Original Research Article

Saudi Medical Journal of Students (SMJS)
Official Journal of Faculty of Medicine University of Tabuk
ISSN: 1658-8274 (Print version); 1658-8282 (Electronic version)

MANAGEMENT AND OUTCOMES OF HYPERTENSIVE CRISES IN EMERGENCY SETTINGS: A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: Hypertensive crises, encompassing both emergencies and urgencies, present with varied symptoms and can lead to significant morbidity and mortality if not managed appropriately. Despite the common use of antihypertensive therapies, optimal management in ED remains a clinical challenge.
Aim: The aim of this study was to assess the effectiveness and outcomes of management strategies for hypertensive crises in emergency settings, guiding clinical practice and identifying gaps in current research.
Methods: A comprehensive systematic review included studies from 1993 to 2023, totaling 27,808 adult patients with hypertensive crises. Adult patients aged 18 years and above with a hypertensive crisis treated in EDs were included. Pregnant women, individuals under 18, and non-ED settings were excluded. Management strategies encompassed IV antihypertensive agents for

emergencies and oral medications for urgencies, focusing on CCBs, β blockers, and other antihypertensive classes. Primary outcomes were mortality, morbidity, and complications related to hypertensive crisis management. Secondary outcomes included patient discharge rates and education on red flag symptoms.

Results: Calcium channel blockers, especially Nicardipine, were predominant in managing hypertensive crises, with significant patient discharge rates post-intervention. Stroke was the most common complication, emphasizing the need for effective blood pressure control; 54.17% of patients were eventually discharged.

Conclusion: Nicardipine is effective in hypertensive crisis management in EDs. Stroke is a notable complication, underscoring the importance of timely intervention. Furthermore, findings support the use of CCBs in hypertensive crises and highlight the need for patient education on symptom monitoring post-discharge. Future research should focus on long-term outcomes, personalized medicine approaches, and randomized controlled trials for novel therapies.

Keywords: Hypertensive Emergency, Hypertensive Urgency, Emergency Department, Emergency Room, Management, Outcome.

To cite this article: Alshalahi SS, Almutairi AH, Almuteri D, Alomar LA, Ezmirly M, Alafaliq D, Alqahtani M, Aldhamer A, Almokhalfi M, Almasoud A, Zaheralliyali A, Aldaghmani A, Alenezi AAK2, Alshanqiti N. Management and Outcomes of Hypertensive Crises in Emergency Settings: A Comprehensive Systematic Review. Saudi Med J Students. 2024;5(1):12-24

INTRODUCTION

Hypertension is a medical condition that occurs when a person's blood pressure exceeds the normal range (140/90 mmHg or higher) [1]. Hypertension may be accompanied by damage to one of the body's organs. In this case, it is called a hypertensive emergency, and work must be done to reduce it immediately with an IV antihypertensive agent. If the hypertension is without any damage to an organ, it is called hypertensive urgency, and it can be reduced gradually within days with an oral antihypertensive [2].

Patients may not feel symptoms due to this increase in blood pressure and may not be aware of this disorder. Common symptoms include headaches, blurred vision, nausea, dizziness, and some chest complications such as difficulty breathing and chest pain [3]. It is considered one of the most common disorders in the world, as the number of people who have hypertension reaches 1.28 billion adults around the world [4]. Hypertensive crisis is a condition frequently found in emergency departments of various ages and symptoms [5], and it is treated using different therapeutic interventions and management strategies in emergency departments [6]. When choosing an antihypertensive medication for both urgencies and emergencies, clinicians should take into account the underlying reasons for the crisis, any comorbidities, and cardiovascular disorders. Many studies have been published that include talking about the management of hypertensive crises in emergency departments. Hypertensive urgencies should be gradually reduced within 24–48 hours using oral treatments (which are

often Captopril, Nifedipine, and Amlodipine drugs), considering onset, duration, contraindications, and side effects. Hypertensive emergencies should be treated with parental treatment, such as Labetalol, to prevent the aggravation of organ damage and reduce the rate of morbidity and mortality. However, rapid reduction of blood pressure should be avoided; blood pressure can be reduced by 25% in the first hour and then gradually reduced over 24–48 hours, provided there is no aggravation of organ damage, and after normal blood pressure is achieved, the patient can be referred to oral treatment [7].

We conducted this systematic review to evaluate and determine the effectiveness of the various strategies used in treating and managing hypertensive crises in adults who attend emergency departments and to be aware of the effectiveness and outcomes of these strategies by evaluating mortality, morbidity, and complications of the therapeutic interventions in emergency departments.

MATERIAL AND METHODS

Material and Methods: This comprehensive systematic review was prospectively registered in PROSPERO (CRD42023479351) and conducted in adherence to the Preferred Reporting Items for Systematic Reviews (PRISMA) guideline [8]. A comprehensive electronic search was conducted on the PubMed, Google Scholar, and Cochrane databases for studies published between January 1, 1993, and October 1, 2023. The search strategy used the PICOS method of searching electronic databases; it was designed by one of the authors (Seham Alshalahi) and was approved by the study team members prior to application. An amalgamation of medical subject headings (MeSH), such as ("hypertensive emergency" OR "hypertensive urgency") AND ("emergency department" OR "emergency room" OR "ER") AND ("management" OR "outcomes" OR "outcome"), were used.

Eligibility Criteria

This review used articles that were published in English for the hypertensive crisis in emergency settings for adult patients aged 18 years old and above who have been treated in emergency departments with a diastolic blood pressure of ≥ 120 mmHg. Exclusion criteria included articles that focused on hypertensive crisis in pregnancy, a study population age below 18 years, whether participants were treated in a department other than an emergency, and systematic and narrative reviews.

Selection of Articles and Data Extraction: Five reviewers independently evaluated the titles and abstracts obtained from the search strategy using Rayyan software (Rayyan Systems Inc., Cambridge, MA) according to the study's eligibility requirements with the agreement of all authors [9]. By this we ensured only relevant studies for the final analysis in this research would be included. Data extracted from the retained studies included year of publication and country of origin, study design, and total number of patients with their ages, genders, and ethnicities.

Study	Selection (0–4)	Comparability (0–2)	Outcomes (0–3)	Total	Risk of Bias 0–3: High; 4–6: Moderate; 7–9: Low
Vlcek et al. (2008)	2	1	1	4	Moderate
Preston et al. (2018)	2	2	3	7	Low
Salvetti et al. (2019)	2	2	3	7	Low
Lin et al. (2021)	2	1	3	6	Moderate
Endo et al. (2023)	4	2	3	9	Low
Kim et al. (2022	4	1	3	8	Low

Table 1. Risk of Bias Assessment (Newcastle Ottawa Scale)

Moreover, their comorbidities, blood pressure readings, and medication were included. In addition, target organ damage, number and type of antihypertensive medications administered in emergency departments, route of administration, admission, discharge, outcomes complication, and death were also included.

Quality Assessment and Risk of Bias: The risk of bias in this study was independently evaluated by four reviewers. They used an assessment tool based on nine criteria distributed across the three following categories: selection, comparability, and outcome. Regardless of perceived bias in the material, the reviewers' assessments were consistent. The Newcastle–Ottawa scale was used for bias assessment in retrospective and prospective cohort studies (Table 1) [10] and for a methodological index for nonrandomized studies (minors) (Table 2) [11], Cochrane risk-of-bias for randomized (Table 3).

Statistical Analysis of Data: Despite our efforts to carry out a basic descriptive statistical analysis, the diverse nature of the articles reviewed and the lack of suitably formatted data prevented the possibility of performing a meta-analysis.

RESULTS

Overview of the Literature (Figure. 1; Tables 1–4)

The study commenced with the identification of 1,096 publications by the first author, consisting of 948 from Google Scholar, 124 from PubMed, and 24 from Cochrane. After eliminating duplicate papers, the titles and abstracts of 1,088 distinct research papers were assessed. Subsequently, the entire texts of 290 publications were thoroughly reviewed, leading to the identification of 9

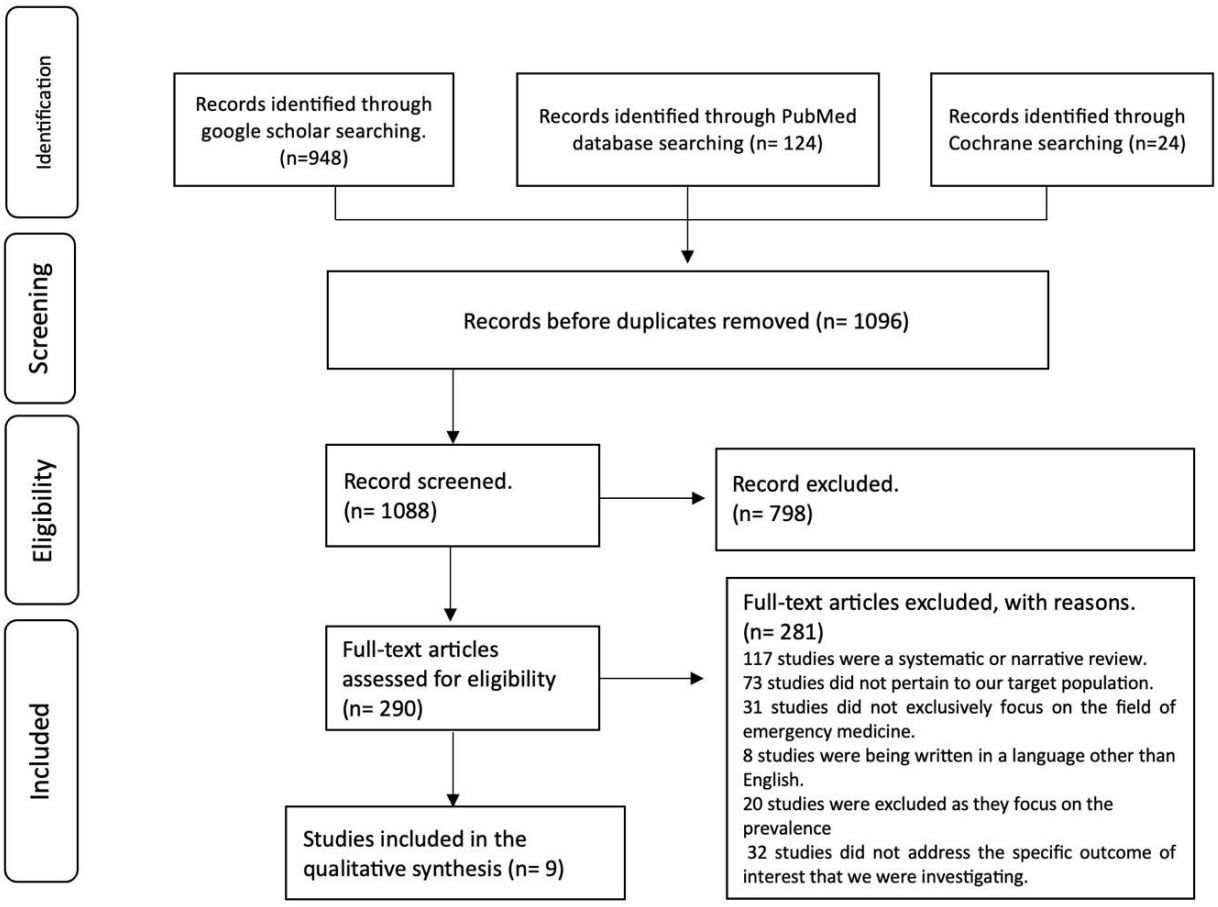

Figure 1. PRISMA chart

papers that met the criteria for inclusion or exclusion. Several factors have contributed to the exclusion of a significant number of articles in our analysis. These factors include the presence of articles that specifically focus on pregnant women, studies that lack relevance to specific patient age groups or target populations, research that fails to mention management outcomes, and studies conducted exclusively within departments other than emergency medicine. (Figure. 1).

In our systematic comprehensive review, we examined a total of nine investigations, each employing a variety of methodologies (three prospective, three retrospective, and three cross-sectional). The geographical diversity was robust, with two studies based in the United States and others originating from Philadelphia, Taiwan, Korea, Sudan, Japan, Austria, and Northern Italy. Spanning a three-decade timespan from 1993 to 2023, these studies included a cohort of 27,808 patients. Gender distribution was nearly balanced, with males comprising 46.23% and females 53.38% of the study population. A

	Salvetti et al. (2019)	Obeid et al. (2020)	Preston et al. (1999)
Clearly stated aim	2	2	2
Inclusion of consecutive patients	1	1	2
Prospective collection data	1	1	1
Endpoint appropriate to the aim study	2	2	2
Unbiased assessment of the study endpoint	1	1	1
Follow-up period appropriate to the aim of study	2	1	1
Loss to follow-up less than 5%	1	0	0
Prospective calculation of the study size	0	0	0
An adequate control group	0	0	0
Contemporary groups	N/A	N/A	N/A
Baseline equivalence of group	N/A	N/A	N/A
Adequate statistical analysis	2	2	2
Total score	12	10	11

Table 2. Instrumental assessment for nonrandomized studies (minors)

common characteristic amongst these patients was the prevalence of preexisting conditions. The age range was broad, typically from 18 to 84 years. Cardiovascular

	McDonald et al. (1993)
Random sequence generation	Low
Allocation concealment	High
Blinding of participants and personnel	High
Blinding of outcome assessment	High
Incomplete outcome data	Low
Selective reporting	Unclear
Other bias	Unclear
Attrition bias	Unclear
Reporting bias	Unclear
Performance bias	High
Detection bias	High
Other (e.g., funding source)	Unclear

Table 3. Cochrane risk-of-bias for randomized

diseases were the most prevalent comorbidities among hypertensive urgency and emergency patients, with a total of 4,492 cases. Specifically, stroke was the predominant condition, accounting for 45.52% of the cases, followed by coronary artery disease at 3.34%. Notably, five studies indicated that out of 27,602 patients, 13,302 had a history of target organ damage (Table 4).

Table 5 enumerates the classes of antihypertensive agents employed in the encompassed studies, including β blockers, CCB, Clonidine, vasodilators, diuretics, alpha-blockers, Urapidil, and RASi. This treatment approach led to observable improvements in patient health outcomes. Upon admission, 54.17% of patients were eventually discharged due to health improvements and after receiving education about red flag symptoms. The complications

Author	Name of journal	Year	Country	Study design	Total number of patients	Age	Sex		Ethnicity		Comorbidities			
							Male	Female	Black	White	Hypertension	Diabetes mellitus	Cardiovascular disease	CKD
McDonald	*The American Journal of Emergency Medicine*	1993	Philadelphia	prospective, randomized open labeled	20	48 ± 19	10	10	20	0	15	N/A	N/A	N/A
Preston	*Journal of Human Hypertension*	1998	USA	cross-sectional	87	54.3 ± 12.5	45	42	N/A	N/A	71	29	48	N/A
Vlcek	*Journal of Hypertension*	2008	Austria	Prospective	384	56 ± 12	199	185	N/A	N/A	N/A	59	62	N/A
Preston	*Journal of Hypertension*	2019	USA	Retrospective cohort	156	54.9	89	67	108	48	N/A	36	41	17
Salvetti	*Journal of Hypertension*	2019	Northern Italy	prospective, analyzed	2,765	70 ± 15	1,191	1,574	N/A	N/A	305	103	105	N/A
Lin	*PLOS ONE*	2021	Taiwan	Retrospective cohort	22,906	60.2	10,516	12,390	N/A	N/A	10,324	2,496	3,948	4,621
Obied	*National Library of Medicine*	2021	Sudan	cross-sectional	50	18 ± 60	20	30	N/A	N/A	N/A	12	2	1
Kim	*Springer Link*	2022	Korea	cross-sectional	1,391	57.4 ± 17.2	749	642	N/A	N/A	674	306	298	172
Endo	*BMC Nephrology*	2023	Japan	Retrospective cohort	49	47.2 ± 11.2	37	12	N/A	N/A	39	4	N/A	N/A

Table 4: Summary of nine studies involved

experienced by the patients varied significantly, with stroke being the most common, affecting 5,782 patients. A general representation of cardiovascular disease was seen in 734 cases. Additionally, acute kidney injury (AKI) was reported in 7 cases, and chronic kidney disease (CKD) was seen in 15 cases, including 10 instances of end-stage renal disease. The approximate count of fatalities was recorded to be 7,436 (Table 6).

DISCUSSION

The primary aim of this systematic review was to evaluate the effectiveness of diverse management strategies for hypertensive crises in emergency settings and their impact on patient outcomes. This systematic review provides valuable insights into the prevalence of comorbidities, age distribution, and treatment outcomes among hypertensive urgency and emergency patients. The findings highlight the importance of cardiovascular disease as a common comorbidity and the potential benefits of calcium channel blockers as the predominant choice of treatment among individuals experiencing hypertensive crises. Furthermore, the discharge of a significant proportion of patients following improved health status and education underscores the significance of patient education and monitoring in hypertension management.

Across all nine studies, we applied in Table 5 all medications that were used; the most commonly used medications were CCBs, including Nicardipine, Amlodipine, and Nifedipine. Among these, Nicardipine emerged as the most frequently prescribed. According to the latest United States study conducted in 2024, Nicardipine was found to be safe and effective, with only one patient (2.6%) in the total population experiencing both hypotension and bradycardia [21].

Table 5. Impact of antihypertensive drugs used in emergency departments

Study	Antihypertensive drug used							
	β blockers	CCB	Clonidine	Vasodilators	Diuretic	Alpha blockers	Urapidil	RASi
[12]	Labetalol (10)	Nifedipine (10)	_	_	_	_	_	_
[13]	_	Nifedipine (15)	Clonidine (68)	_	_	_	_	_
[14]	_	Amlodipine (NM)	_	_	_	_	_	Captopril (NM)
[15]		Nifedipine (31) Amlodipine (9)	Clonidine (61)	Hydralazine (21)	_	_	_	Lisinopril (10)
[16]	Labetalol (54)	DHP (63) , NDHP (16)	–	Nitrates (129)	Thiazides (3) Furosemide (123)	Doxazosin (9)	Urapidil (6)	NM
[17]	NM	NM	_		NM	NM		NM
[18]	_	_	_	_	_	_	_	Captopril (50)
[19]	Labetalol (35) Esmolol (14) Carvedilol, Nebivolol, Propranolol, Atenolol, and Bisoprolol (62)	Nicardipine (453), Amlodipine, and Nifedipine (170)		Nitroglycerin (284)	–	–	–	Perindopril, Candesartan, Losartan, and Fimasartan (22)
[20]	NM	NM	_	_	_	_	_	NM
Total	175 (10.32%)	767 (45%)	129 (7.56%)	434 (25.43%)	126 (7.39%)	9 (0.53%)	6 (0.35%)	82(4.74%)

Additionally, a study conducted in 2011 compared treatment with intravenous Nicardipine to intravenous Labetalol. Within 30 minutes, 91.7% of patients treated with intravenous Nicardipine achieved the target blood pressure level, compared to 82.5% of patients treated with intravenous Labetalol. Furthermore, a subgroup analysis of this study included 141 patients exhibiting signs or symptoms of target organ damage. Within 30 minutes, 91.4% of patients randomized to intravenous Nicardipine reached their target blood pressure level, whereas only 76.1% of patients randomized to intravenous Labetalol achieved the same [22]. This demonstrates that Nicardipine is a more effective antihypertensive drug, particularly when compared to Labetalol. Additionally, in a study conducted by McDonald, the rate of response to Labetalol was reported to be 80%, whereas the response rate for Nifedipine was 100% [12, 13]. Nifedipine causes a fast and notable decrease in blood pressure, typically within 5 to 20 minutes. The maximum effects are observed between 30 to 60 minutes after administration, and its impact can last up to 6 hours [23]. Another comparative study conducted in Korea examined the efficacy of nicardipine and nitroprusside in the treatment of hypertensive emergencies. Both medications demonstrated significant reductions in blood pressure with comparable effectiveness. However, nicardipine exhibited additional favorable outcomes, including improved heart rate and decreased noradrenaline levels [24]. In the same vein, Nicardipine demonstrated comparable efficacy to sodium nitroprusside in achieving the target blood pressure, but with the advantage of avoiding the risk of thiocyanate toxicity. Nicardipine also resulted in faster attainment of the target

Table 6. Complications of hypertensive crises

Study	Hypertensive encephalopathy	Congestive heart failure	Cerebrovascular accident	Acute coronary syndrome	Stroke	Atrial fibrillation	Acute left ventricular failure	Heart failure
[12]	_	_	_	_	_	_	_	_
[13]	3 (3.44%)	3 (3.44%)	2 (2.29%)	2 (2.29%)	_	_	_	_
[14]	_	_	_	40 (10.41%)	26 (6.77%)	5 (1.30%)	17 (4.42%)	_
[15]	_	_	12 (7.69%)	29 (18.58%)			4 (2.56%)	29 (18.58%)
[16]	_	_	_	_	_	_	_	571
[17]	_	_	_	_	5,756 (25.12%)	_	_	_
[18]	_	_	_	_	_	_	_	_
[19]	_	_	_	_	_	_	_	_
[20]	1 (2%)	_	_	2 (4.1%)	_	_	_	8 (16.3%)
Continued	**Myocardial infarction**	**Aortic dissection**	**Fatal cardiac arrest**	**Acute kidney injury**	**Chronic kidney disease**	**ESRD**	**TMA**	**Death**
[12]	_	_	_	_	_	_	_	_
[13]	_	_	_	_	_	_	_	_
[14]	_	_	_	_	_	_	_	_
[15]	4 (2.56%)	1 (0.64%)	4 (2.56%)	7 (4.48%)	5 (3.2%)	4 (2.56%)	_	4 (2.56%)
[16]	_	9	_	_	_	_	_	6 (3.84%)
[17]	_	_	_	_	_	_	_	6,364 (27.78%)
[18]	_	_	_	_	_	_	_	_
[19]	_	_	_	_	_	_	_	241 (17.3%)
[20]	2 (4.1%)	_	_	_	_	6 (12.24%)	5 (10.2%)	_

blood pressure with reduced variability [23]. Hypertension Nitroglycerin was applied in 16.65% of hypertensive crisis patients. Nitroglycerin is a potent vasodilator that primarily affects the veins, and its impact on arterial tone is noticeable only at high doses. It can lead to hypotension and reflex tachycardia, which can be worsened by the reduced blood volume often seen in hypertensive emergencies [25]. In Sri Lanka, only 2 patients (5.4%) experienced an excessive decrease in blood pressure. It took a minimum of 15 minutes to prepare and administer nitroglycerin through an intravenous infusion. To provide rapid blood pressure control in hypertensive emergencies, sublingual nitroglycerin spray can be used as a useful temporary measure while the intravenous infusion is being prepared [24]. Furthermore, in the management of postoperative surgical hypertension, nitroglycerin and nicardipine are considered the drugs of choice [26]. In addition, in a 2022 cross-sectional study conducted in Eastern Ethiopia involving 363 patients, it was discovered that 70.2% of them received Captopril, whereas 29.8% were given intravenous hydralazine for the

management of hypertensive crisis. Among these patients, 27% had an unfavorable treatment outcome. The study highlighted a significant association between the choice of emergency medication administered upon admission and an increased probability of experiencing a poor treatment outcome in cases of hypertensive crisis [27]. Similar results were reported by Obied et al., who found that 30% of patients progressed after receiving Captopril treatment [18]. in the elderly, certain medications are preferred due to their efficacy and tolerability. Clevidipine, nicardipine, labetalol, esmolol, and fenoldopam are recommended choices. However, caution should be exercised when considering nitroprusside, hydralazine, and nifedipine for elderly patients. Due to the increased risk of complications and unpredictable reactions [28].

Among patients with hypertensive crises, stroke was the most common complication, accounting for approximately 88.18% of all reported complications. This high percentage was followed by heart failure, acute coronary syndrome, and acute left ventricular failure, which accounted for 9.15%, 1.11%, and 0.32% of cases, respectively. Additionally, a meta-analysis study conducted in 2023 revealed similar findings, indicating that stroke was the most prevalent complication of hypertensive crises, accounting for approximately 42.7% of cases. Acute heart failure, acute coronary syndrome, and renal failure accounted for 24.1%, 10.8%, and 8.0% of cases, respectively [29]. Furthermore, in Northeastern Thailand, a retrospective cohort study conducted in 2021, the outcomes of hypertensive emergency patients indicated that the highest prevalence of target organ damage was observed in stroke cases, accounting for 49.8% of the patients. This was followed by acute heart failure, which affected 19.3% of the patients, and acute coronary syndrome, which was observed in 6.5% of the cases [30]. In another cross-sectional study carried out in Cleveland (US), it was observed that within a span of six months, 0.85% of patients encountered major adverse cardiovascular events (MACEs), 0.35% experienced episodes of acute coronary syndrome, and 0.51% had episodes of stroke or transient ischemic attacks [31].

Our systematic review highlighted multiple limitations in the existing literature. First, several studies reported medication administration without specifying patient sample size. Second, numerous studies mentioned only the general class of drugs used, omitting the specific subclasses within those categories. Finally, there was a lack of uniformity in the reporting of admission procedures and post-management follow-up in cases of hypertensive crises across the reviewed studies.

CONCLUSION

This systematic review presents empirical evidence on the effectiveness of various management strategies for hypertensive crises in emergency department settings. Among these strategies, calcium channel blockers (CCBs), specifically Nicardipine, have been found to be a commonly recommended medication for effectively and safely managing hypertensive crises. Hypertensive crises are associated with complications such as cardiovascular events,

particularly strokes, highlighting the importance of promptly and effectively controlling blood pressure to reduce the risk of such events.

Based on the findings of this review, several directions for future research can be proposed. First, longitudinal studies are needed to assess the long-term effects of interventions for hypertensive crises, focusing on the sustained efficacy of treatment and the impact on patients' quality of life post-intervention. Second, personalized medicine approaches should be explored, taking into account individual patient characteristics, including genetic factors, to improve the specificity and effectiveness of antihypertensive treatments. Last, rigorous randomized controlled trials are necessary to evaluate the potential of new therapeutic agents and tailored intervention strategies, thus expanding the evidence base for managing hypertensive crises.

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