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Prevalence and factors associated with Uncontrolled blood pressure in dialysis patients using antihypertensive: a narrative review

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ABSTRACT

Hypertension in patients with end-stage chronic kidney disease undergoing hemodialysis is difficult to control leading to a significant risk factor for a cardiovascular event. The aimed of this review is to summarize the prevalence of uncontrolled blood pressure in dialysis patients. This review hopefully can serve as a valuable reference and source of insight for clinicians in their efforts to attain controlled blood pressure in dialysis patients. The relevant literatures was undertaken from PubMed, Scopus, and Google Scholar for studies addressing the factor associated with uncontrolled blood pressure in hemodialysis patients using antihypertensives from 2013 to 2023. Combinations of search terms were "uncontrolled" and "blood pressure" and "dialysis" and "antihypertensive". Any study in English, including randomized control trials, cohort, case-control, and cross-sectional studies was included. Uncontrolled blood pressure is very common among hypertension in dialysis patients (28.7 - 78.33% of cases). Factors affecting blood pressure in dialysis patients include age, obesity, and comorbidity (diabetes and stage of chronic kidney disease). Although the relationship between gender, the number of antihypertensive, the number of dialysis, and the length of dialysis sessions with blood pressure varies, some studies have shown a positive association.

ABSTRAK

Hipertensi pada pasien dengan penyakit ginjal kronis stadium akhir yang menjalani hemodialisis sulit dikendalikan, dan merupakan faktor risiko yang signifikan untuk kejadian kardiovaskular. Tujuan dari review ini adalah untuk merangkum prevalensi tekanan darah tidak terkontrol pada pasien dialisis. Review diharapkan juga dapat sebagai acuan dan pertimbangan bagi klinisi dalam upaya mencapai tekanan darah terkontrol pada pasien dialisis. Pustaka yang relefan diambil dari PubMed, Scopus, dan Google Scholar untuk kajian tentang faktor yang terkait dengan tekanan darah yang tidak terkontrol pada pasien hemodialisis yang menggunakan antihipertensi dari tahun 2013 hingga 2023. Kombinasi istilah pencarian adalah "*uncontrolled*" dan "*blood pressure*" dan "*dialysis*" dan "*antihypertension*". Semua penelitian yang ditulis dalam bahasa Inggris dianalisis, termasuk uji coba kontrol acak, kohort, kasus kontrol, dan penelitian potong-lintang. Tekanan darah yang tidak terkontrol umum terjadi di antara hipertensi pada pasien dialisis (28,7- 78,33%). Faktor-faktor yang mempengaruhi tekanan darah pada pasien dialisis meliputi usia, obesitas, dan komorbiditas (diabetes dan stadium penyakit ginjal kronis). Meskipun hubungan antara jenis kelamin, jumlah obat antihipertensi, jumlah dialisis, dan lama sesi dialisis dengan tekanan darah bervariasi, beberapa penelitian menunjukkan hubungan yang positif.

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INTRODUCTION

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative, recommended that the respective targets for pre- and post-dialysis blood pressure should be less than 140/90 mmHg and less than 130 mmHg, respectively.[1] However, hypertension in patients with end-stage chronic kidney disease (ESCKD) undergoing hemodialysis is difficult to control, and a significant risk factor for a cardiovascular event.[2-5] Therefore, it is crucial to understand the factors that influence blood pressure in dialysis patients.

Studies related to the prevalence of uncontrolled blood pressure in routine hemodialysis patients and the influencing factors have been conducted using various methods. However, narrative study based on electronic literature searches is still limited. The aim of this article review is to summarize the prevalence of uncontrolled blood pressure in dialysis patients in several countries. This review also can serve as a valuable reference and source of insight for clinicians in their efforts to attain controlled blood pressure in dialysis patients.

MATERIAL AND METHODS

PubMed, Scopus, and Google Scholar were employed to summarize the prevalence of uncontrolled blood pressure in hemodialysis patients and to identify any factors influencing it in patients using antihypertensive. The articles were obtained from 2013 to 2023. Combinations of search terms were “uncontrolled” and “blood pressure” and “dialysis” and “antihypertensive”. Any study written in English was collected, including randomized control trials, cohort, case-control, and cross-sectional studies. Non-dialysis studies, case reports, studies involving post-renal transplantation patients, any articles or studies published before 2013 were excluded.

RESULTS

A total of 175 articles were identified through database searches, comprising 27 from PubMed, 30 from Scopus and 118 from Google Scholar. Furthermore, a total of 160 articles were excluded for various reasons, including duplicates (6), irrelevant (24), non-dialysis (58), not original research (24), case reports (44), and post-renal transplantation (4). Therefore, the full-text articles assessed for eligibility was 15 (FIGURE 1).

The primary objective of the research focus on consolidating information regarding the prevalence of uncontrolled blood pressure in dialysis patients across various countries and identifying the factors associated with uncontrolled blood pressure in this patient population. The prevalence of uncontrolled blood pressure in routine hemodialysis patients is high and varies among several countries (TABLE 1). Factors that affect uncontrolled blood pressure in dialysis patients are presented in TABLE 2.

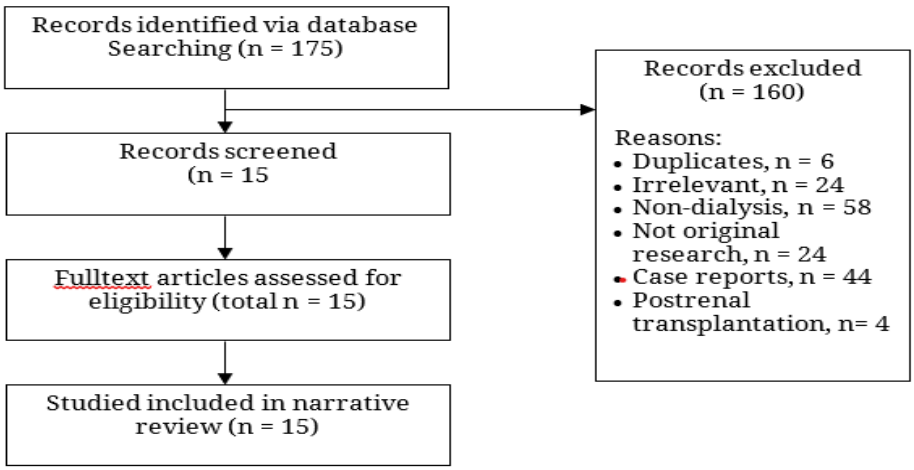

FIGURE 1. Study selection flowchart

TABLE 1. Prevalence of uncontrolled blood pressure in dialysis patients in some countries

Authors	Patient and population	Country	Uncontrolled blood pressure definition	Methods	Prevalence [% (n)]
Nugraha *et al.*[6]	65 patients receiving regular hemodialysis	Bali (Indonesia)	Pre-dialysis BP measurement >140/90 mmHg and/or taking the antihypertensive regularly	Cross-sectional	65.6 (42)
Amr *et al.*[7]	390 adult patients at three hemodialysis units	South of Palestine	Predialysis BP of ≥ 140/90 mmHg and post-dialysis BP of ≥130/80 mmHg	Cross-sectional	59 (231)
Sarafidis *et al.*[8]	396 hemodialysis adult patients in 16 hemodialysis unit	Three countries (Italy, Greece, and Slovenia)	Pre-hemodialysis BP ≥140/ 90 mmHg or current treatment with any antihypertensive; ambulatory 48-h BP ≥130/80 mmHg or current treatment with any antihypertensive	Cross-sectional	46 (186)
Al Sahlawi[9]	339 hemodialysis patients at a large tertiary hospital	Saudi Arabia	The mean of 3 BP readings ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg	Observational retrospective	64 (216)
Burmeister *et al.*[10]	1215 hemodialysis patients in Porto Alegre	Porto Alegre (Brazil)	All patient which use antihypertensive, or those with mean pre-dialysis BP in stage 1 or up of the Seventh Report of JNC on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classification	Cross-sectional	72 (875)
Mallamaci *et al.*[11]	506 hemodialysis patients from 10 renal units in Europe (data was taken from the registry of European Renal and Cardiovascular Medicine (EURECAm))	Europe	Pre-hemodialysis BP at least 140/90 mmHg or current treatment with any antihypertensive agent; ambulatory 44-h BP at least 130/80 mmHg or current treatment with any antihypertensive	Cross-sectional	58 (296)
Bakri *et al.*[12]	60 outpatients at the Dialysis Installation of RSUD dr. Zainoel Abidin Banda Aceh	Banda Aceh (Indonesia)	Pre-hemodialysis 140/90 mmHg; intra-dialysis 135/85 mmHg; and post-hemodialysis 130/80 mmHg	Cross-sectional	a. 78.33 (47)* b. 85 (51)** c. 95 (57)***
Li *et al.*[13]	1871 peritoneal dialysis at 9 centers from 5 tertiary hospitals and 4 secondary hospitals	Guangdong (China)	SBP ≥130 mmHg or DBP ≥80 mmHg with concurrent use of at least three antihypertensive of different classes, or BP controlled by at least 4 medications	Cross-sectional	42.2 (755)
Gulalai *et al.*[14]	237 hemodialysis patients from the Balochistan Institute of Nephrology Urology Quetta (Pakistan)	Pakistan	If a hypertensive diagnosis was documented in the medical record or the patient was receiving antihypertensive drugs.	Retrospective observational	28.7 (68)

Note: HT: hypertension; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; *:prehemodialysis; **: intradialysis; ***

TABLE 2. Factors associated with uncontrolled BP on dialysis patients

Authors	Patient, population, and problem	Uncontrolled BP definition	Methods	Results													
				Age	Gender	Work status	Smoking	Education level	DM	Obesity	CKD stage	Frequency	Dialysis duration	Number of medications	Depression	Medication adherence	HD adherence
Nugraha *et al.*[6]	65 patients receiving regular hemodialysis at Wangaya General Hospital, Bali (Indonesia)	Pre-dialysis BP measurement >140/90 mmHg and/or taking the antihypertensive regularly	Cross-sectional	X	X	-	-	-	-	-	-		V	V	-	-	-
Amr *et al.*[7]	390 adult patients at 3 hemodialysis units in the south of Palestine	Pre-dialysis BP of ≥140/90 mmHg and post-dialysis BP of ≥130/80 mmHg	Cross-sectional	X	V	X	X	X	-	-	-	X	X	X	-	-	-
Al Sahlawi[9]	339 hemodialysis patients at a large tertiary hospital in Saudi Arabia	The mean of 3 SBP readings ≥140 mmHg and/or DBP ≥90 mmHg	Cross-sectional	V	X	-	-	-	V	V	V	-	-	-	-	-	-
Bakri *et al.*[12]	60 outpatients at the Dialysis Installation of dr. Zainoel Abidin District Hospital, Banda Aceh	Pre-hemodialysis 140/90 mmHg; intra-dialysis 135/85 mmHg; and post-hemodialysis 130/80 mmHg	Cross-sectional	-	-	-	-	-	-	-	-	-	-	-	-	X	-
Li *et al.*[13]	1871 hypertensive patients from 5 tertiary and 4 secondary hospitals in Guangdong Province, China, from December 1st, 2019 to March 31st, 2021	SBP ≥130 mmHg or DBP ≥80 mmHg with concurrent use of at least 3 antihypertensive of different classes, or BP controlled by at least 4 antihypertensive	Cross-sectional	V	-	-	V	-	-	V	-	-	-	-	-	-	-
Gulalai *et al.*[14]	237 hypertensive hemodialysis patients recruited at the Balochistan Institute of Nephrology Urology Quetta (Pakistan)	If the hypertensive diagnosis was documented in the medical record or the patient was receiving antihypertensive	Retrospective observational	X	X	X	X	-	-	-	-	-	-	-	-	-	-

TABLE 2. Cont.

Authors	Patient, population, and problem	Uncontrolled BP definition	Methods	Results													
				Age	Gender	Work status	Smoking	Education level	DM	Obesity	CKD stage	Frequency	Dialysis duration	Number of medications	Depression	Medication adherence	HD adherence
Shwaib *et al.*[15]	122 dialysis patients in Al-Academy Teaching Hospital	An average SBP of ≥140 mmHg or DBP of ≥90 mmHg, or all patient who were taking antihypertensive eventhough their BP was normal at the time of measurement	Cross-sectional	V	-	-	-	-	-	-	-	-	-	-	-	-	-
Tanaka *et al.*[16]	2999 adult outpatients undergoing hemodialysis in 39 dialysis facilities between 31 December 2006 and 31 December 2007, were followed prospectively until 31 December 2016	ATRH: uncontrolled BP (SBP ≥140 mmHg and DBP ≥90 mmHg) despite the use of ≥ 3 classes of antihypertensive, or ≥4 classes of antihypertensive in any of BP level	Q-Cohort study	V	V	-	-	-	V	-	-	-	X	-	-	-	-
Kotanko *et al.*[17]	Daily trial: 245 patients were randomized to 12 months of 6 x weekly HD or 3 x weekly in-center HD. The Nocturnal Trial: 87 patients were randomized to 12 m.o. of 6 x weekly nocturnal hemodialysis versus 3 x weekly predominantly home-based hemodialysis	Baseline pre-hemodialysis SBP >145 mmHg	Multicenter, randomize, prospective trial	-	-	-	-	-	-	-	-	V	-	-	-	-	-
Kauric-Klein[18]	118 hemodialysis participants from 6 ambulatory units in Michigan	Pre-hemodialysis BP >150 mmHg or diastolic >90 mmHg	RCT	-	-	-	-	-	-	-	-	-	-	-	-	V	V

TABLE 2. Cont.

Authors	Patient, population, and problem	Uncontrolled BP definition	Methods	Results													
				Age	Gender	Work status	Smoking	Education level	DM	Obesity	CKD stage	Frequency	Dialysis duration	Number of medications	Depression	Medication adherence	HD adherence
Kauric-Klein[19]	118 participants from 6 outpatient hemodialysis units in Michigan	4 wk average pre-hemodialysis BP >150 mmHg or DBP >90 mmHg	Descriptive comparative study	-	-	-	-	-	-	-	-	-	-	X	-	-	-
Huang *et al.*[20]	90 adults of hemodialysis patients in Peking Union Medical College Hospital dialysis center between September 2011 and August 2012.	SBP ≥140 mmHg or DBP ≥90 mmHg based on the average of 6 automated measurements or who were taking antihypertensive.	Pilot cluster randomized controlled trial	-	-	-	-	-	-	-	-	-	-	-	-	V	-

Note: HT: hypertension; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus, HD: hemodialysis; ATRH: apparent treatment-resistant hypertension; RCT: randomized control trial; V: significantly related; X: not related; -: no data available.

DISCUSSION

Prevalence of uncontrolled blood pressure

Although many hypertensive patients undergoing routine dialysis used antihypertensive therapy, the prevalence of uncontrolled blood pressure is quite large and varied. The highest prevalence of uncontrolled blood pressure in hemodialysis patients was found in Indonesia, ranging from 65.6 - 78.33%.[6,12] The second highest prevalence was in Brazil with 72%, followed by 64% in Saudi Arabia, 59% in studies in South of Palestine, 58% in studies in Europe, 46% in studies in 3 countries (Italy, Greece and Slovenia), and 28.7% in studies in Pakistan.[7-11,14] Not only in hemodialysis patients, but also the prevalence of uncontrolled blood pressure in peritoneal dialysis patients is quite high, namely 42.2%.[13]

Sosio-demographic

Nugraha *et al.*[6] study in Indonesia demonstrated that age did not exhibit any correlation with blood pressure levels among routine hemodialysis patients. Similar findings were observed in a study conducted in Palestine, where patients were categorized into three distinct age groups of 18-40, 41-60, and >60 y.o. This study revealed no statistically significant disparities among the three age groups in either the controlled or uncontrolled blood pressure patients.[7] It is noteworthy that both of these studies were executed with relatively small sample sizes, encompassing 65 and 390 patients,

respectively. Additionally, both studies employed a cross-sectional methodology.

However, contrasting findings were observed in some studies. A study at a large tertiary hospital in Saudi Arabia, involving a total of 339 hemodialysis patients, showed that the age group of 18-39 y.o. or those over 60 y.o. were associated with uncontrolled blood pressure ($p<0.001$).[9] A cross-sectional study by Shwaib *et al.*[15] that compared three groups of hemodialysis patients (18-45, 46-65, and over 65 y.o.) concluded that 69% of the patients in the first group had hypertensive for SBP and DBP, respectively. For the second group, 55.1% were hypertensive. In the last group, 51.6% were hypertensive. Furthermore, an additional study by Tanaka *et al.*[16] which was carried out with a larger sample size of 2999 patients and was conducted a 10-yr prospective cohort study, echoed these findings. The results concluded that younger people were at risk of uncontrolled blood pressure in hemodialysis patients. Age was also a risk factor in peritoneal dialysis patients.[13] Age emerged as a significant determinant concerning adherence to the hemodialysis regimen, with elderly patients showing a higher tendency to comply with the regimen.[21] Another study concluded that younger age is related to non-adherence to fluid restriction. Excessive fluid intake leads to hypervolemia which can cause hypertension.[22] In addition, younger participants had lower levels of self-efficacy for sodium restriction and were more likely to experience difficulties controlling their hemodialysis diet. Younger participants had higher median sodium intake and average adjusted interdialytic weight gain, which is consistent with these results.[23]

Different findings have emerged from several studies regarding the association between gender and blood pressure in hemodialysis patients. A cross sectional study and an observational retrospective concluded that gender was not related to uncontrolled blood pressure in regular hemodialysis patients ($p = 0.878$ and $p = 0.83$).[6,14] There was also no significant difference between the controlled and uncontrolled blood pressure groups in hemodialysis patients.[9]

However, the findings of these studies did not concur with the cross-sectional study of Amr *et al.*[7] which concluded that gender was significantly associated with blood pressure ($p = 0.002$). Another study conducted by Tanaka *et al.*[16] with a larger sample size of 2999 patients, and spanning a 10-yr prospective cohort study, concluded that patients with ATRH had a significantly higher frequency of male gender compared to those without ATRH.

Other socio-demographic factors including work status, smoking, education level, and dialysis period were found to have no impact on the blood pressure of hemodialysis patients.[7,14] These results are in accordance with study from Khan *et al.*[24] which also showed that smoking is not related to blood pressure in hemodialysis patients. A study by Tanaka *et al.*[16] identified that a shorter dialysis period was a risk factor for aTRH in hemodialysis patients. In aTRH group, the mean of dialysis vintage was 4.8 years (interquartile range 2.0-9.3) whereas, in the non-aTRH group, the mean of dialysis vintage was 5.0 yr (interquartile range 2.0-10.8 yr). The adverse effects of insufficient educational guidance on lifestyle habits including salt restriction may independently explain the association between younger age, shorter dialysis period, and aTRH.

Several comorbidities were also found to be significantly related to blood pressure in dialysis patients. A study at a large tertiary hospital in Saudi Arabia showed that diabetes ($p <0.001$) and obesity ($p <0.003$) were significantly associated with uncontrolled blood pressure. Obesity was widespread, with 44.5% of patients having a body mass index (BMI) of 30 kg/m^2 or higher.[9] Similar findings in a study by Li *et al.*[13] concluded that a higher BMI was linked to higher incidence of aTRH. In addition

to diabetes and obesity, a study at a large tertiary hospital in Saudi Arabia showed that the more advanced the stage of chronic kidney disease, the stronger the association with uncontrolled BP. Even though stage G3a chronic kidney disease was not associated with uncontrolled BP, stage G3b, G4 and G5 were significantly associated with uncontrolled BP ($p = 0.023$; $p = 0.007$ and $p = 0.0005$).[9]

Hemodialysis regimen

Blood pressure in hemodialysis patients is also affected by the HD regimen. The Daily Trial, a randomized trial that compared 6x ("frequent") to 3x ("conventional") weekly, and the Noctural Trial, which compared 6 x weekly nocturnal hemodialysis versus 3 x weekly predominantly home-based hemodialysis, concluded that frequent hemodialysis reduces blood pressure and the number of prescribed antihypertensive.[17] However, these findings do not align with the study by Amr *et al.*[7] A cross-sectional study concluded that the number of dialysis and length of dialysis sessions were not significantly associated with blood pressure.[7] But this study analyzed the number of dialysis categories 1, 2, 3, and 4 x weekly hemodialysis and the length of dialysis categories ≤ 180 min and ≥ 210 min. Missed hemodialysis regimen also affects blood pressure in dialysis patients. A study by Kauric-Klein[18] concluded that total missed hemodialysis treatments had a significant effect on both systolic and diastolic blood pressure. The possible reason for this finding was that missed hemodialysis treatment results in volume overload and increased blood pressure in hemodialysis population.

Antihypertensive regimen

A study showed that number of antihypertensive was correlated with uncontrolled blood pressure.[6] Most patients received 2 antihypertensives (46.2%). However, this result was inconsistent with another study. The study by Amr *et al.*[7] concluded that there was no correlation between the number of medications (≤5 and >5 antihypertensive) and blood pressure control. In Kauric-Klein's[19] study, it was shown that most patients received 3 antihypertensive (38.1%).

Compliance with antihypertensive regimens is also affected by blood pressure. Over half of dialysis patients do not stick to their antihypertensive therapy, and poor medication adherence is a well-known issue in this population.[11,25] A study by Kauric-Klein18 concluded that blood pressure medication adherence was significantly correlated to average systolic blood pressure and average diastolic blood pressure. However, Bakri *et al.*[12] study revealed the reverse, namely that there was no significant correlation between blood pressure control and the degree of compliance with antihypertensive use in ESRD patients receiving hemodialysis ($p = 0.301$). In this study, it can also be seen that some of the causes of patient non-adherence to treatment include: patients forgetting to take antihypertensive medication and patients stopping taking medication because they feel their body condition is getting better.

To increase adherence to antihypertensive medication, a variety of strategies can be used. A quasi-experimental study compared the counseling group (home pharmacy care intervention) and the non-counseling group. The results showed that increasing adherence was correlated with controlled blood pressure.[26] A cluster randomized controlled trial study concluded that self-management support could improve salt restriction and medication adherence, which led to better blood pressure control.[20]

CONCLUSION

In general, the prevalence of hypertension in hemodialysis patients is 78.33-98.5%. Hypertension is more

common among dialysis patients of the Asian race on average, and this prevalence is greater than that of the European race. Uncontrolled blood pressure is very common among hypertension in dialysis patients, occurring in 28.7 - 78.33% of cases. Factors that affect blood pressure in dialysis patients are including age, obesity, and comorbidity (diabetes and stage of chronic kidney disease). Although the relationship between gender, the number of antihypertensive, the number of dialysis, and the length of dialysis sessions with blood pressure varies, several studies have shown a positive association.

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