

Original Research Article

A COMPARATIVE STUDY ON ASSOCIATION BETWEEN CREATININE KINASE AND HYPERTENSION

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ABSTRACT

Background: Hypertension is chronic elevation of blood pressure and is ranked as third most important risk factor for attributed burden of diseases and most common cause for premature death worldwide affecting around 1.13 billion people worldwide. Prevalence of hypertension in urban areas is around 25% and around 10% in rural areas in India. Hypertension is asymptomatic until diagnosed. High creatinine kinase activity promotes hypertension through enhanced vascular contractility and sodium retention in kidneys.

Materials and Methods: We adopted a comparative study where we included 50 hypertensive patients and 50 healthy individuals after appropriate matching. Hypertensive patients were recruited from the OPD under General Medicine and control group were recruited from other inpatients, outpatients or relatives/attenders of the patients. Creatinine kinases, other investigations were conducted and possible association were established with appropriate statistical analysis tools.

Results: Duration of hypertension was positively associated with elevated CKMB levels. BMI did not show any association with CKMB values.

Conclusion: Blood pressure among hypertensive patients was significantly higher compared to control group. Lipid parameters were also significantly higher among hypertensive patients. Creatinine kinase values was very significantly higher among hypertensive patients, which indicated a strong association between creatinine kinase levels and elevated blood pressure, also higher CKMB values had negative outcome.

Keywords: Hypertension, Creatinine Kinase, CKMB.

INTRODUCTION

Hypertension is chronic elevation in blood pressure which is a major contributor to cardiovascular disease and its associated complications worldwide.^[1] It is characterized by persistently high blood pressure in the arteries: pressure that is exerted on the arterial walls when the heart contracts and pressure when the heart relaxes.^[2] Hypertension is ranked third most important risk factor for attributed burden of disease in South Asia and as per WHO hypertension is one of the most important causes for premature death worldwide with its prevalence of 25% in urban and 10% in rural India.³ Hypertension is considered a major global public health problem affecting an estimated 1.13 billion people worldwide with its complications accounting 9.4 million deaths every year. Hypertension contributes to pathogenesis of

microvascular complications and as a risk factor for diabetic retinopathy.^[4]

Development of essential hypertension is mechanized by cardiac output, peripheral resistance, renin angiotensin aldosterone system and autonomic nervous system. Other factors include Bradykinin, Endothelin, EDRF, or nitric oxide, ANP and Ouabain.^[5] Genetic factor for hypertension and cardiovascular disease proposed recently revealed activity of ATP generating enzyme creatine kinase and that high creatine kinase activity promoted hypertension through enhanced vascular contractility and sodium retention in kidney.^[6]

Creatine kinase is an enzyme which is found in both cytosol and mitochondria of tissues where energy demands are high.^[7] It is an intracellular enzyme present in greatest amount in skeletal muscles, myocardium, brain and small quantities are present in

other visceral tissue.^[8] Studies and evidence indicate that tissue CK increases hypertension risk and the circulating plasma CK increase bleeding risk.^[9] Creatinine kinase activity promotes hypertension through enhanced vascular contractility and sodium retention in kidneys. CK has shown to be a significant independent predictor for blood pressure levels.^[10] Our study aim was to determine whether creatinine kinase was associated with hypertension.

MATERIALS AND METHODS

We adopted a hospital based comparative study design to enrol 50 patients diagnosed with hypertension and 50 individuals with no history of hypertension as control group. Our study was conducted in the department of General Medicine at Chikmagalur Institute of Medical Science, Karnataka. Once enrolled patients and control group were informed about our study and written informed consent was obtained. A detailed history was taken from the patients using a pretested proforma, also history regarding duration of hypertension, history of diabetes, family history of hypertension, smoking pack years was collected. General physical examination was conducted and details related to BMI, waist to hip ratio, pulse rate, standing and supine blood pressure were noted. We selected patients and control group aged more than 40 years, while patients diagnosed with chronic kidney disease, ischaemic heart disease, stroke were excluded.

RESULTS

The mean age of our hypertensive patients was 69.15 ± 10.94 years and in control group it was $69.49 \pm$

10.86 years. In total 61% were males and 39% were females. Among hypertensive patients, 20% had history of diabetes, 27% had family history of hypertension and 20% had history of smoking. Similarly, in control group 16% had history of diabetes, 8% had family history of hypertension and 14% had history of smoking. [Table 1] The mean duration of hypertension among patients was 4.99 ± 2.61 years with 38% of them having history of hypertension for more than 5 years. The mean systolic blood pressure and diastolic blood among hypertensives was 166.08 ± 12.73 mmHg and 95.78 ± 6.72 mmHg respectively. [Graph 1] The laboratory investigative findings revealed that difference in serum sodium, serum potassium, random blood sugar levels were significant. (Table 2 & 3) Mean creatinine kinase levels among hypertensives was 19.78 ± 4.45 and among control group it was 14.17 ± 3.39 . With increase in duration of hypertension, there was a significant increase in creatinine kinase levels. [Table 4]

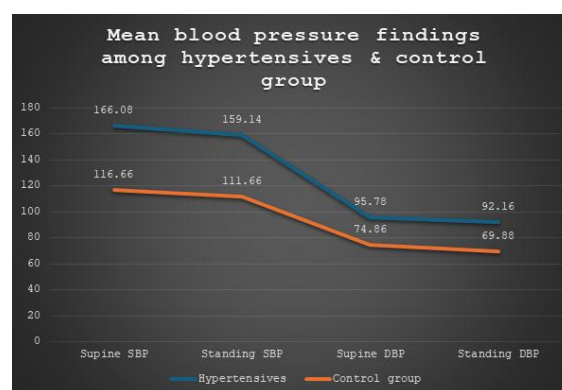


Figure 1: Blood Pressure levels

Table 1: Socio-demographic parameters

Sl. No	Particulars	Hypertensives (n=50)	Control group (n=50)
01	Age (in years)	69.15 ± 10.94	69.49 ± 10.86
02	History of diabetes	10 (20%)	08 (16%)
03	Family h/o hypertension	14 (28%)	04 (8%)
04	History of smoking	10 (20%)	07 (14%)
05	Duration of hypertension	4.99 ± 2.61 years	---

Table 2: Laboratory findings

Sl. No	Laboratory parameters	Hypertensives		Control group		p value
		Mean	SD	Mean	SD	
01	Haemoglobin (gm%)	9.575	1.32	10.377	1.63	0.0002 *
02	Random blood sugar (mg/dl)	168.58	52.90	152.06	29.89	0.0071 *
03	Blood urea (mg/dl)	27.49	10.73	29.26	6.41	0.1583 NS
04	Serum creatinine (mg/dl)	1.16	0.47	1.66	0.67	0.5160 NS
05	Serum sodium (mg/dl)	138.21	3.07	136.07	4.55	0.0001 *
06	Serum potassium (mg/dl)	3.69	0.43	3.873	0.52	0.0073 *

(t test: NS is Not significant, * is Significant, at p value <0.05)

Table 3: Lipid profile and creatinine kinase levels

Sl. No	Laboratory parameters	Hypertensives		Control group		p value
		Mean	SD	Mean	SD	
01	Total Cholesterol (mg/dl)	177.75	36.16	170.05	10.55	0.0423 *
02	LDL (mg/dl)	51.70	16.35	83.41	11.68	<0.0001 *
03	HDL (mg/dl)	41.24	6.81	37.21	5.91	<0.0001 *
04	Creatinine Kinase (IU)	19.78	4.45	14.17	3.39	<0.0001 *

(t test: NS is Not significant, * is Significant, at p value <0.05)

Table 4: Association between creatinine kinase and hypertension variables

Sl. No	Parameters	Creatinine kinase		p value
		Normal (<25 IU)	Elevated (>25IU)	
01	Systolic blood pressure	160.75 ± 11.96	166.89 ± 13.92	0.0223 *
02	Diastolic blood pressure	96.47 ± 7.31	99.56 ± 5.28	0.0282
03	Duration of hypertension	4.81 ± 2.79	5.89 ± 2.25	0.0498 *
04	Total cholesterol	170.59 ± 37.30	186.92 ± 32.07	0.0297 *
05	LDL	50.91 ± 17.67	53.11 ± 13.56	0.5191 NS
06	HDL	40.44 ± 6.39	42.67 ± 7.27	0.1143 NS

(t test: NS is Not significant, * is Significant, at p value <0.05)

DISCUSSION

Brewster et.al., conducted a systemic review on creatine kinase and blood pressure, which confirmed the association between Creatine kinase and blood pressure. ATP (Adenosine triphosphate) buffer capacity is a relevant factor in the generation of blood pressure. High creatine kinase activity carries the risk for hypertension which is difficult to treat. Creatine kinase related hypertension and cardiovascular diseases has been substantiated by experimental evidence, including reduction of blood pressure with creatine kinase inhibitors.^[10] L M BREWSTER revealed that creatine kinase activity in cardiovascular muscle and other tissues with high energy demands could increase cardiovascular contractile reserve, enhance trophic responses and increase renal tubular ability to retain salt. All these would facilitate the development of arterial hypertension under chronic proactive circumstances and with higher mean blood pressure, more left ventricular hypertrophy and relatively few ischaemic events. The study concluded that greater cellular activity of creatine kinase might explain the greater hypertension risk and clinical characteristics of hypertension diseases was observed in black population.^[11]

Fares A, conducted a study on Resistance artery creatine kinase mRNA and blood pressure and according to them, human resistance artery creatine kinase mRNA levels increased progressively with blood pressure, which nearly doubled among hypertensives. In general population circulating creatine kinase was the main predictor of blood pressure and that human resistant artery contractility was highly creatine kinase dependent.^[12] Inge oudman et.al., conducted a study on creatine kinase associated with failure of hypertensive treatment. They concluded that creatine kinase increased blood pressure through sodium retention and cardiovascular contractility by rapidly providing ATP for function. They also concluded that high creatine kinase was associated with failure of antihypertensive treatment.^[13] Thomas et.al., in their study on muscular hypertension and was creatine kinase responsible for hypertension in blacks? stated that there was significant relationship between Creatine kinase and blood pressure and this was independent of demographic factors and ethnicity, also higher creatine kinase was associated with high blood pressure.^[14]

Stein H Johnsen et.al., conducted a study on creatine kinase as a predictor of blood pressure and hypertension, was it all about body mass index and according to their study there was correlation between creatine kinase and systolic blood pressure and diastolic blood pressure. Baseline creatine kinase was significantly corelated with diastolic blood pressure, creatine kinase effect was clearly modified by body mass index. The proposed biological link between muscle fibre phenotype and creatine kinase activity with hypertension and obesity was intriguing but needed further confirmation.^[15] Lizzy et.al., in their study on whether creatine kinase was associated with cardiovascular hemodynamic, the HELIUS study stated that the ATP - regenerating enzyme creatine kinase was strongly associated with blood pressure, which lowered upon experimental creatine kinase inhibition. The study indicated that the association of creatine kinase and blood pressure likely resulted due to enhanced systemic vascular resistance, stroke volume and cardiac contractility.^[16] Johnsen S H, et al conducted a study to understand the creatinine kinase activity and blood pressure and they concluded that creatinine kinase was associated with blood pressure and that creatinine kinase effect on blood pressure was independent of antihypertensive medication and there was no difference in creatinine kinase level among controlled and uncontrolled hypertensive patients.^[17]

CONCLUSION

It was observed that among hypertensive patients the blood pressure levels was significantly higher as compared to control group and also, difference in random blood sugar levels, serum sodium and serum potassium levels were significant. Among hypertensive patients, 36% of them had significantly elevated creatinine levels. It was also seen that elevated creatinine kinase levels were significantly associated with elevated standing and supine blood pressure levels, duration of hypertension, elevated total cholesterol levels and negative outcome.

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