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ORIGINAL RESEARCH

Urinary albumin creatinine ratio (ACR) assessment in hypertensive non diabetics and its association with estimated glomerular filtration rate (eGFR)

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Abstract
Microalbuminuria in hypertension has been described as an early sign of kidney damage and a predictor for end stage renal disease and cardiovascular disease. Thus, it is of great importance to study the association between urinary albumin creatinine ratio and progression of kidney disease in hypertensive patients. The presence of microalbuminuria has been shown to correlate with the other cardiovascular risk factors commonly seen in hypertensive patients. This fact indicates that the detection of an increased urinary albumin excretion could probably be the best index of an increased global cardiovascular risk in a hypertensive patient. BP control is accompanied by a fall in the content of albumin in urine. Agents with the capacity to block the renin-angiotensin system have shown a capacity to decrease urinary albumin excretion, which is independent of their ability to lower blood pressure. In the present study two groups of patients, 50 non diabetic hypertensive (case) and 50 non diabetic normotensive (control) were evaluated for urinary ACR in spot urinary sample and their eGFRwas calculated. Written informed consent was taken from all the candidates enrolled for the study. The approval of institutional thesis committee was obtained before the study.
Key Words: eGFR, Microalbuminuria, Normotensive, Hypertensive, Urinary ACR

Introduction

Hypertension is a major public health issue in both developed as well as developing countries, impacting one in every four individuals.[1]

Towards the end of 2017, new guidelines on the appropriate range for blood pressure readings were released in a joint consensus between the American College of Cardiology along with the American Heart Association.[2]

Blood Pressure Category	Systolic	Diastolic
Normal	120mmHg	<80mmHg
Elevated	120-129mmHg	<80mmHg
Hypertension stage I	130-139mmHg	80-89mmHg
Hypertension stage II	>140mmHg	>90mmHg

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Hypertensive nephropathy rank second most frequent reason for end-stage renal disease (ESRD) following diabetes. Most of the individuals with hypertension experience mild to moderate hypertensive nephrosclerosis. The number of patients developing ESRD increases significantly when blood pressure (BP) levels remains uncontrolled for long period of time.[3]
Capillary tuft damage from elevated intraglomerular pressure resulting in nephrosclerosis&hyalinosis as well as renin- angiotensin system abnormalities have been implicated in pathogenesis of hypertensive nephropathy from a long period of time.[3-6]
Chronic Hypertension results in increase in intraglomerular pressure which causes damage to capillary tuft endothelium & activation of mesangial cells, which results in release of various vasoactive &proinflammatory agents like angiotensin. These vasoactive molecules causes activation of AT1 receptors which contribute to pathogenesis of renal damage.[7]
In a normally functioning kidney, the blood proteins which are filtered through the glomerular filtration membrane are almost completely reabsorbed in the proximal convoluted tubules via cotransport mechanism across the apical plasma membrane & then enter the peritubular blood microcirculation. But in chronic hypertension, persistently elevated increased pressure load along with increased peripheral resistance results in alteration of renal hemodynamic & damage the microvasculature of renal system. This results in filtration of the albumin to a level that exceeds the reabsorption capacity of renal proximal tubules. [8-10]
Presence of Microalbuminuria (MAU) in hypertension is significantly link with the elevated morbidity & mortality. Moreover, Microalbuminuria has been identified as an early predictor of renal injury & marker of ESRD (End stage renal disease).[11]Microalbuminuria (MAU) refers to an elevated excretion of urinary albumins (30-300 mg/24 h) that is not detected by using routine dipstick method.[12] Most commonly used method for measurement of albuminuria is urinary ACR (albumin creatinine ratio) in a spot r&om urinary sample. In the study albuminuria is classified as.[13]

Category	Description	UACR
A1	Normal to mildly increased	<30 mg/mmol
A2	Moderately increased	30-300 mg/mmol
A3	Severely increased	>300 mg/mmol

The elevated pressure in the renal blood vessels causes damage to tiny filtering structures of the kidney-called nephrons. Due to this the kidneys' lose their ability to filter waste products & excrete extra fluids which is estimated by a reduced glomerular filtration rate (GFR).[14] The estimated glomerular filtration rate (eGFR) test typically uses a formula based on creatinine levels, a waste product produced by the body's muscles, in the blood.[15] The duration & degree of hypertension among hypertensive patient correlates with fall in kidney function which can be assessed by measuring eGFR.[16]
The eGFR is calculated by using Cockcroft Gault equation.[17]

- In Males: eGFR = 140-age (in years) x weight (in kg)/[72 x serum creatinine (mg/dl).
- In Females: eGFR = 140-age (in years) x weight (in kg) x0.85/[72 x serum creatinine (mg/dl).

Aims & objectives

To determine the prevalence of microalbuminuria in non-diabetic hypertensive patients.To study the correlation between urinary ACR &eGFR among non-diabetic hypertensive patients & non-diabetic normotensive patients.

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Material & methods

This cross-sectional study was conducted in 100 individual who were admitted or attending the Medicine Emergency or OPD of Medicine in GNDH attached to GMC, Amritsar. These patients were divided into two groups. Group A (Case) - Non-diabetic hypertensive patients (50 patients). Group B (Controls) - Non-diabetic normotensive patients (50 patients).

Inclusion Criteria

- Non diabetic hypertensive with age between 30 years to 70 years (cases)
- Non diabetic normotensive with age between 30 years to 70 years (Control)
- Written informed consent.

Exclusion Criteria

- Age 70 years.
- Diabetic patients.
- Pregnant patients
- Patients with urinary tract infection (UTI).
- Patients with chronic kidney disease.
- Nephrotic syndrome.

Method of Study

- After selection for the study, detailed history was taken & thorough physical examination was conducted including measurements of vitals, other examinations relevant to the hypertension.
- Clinical criteria for defining hypertension have been based on average of two or more outpatient visits & patient are categorised into various stages of hypertension on the basis of guideline released in a joint consensus between the American College of Cardiology & the American Heart Association.
- Patientscreatinine was calculated by using creatinine enzymatic method. Albuminuria was quantified in ar&om spot urine sample by nephelometry& then interpreted as albumin creatinine ratio & then categorized into normal (<30mg/mmol), microalbuminuria (30-300mg/mmol) &macroalbuminuria (>300 mg/mmol).

The formula of Cockcroft &Gault equation was used to calculate eGFR.

- In males:eGFR = 140-age (in years) × weight (in kg) /[72 × serum creatinine (mg/dl)].
- In females:eGFR = 140-age (in years) × weight (in kg) ×0.85/[72 × serum creatinine (mg/dl)].

Statistical Analysis

Data was recorded in a Microsoft excel spread sheet & analysed using Statistical Package for the IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp., Chicago. Numerical variables were normally distributed & analysed using independent t- test, One way ANOVA test & Pearson's Correlation test. Categorical variables were analysed using chi square test. 'p' value less than 0.05 was taken as statistically significant.

Observations

TABLE I: AGE & GENDER WISE DISTRIBUTION OF STUDY POPULATION

	No.	**%age**	**No.**	**%age**
AGE				
30-40	8	16.00	6	12.00
41-50	12	24.00	14	28.00

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51-60	24	48.00	22	44.00
61-70	6	12.00	8	16.00
Total	50	100.00	50	100.00
GENDER				
Female	21	42.00	23	46.00
Male	29	58.00	27	54.00
Total	50	100.00	50	100.00
Meanage	50.82±10.07		51.84±10.84	
p-value	0.627			

TABLE 2: CORRELATION OF STAGE OF HYPERTENSION WITH UACR & HYPERTENSION WITH eGFR

Stage of hypertension	No. of cases	UACR	eGFR
		Mean±S.D.	Mean±S.D.
Stage 1	19	44.07±27.83	85.05±14.55
Stage 2	31	206.79±119.75	56.43±16.54
Total	50	144.96±124.22	67.31±21.03
‘r’ value	0.642		
‘p’ value	0.001		

TABLE 3: CORRELATION OF DURATION OF HYPERTENSION WITH UACR &eGFR

Duration ofHypertension	No.ofcases	UACR	eGFR
		Mean±S.D.	Mean±S.D.
1-2	17	38.67±16.92	86.88±12.96
3-4	9	80.97±32.05	69.54±13.45
5-6	12	184.66±96.20	55.13±9.63
7-8	5	244.00±73.10	47.85±5.57
9-10	7	346.57±80.34	46.02±6.91
Total	50	144.96±124.22	66.52±19.66
‘r’ value	0.891		
‘p’ value	0.001		

TABLE 4: UACR DISTRIBUTION OF STUDY POPULATION

UACR	Normotensive(Control)		Hypertensive (Cases)	
	No. of Cases	Percentage (%)	No. of Cases	Percentage (%)
<30	44	88.00	10	20.00
30-300	6	12.00	34	68.00
>300	-	-	6	12.00
Total	50	100.00	50	100.00

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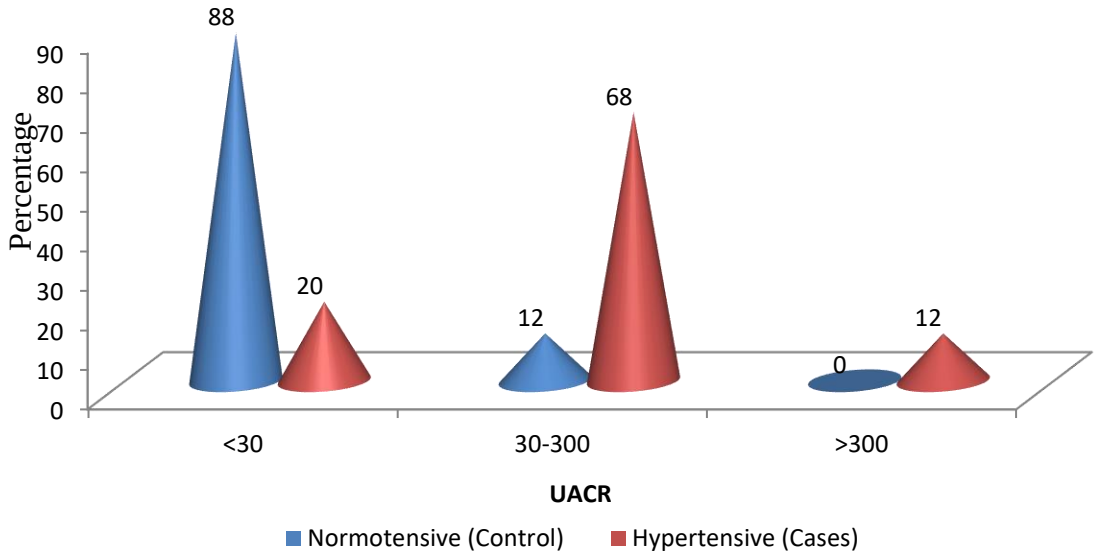

TABLE 5: COMPARISON OF UACR &eGFR BETWEEN HYPERTENSIVES & NORMOTENSIVES

Age group	UACR		eGFR	
	Normotensive (Mean±S.D.)	Hypertensive (Mean±S.D.)	Normotensive (Mean±S.D.)	Hypertensive (Mean±S.D.)
30-40	26.25±4.56	46.90±13.16	105.79±7.52	91.82±9.95
41-50	22.58±5.43	53.24±35.08	98.55±7.84	78.18±16.78
51-60	26.21±4.91	176.88±127.07	87.94±4.98	58.60±15.15
61-70	21.00±5.90	291.25±66.57	79.25±4.39	48.89±7.05
Total	24.72±5.36	144.96±124.22	92.30±10.24	66.52±19.66
'p' value	0.001 (p value <0.001; Highly Significant)			

TABLE 6: CORRELATION OF UACR WITH eGFR

UACR	No.ofcases	EGFR	
		Mean	SD
<30	10	83.7160	13.06030
30-300	34	65.3535	18.51336
>300	6	44.4433	5.70116
Total	50	66.5168	19.65820
'r' value	-0.709		
'p' value	0.001		

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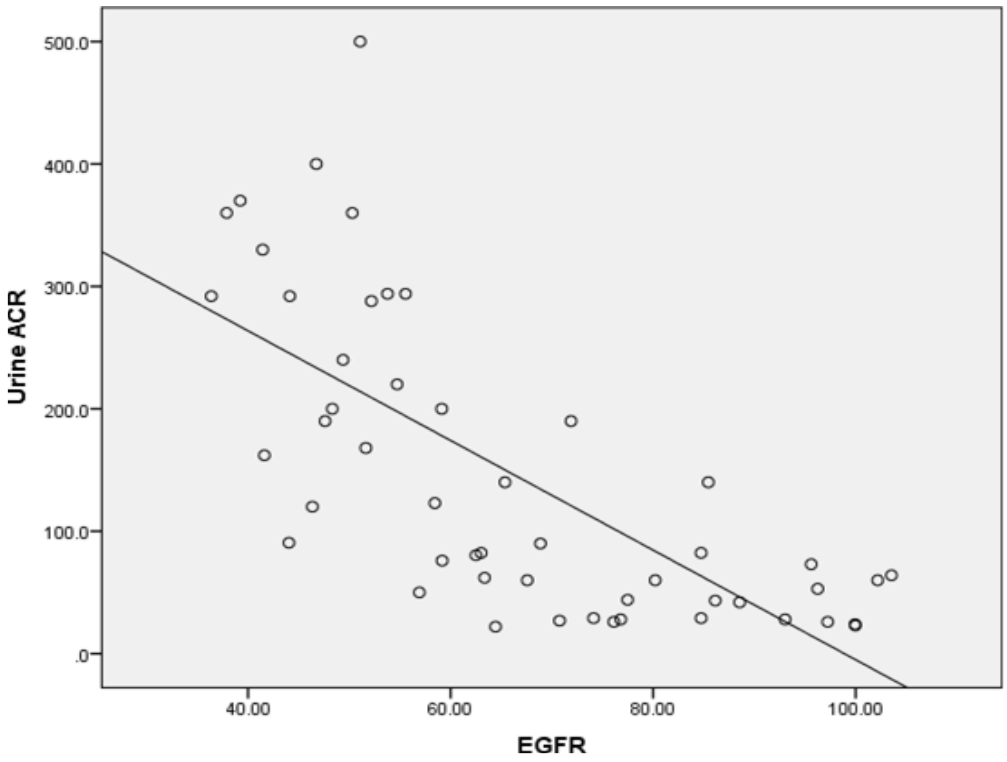

Discussion

The age group of study population ranges from 30 year to 70 year & majority of patients were in age group of 40-60 years comprising of 36 hypertensive cases & 36 normotensive controls. The study population sex wise distribution comprises of 21 females & 29 males in cases & 23 females & 27 males in controls. All the subject in study population were non-diabetic with hbA1c of <6.4 in both cases & control. The study population was assessed for albuminuria by using urinary albumin creatinine ratio (UACR) & their respective eGFR was calculated by using Cockcroft &Gault equation. The cases & controls were than compared according to their duration of hypertension, stage of hypertension, albuminuria with their respective UACR &eGFRin a specific age group categories.

In our study, it was observed that UACR increase significantly with increase in duration of hypertension which show statistically significant association with 'p' value of 0.001. Aggarwalet al[18], in a similar study also observed that urinary ACR increase with increase in duration of hypertension.

In our study 19 patients had stage 1 hypertension with their Mean±SD UACR of 44.07 while 31 patients had stage 2 hypertension with their Mean±SD UACR of 206.79. This data concluded that UACR has significant association with severity of hypertension in a way that higher the stage of hypertension more will the UACR with statistically significant p value is 0.001. Aggarwalet al[18], in a similar study also observe that urinary ACR increase significantly with increase in stage & severity of hypertension.

This study also accessed the distribution of UACR among cases (hypertensive) & controls (normotensive) in different age groups between 30-70 years. The Mean±SD UACR of control (normotensive) was 24.72 (normoalbuminuria) while the Mean±SD UACR of cases (hypertensive) was 144.96 (microalbuminuria). This data distribution concluded that prevalence of microalbuminuria was significantly higher in hypertensive cases as compared to normotensive controls with statically significant p-value of 0.001. Lee JH[19] in their study also concluded that prevalence of albuminuria was significantly higher in hypertensive patients as compared to normotensives.

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This study also estimate the difference between eGFR among hypertensive cases & normotensive controls. The mean±SDeGFR of normotensive controls was 92.29 while the Mean±SDeGFR of hypertensive cases was 66.51 in their respective age groups. This data shows that hypertensive patient had a significant decline in kidney function (eGFR) as compare to normotensive controls with a statically significant p-value of 0.001. Lee JH[19] in their study also concluded that hypertension was strongly associated with decreased eGFR.
In the present study, albuminuria was estimated by testing patients r&om spot urine sample for urinary albumin creatinine ratio. Ten cases had UACR less than 30 with their respective Mean±SDeGFR of 83.71 34 cases had UACR between 30- 300 with their Mean±SDeGFR of 65.35 & 6 cases had UACR more than 300 with their respective Mean±SDeGFR of 44.44. As per this data UACR has strong association with eGFR in hypertensive patients such that as UACR increases the eGFR fall with the statistically significant p-value of 0.001. Thus degree of albuminuria correlate decline in kidney function. Chou et al[20] in his study also observed that degree of albuminuria correlate with decline in kidney function.

Conclusions

This study concluded that the prevalence of albuminuria is significantly higher in hypertensive patient as compared to normotensive patients. The degree & the duration of hypertension among hypertensive patients correlate significantly with decline with kidney function such that longer the duration & higher the stage of hypertension, more severe will be the kidney dysfunction & lower the eGFR. So early detection & treatment of hypertension may prevent further kidney damage & progression to end stage renal disease (ESRD). This study also concluded that measurement of albuminuria in hypertensive patients using UACR is an important marker of kidney dysfunction. Degree of albuminuria correlates significantly with the severity of kidney damage. Thus, regular screening of albuminuria in hypertensive patients is helpful in early detection of hypertension induced renal damage.

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