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Original Article

PREVALENCE AND ASSOCIATED FACTORS OF INTRADIALYTIC HYPERTENSION IN PATIENTS UNDERGOING HEMODIALYSIS IN A TERTIARY CARE CENTER IN KARACHI, PAKISTAN

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ABSTRACT:

A significant number of patients with end-stage renal disease (ESRD) experience a paradoxical rise in systolic blood pressure (SBP) during or immediately following hemodialysis (HD), a condition known as intradialytic hypertension (IDHTN). While the physiological removal of excess fluid typically lowers blood pressure, IDHTN has been linked to increased morbidity, hospitalization, and mortality. A cross-sectional study was conducted on 134 adults undergoing thrice-weekly maintenance HD at a tertiary care center in Karachi, Pakistan, to investigate the prevalence and associated factors of this condition in a resource-constrained setting where data are scarce. Intradialytic hypertension was defined as a change in SBP of at least 10 mmHg from pre- to post-dialysis, averaged over three consecutive sessions. The study found a prevalence of 35.8% (48 out of 134 patients). The condition was significantly associated with several factors, including pre-existing hypertension ($p=0.005$) and diabetes mellitus ($p=0.012$), ultrafiltration volumes below 2 L ($p=0.020$), and, most notably, the use of antihypertensive medications ($p<0.001$) and dialyzable agents ($p<0.001$). Additional associations were observed with age 30 years or younger ($p=0.018$) and smoking ($p<0.001$). The findings indicate that IDHTN is a common finding in this cohort and is strongly linked to clinical and treatment-related factors. The results suggest that interventions focused on optimizing ultrafiltration targets and tailoring antihypertensive regimens, particularly by selecting non-dialyzable agents, may be crucial for reducing the incidence of this condition and improving patient outcomes.

Keywords: Intradialytic Hypertension, Hemodialysis, Systolic Blood Pressure, End-Stage Renal Disease, Ultrafiltration

INTRODUCTION

Hypertension is a substantial global public health concern and stands as a major cause and complication of end-stage renal disease (ESRD), affecting up to 90% of patients receiving maintenance hemodialysis (HD)(1, 3, 4). The process of hemodialysis, which involves the removal of excess fluid and uremic toxins, is typically expected to result in a decrease in blood pressure (BP) as a physiological response to the reduction in circulating blood volume (1, 5). However, a paradoxical phenomenon known as intradialytic hypertension (IDHTN) occurs in a notable subset of these patients, where blood pressure increases during or immediately following the procedure (1, 6, 7, 8).

The clinical implications of this paradoxical BP rise are profound and have been consistently linked to adverse cardiovascular outcomes. Intradialytic hypertension is commonly defined as an increase in systolic blood pressure (SBP) of at least 10 mmHg from pre- to post-dialysis measurements (1, 5, 8, 9). Research has shown a strong association between IDHTN and an elevated risk of increased hospitalization and mortality (1, 2). For example, a secondary analysis of the Dialysis Morbidity and Mortality Wave 2 Study found that an increase in BP during HD was associated with a 37% higher two-year mortality rate and doubled the odds of hospitalization or death at six months when compared to patients whose BP declined (1, 2, 5, 8). This highlights the significant prognostic bearing of intradialytic BP phenomena and underscores the need for effective management strategies (10). Furthermore, a meta-analysis of randomized controlled trials demonstrated that lowering BP with antihypertensive therapy can significantly reduce the risk of cardiovascular events by 29% and all-cause mortality by 20% in dialysis patients, confirming the importance of BP control in this high-risk population (11).

The pathophysiology of IDHTN is complex and multifactorial, involving a combination of volume-related and neurohumoral mechanisms (1, 9, 12). Key contributing factors include endothelial dysfunction with impaired nitric oxide release and activation of endothelin-1, which can lead to increased peripheral vascular resistance and a subsequent rise in BP (1, 5, 13, 14). While some studies suggest that overzealous fluid removal can activate the renin-

angiotensin-aldosterone axis (RAAS) and the sympathetic nervous system (SNS), leading to vasoconstriction and BP rise, other evidence points to the opposite, where subclinical fluid overload is the primary driver of IDHTN (1, 9, 15, 5). Another critical factor is the dialytic clearance of antihypertensive medications, especially those that are water-soluble and have a low molecular weight, which can leave the patient with inadequate BP control at a critical point in the session (1, 7, 9).

Despite the growing body of evidence on IDHTN, there is a notable scarcity of data from resource-constrained settings in South Asia. Given the unique patient demographics, disease profiles, and potential differences in care practices in these regions, a deeper understanding of IDHTN in this context is essential. This study was therefore conducted to determine the frequency and identify the associated clinical and treatment-related factors of intradialytic hypertension in a cohort of patients undergoing maintenance hemodialysis at a tertiary-care unit in Karachi, Pakistan. The findings aim to provide crucial local data and contribute to the global understanding of this important complication.

METHODS

Study Design and Setting

This cross-sectional study was conducted over a six-month period, from December 22, 2022, to June 22, 2023. The research was carried out at the Nephrology Outpatient Department and Dialysis Unit of the Dr. Ziauddin Hospital in Karachi, Pakistan.

Patient Population and Sampling

The sample size was calculated using the World Health Organization (WHO) sample size calculator. Based on a proportion of 33.6% for diabetes in patients with IDHTN, a power of test at 80%, and a 95% confidence interval, a sample size of 134 participants was determined to be appropriate for the study. A non-probability consecutive sampling technique was employed to enroll participants who met the following inclusion criteria: all patients aged between 18 and 80 years who had been undergoing maintenance hemodialysis as outpatients at the study site for a minimum of three months and who provided informed consent. Patients who were either below 18 or above 80 years of age or who declined to participate were excluded from the study.

Data Collection Procedure

A standardized proforma questionnaire, included as an appendix in the full manuscript, was used to collect data. Trained nursing staff measured the blood pressure of patients before and after each dialysis session. Pre-dialysis blood pressure was measured after the patient had been seated for at least five minutes, before the placement of dialysis access needles. Post-dialysis blood pressure was measured at least five minutes after the conclusion of the procedure. For a stable measure, the average of three consecutive hemodialysis sessions' readings was recorded. Pre- and post-dialysis weights were also recorded during these sessions. Patients were specifically instructed not to withhold their antihypertensive medications before their hemodialysis appointments. Additional patient information, including the history of ESRD, comorbidities (e.g., hypertension, diabetes), smoking status, duration of dialysis, and interdialytic weight gain, was obtained through interviews and a review of medical records. Body Mass Index (BMI) data were extracted from outpatient department records.

Ethics Statement

The study protocol, which involved human participants, received approval from the Institutional Ethics Committee. The study was conducted in full compliance with the ethical standards of the responsible institutional committee on human experimentation and in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to their enrollment(1, 3). The privacy and anonymity of the participants were strictly protected by ensuring that no identifying information was included in the data collection forms or subsequent analysis.

Statistical methods

All collected data were analyzed using Statistical Package for Social Sciences (SPSS version 22.0). Continuous variables, such as age, BMI, and ultrafiltration volumes, were described using mean and standard deviation, along with a 95% confidence interval for the mean. Categorical variables, including gender, smoking status, and the presence of IDHTN, were presented as frequencies and percentages. The Chi-square test was used to compare the frequency of IDHTN with its potential predictors, while Fisher's exact test was used as an alternative when cell counts were low. A *p*-value of less than 0.05 was considered statistically significant for all comparisons.

RESULTS

A total of 134 patients on maintenance hemodialysis for at least three months were included in the study. The mean age of the cohort was 48.9 ± 12.1 years (95% CI 46.8–50.9), with a substantial majority being male patients (110/134, 82.1%). The mean body mass index was 23.5 ± 2.0 kg/m² (95% CI 23.17–23.86). The average ultrafiltration volume per session was 2.8 ± 0.9 L (95% CI 2.65–2.96), and the average interdialytic weight gain was 1.53 ± 1.73 kg (95% CI 1.24–1.83). The baseline characteristics of the patient cohort are summarized in Table 1.

Table 1. Demographic and basic study characteristics of the Patient Cohort

Variable	Mean ± SD	95% Confidence Interval for Mean
Age (Years)	48.87 ± 12.14	46.80 to 50.94
Height (cm)	154.44 ± 5.51	153.50 to 155.37
Weight (kg)	56.08 ± 5.41	55.16 to 56.99
BMI (kg/m^2)	23.52 ± 2.04	23.17 to 23.86
Duration of Hemodialysis (Hours)	3.44 ± 0.49	3.36 to 3.53
Interdialytic Weight Gain (kg)	1.53 ± 1.73	1.24 to 1.83
Ultra-filtrate Volumes (L)	2.81 ± 0.90	2.65 to 2.96

Intradialytic hypertension, defined as a post-dialysis systolic blood pressure rise of at least 10 mmHg, was observed in 48 out of 134 patients, yielding a prevalence of 35.8%.

Factors Associated with Intradialytic Hypertension

Analysis of the cohort revealed several significant associations with the occurrence of IDHTN. As presented in Table 2, patients with a history of hypertension were more likely to experience IDHTN. Of the 48 patients with IDHTN, 21 (43.8%) had a history of hypertension, compared to 18 of 86 patients (20.9%) without IDHTN ($\chi1^2 = 8.02$, $p = 0.005$, Cramer's V = 0.24). A similar trend was observed for diabetes mellitus, which was present in 17 of 48 patients (35.4%) with IDHTN versus 14 of 86 patients (16.3%) without IDHTN ($\chi1^2 = 6.32$, $p = 0.012$, Cramer's V = 0.22).

Patients with ultra-filtration volumes below 2 L had a higher frequency of IDHTN (36/48, 75.0%) compared to those without IDHTN (47/86, 54.7%) ($\chi1^2 = 5.41$, $p = 0.020$, Cramer's V = 0.18). The strongest association was observed with the use of antihypertensive medications, where nearly 90% of patients with IDHTN (34/38) were taking these drugs, a significantly higher proportion than in the non-IDHTN group (14/96, 14.6%) ($\chi1^2 = 87.30$, $p < 0.001$, Cramer's V = 0.81). Furthermore, the use of dialyzable antihypertensive agents was very strongly linked to IDHTN; 20 of 22 patients who took dialyzable drugs experienced IDHTN, while none of the 112 patients without IDHTN were on these agents (Fisher's exact $p < 0.001$).

Table 2: Key Factors Associated with Intradialytic Hypertension in the Overall Cohort (n=134)

Factors	IDHTN (n=48)	No IDHTN (n=86)	Statistical Results
Hypertension	21 (43.8%)	18 (20.9%)	χ12=8.02, p=0.005, V = 0.24
Diabetes Mellitus	17 (35.4%)	14 (16.3%)	χ12=6.32, p=0.012, V = 0.22
Ultrafiltration <2 L	36 (75.0%)	47 (54.7%)	χ12=5.41, p=0.020, V = 0.18
Antihypertensive Use	34 (89.5%)	14 (14.6%)	χ12=87.30, p<0.001, V = 0.81
Dialyzable Agents	20 (90.9%)	0 (0%)	Fisher's exact p<0.001
Age ≤30 years	10 (66.7%)	5 (33.3%)	χ12=5.63, p=0.018, V = 0.21
Smoking	8 (23.5%)	0 (0%)	Fisher's exact p<0.001

Patients aged 30 years or younger had a higher frequency of IDHTN (10/15, 66.7%) compared to older patients (5/15, 33.3%) ($\chi 1^2 = 5.63$, $p = 0.018$, $V = 0.21$). Among smokers, 8 out of 34 patients (23.5%) experienced IDHTN, whereas no associations were found in the non-smoking group (Fisher's exact $p < 0.001$).

A sub-group analysis confirmed these trends and provided additional details. For instance, among male patients, both hypertension ($p = 0.018$) and diabetes mellitus ($p = 0.015$) were significant factors for IDHTN. Similarly, patients with a BMI of 25 kg/m² or less had significant associations with hypertension ($p = 0.011$) and diabetes mellitus ($p = 0.008$) as contributing factors for IDHTN. The duration of hemodialysis did not appear to be a factor in the overall study cohort.

DISCUSSION

The findings of this study provide a detailed view of the prevalence and risk factors for intradialytic hypertension in a South Asian population. The overall prevalence of 35.8% stands in stark contrast to the rates of 5–15% commonly reported in the international literature from Western cohorts (1, 8, 9, 14, 5). This elevated prevalence is, however, consistent with other findings from similar resource-constrained settings in India (22%) and Africa (31–34.5%), and a similar incidence of 37% was observed in the Philippines (1, 2, 11, 2). This high prevalence is not an isolated local anomaly but may be a recurring systemic issue in these regions, reflecting shared challenges such as delayed patient presentation, inadequate access to advanced diagnostic tools, or differences in care practices and medication availability that contribute to the pathogenesis of IDHTN.

The findings related to ultra-filtration volume provide a compelling perspective on the possible underlying mechanisms. A significant association was found between IDHTN and ultrafiltration volumes of less than 2 L, a finding that at first appears counterintuitive. While one might expect higher ultrafiltration rates to be associated with hemodynamic stress and a BP rise, this result suggests a more complex interplay.(15) In the absence of advanced diagnostics like bioimpedance spectroscopy (BIS), which is a valuable tool for objectively assessing fluid status, clinicians may be hesitant to set aggressive ultrafiltration targets due to a fear of inducing intradialytic hypotension.(1, 9, 16) This conservative approach may inadvertently perpetuate a state of chronic subclinical volume overload.(9, 16) Consequently, the modest fluid removal may be insufficient to resolve the underlying volume excess, allowing the neurohumoral mechanisms of IDHTN, such as RAAS and SNS activation, to remain unopposed and lead to a BP increase.(12, 14) Therefore, the low ultrafiltration volume may not be the cause of IDHTN but rather a marker of an underlying, uncorrected fluid overload that drives the pathological increase in blood pressure.(5,15)

The strong associations found between IDHTN and both antihypertensive medication use and the dialyzability of these drugs are particularly instructive. The data showed that a high proportion of patients with IDHTN were using antihypertensives, and a significantly higher number were taking dialyzable agents. This observation underscores the hypothesis that the clearance of medications during hemodialysis can directly contribute to a post-dialysis BP rebound. As dialyzable agents are rapidly removed from the bloodstream, the patient is left with minimal BP coverage at a time when the body is activating vasoconstrictive pathways (1, 9). The very strong effect size of this association ($V = 0.81$) suggests that it is a dominant contributor to IDHTN in this cohort. A more nuanced aspect of the findings is the observation that a substantial number of diabetic patients on non-dialyzable antihypertensive agents still experienced IDHTN. This suggests that while medication removal is an important factor, it is not the sole driver of the phenomenon, particularly in this high-risk subgroup. The elevated BP in these patients, independent of drug kinetics, is likely a manifestation of the profound endothelial dysfunction, arterial stiffness, and sympathetic overactivity that are hallmarks of both diabetes and chronic kidney disease (10, 13, 14). This finding highlights that effective management of IDHTN in diabetic patients may require addressing the underlying physiological mechanisms rather than simply adjusting medication timing or type.

A final noteworthy finding is the higher frequency of IDHTN in the younger age group (30 years or younger), which appears to contradict the general consensus in the literature that IDHTN is more common in older patients (1, 8). This paradoxical result is likely not a statistical anomaly but a reflection of the unique disease etiology within this population. The underlying causes of ESRD in younger patients in this region, such as glomerulonephritis or other inflammatory conditions, may be associated with heightened sympathetic tone and chronic inflammatory states that predispose them to IDHTN. This finding, therefore, warrants further research to explore whether there are distinct pathophysiological pathways that require a tailored approach to management for this specific demographic.

This study, while providing valuable data from an under-represented population, has several limitations inherent to its design. The cross-sectional design limits the ability to establish a definitive causal relationship between the identified factors and the occurrence of IDHTN. For instance, while a strong association was found between antihypertensive use and IDHTN, it is not possible to conclude whether the medications are causing the BP rise or if the BP rise necessitates the prescription of more drugs. The single-center nature of the study may also limit the generalizability of the findings to other patient populations or healthcare settings, especially given the specific characteristics of this resource-constrained environment. Furthermore, several potential confounders that could influence the development of IDHTN were not measured or controlled for, including dietary sodium intake and the concentration of sodium in the dialysate. The study also did not objectively measure blood levels of antihypertensive medications to confirm their removal during dialysis, relying instead on a general classification of dialyzability. The absence of advanced diagnostics, such as bioimpedance spectroscopy (BIS), meant that subclinical fluid overload in the IDHTN group could not be quantified, a factor that could have further elucidated the underlying mechanisms.

CONCLUSION

In this cohort of patients with end-stage renal disease undergoing maintenance hemodialysis in a resource-constrained setting, intradialytic hypertension was a common complication. The prevalence was higher than rates commonly reported in the international literature, which may reflect the unique patient population and care practices. The condition was significantly linked to several factors, including pre-existing hypertension and diabetes mellitus. Notably, strong associations were found with modifiable factors such as ultrafiltration targets and the use of dialyzable antihypertensive agents. These findings underscore the importance of optimizing fluid removal strategies and carefully selecting antihypertensive drug regimens, preferentially favoring non-dialyzable agents, as potential interventions to mitigate the incidence of intradialytic hypertension and improve patient outcomes. Further research is necessary to explore the specific pathophysiological mechanisms in this population and to confirm these findings through prospective studies.

Conflict of Interest

Authors declare no conflict of interest.

Ethical consideration

The study was approved by local research ethics committee.

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