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

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. 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. 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

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient and population</th>
<th>Country</th>
<th>Uncontrolled blood pressure definition</th>
<th>Methods</th>
<th>Prevalence [% (n)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nugraha et al.⁶</td>
<td>65 patients receiving regular hemodialysis</td>
<td>Bali (Indonesia)</td>
<td>Pre-dialysis BP measurement &gt;140/90 mmHg and/or taking the antihypertensive regularly</td>
<td>Cross-sectional</td>
<td>65.6 (42)</td>
</tr>
<tr>
<td>Amr et al.⁷</td>
<td>390 adult patients at three hemodialysis units</td>
<td>South of Palestine</td>
<td>Predialysis BP of ≥ 140/90 mmHg and post-dialysis BP of ≥130/80 mmHg</td>
<td>Cross-sectional</td>
<td>59 (231)</td>
</tr>
<tr>
<td>Sarafidis et al.⁸</td>
<td>396 hemodialysis adult patients in 16 hemodialysis unit</td>
<td>Italy, Greece, Slovenia</td>
<td>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</td>
<td>Cross-sectional</td>
<td>46 (186)</td>
</tr>
<tr>
<td>Al Sahlawi⁹</td>
<td>339 hemodialysis patients at a large tertiary hospital</td>
<td>Saudi Arabia</td>
<td>The mean of 3 BP readings ≥140 mmHg and/or diastolic BP ≥90 mmHg</td>
<td>Observational retrospective</td>
<td>64 (216)</td>
</tr>
<tr>
<td>Burmeister et al.¹⁰</td>
<td>1215 hemodialysis patients in Porto Alegre (Brazil)</td>
<td>Porto Alegre</td>
<td>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</td>
<td>Cross-sectional</td>
<td>72 (875)</td>
</tr>
<tr>
<td>Mallamaci et al.¹¹</td>
<td>506 hemodialysis patients from 10 renal units in Europe (data was taken from the registry of European Renal and Cardiovascular Medicine (EURECAm))</td>
<td>Europe</td>
<td>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</td>
<td>Cross-sectional</td>
<td>58 (296)</td>
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<tr>
<td>Bakri et al.¹²</td>
<td>60 outpatients at the Dialysis Installation of RSUD dr. Zainoel Abidin Banda Aceh</td>
<td>Banda Aceh</td>
<td>Pre-hemodialysis 140/90 mmHg; intra-dialysis 135/85 mmHg; and post-hemodialysis 130/80 mmHg</td>
<td>Cross-sectional</td>
<td>a. 78.33 (47) b. 85 (51) c. 95 (57)¹³¹³</td>
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<tr>
<td>Li et al.¹³</td>
<td>1871 peritoneal dialysis at 9 centers from 5 tertiary hospitals and 4 secondary hospitals</td>
<td>Guangdong (China)</td>
<td>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</td>
<td>Cross-sectional</td>
<td>42.2 (755)</td>
</tr>
<tr>
<td>Gulalai et al.¹⁴</td>
<td>237 hemodialysis patients from the Balochistan Institute of Nephrology Urology Quetta (Pakistan)</td>
<td>Pakistan</td>
<td>If a hypertensive diagnosis was documented in the medical record or the patient was receiving antihypertensive drugs</td>
<td>Retrospective observational</td>
<td>28.7 (68)</td>
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Note: HT: hypertension; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure; “: pre-hemodialysis; “”: intradialysis;”¹³
<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient, population, and problem</th>
<th>Uncontrolled BP definition</th>
<th>Methods</th>
<th>Age</th>
<th>Gender</th>
<th>Work status</th>
<th>Smoking</th>
<th>Education level</th>
<th>DM</th>
<th>Obesity</th>
<th>CKD stage</th>
<th>Frequency</th>
<th>Dialysis duration</th>
<th>Number of medications</th>
<th>Depression</th>
<th>Medication adherence</th>
<th>HD adherence</th>
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<td>Nugraha et al.</td>
<td>65 patients receiving regular hemodialysis at Wangaya General Hospital, Bali (Indonesia)</td>
<td>Pre-dialysis BP measurement &gt;140/90 mmHg and/or taking the antihypertensive regularly</td>
<td>Cross-sectional</td>
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<td>Amr et al.</td>
<td>390 adult patients at 3 hemodialysis units in the south of Palestine</td>
<td>Pre-dialysis BP of ≥140/90 mmHg and post-dialysis BP of ≥130/80 mmHg</td>
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<td>Li et al.</td>
<td>1871 hypertensive patients from 5 tertiary and 4 secondary hospitals in Guangdong Province, China, from December 1st, 2019 to March 31st, 2021</td>
<td>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</td>
<td>Cross-sectional</td>
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<td>Gulalai et al.</td>
<td>237 hypertensive hemodialysis patients recruited at the Balochistan Institute of Nephrology Urology Quetta (Pakistan)</td>
<td>If the hypertensive diagnosis was documented in the medical record or the patient was receiving antihypertensive</td>
<td>Retrospective observational</td>
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<td>Shwaib et al.</td>
<td>122 dialysis patients in Al-Academy Teaching Hospital</td>
<td>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</td>
<td>Cross-sectional</td>
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<td>Tanaka et al.</td>
<td>2999 adult outpatients undergoing hemodialysis in 39 dialysis facilities between 31 December 2006 and 31 December 2007, were followed prospectively until 31 December 2016</td>
<td>ATRH: uncon-trolled BP (SBP ≥140 mmHg and DBP ≥90 mmHg) despite the use of ≥3 classes of antihyper-tensive, or ≥4 classes of antihypertensive in any of BP level</td>
<td>Q-Cohort study</td>
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<td>Kotanko et al.</td>
<td>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</td>
<td>Baseline pre-hemodialysis SBP &gt;145 mmHg</td>
<td>Multicenter, randomize, prospective trial</td>
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<td>Kauric-Klein</td>
<td>118 hemodialysis participants from 6 ambulatory units in Michigan</td>
<td>Pre-hemodialysis BP &gt;150 mmHg or diastolic &gt;90 mmHg</td>
<td>RCT</td>
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TABLE 2. Cont.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patient, population, and problem</th>
<th>Uncontrolled BP definition</th>
<th>Methods</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kauric-Klein&lt;sup&gt;19&lt;/sup&gt;</td>
<td>118 participants from 6 outpatient hemodialysis units in Michigan</td>
<td>4 wk average pre-hemodialysis BP &gt;150 mmHg or DBP &gt;90 mmHg</td>
<td>Descriptive comparative study</td>
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<tr>
<td>Huang et al.&lt;sup&gt;20&lt;/sup&gt;</td>
<td>90 adults of hemodialysis patients in Peking Union Medical College Hospital dialysis center between September 2011 and August 2012.</td>
<td>SBP ≥140 mmHg or DBP ≥90 mmHg based on the average of 6 automated measurements or who were taking antihypertensive.</td>
<td>Pilot cluster randomized controlled trial</td>
<td>- - - - - - - V - -</td>
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</table>

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%.<sup>6,12</sup> 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.<sup>7-11,14</sup> Not only in hemodialysis patients, but also the prevalence of uncontrolled blood pressure in peritoneal dialysis patients is quite high, namely 42.2%.<sup>13</sup>

Sosio-demographic

Nugraha et al.<sup>6</sup> 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.<sup>7</sup> 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). A cross-sectional study by Shwaib et al. 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. 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. Age emerged as a significant determinant concerning adherence to the hemodialysis regimen, with elderly patients showing a higher tendency to comply with the regimen. Another study concluded that younger age is related to non-adherence to fluid restriction. Excessive fluid intake leads to hypervolemia which can cause hypertension. 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.

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). There was also no significant difference between the controlled and uncontrolled blood pressure groups in hemodialysis patients. However, the findings of these studies did not concur with the cross-sectional study of Amr et al. which concluded that gender was significantly associated with blood pressure (p = 0.002). Another study conducted by Tanaka et al. 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. These results are in accordance with study from Khan et al. which also showed that smoking is not related to blood pressure in hemodialysis patients. A study by Tanaka et al. 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. Similar findings in a study by Li et al. 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 \( (p = 0.023; p = 0.007 \text{ and } p = 0.0005) \).

**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 Nocturnal 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.\(^{18}\) 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-Klein\(^{18}\) 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.

ACKNOWLEDGMENT

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