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## Intradialytic hypertension prevalence and predictive factors: A single centre study

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### ABSTRACT

**Introduction:** Intradialytic hypertension (IDH) is associated with significant vascular and cardiac adverse outcomes.

**Objectives:** This study was performed to know the prevalence and factors predicting IDH.

**Patients and Methods:** A single-center cross-sectional observational study at a tertiary care hospital. After ethics committee approval and informed consent, all patients over 18 years on twice weekly hemodialysis were included, those on peritoneal dialysis and acute kidney injury excluded. Primary outcome was prevalence of IDH based on three definitions and secondary outcome was predictive factors. IDH was defined as  $\geq 10$  mm Hg surge in systolic blood pressure (SBP) between pre- and post-dialysis in 4 of 6 successive sessions or  $>15$  mm Hg rise in mean arterial pressure (MAP) between start and end of dialysis or symptomatic rise in blood pressure requiring intervention. SBP and MAP were measured on standardized monitors before, hourly and 30 minutes post dialysis.

**Results:** Of 136 patients, prevalence of intra-dialytic hypertension was 78/136 (57%), 33/136 (24%), 15/136 (11%) based on systolic rise, rise in MAP and symptomatic rise in BP respectively. Among those with systolic rise, diabetes mellitus ( $P=0.03$ ), undernourishment ( $P=0.03$ ), inter-dialytic weight gain  $>3$  kg ( $P<0.001$ ) and dialysis vintage  $>3$  years ( $P<0.001$ ) were significantly associated with IDH.

**Conclusion:** IDH prevalence varied from 11 to 57% with different definitions. Diabetes mellitus, under nutrition, inter-dialytic weight gain  $>3$  kg and dialysis vintage  $>3$  years predicted IDH.

### *Implication for health policy/practice/research/medical education:*

This study highlights the fact that prevalence of intradialytic hypertension varies when different definitions are used and there is a requirement for a uniform definition/criterion which can be utilized by nephrologist's across the world.

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### Introduction

Hypertension is seen in 85% patients on maintenance hemodialysis (HD) and is often difficult to manage, with adequate blood pressure (BP) control seen in only 35%-40% of them despite effective use of antihypertensive drugs (1). In most patients HD reduces BP, however few may have a paradoxical rise known as intradialytic hypertension (IDH), the prevalence of which varies from 5 to 20 % and leads to various cardiac and vascular complications (2).

Intradialytic hypertension has been a frequently recognized phenomenon for several years in maintenance HD population however there are no accepted criteria to define the same. The three most frequently considered definitions in descending order are  $\geq 10$  mm Hg rise in systolic blood pressure (SBP) in at least four of six successive HD sessions or  $>15$  mm Hg rise in mean arterial pressure (MAP) from beginning to end of the dialysis or any symptomatic rise in BP during ongoing HD (2). Other definitions suggested are BP higher at

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end of dialysis when compared to beginning in more than half or in consecutive four dialysis sessions (3).

## Objectives

In analysis of IDH consistency of definition is a fundamental criterion, nevertheless there is limited Indian data available on its prevalence and disparity because of different definitions. We studied prevalence of IDH in Indian patients on maintenance HD based on three most used definitions and associated factors.

## Patients and Methods

### Study design

This was a single-centre, observational study conducted over three months from November 2015 to January 2016 at a tertiary care hospital.

Inclusion criteria; all HD-dependent-chronic kidney-disease (CKD5D) patients aged above 18 years on twice-weekly maintenance HD lasting five hours each session.

Exclusion criteria; patients on peritoneal dialysis and those with acute kidney injury.

Primary and secondary outcome: Primary outcome was prevalence of IDH based on mentioned definitions and secondary outcome was factors associated with IDH.

### Definitions

IDH was defined as either;

1.  $\geq 10$  mm Hg increase in SBP between pre- and post-dialysis in at least 4 of 6 successive sessions or
2.  $>15$  mm Hg rise in MAP between the start and end of the dialysis session or
3. Any symptomatic rise (headache, blurring of vision, vomiting) in BP during dialysis requiring intervention

Pulse rate, SBP, diastolic blood pressure (DBP) and MAP were measured on standardized BP monitors using oscilloscopic method before, hourly and up to half an hour after dialysis. Pre HD BP was measured in the non-access arm in supine position before insertion of needle and post HD BP was obtained similarly after the needle removal by the same individual.

IDH definition involving a rise in SBP was utilized for analyzing associated factors as this is the most frequently used definition in prior studies. Potential factors that were studied included age, gender, comorbidities like diabetes mellitus, hypertension, ischemic heart disease, body mass index, inter-dialytic weight gain, and dialysis vintage. Formulae for calculating;

1. Inter-dialytic weight gain (IDWG) = Pre-dialysis weight – Post dialysis weight of the previous HD session.
2. Ultrafiltration rate (UFR) = Ultrafiltration volume (mL)/Duration of dialysis session (hours).

### Statistical analysis

Analysis was done on IBM SPSS statistical software version 20.0 for Windows (SPSS Incorporation, Chicago, Illinois, USA). Data was conveyed as mean for continuous variables and percentage frequency for categorical variables. Chi-square test was applied to analyses any significant difference between groups and p-value was checked at a 5% level of significance.

## Results

Of 136 patients, baseline characteristics are described in Table 1. Among them IDH was seen in 78 patients based on SBP rise. In this group, patients aged  $<60$  years were 59 (75.6%) and 53 (67.9%) were males.

### Primary outcome

The prevalence of IDH varied as per definitions for diagnosis. IDH was seen based on  $\geq 10$  mm Hg increase in SBP between pre- and post-dialysis in at least 4 of 6 successive sessions in 78/136 (57.3%) (Figure 1A), based on  $>15$  mm Hg rise in MAP between start and end of dialysis seen in 33/136 (24.2%) (Figure 1B) and based on symptomatic rise in BP in 15/136 (11%) (Figure 1C).

### Secondary outcome

Factors associated with IDH were analyzed (Table 1). Diabetes mellitus was seen in 45/78 (57.7%,  $P=0.03$ ), hypertension in 26 (33.3%), ischemic heart disease in 7 (9%) and below normal weight in 47 (60.2%,  $P=0.03$ ), overweight in 13 (16.8%), IDWG  $>3$  kg in 59 (75.6%,  $P<0.001$ ), and dialysis vintage  $>3$  years in 64 (82%,  $P<0.001$ ).

## Discussion

IDH is frequent in maintenance HD population and has considerable cardiovascular morbidity and mortality. IDH is multifactorial and has a complex mechanism.

Several hypotheses have been proposed for IDH such as excessive ultrafiltration causing hypovolemia, renin-angiotensin and sympathetic over activity, dialysate temperature, potassium and calcium variations, vasoconstriction due to hemoconcentration favored by erythropoietin supplementation, volume excess causing increased cardiac output, endothelin induced vasoconstriction and lastly antihypertensive removal during HD (4). As a unifying criterion for diagnosis of IDH has not been proposed till date, Chazot et al (3) analyzed various studies using different definitions for IDH and mentioned the frequency to vary between 5 to 20 %. Recent Indian studies show a higher prevalence. Studies by Kumar et al (5) on 100 patients followed up for 12 months, IDH was seen in 49%, by Nilrohit et al (6) in which 142 patients were studied for two and a

**Table 1.** Baseline characteristics and factors associated with IDH

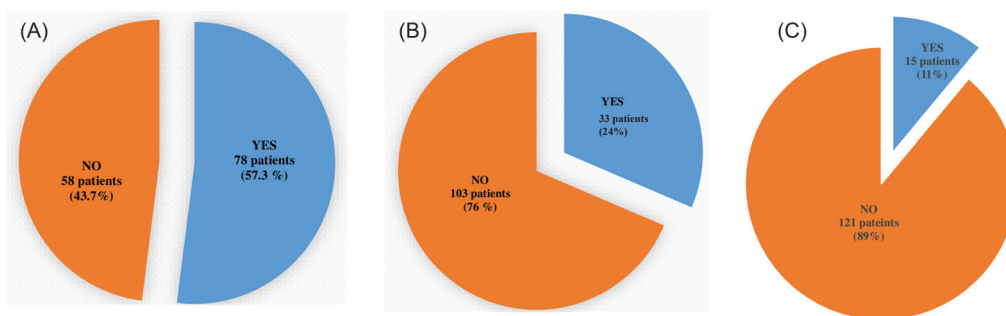
Factors	With IDH (n=78)	No IDH (n=58)	P value <sup>a</sup>
Age (y)			
<60	59 (75.6%)	39 (67.2%)	0.28
>60	19 (24.4%)	19 (32.8%)	
Gender			
Males	53 (67.9%)	45 (77.5%)	0.21
Co-morbidities			
Diabetes mellitus	45 (57.7%)	23 (39.6%)	0.03 <sup>a</sup>
Hypertension	26 (33.3%)	27 (46.6%)	0.11
Ischemic heart disease	7 (9%)	8 (13.8%)	0.41
Body mass index (kg/m <sup>2</sup> )			
Underweight	47 (60.2%)	45 (77.5%)	0.03 <sup>a</sup>
Normal	18 (23%)	7 (12%)	0.10
Overweight	13 (16.8%)	6 (10.5%)	0.29
Interdialytic weight gain (kg)			
<3	19 (24.4%)	49 (84.4%)	<0.001 <sup>a</sup>
>3	59 (75.6%)	9 (15.6%)	
Dialysis vintage (y)			
<3	14 (18%)	27 (46.5%)	<0.001 <sup>a</sup>
>3	64 (82%)	31 (53.5%)	

<sup>a</sup> Statistically significant ( $P < 0.05$ ).

half years showed a prevalence of 34.5%. Prevalence of IDH based on definition involving SBP rise was done in three studies, firstly CLIMB study (7) on 438 taking SBP rise of  $\geq 10$  mm Hg as criteria and 13.2% patients had IDH, second Wave II study (8) on 1748 HD patients from the United States renal data system (USRDS) with an average rise in SBP of  $>10$  mm Hg from three successive dialysis sessions as the criteria concluded that 12.2% of patients satisfied the criteria and lastly study by Van Buren et al (9) wherein 362 patients were followed up for 6 months and found 22.3% patients had IDH.

We found a prevalence of IDH based on  $\geq 10$  mm Hg SBP in 78 (57.3%) patients which is higher than other studies however similar to recent ones from India (5, 6). We found prevalence of IDH based on  $>15$  mm Hg rise in MAP in 33 (24.2%) patients which is higher than 8% shown by Amerling et al (10). Symptomatic rise in BP during dialysis requiring intervention was seen in 15 (11%) patients which is higher than 8% shown by Van Buren et al (9). Possible reason for an increased prevalence of IDH based on all three definitions in our setting may be higher inter-dialytic weight gains due to twice a week HD schedules followed in most centers with ultrafiltration inadequacy, poor adherence to salt and water restriction and undernourishment with difficulties in dry weight assessment (11). Based on studies from previous decade IDH occurs more frequently in elderly, diabetes mellitus, undernourished with low-serum creatinine, those on two or more antihypertensive medications and on longer dialysis vintage (2,7-9). We studied factors associated with IDH defined based on SBP rise as this was the commonest definition used (5-7). IDH was seen in 78/136 patients with only 19 (24.4%) being older than 60 years which is not similar to study by Inrig et al (2) probably reflecting a younger population on dialysis. We did not find a gender difference similar to previous studies (5, 6). IDH was seen in 45 (57.7%) patients with diabetes mellitus which was statistically significant and is similar to study by Van Buren et al (12) possible mechanisms being excess salt retention, sympathetic nervous system and renin-angiotensin-aldosterone system activation, endothelial dysfunction and oxidative stress in these patients.

We found low body mass index (BMI) to be associated with IDH similar to Inrig et al (5) and Nilrohit et al (6). Possible explanations are smaller inter-dialytic weight gain leading to less ultrafiltration prescribed causing chronic extracellular volume excess and hence preserved intravascular fluid volume which contributes to IDH. Additionally, high concentration of vasoconstrictor



**Figure 1.** (A) IDH prevalence based on rise in systolic blood pressure. (B) IDH prevalence based on rise in mean arterial pressure. (C) IDH prevalence based on symptomatic rise in blood.

endothelin-1 and less levels of vasodilator nitric oxide which leads to higher BPs.

Inter-dialytic weight gain >3 kg was associated with more IDH similar to Ipema et al (13). Possible mechanisms suggested are presence of high DBPs pre and post dialysis in them, less chances of reaching their dry weight leading to lesser blood viscosity, higher cardiac output and thus increased peripheral vascular resistance and lastly these patients have a lower sodium concentration at the beginning of the dialysis session which is not corrected during dialysis despite diffusive transfer of sodium to the patient. Hence it is seen that every 1% increase in IDWG is associated with a 1 mm Hg increase in pre- and intradialytic SBP (13).

In this study, IDH was more in those with a longer dialysis vintage (>3 years) similar to Inrig et al (2) wherein increased arterial stiffness and unrecognized accelerated arteriosclerosis were observed causing increased chances of IDH.

### Conclusion

Prevalence of IDH in our population varied from 11-57% based on different definitions. Diabetes mellitus, undernourishment, inter-dialytic weight gain of >3 kg, and dialysis vintage of >3 years were significantly associated with IDH.

### Limitations of the study

Factors known to influence IDH like dialysate sodium, conductivity, temperature, class and number of antihypertensive and role of erythropoietin supplementation were not assessed.

### Authors' contribution

RAP, BN and MVB were the principal investigators of the study. RAP, BN, MVB and IRR were included in preparing the concept and design. SVS, SPN and DR revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

### Conflicts of interest

The authors declare that they have no competing interests.

### Ethical issues

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research

committee. The study protocol was approved by the institutional ethics committee of Kasturba Medical College, Manipal Academy of Higher Education (IEC 775/2015). Accordingly, informed consent was obtained from each patient enrolled in the study. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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