobin with microalbuminuria in patients with type 2 diabetes mellitus.
25. Festa, A., D'agostino Jr, R., Howard, G., Mykkänen, L., Tracy, R. P., & Haffner, S. M. (2000). Inflammation and microalbuminuria in nondiabetic and type 2 diabetic subjects: The Insulin Resistance Atherosclerosis Study. *Kidney international*, *58*(4), 1703-1710.
26. Schmitz, A., & Vaeth, M. (1988). Microalbuminuria: a major risk factor in non-insulin-dependent diabetes. A 10-year follow-up study of 503 patients. *Diabetic Medicine*, *5*(2), 126-134.
27. Hoque, S., Muttalib, M. A., Islam, M. I., Khanam, P. A., Akter, N., & Akber, T. (2017). Prevalence of nephropathy with evaluation of HbA1c level and other associated risk factors in type 2 diabetic patients in a tertiary level hospital. *KYAMC Journal*, *8*(1), 21-26.
28. Kundu, D., Roy, A., Mandal, T., Bandyopadhyay, U., Ghosh, E., & Ray, D. (2013). Relation of microalbuminuria to glycosylated hemoglobin and duration of type 2 diabetes. *Nigerian journal of clinical practice*, *16*(2), 216-220.
29. Bakris, G. L., & Molitch, M. (2014). Microalbuminuria as a risk predictor in diabetes: the continuing saga. *Diabetes care*, *37*(3), 867-875.
30. Rabbat, C. G., Treleaven, D. J., Russell, J. D., Ludwin, D., & Cook, D. J. (2003). Prognostic value of myocardial perfusion studies in patients with end-stage renal disease assessed for kidney or kidney-pancreas transplantation: a meta-analysis. *Journal of the American Society of Nephrology*, *14*(2), 431-439.
31. Ibsen, H., Olsen, M. H., Wachtell, K., Borch-Johnsen, K., Lindholm, L. H., Mogensen, C. E., ... & Wan, Y. (2005). Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients: losartan intervention for endpoint reduction in hypertension study. *Hypertension*, *45*(2), 198-202.
32. XU, J., MA, J., CHEN, X., YAN, L., CAI, X., & WU, J. (2019). Association between microalbuminuria and cardiovascular risk factors in general population. *Chinese Journal of Nephrology*, 30-35.
33. Llisterri, J. L., Micó-Pérez, R. M., Velilla-Zancada, S., Rodríguez-Roca, G. C., Prieto-Díaz, M. Á., Martín-Sánchez, V., ... & Cinza-Sanjurjo, S. (2021). Prevalence of chronic kidney disease and associated factors in the Spanish population attended in primary care: Results of the IBERICAN study. *Medicina Clínica (English Edition)*, *156*(4), 157-165.
34. Hari, M. L. (2014). A study of microalbuminuria in type II diabetes mellitus. *Int. J. Modn. Res. Revs*, *2*(10), 433-437.
35. Garg, P., Misra, S., Yadav, S., & Singh, L. (2018). Correlative study of diabetic retinopathy with HbA1c and microalbuminuria. *International Journal of Ophthalmic Research*, *4*(2), 282-286.
36. Fowler, M. J. (2011). Microvascular and macrovascular complications of diabetes. *Clinical diabetes*, *29*(3), 116-22.
37. Bell, D. S., Ketchum, C. H., Robinson, C. A., Wagenknecht, L. E., & Williams, B. T. (1992). Microalbuminuria associated with diabetic neuropathy. *Diabetes Care*, *15*(4), 528-531.