



ASSESSMENT OF FACTORS ASSOCIATED WITH END-ORGAN DAMAGE IN PATIENTS PRESENTING WITH HYPERTENSIVE CRISES IN A TERTIARY CARE HOSPITAL

General Medicine

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ABSTRACT

Background: Hypertensive crises are common clinical presentations seen in the outpatient and emergency department on daily basis. It is important to find out whether patient has any end organ damage to label the patient as hypertensive emergency or urgency. The preset study was done to assess clinical profile and end organ damage of patients presenting with hypertensive. **Methodology:** 120 patients aged >18 years, known case of hypertension, case of de novo hypertension and pregnancy with hypertension were included. Additional workup like CT scan, MRI or USG for related organ to rule out end organ damage on emergency basis were undertaken for further assessment and management. Presence of end organ damage was correlated with various clinical and demographic risk factors. **Results:** End organ damage was significantly higher in patients with limb weakness/facial deviation (100%), history of IHD(100%), in diabetics(88%) and hypertensives (76.04%). Based on investigations, end organ damage was significantly higher in patients with concentric LVH(100%), diastolic dysfunction (100%), valvular disease(100%), concentric LVH+DD, grade 1(100%), grade 2(100%), grade 3(100%) of HTR and pulmonary edema(73.33%). Distribution of end organ damage was comparable with bronchial asthma, hypothyroidism, chronic kidney disease. Mean of ejection fraction (%) in patients with end organ damage was and in patients without end organ damage was were comparable and no significant association between them. (p value=0.298). **Conclusion:** 70% of the patients presenting with hypertensive crisis admitted in emergency department had end organ damage. Presence of diabetes and hypertension has a greater risk of acute target organ damage. Heart is the most common target organ affected in hypertensive emergencies followed by retina, kidneys and brain. Clinical history, examination and radiological investigations like 2D echo, ECG, USG and Fundoscopy are necessary in complete evaluation of hypertensive crisis and related end-organ damage.

KEYWORDS

Hypertensive Crises, Clinical Profile, End Organ Damage, Hypertensive retinopathy.

INTRODUCTION

Hypertension is one of the leading causes of global burden of disease. It affects more than 1 billion individuals yearly with mortality at the rate of 9.4 million deaths per year. Hypertension is the most common comorbidity affecting the Indian Population⁽¹⁾. Hypertensive crises are common clinical presentations seen in the outpatient and emergency department on daily basis. It doubles the risk of coronary heart disease (CHD), Congestive heart failure (CHF), Ischemic and hemorrhagic stroke, renal failure and peripheral arterial disease (PAD). Defined as systolic blood pressure (SBP) of >140 mmHg, diastolic blood pressure of >90 mmHg, or anyone taking antihypertensive medications⁽²⁾.

Physicians in emergency department (ED) frequently triage patients with 'Hypertensive-crisis'. This crisis has been further subdivided into Hypertensive 'Emergency' and 'Urgency'. Hypertensive crises occur in up to 2-3% of hypertensive patients. With prevalence of 24% and 76% respectively for hypertensives emergencies and urgencies⁽³⁾. 6 out of 1000 patients who seek emergency services are in hypertensives crises⁽⁴⁾.

Risk Factors include Non adherence to medications, Long standing hypertension, Higher number of antihypertensive drugs, Female sex, Perioperative period, Stroke, Head trauma, Eclampsia, Cocaine and similar drugs, Acute withdrawal of clonidine and beta blockers, Pheochromocytoma, obesity, Anxiety states etc. If there is a clinical suspicion of end organ damage the clinician must strongly consider additional workup if available⁽⁵⁾. The main areas of focus should be neurological, cardiovascular and renal systems. The key point in making the diagnosis is to find out whether patient has any end organ damage which will allow to label the patient as hypertensive emergency or urgency.

Additional workup required according to clinical suspicion would include ECG, Chest Xray, Serum electrolyte, BUN, Serum Creatinine, Urine analysis, Fundoscopy, 2D echo (if required), Ultrasound with doppler assessment (if required), Brain imaging (CT or MRI) (if required), Cardiac Biomarkers (if required), Chest/Abdominal Contrast CT (if required).

Thorough knowledge and review is needed to throw light on the accurate assessment and management of this complication, in Indian settings where workforce is overburdened and diagnostic work up is not yet well established in some parts of the subcontinent. Aggressive

management can be deleterious as with hypertensive urgencies but prompt and rapid correction is needed in hypertensive emergencies.

Objectives

To study the clinical profile of patients presenting with hypertensive crises and to estimate the presence of end organ damage in patients with hypertensive emergency.

MATERIALS AND METHOD

The present study was conducted on 120 patients aged >18 years, known case of hypertension, case of de novo hypertension and pregnancy with hypertension, who presented with crises in emergency department or OPD. Patients in hypertensive pseudo-crisis were excluded. The study was started after getting approval from Institutional Ethics Committee. After obtaining written consent from patient as well as legally acceptable representative, a pre-tested semi-structured proforma were used to collect information about subjects.

Individuals presenting to the emergency department or OPD, were asked detailed history and clinical examination was performed. Data regarding demographical parameters like Age, sex, socioeconomic status, marital status, profession and any co-morbidity was collected. If indicated, additional workup like CT scan, MRI or USG for related organ to rule out end organ damage on emergency basis were undertaken for further assessment and management. Blood Pressure control was done in the ED itself according to the current treatment protocols. Diagnosis of hypertensive crises was in lieu with the Seventh report of Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure⁽⁶⁾ with attention and critical sense based mainly on the signs and symptoms. The blood pressure measurement was performed using the indirect method, with auscultatory technique and the use of mercury sphygmomanometers.

To identify the clinical manifestations, along with management and treatment of patients, all information in the emergency department records were considered along with information about the patient condition, work-up and treatment if patients admitted indoor in the institution. Investigations like ECG, Chest Xray, Serum electrolyte, BUN, Serum Creatinine, Urine analysis, Fundoscopy were performed in all patients. Some investigations like 2D echo, Ultrasound with doppler assessment, Brain imaging (CT or MRI), Cardiac Biomarkers, Chest/Abdominal Contrast CT were done if indicated. Assessment of presence of end organ damage was done and this occurrence was

correlated with various clinical and demographic risk factors.

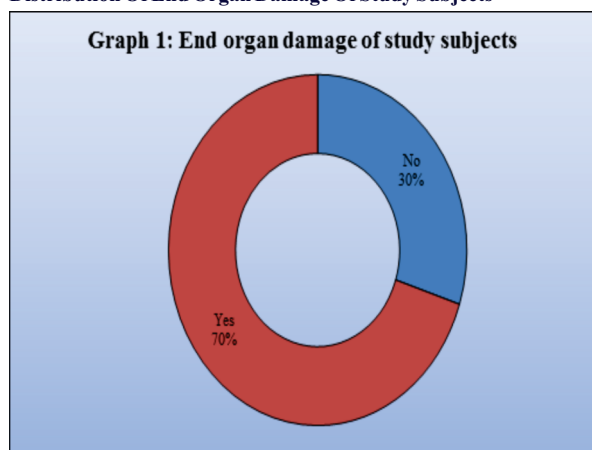
Necessary statistical tests, INOVA software and applications like Microsoft Excel was used as required. R value for each risk factor was calculated. The categorical data was summarized as percentage and proportions while continuous variable as mean and standard deviation.

RESULTS

52(43.33%) patients belonged to age group 51-60 years followed by 61-70 years [32(26.67%)]. Mean value of age(years) of study subjects was 55.56 ± 10.8 with median (25th-75th percentile) of 58 (50-63.25). 83(69.17%) patients were males and 37(30.83%) patients were females. In majority [31(25.83%)] of patients, chief complaint was lower limb swelling followed by limb weakness/facial deviation (20%) and decreased urine output (16.67%).

Majority (70.83%) of patients did not have past history. IHD was present in 15(12.50%) patients. Past history of CVA and pulmonary TB was present in only 10 out of 120 patients (8.33%) each. In majority (80%) of patients, hypertension was present followed by diabetes mellitus (20.83%), bronchial asthma (17.50%), hypothyroidism (9.17%) and chronic kidney disease (8.33%).

Distribution Of End Organ Damage Of Study Subjects



Majority [84(70%)] of patients had end organ damage. 77(64%) patients had cardiac involvement, 58(48.3%) had retinopathy, 32(26%) had nephropathy and 24(20%) had neurological involvement. 118 (98.4%) patients were discharged and 2 (1.6%) patients died (Graph 1).

Association Of Age(years) And Gender With End Organ Damage

Distribution of end organ damage was comparable with age(years). (21-30(100%) vs 31-40(57.14%) vs 41-50(77.78%) vs 51-60(69.23%) vs 61-70(68.75%) vs 71-80(100%)). (p value=0.772). Mean $\pm$ SD of age(years) in patients with end organ damage was 55.88 ± 10.87 and in patients without end organ damage was 54.81 ± 10.68 with no significant association between them. (p value=0.619) Distribution of end organ damage was comparable with gender. (Female 72.97% vs Male 68.67%, p value=0.635) (Table 1).

Table 1:- Association Of Age(years) And Gender With End Organ Damage:

Demographic Variables		With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
Age (years)	21-30	2 (100%)	0 (0%)	2 (100%)	0.772*
	31-40	8 (57.14%)	6 (42.86%)	14 (100%)	
	41-50	14 (77.78%)	4 (22.22%)	18 (100%)	
	51-60	36 (69.23%)	16 (30.77%)	52 (100%)	
	61-70	22 (68.75%)	10 (31.25%)	32 (100%)	
	71-80	2 (100%)	0 (0%)	2 (100%)	
	Mean $\pm$ SD	55.88 ± 10.87	54.81 ± 10.68	55.56 ± 10.78	0.619†
Gender	Female	27 (72.97%)	10 (27.03%)	37 (100%)	0.635†
	Male	57 (68.67%)	26 (31.33%)	83 (100%)	
Total		84(70%)	36(30%)	120(100%)	

†Independent t test, *Fisher's exact test

Table 2:- Association Of Chief Complaints With End Organ Damage:

Chief complaints	With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
Abdominal pain	6 (75%)	2 (25%)	8 (100%)	1*
Blurring of vision	2 (40%)	3 (60%)	5 (100%)	0.159*
Limb weakness/facial deviation	24 (100%)	0 (0%)	24 (100%)	<.0001*
Altered sensorium	8 (100%)	0 (0%)	8 (100%)	0.104*
Fever	13 (68.42%)	6 (31.58%)	19 (100%)	0.87†
Reduced urine output	17 (85%)	3 (15%)	20 (100%)	0.18*
Lower limb swelling	21 (67.74%)	10 (32.26%)	31 (100%)	0.75†
Breathlessness	23 (65.71%)	12 (34.29%)	35 (100%)	0.511†
Chest pain	16 (84.21%)	3 (15.79%)	19 (100%)	0.178*
Total	84(70%)	36(30%)	120(100%)	

*Fisher's exact test, †Chi square test

Distribution of end organ damage was comparable with abdominal pain, blurring of vision, altered sensorium, fever, decreased urine output, lower limb swelling, breathlessness, chest pain, others. End organ damage was significantly higher in patients with limb weakness/facial deviation (100%) as compared to without limb weakness/facial deviation (62.50%). (p value<0.0001) (Table 2).

Table 3:- Association Of Past History, Comorbidities And Addictions With End Organ Damage

Past History, Comorbidities, Addictions	With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
Past history				
CVA	7 (70%)	3 (30%)	10 (100%)	0.022*
IHD	15 (100%)	0 (0%)	15 (100%)	
Pulmonary TB	7 (70%)	3 (30%)	10 (100%)	
NAD	55 (64.71%)	30 (35.29%)	85 (100%)	
Comorbidities				
Diabetes mellitus	22 (88%)	3 (12%)	25 (100%)	0.029*
Hypertension	73 (76.04%)	23 (23.96%)	96 (100%)	0.004†
Bronchial asthma	14 (66.67%)	7 (33.33%)	21 (100%)	0.714†
Hypothyroidism	9 (81.82%)	2 (18.18%)	11 (100%)	0.502*
Chronic kidney disease	4 (40%)	6 (60%)	10 (100%)	0.064*
Addictions				
Tobacco chewing	36 (78.26%)	10 (21.74%)	46 (100%)	0.119†
Alcohol	25 (69.44%)	11 (30.56%)	36 (100%)	0.931†
Smoking	44 (73.33%)	16 (26.67%)	60 (100%)	0.426†

*Fisher's exact test, †Chi square test

Proportion of patients with end organ damage was significantly higher in IHD(100%) as compared to NAD(64.71%), CVA(70%), pulmonary TB(70%). (p value=0.022) Also in was significantly higher in diabetics(88%) and hypertensives (76.04%) as compared to non-diabetics (65.26%), p value=0.029 and non-hypertensives (45.83%), p value=0.004. Distribution of end organ damage was comparable with bronchial asthma, hypothyroidism, chronic kidney disease as well as with addictions.

Table 4:- Association Of Edema, Systemic Examination Findings With End Organ Damage

Odema, Systemic Examination findings		With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
Edema	No	63 (70.79%)	26 (29.21%)	89 (100%)	0.75†
	Grade 1 {Pitting pedal edema}	21 (67.74%)	10 (32.26%)	31 (100%)	
RS	AEBE	61 (71.76%)	24 (28.24%)	85 (100%)	0.511†

	Basal Crepts	23 (65.71%)	12 (34.29%)	35 (100%)	
CNS	No FND	60 (62.50%)	36 (37.50%)	96 (100%)	<0.001*
	Limb weakness	24 (100%)	0 (0%)	24 (100%)	

*Chi square test, *Fisher's exact test

Distribution of end organ damage was comparable with edema. (No oedema 70.79% vs Grade 1 edema 67.74%, p value=0.75). Distribution of end organ damage was comparable with respiratory system. (AEBE 71.76% vs Basal Crepts 65.71%). (p value=0.511). Proportion of patients with end organ damage was significantly higher in limb weakness(100%) as compared to no FND(62.50%). (p value <.0001)

Table 5:- Association Of 2d Echo Findings And Presence Of Hypertensive Retinopathy (HTR) With End Organ Damage:

2d Echo and HTR	With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
2D echo Findings				
Concentric LVH	72(100%)	0(0.00%)	72(100%)	<.0001*
Diastolic dysfunction	35(100%)	0(0.00%)	35 (100%)	<.0001*
Valvular disease	36(100%)	0(0.00%)	36 (100%)	<.0001*
Concentric LVH+DD	30(100%)	0(0.00%)	30 (100%)	<.0001*
Ejection fraction (%) Mean $\pm$ SD	51.9 $\pm$ 5.14	50.83 $\pm$ 5.14	51.58 $\pm$ 5.14	0.298‡
Hypertensive Retinopathy (HTR)				
Grade 0	38 (51.35%)	36 (48.65%)	74 (100%)	<.0001*
Grade 1	30 (100%)	0 (0%)	30 (100%)	
Grade 2	14 (100%)	0 (0%)	14 (100%)	
Grade 3	2 (100%)	0 (0%)	2 (100%)	

‡Independent t test, *Fisher's exact test

End organ damage was significantly higher in patients with concentric LVH(100%), patients with diastolic dysfunction (100%), with valvular disease(100%) and with concentric LVH+DD. Mean of ejection fraction (%) in patients with end organ damage was and in patients without end organ damage was were comparable and no significant association between them. (p value=0.298). Proportion of patients with end organ damage was significantly higher in grade 1(100%), grade 2(100%), grade 3(100%) as compared to grade 0(51.35%). (p value <.0001)

Table 6:- Association Of X Ray Chest With End Organ Damage.

X ray chest	With end organ damage (n=84)	Without end organ damage (n=36)	Total	P value
X ray chest Findings				
Cardiomegaly	11 (45.83%)	13 (54.17%)	24 (100%)	0.018*
Pulmonary edema	11 (73.33%)	4 (26.67%)	15 (100%)	
NAD	62 (76.54%)	19 (23.46%)	81 (100%)	
USG Findings				
Renal disease	4 (40%)	6 (60%)	10 (100%)	0.064*
ECG Findings				
LVH	73 (76.04%)	23 (23.96%)	96 (100%)	0.004†
NAD	11 (45.83%)	13 (54.17%)	24 (100%)	
Total	84 (70%)	36 (30%)	120 (100%)	

*Fisher's exact test

Proportion of patients with end organ damage was significantly higher in patients with pulmonary edema(73.33%) as compared to patients without pulmonary edema (26.67%). (p value=0.018). But it was comparable with present of renal disease (based on USG). (No(72.73%) vs Yes(40%)). (p value=0.064). Based on ECG, Proportion of patients with end organ damage was significantly higher in LVH(76.04%) as compared to patients without any abnormality (45.83%). (p value=0.004).

DISCUSSION

Lack of knowledge about control of hypertension and poor compliance to antihypertensive medications is a major issue. Also, lack of proper health infrastructure in public sector leading to inability of the poor population to access healthcare adds onto the severity of hypertension in the patient as shown in a study done by Mohammad KB et al⁽⁷⁾.

In our study, 70% of patients had end organ damage. Cardiac involvement was highest (64%) followed by retinopathy (48.3%) and nephropathy in 26% of patients. Zamapglione et al⁽⁸⁾ in their study observed target organ damage in the form of intracerebral hemorrhage seen in 4.5% patients, left ventricular failure seen in 23% patients and acute ischemic stroke seen in 24% patients.

In the present study, Percentage of end organ damage was higher in extreme of ages. Mean age(years) in patients with end organ damage was slightly higher but lacks statistical significance. Study done by Almas A et al⁽⁹⁾ demonstrated that mean age of patients with end organ damage was 56.7 $\pm$ 14.7 years and 45.2% of patients were male with no significant association between them with p value of 0.310. It is clear that end organ damage in patients with hypertensive crisis is significantly related to the age of the patient.

Present study shows that percentage of Females having end organ damage was 72.97% and percentage of Males having end organ damage was 68.67% with p value of 0.635. In a study done by Rao et al⁽¹¹⁾ and Zampoglione et al⁽⁸⁾ gender predisposition was not seen to be correlated with end organ damage. Gender differences in hypertension are due to biological and behavioural factors like lifestyle, stress, diet and physical activity according to Sandberg and Ji et al⁽¹⁰⁾. So, there is no significant gender predisposition when end organ damage is considered.

The proportion of patients with end organ damage was significantly higher in diabetics (88%, p value 0.035) and in known hypertensives was (76.04%, p value 0.036). Study done by Rao et al⁽¹¹⁾ demonstrated that Metabolic abnormalities like hyperglycemia, hyperinsulinemia, and dyslipidemia may play important role in the pathogenesis and complications of arterial hypertension.

The proportion of patients with end organ damage was significantly higher in patients with longer duration of hypertension. Patients who had end organ damage with duration of hypertension greater than 5 years was 84.4% compared to patients who were hypertensive for 5 years or less (41.4%) with significant p value of 0.026. The end organ damage most commonly encountered in hypertensives with duration of disease 5 years or less was hypertensive retinopathy as opposed to patients with disease duration of greater than 5 years in whom LVH and nephropathy was more common. Similar findings were noted in study done by Rao et al⁽¹¹⁾ which demonstrated that higher the duration of hypertension greater is the risk of developing end organ damage.

Our study revealed that the proportion of patients with end organ was compared with BMI. 71.4% of Obese patients with BMI >27.5 had end organ damage compared 69.7% of non-obese patients who had end organ damage with p value of 0.088. Pierin et al⁽¹²⁾ demonstrated that obese individuals with BMI>30 had higher risk of end organ damage than non-obese individuals with p value of 0.038. But our study showed no significance of BMI with end organ damage

Tobacco chewing was significantly associated with organ damage (p value 0.042) in our study. Alcohol and smoking don't show significant association with organ damage. Shao J et al⁽¹³⁾ found that nearly half of patients with end organ damage had addition to tobacco chewing as well as smoking. Intake of alcohol when compared to end organ damage in hypertensives showed no significant association as per their study.

In our study, presence of LVH and diastolic dysfunction was considered as end organ damage to heart. Percentage of patients having end organ damage without valvular disease was 69.05% while those with valvular disease was 72.22% (p value 0.728). Median of ejection fraction in patients with and without end organ damage was similar. In previous studies done by No significant association was seen with valvular involvement and end organ damage in studies by Bender et al⁽¹⁴⁾ and Zampoglione et al⁽⁸⁾, which are similar to our study.

The proportion of patients with end organ damage was significantly

higher in HTR grade 1 (p value <0.0001) in our study. Study by Rao et al⁽¹¹⁾ demonstrated that evaluation of fundus revealed changes ranging from hypertensive retinopathy to papilledema in 50% of patients. Papilledema was seen in 12 % patients which is an evidence of ongoing target organ damage.

A study by Rao et al⁽¹¹⁾ demonstrated that 58% of their patients had hypertensive nephropathy. Longer duration of hypertension and male gender had higher risk of developing hypertensive nephropathy according to this study. Similar findings were noted in our study where hypertension of more than 5 years showed development of nephropathy more commonly than other target organ damages. Development of ESRD secondary to hypertensive nephropathy has highest morbidity associated with it secondary to renal replacement therapy and maintenance dialysis thus signifying its prevention rather than treating it later after its development.

In our study, the proportion of patients with end organ damage was significantly higher with pulmonary edema (p value 0.018). Brian et al⁽¹⁵⁾ showed significant difference between aortic knob width in hypertensives and normotensives as seen on chest X ray (3.69 cm vs 3.28 cm) and cardiomegaly was also significantly correlated with end organ damage with p value of <0.02.

Pierin et al⁽¹²⁾ showed that out of all patients in their study who had hypertensive crisis, 75% patients had LVH criteria fulfilled on ECG of whom 55% were confirmed to have LVH on the basis of 2D echo findings. Similarly, we found that proportion of end organ damage was compared with ECG findings and it was seen that 76.04% of patients having LVH on ECG had end organ damage while the remaining 23.96% patients had no end organ damage.

We observed, 118 patients improved and were discharged, while 2 patients expired. Both expired patients had intracranial hemorrhage. A study done by Rao et al⁽¹¹⁾ demonstrated that out of 50 patients with hypertensive emergencies, 7 patients expired before discharge. Hospital mortality was 14%. All expired patients had Intracerebral hemorrhage (ICH) and acute LVF. Study done by Shao J et al⁽¹³⁾ demonstrated that In-hospital mortality among patients with hypertensive emergency was 26.8%. While factors contributing to the high mortality might include severity of illness and existing comorbidities, the most important factor was likely the inability to provide advanced care to critically ill patients due to lack of resources.

CONCLUSION

In our study, the majority of patients presenting with hypertensive crisis getting admitted had an emergency, as 70% of them had end organ damage. Maximum patients belonged to the 6th and 7th decade of life with male predominance. Presence of diabetes and hypertension has a greater risk of acute target organ damage. Heart is the most common target organ involved followed by the retina, kidneys and the brain. Clinical history and examination along with radiological investigations like 2D echo, ECG, USG and Fundoscopy are necessary in complete evaluation of hypertensive crisis and related end-organ damage.

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