A CROSS SECTIONAL STUDY TO FIND THE DIFFERENCE IN SYSTOLIC BLOOD PRESSURE BETWEEN ARMS AS A RISK MARKER FOR DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetic nephropathy is the commonest cause of end-stage renal disease in the developed world. Recent studies have demonstrated that a difference in systolic blood pressure between arms is associated with cardiovascular disease and microalbuminuria. It is considered a predictor for cardiovascular disease and a surrogate marker for early kidney damage among patients with both type 2 diabetes and hypertension.

AIMS AND OBJECTIVES

The aim was to investigate an association between arm difference in systolic blood pressure and microalbuminuria which can serve as a marker for diabetic nephropathy.

MATERIALS AND METHOD

This study was conducted on 200 patients with diabetes mellitus and an inter-arm difference in systolic blood pressure was present in 35.7% of the study population. Presence of systolic blood pressure difference of more than 10 mmHg between arms correlated with microalbuminuria and duration of diabetes mellitus with a p value of <0.001. We also found a correlation between arm difference in blood pressure and duration of diabetes mellitus, presence of hypertension and body mass index.

CONCLUSION

The inter-arm difference in blood pressure could serve as a risk marker for renal damage in diabetes mellitus.

KEYWORDS

Systolic Blood Pressure, Diabetic Nephropathy, Type 2 Diabetes.

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INTRODUCTION: Diabetic kidney disease occurs in 20–40% of patients with diabetes and is the leading cause of end-stage renal disease (ESRD). Nephropathy is a major cause of illness and death in diabetes. Diabetic nephropathy is the single most common cause of ESRD in Europe, Japan, United States and India. In a recent study conducted in south India, the prevalence of overt nephropathy was 2.2%.(1) Microalbuminuria was present in 26.9% of the population. The excess mortality of diabetes occurs mainly in proteinuric diabetic patients and results not only from end-stage renal disease(ESRD) but also from cardiovascular disease, the latter particularly in type 2 diabetic patients.(2)

Microalbuminuria and gross proteinuria were significantly associated with subsequent mortality from all causes and from cardiovascular, cerebrovascular, and coronary heart diseases. These associations were independent of known cardiovascular risk factors and diabetes-related variables.(3) Although microalbuminuria interacts with the traditional cardiovascular risk factors, it has an independent relationship to renal and cardiovascular outcomes. Elevated rates of urinary albumin excretion predict target organ damage, notably renal disease, but are also related to left ventricular dysfunction, stroke, and myocardial infarction.(4)

Diabetic nephropathy screening is made by measuring albumin in spot urine. Additionally, it is recommended that glomerular filtration rate be routinely estimated for appropriate screening of nephropathy, because some patients present a decreased glomerular filtration rate when urine albumin values are in the normal range. The two main risk factors for diabetic nephropathy are hyperglycaemia and arterial hypertension, but the genetic susceptibility in both type 1 and type 2 diabetes is of great importance. Other risk factors are smoking, dyslipidaemia, proteinuria, glomerular hyperfiltration and dietary factors.

Multiple studies have demonstrated that a difference in systolic blood pressure (SBP) between arms is associated with both vascular disease and mortality.(5) A recent study demonstrated that a difference of blood pressure between arms correlated with albuminuria.(6) This study was conducted with the objective of finding an association between arm difference in blood pressure and

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microalbuminuria, which could result in the earlier diagnosis of diabetic nephropathy and prevent the progression of the disease by the prompt institution of therapy.

Hence, this study evaluated relationship between a difference in SBP between arms and microalbuminuria and estimated glomerular filtration rate (eGFR).

MATERIALS AND METHODS: A sample size of 200 attending the outpatient clinic at Karnataka Institute of Medical Sciences and inpatients in the same institute for a period of 3 years from September 2013 to September 2015 were selected by simple random sampling method and based on the CURES Study which detected a prevalence of microalbuminuria of 26.9% in a south Indian population.[2] Adults with type 2 diabetes mellitus were included and patients with advanced renal dysfunction (serum creatinine >4.2 mg/dL), urinary infections, and haematuria were excluded.

A difference in systolic blood pressure of 10 mmHg and diastolic blood pressure of 5 mmHg was considered significant. A creatinine clearance value of 150 mL/min. was chosen as the cut-off for glomerular hyperfiltration.[7]

Patients were explained about the study in their own language and informed consent was obtained. Blood pressure was measured in both the limbs simultaneously using 2 automated sphygmomanometers and the interarm difference in blood pressure was calculated. Weight was measured using digital weighing scale. Microalbuminuria was assessed on a spot sample of urine using a microalbumin test kit. Serum creatinine was measured in the biochemistry laboratory at KIMS, Hubli.

The eGFR of the subjects will be calculated using the formula as (140-age) x weight (kg)/72 (x 0.85 if women) x plasma creatinine.

STATISTICAL ANALYSIS: The results were analysed by calculating percentages, Chi-square test & proportion test. A p value of less than 0.05 was considered statistically significant. These values were compared using Student's t test to calculate statistical significance.

RESULTS AND ANALYSIS: A total of 200 patients were studied, 53.5% (=107 females) of whom were women and 48.5% were men. In our study, the presence of systolic blood pressure difference of more than 10 mmHg between arm correlated with microalbuminuria with a p value of <0.001 (Table 7). In our study, the presence of a difference in diastolic blood pressure of more than 5 mmHg between arms co-related with the presence of microalbuminuria with a p value of 0.001 (Table 8). In our study, the presence of systolic blood pressure difference of more than 10 mmHg between arms correlated with the duration of diabetes with a p value of < 0.001 (Table 9). In our study, the presence of diastolic blood pressure difference of more than 5 mmHg correlated with the duration of diabetes with a p value of <0.001 (Table 10). The presence of systolic blood pressure difference of more than 10 mmHg correlated with the presence of hypertension with a p value of <0.001 (Table 11).

DISCUSSION: Recent studies have found that a difference in SBP of 10 mmHg between inter-arms was associated with vascular disease and mortality,[7] the relationship of a difference in SBP and microalbuminuria has not been extensively investigated. Hence, the aim of our study was to evaluate a relationship between difference in SBP between and microalbuminuria and to evaluate a relationship between difference in SBP between arms and estimated glomerular filtration rate (eGFR).

A recent review of literature on systolic blood pressure by Clark et al[8,9] revealed a prevalence of 19.6% of the inter-arm difference in systolic blood pressure. Our study was conducted on 200 patients with diabetes mellitus and an inter-arm difference in systolic blood pressure was present in 35.7% of the study population whereas Weinberg et al reported in 9.4% of population.[10]

A recent study by Okada et al[11] demonstrated that a difference in SBP between arms correlated with urinary albumin excretion. In our study, the presence of systolic blood pressure difference of more than 10 mmHg between arms correlated with microalbuminuria (p value of <0.001). Our study also demonstrated a correlation between arm difference in blood pressure and duration of diabetes, presence of hypertension and body mass index. Clark et al[12] suggested that a difference in SBP between arms may be a marker of peripheral arterial disease (PAD). Thus, there is some evidence to support the association of a difference in SBP with PAD. It is well known that PAD is associated with renal damage; Norgren[13] reported that 23–42% patients with PAD have renal artery stenosis of 50% or greater. Hence, it is hypothesised that the inter-arm difference in blood pressure could serve as a risk marker for renal damage in diabetes mellitus.

Glomerular hyperfiltration, defined as a eGFR more than 150 mL/min.,[14],[15],[16],[17] occurs early in a variety of kidney diseases including diabetic nephropathy.[18],[19],[20] In our study, 2.5% of the population studied had glomerular hyperfiltration and it did not correlate with inter-arm difference in blood pressure.

Our study also demonstrated a correlation between an inter-arm difference in diastolic blood pressure of 5 mmHg and microalbuminuria, duration of diabetes and peripheral vascular disease (p value<0.001). Seventy one patients (35.5%) had an inter-arm difference. Out of 200 patients studied, 61% had inter-arm difference in diastolic blood pressure of more than 5 mmHg, 25% had glomerular hyperfiltration. overall 65.8% of the patients had microalbuminuria, 12.1% (24) had macroalbuminuria and 22.1% (44) had normal urine albumin excretion. Presence of systolic blood pressure difference of more than 10 mmHg correlated with microalbuminuria and duration of diabetes with a p value of <0.001. Difference in diastolic blood pressure of more than 5 mmHg correlated with the presence of microalbuminuria and duration of diabetes with a p value of< 0.001. Peripheral vascular disease did correlate with Diastolic BP difference between arms (p Value <0.001). Body mass index (BMI) co-related with a Systolic BP Difference between arms (p value <0.001). In our study,

history of smoking did not correlate with systolic blood pressure (p value 0.211). In our study, presence of hypertension did not correlate with diastolic BP difference between arms (p value 0.846). In our study, peripheral vascular disease did not correlate with systolic BP difference between arms (p Value 0.270).

Our cross sectional data does not show the precise demonstration of a cause–effect nature of the relationship. Results in this study may not be applicable to the general population or to the patients with diabetes in a primary care clinic because the patients in this study were selected from a tertiary care hospital. Large, prospective trials, including patients with both Type 1 and Type 2 diabetes, are needed to better assess the relationship between a difference in BP between arms and between lower limbs and the degree of urine albumin excretion in patients with diabetes.

CONCLUSION: A difference in SBP between arms could be a novel risk marker for diabetic nephropathy in patients with Type 2 diabetes.

Duration of Diabetes in Months	No. of patients	Percent
<10 Months	64	32.2
10-25 Months	39	19.6
25-50 Months	21	10.6
50-100 Months	36	18.1
>100 Months	39	19.6
Total	**199**	**100**

Table 1: Distribution of Patients According to Duration of Diabetes in Months

BMI	No. of patients	Percent
Underweight	18	9
Normal	79	39.7
Overweight	11	5.5
Obese	12	6
	120	60.3
Total	199	100

Table 2: Distribution of Patients According to BMI

Systolic BP Difference	No. of patients	Percent
<=10	128	64.3
>10	71	35.7
Total	**199**	**100**

Table 3: Distribution of Patients According to Inter-Arm Systolic Blood Pressure (BP) Difference

Diastolic BP Difference	No. of patients	Percent
<=5	77	38.7
>5	122	61.3
Total	**199**	**100**

Table 4: Distribution Of Patients According To Inter-Arm Diastolic Blood Pressure(BP) Difference

Creatinine Clearance (mL/min.)	No. of patients	Percent
Less Than 150	194	97.5
More Than 150	5	2.5

Table 5: Percentage Of Patients With Glomerular Hyperfiltration

Albuminuria	No. of patients	Percent
Normal urine albumin excretion (<=30)	44	22.1
Microalbuminuria (30-300)	131	65.8
Macroalbuminuria (>300)	24	12.1
Total	**199**	**100**

Table 6: Percentage Of Patients With Albuminuria

			Systolic BP Difference		Total
			<=10	>10	
Albuminuria	<=30	% with Systolic BP Difference	31.2%	5.6%	22.1%
	30-300	% with systolic BP difference	57.8%	80.3%	65.8%
	>300	% with systolic BP difference	10.9%	14.1%	12.1%
Total		**Count**	**128**	**71**	**199**

Table 7: Correlation Between Albuminuria And Systolic BP Difference Between Arms

			Diastolic BP Difference		Total
			<=5	>5	
Microalbumin (30-300)	<=30	Count	10	34	44
		% with Diastolic BP Difference	13.0%	27.9%	22.1%
	30-300	Count	63	68	131
		% with Diastolic BP Difference	81.8%	55.7%	65.8%
	>300	Count	4	20	24
		% with Diastolic BP Difference	5.2%	16.4%	12.1%
Total		**Count**	**77**	**122**	**199**

Table 8: Correlation Between Albuminuria And Diastolic BP Difference Between Arms

			Systolic BP Difference		Total
			<=10	>10	
Duration of diabetes mellitus in months	<10 Months	Count	31	33	64
		% with Systolic BP Difference	24.2%	46.5%	32.2%
	10-25 Months	Count	32	7	39
		% with Systolic BP Difference	25.0%	9.9%	19.6%
	25-50 Months	Count	12	9	21
		% with Systolic BP Difference	9.4%	12.7%	10.6%
	50-100 Months	Count	19	17	36
		% with Systolic BP Difference	14.8%	23.9%	18.1%
	>100 Months	Count	34	5	39
		% within Systolic BP Difference	26.6%	7.0%	19.6%
Total		**Count**	**128**	**71**	**199**

Table 9: Correlation Between Duration Of Diabetes mellitus And Systolic BP Difference Between Arms

			Diastolic BP Difference		Total
			<=5	>5	
Duration Of Diabetes Mellitus In Months	<10 Months	Count	36	28	64
		% with Diastolic BP Difference	46.8%	23.0%	32.2%
	10-25 Months	Count	10	29	39
		% with Diastolic BP Difference	13.0%	23.8%	19.6%
	25-50 Months	Count	14	7	21
		% with Diastolic BP Difference	18.2%	5.7%	10.6%
	50-100 Months	Count	8	28	36
		% with Diastolic BP Difference	10.4%	23.0%	18.1%
	>100 Months	Count	9	30	39
		% with Diastolic BP Difference	11.7%	24.6%	19.6%
Total		**Count**	**77**	**122**	**199**

Table 10: Correlation Between Duration Of Diabetes mellitus And Diastolic BP Difference

			Systolic BP Difference		Total
			<=10	>10	
Hypertension	No	Count	54	58	112
		% with Systolic BP Difference	42.2%	81.7%	56.3%
	Yes	Count	74	13	87
		% with Systolic BP Difference	57.8%	18.3%	43.7%
Total		**Count**	**128**	**71**	**199**

Table 11: Correlation Between Presence Of Hypertension And Systolic BP Difference Between Arms

			Systolic BP Difference		Total
			<=10	>10	
BMI	Underweight	Count	6	12	18
		% with Systolic BP Difference	7.8%	27.9%	15.0%
	Normal	Count	59	20	79
		% with Systolic BP Difference	76.6%	46.5%	65.8%
	Overweight	Count	2	9	11
		% with Systolic BP Difference	2.6%	20.9%	9.2%
	Obese	Count	10	2	12
		% with Systolic BP Difference	13.0%	4.7%	10.0%
Total		**Count**	**77**	**43**	**120**

Table 12: Correlation Between BMI and Systolic BP Difference between Arms was Significant (p value <0.001)

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