



Original Article

Hemodynamic Instability during Intermittent Hemodialysis in ICU Patients with Abnormal Capillary Refill Time

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ABSTRACT

Intradialytic Hemodynamic Instability (IHI) may cause delay in renal recovery and also increases risk of mortality. Capillary Refill Time (CRT) was a stress free method used for peripheral perfusion that becomes worse during circulatory failure. **Objective:** To determine Hemodynamic Instability during Intermittent Hemodialysis in ICU Patients with Abnormal Capillary Refill Time at a tertiary care hospital, Karachi, Pakistan. **Methods:** This was the 06 months' data collection, 1-year prospective observational study. Overall 137 patients were evaluated via sampling technique of non-probability consecutive sampling technique. For each intermittent hemodialysis session, index CRT was recorded. IHI was noted down 30 minutes before the beginning of intermittent hemodialysis and then 60 minutes, 120 minutes and 180 minutes. Entire data were recorded as a predesigned proforma. The natural distribution of patients into subgroups was done using Chi Square test considering p-value ≤ 0.05 as significant. **Results:** The total population was 98 men (71.5%) and 39 women (28.5%) Average age was 61.51 ± 15.37 years. 45 (17.5%) patients observed abnormal Capillary refill time. 20 (14.6%) patients experienced intradialytic hemodynamic instability. Among patients diagnosed with intradialytic hemodynamic instability, 9 (45%) had abnormal CRT. Compared to patients with normal CRT, individuals with aberrant CRT had a higher risk of hemodynamic instability (OR = 5.564, $p < 0.001$). **Conclusions:** IHI was most at risk when it comes to initiating intermittent hemodialysis, especially in the first hour of the first session. The increase in index capillary refill time was linked to IHI.

INTRODUCTION

Chronic Kidney Disease (CKD) represents a critical global public health challenge, frequently progressing to End-Stage Renal Disease (ESRD), which necessitates dialysis or kidney transplantation. The prevalence of hypertension rises as Glomerular Filtration Rate (GFR) declines, making it a common comorbidity in both CKD and ESRD. Intradialytic Hypotension (IDH) is a prevalent complication during intermittent hemodialysis, primarily due to the need for rapid fluid removal over short treatment periods. Reported rates of IDH in ESRD patients vary widely, ranging from 5% to 40% across different patient populations [1]. IDH is linked to a range of severe complications, including disabling symptoms, inadequate dialysis, vascular access

thrombosis, accelerated kidney function decline, cardiovascular events, and increased mortality. The prevalence of IDH varies depending on the definitions applied, as there is no universally accepted "safe" blood pressure range for dialysis patients. This makes defining IDH particularly challenging. Most definitions incorporate one or more of the following criteria: a drop in blood pressure below a specific threshold or nadir, a decline in blood pressure during dialysis, patient-reported symptoms occurring during dialysis, and medical interventions during dialysis aimed at restoring blood volume [1]. ESRD can further complicate the relationship between blood pressure and tissue perfusion due to factors such as



upstream vascular stenosis, endothelial dysfunction, and capillary rarefaction. While it is typically assumed that these limits are reached when mean arterial pressure drops below 60 mm Hg, a recent study in dialysis patients found the mean limit to be 74 mm Hg, with a significant range from 39 to 103 mm Hg. [2]. Some studies have employed alternative threshold values to characterize IDH was 68% based on these cut-off values [3]. Because of the comparatively short treatment durations that require quick volume clearance of excess fluid gains, IDH is a commonly encountered consequence of intermittent hemodialysis [4]. Remarkably, immediate Renal Replacement Treatment (RRT) is needed for 10–20% of AKI patients in the ICU, and their predicted death rate is close to 50% [5]. However, RRT is linked to a significant death rate and is necessary for 5–20% of patients. [6–9]. In the absence of emergent criteria, identifying individuals in whom the commencement of RRT should be reevaluated could be facilitated by the identification of risk factors for IHI by physicians [10]. In response to circulatory dysfunction, the body's compensatory mechanisms prioritize blood flow to vital organs, reducing circulation to non-essential areas like the skin. This shift makes the skin a valuable area for clinical assessment of circulatory issues. Bedside evaluation of peripheral perfusion parameters is straightforward and often used to determine the need for fluid resuscitation in patients with sepsis-induced acute circulatory dysfunction [11]. Capillary Refill Time (CRT), an inexpensive and readily accessible tool, has gained attention as a promising target for guiding resuscitation efforts in septic shock [12]. CRT is convenient-to-use bedside indicator of the perfusion in the periphery. Its applicability in pre-hospital patient triage has been established as well as in the emergency room [13–15]. An earlier clinical study involving adult patients with septic shock compared two resuscitation strategies: one aimed at normalizing CRT and the other focused on serum lactate levels. The results showed comparable effectiveness in reducing 28-day mortality rates. However, a more recent meta-analysis of 10 studies, encompassing 917 septic shock patients, identified a weak inverse relationship between Mean Arterial Pressure (MAP) and CRT [15]. In order to find out the intradialytic hemodynamic instability by abnormal CRT in order to maintain the hemodynamic stability among ICU patients.

As a secondary objective this study defined CRT in IDH future management strategies which should be can be formed for better management of patients who need intermittent hemodialysis.

METHODS

This cross-sectional study was conducted over six months, from August 2022 to January 2023, within the Intensive Care Unit of Ziauddin Hospital in Karachi, Pakistan. With ethical approval secured from Ziauddin University Hospital

(Ref code: 5660622AJCCM), all eligible patients were thoroughly briefed on the study's goals, potential benefits, and any associated risks. Informed written consent was obtained, ensuring that each participant's privacy was protected by assigning them a unique encrypted code. Participants were selected using a non-probability consecutive sampling method. The data gathered will be kept strictly confidential, shared only with authorized personnel and the study's principal investigators. Patients undergoing IHD at the ICU and met the following criteria were included in this study: they were 18 years of age or older, of any gender, and undergoing intermittent hemodialysis. Patients were excluded from the study if they refused to provide consent or if CRT could not be assessed due to conditions such as Raynaud syndrome or severe hypothermia. Prior to inclusion the purpose, procedure, risk and benefits of the study was explained to all participants. Demographic profile of the patients was recorded like gender and age. History of the patients was taken regarding hypertension, diabetes mellitus and noted in predesigned proforma. All IHD must be advised by consultant nephrologist of experience more than 5 years. It usually occurs at the initiation of intermittent hemodialysis during the first hour of the first session despite the absence of fluid removal. It was found that there was association of Index CRT ≥ 3 s with the occurrence of IHI. Taking SOCRATE study [16, 17], first and later sessions made up the 211 sessions, with 72 (34%) being first sessions and 139 (66%) later sessions, sample size of this study was 137, with a 95% confidence interval and a 5% margin of error. Non-probability, Consecutive Sampling technique was used for data collection. In the absence of strong evidence supporting the use of one modality of RRT over the other, guidelines from both national and international organizations recommended IHD to maximize hemodynamic tolerance. The occurrence of an IHI was recorded 30 minutes just before started IHD and after 60 minutes, 120 minutes and 180 minute intervals. For each IHD session, the index CRT was recorded just before the start of the session (T0). The cut-off values defining tissue hypoperfusion were based on previously published studies, with an index CRT of ≥ 3 seconds. The index CRT was measured 30 minutes before the hemodialysis by applying firm pressure to the distal phalanx of the right index finger for 10 seconds. The time for the normal colour to return to the ventral surface was recorded using a mobile phone chronometer. The selected cut-off value for CRT was ≥ 3 seconds, and all measurements were performed by the principal investigator to ensure consistency and avoid variability. Confounding variables and biasness was controlled by strictly adhering to inclusion and exclusion criteria and stratification. Patient information will be kept secured and available to authorized person only. Only

authorized individuals had access to patient information, which was maintained safely. SPSS version-21.0 (IBM Corp., 2012) was used for data entry and analysis. IBM SPSS Statistics, Version 21.0, for Windows. IBM Corp., Armonk, NY. For quantitative (continuous) characteristic like age (years) and descriptive statistics like mean ± SD, skewness, median (IQR) and for the accurate computation of maximum and minimum values, the Shapiro-Wilk test was utilized to validate the hypothesis of normality. Frequency and percentages will be computed for categorical variables like age, gender, hypertension, type 2 diabetes, aberrant CRT time, and hemodynamic instability. Using stratification, effect modifiers including age groups, type 2 diabetes and hypertension were managed. Applications included the Fisher Exact Test and the Post-Stratification Chi-Square Test. The significant level was set at the level of less than 0.05.

RESULTS

Out of 137 patients, there were 28.5% women and 71.5% men with an average age was 61.51 ± 15.37 years, however the majority 110 (80.3%) were over 50 years. 75 (54.7%) patients diagnosed with diabetes mellitus and 98 (71.5%) with hypertension. Total 45 (17.5%) patients observed abnormal capillary refill time. In our study, 20 (14.6%) patients experienced intradialytic hemodynamic instability (Table 1).

Table 1: Descriptive Data for the Population under Investigation (n=137)

Variables	N (%) / Mean ± SD
Gender	
Males	98 (71.5%)
Females	39 (28.5%)
Age (Years)	
Mean ± S.D	61.51 ± 15.37
Groups	
≤50 Years	27 (19.7%)
>50 Years	110 (80.3%)
Diabetes Mellitus	
Yes	75 (54.7%)
No	62 (45.3%)
Hypertension	
Yes	98 (71.5%)
No	39 (28.5%)
Abnormal CRT	
Yes	24 (17.5%)
No	113 (82.5%)
Intradialytic Hemodynamic Instability	
Yes	20 (14.6%)
No	117 (85.4%)

Fifteen patients (75%) among 20 intradialytic hemodynamic instability patients were discovered in the first hour, while 3 (15%) in the second hour, and 2 (10%) in the third hour (Figure 1).

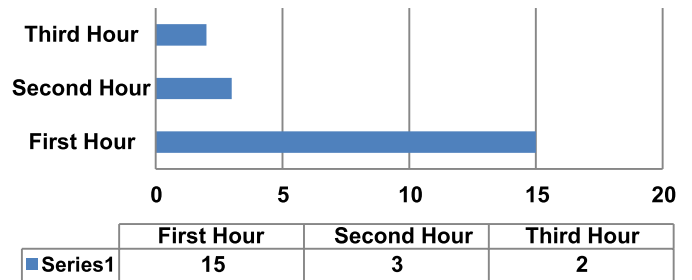


Figure 1: Intradialytic Hemodynamic Instability during Hour. Ninety-five percent of the 19 patients were older than 50. Among these, 11 (55%) of the patients have diabetes mellitus, 13 (65%) have hypertension, and 9 (45%) have abnormal CRT. Intradialytic hemodynamic instability was shown to be significantly associated with abnormal CRT (p = 0.002), but not with gender (p = 0.484), age group (p = 0.107), diabetes mellitus (p = 0.980) or hypertension (p = 0.484) (Table 2).

Table 2: Association of Intradialytic Hemodynamic Instability with Demographic Profile and Co-Morbid

Variables	Intradialytic Hemodynamic Instability N (%)		p-Value
	Yes	No	
Gender			
Male	13 (65%)	85 (72.6%)	0.484
Female	7 (35%)	32 (27.4%)	
Age Groups			
≤50 Years	1 (5%)	26 (22.2%)	0.124
>50 Years	19 (95%)	91 (77.8%)	
Diabetes Mellitus			
Yes	11 (55%)	64 (54.7%)	0.980
No	9 (45%)	53 (45.3%)	
Hypertension			
Yes	13 (65%)	85 (72.6%)	0.484
No	7 (35%)	32 (27.4%)	
Abnormal CRT			
Yes	9 (45%)	15 (12.8%)	0.002*
No	11 (55%)	102 (87.2%)	

A chi-square or Fisher exact test was applied. Significant at 0.05 levels IHD instability was less common in male patients than in female patients (OR = 0.699, p = 0.485). Patients under 50 were less likely to experience intradialytic hemodynamic instability compared to those over 50 (OR=0.184, p = 0.107). Compared to patients with normal CRT, individuals with aberrant CRT had a higher risk of hemodynamic instability (OR = 5.564, p < 0.001) (Table 3).

Table 3: Odds Ratio for Intradialytic Hemodynamic Instability

Variables	Odds Ratio (95% CI)	p-Value
Gender		
Male	0.699 (0.256 - 1.910)	0.485
Female	1.000	
Age Groups		
≤50 Years	0.184 (0.024 - 1.442)	0.107

>50 Years	1.000	
Diabetes Mellitus		
Yes	1.012 (0.390 - 2.625)	0.980
No ^{c/o}	1.000	
Hypertension		
Yes	0.699 (0.256 - 1.910)	0.485
No ^{c/o}	1.000	
Abnormal CRT		
Yes	5.564 (1.978 - 15.652)	0.001*
No ^{c/o}	1.000	

^{c/o}: Reference Category

Binary logistic regression was applied

*Significant at 0.05 level

DISCUSSION

Despite optimization through protocols, IHI was still a common problem in critically ill patients. In our study 14.6% patients experienced Intradialytic Hemodynamic Instability (IHI) and among them IHI was observed 75% in first hour, 15% in the second hour and 10% in the third hour. Furthermore, among 20 patients diagnosed with IHI, 65% were male and 35% were female. 95% patients were over the age of fifty years. According to Bangash IA *et al.*, the frequency of IHI was quite significant and it varies between 10% and 50% due to the significant variations in its description [17]. In contrast, a different study found that the first 25% of the session was when IHI frequency was highest [18-20]. We observed that patients with abnormal CRT were significantly more likely to experience IHI compared to those with normal CRT ($p = 0.002$). Additionally, female patients and those aged 50 years or older were at a higher risk for developing IHI. Moreover, the development of IHI was documented within the first 30 minutes of the hemodialysis session, highlighting the importance of early monitoring and intervention. Similar to our findings, the SOCRATE Study identified CRT as a significant predictor of IHI. This study further emphasized the role of cardiovascular parameters, such as the SOFA score and lactate levels, in predicting hemodynamic instability, which aligns with our observation that abnormal CRT was a critical marker for IHI [16]. Unlike our study, which did not focus on PRR, Wang AY and Bellomo R highlighted PRR as a crucial factor influencing IHI. This study found that a high PRR at the start of dialysis was protective, while a consistently high PRR during dialysis increased the risk of hypotension. This suggests that, in addition to CRT, PRR could be another valuable marker for predicting IHI risk [5]. Flythe JE *et al.*, found that the prevalence of IHI varied greatly. Consequently, they demonstrated that when the cut-off value of IHI was defined as a drop in systolic blood pressure of greater than 20 mmHg, 68% of the patients experienced IHI during dialysis [20]. Contrary to our findings, Islam F *et al.*, indicated that the frequency of IHI during dialysis was approximately 12%. IHI frequency was observed to be

similar in both genders in the Bangash IA *et al.*, study (23.2% in males versus 26.3% in females) [17, 21]. Contrary to our findings, previous studies have identified female sex as a significant risk factor for developing Intradialytic Hemodynamic Instability (IHI) [22]. This discrepancy may be attributed to variations in the study populations and methodologies. Moreover, it was logical to anticipate an increased incidence of IHI with advancing age, given the higher prevalence of comorbid conditions that were known to elevate the risk of IHI [23]. However, our results challenge this assumption, as we found no significant correlation between age and the frequency of IHI. IHI was associated with significant morbidity and mortality, underscoring the necessity for effective preventative strategies [24]. In a prospective study conducted in an intensive care unit, Bige N *et al.*, identified that IHI frequently occurred within the first hour of intermittent hemodialysis, even in the absence of fluid loss. This instability was significantly associated with two measures of tissue hypoperfusion: A Capillary Refill Time (CRT) of ≥ 3 seconds and a lactate level > 2 mmol/L, alongside a cardiovascular SOFA score of ≥ 1 [17]. The risk of IHI increased proportionally with the number of abnormal parameters observed. In another cohort study, the incidence of IHI was reported to be 23% while Monnet X *et al.*, documented a higher incidence rate of 33%, albeit in a population where all patients underwent fluid removal [25]. The convergence of results across multiple studies suggests that a multifaceted approach, incorporating early detection markers like CRT and PRR along with adherence to practice guidelines, may enhance patient outcomes during hemodialysis.

CONCLUSIONS

The findings indicate that the incidence of Intradialytic Hemodynamic Instability (IHI) in individuals undergoing hemodialysis was relatively low. However, dialysis remains an essential intervention for critically ill patients suffering from Acute Kidney Injury (AKI), despite the inherent concerns regarding its frequency, as it was a non-negotiable treatment for these patients. The commencement of intermittent hemodialysis presents the highest risk for IHI, particularly within the first hour of the initial sessions. This increased risk was significantly associated with prolonged index capillary refill times. Therefore, early and vigilant monitoring during the initial phases of dialysis was crucial to reduce the risk of IHI and its associated complications.

Authors Contribution

Conceptualization: MH

Methodology: SM

Formal analysis: GR

Writing, review and editing: AJ, BA, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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