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Study of Intradialytic Hypertension in Chronic Kidney Disease at a tertiary care centre

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Abstract: *Hypertension is perhaps one of the most common problems of patients with end stage renal disease(ESRD). Hypertension is highly prevalent ESRD in patients on maintenance hemodialysis (HD). Intradialytic hypertension (IDH) is one such complication responsible for increased morbidity and mortality in chronic kidney disease (CKD) patients undergoing hemodialysis. In India, there is limited data available in the literature for the incidence of IDH in CKD patients on hemodialysis. In this observational study, we evaluated the incidence of IDH in Indian CKD patients undergoing hemodialysis. We found a higher incidence of IDH (31%) in our study than in Western studies. The data was analyzed to access the association of IDH with demographic, biochemical, and other parameters. IDH was associated with higher interdialytic weight gain and higher cholesterol level which are modifiable risk factors. Pre-HD systolic blood pressure (SBP) was independent risk factor for IDH. Patients with higher overall BP burden are more likely to have IDH.*

Key Words: *Intradialytic hypertension; chronic kidney disease (CKD); Hemodialysis.*

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I. Introduction

Chronic Kidney Disease (CKD) is a global health burden with high economic cost to health system. CKD and hypertension are inextricably intertwined: the majority (70%) of individuals in the general population who have an elevated serum creatinine are hypertensive, and hypertension is both a cause and a consequence of CKD[1]. While hemodialysis lowers blood pressure (BP) in most hypertensive end stage renal disease patients, some patients exhibit a paradoxical increase in BP during hemodialysis.The pathophysiology is poorly understood and the clinical consequences have only recently been investigated[1].

The prevalence of hypertension in patients undergoing hemodialysis ranges from 65% to 85% [2]. Hypertension results in cardiovascular complications in hemodialysis patients. It is also a powerful predictor of mortality[3]. Intra-dialytic hypertension (IDH), a unique form of hypertension observed in hemodialysis patients, has recently emerged as an important issue[4]. This study was carried outto evaluate the prevalence of IDH in CKD patients on maintenance hemodialysis (MHD).

II. Materials And Methods

We enrolled 100 patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis at tertiary care dialysis unit in western part of India. This was a singlecentre prospective observational study over a period of 18months from January 2017 to June 2018.

All CKDpatients (age >18 years) undergoing MHD (HD vintage > 30 days) were included. Patients of acute kidney injury were excluded.IDH was defined as an increase in systolic blood pressure of more than 10 mmHg during hemodialysis in two or more consecutive hemodialysis sessions[5].Patients were classified into IDH &Non-IDH categories for analysis with above mentioned definitions. Clinical parameters and biochemical parameters were noted for each subject.

Blood pressure was recorded every 30 minutes, using NIBP model - G 30, Philips Goldway,during each dialysis sessions. Pre HD BP was measured in the non access arm after 5 min rest in the supine position before insertion of needle.Similarly, Post HD BP was obtained after 5 minutes of termination of dialysis sessions.

Statistical Analysis:

SPSS software version 20 was used for the analysis of this data. Chi-square test was applied to compare non-continuous variables in IDH & non-IDH groups. Continuous variables were compared using unpaired t test (level of significance was at $p < 0.005$)

III. Results

Out of 100 patients, 31 (31%) patients were found to have intradialytic hypertension (IDH). In this study, 75 (75%) were males and 25(25%) were females. 31 patients were above 50 years of age.

Out of 31 subjects in IDH group , 18 (58%) were diabetic and 13(42%) were non-diabetic. In non-IDH group (n=69), 18 (26%) were diabetic and 51 (74%) were non-diabetic. It was observed that prevalence of IDH was higher in diabetic patient which was statistically significant (P = 0.0052).

It was found that prevalence of IDH was greater in patients with higher HD Vintage which was statistically significant. (P = 0.001) In this study, interdialytic weight gain was significantly higher in IDH group (p-0.004).(Demographic details mentioned in Table 1)

When biochemical parameters were compared in IDH & non IDH group, serum cholesterol level was significantly higher in IDH group. (p=0.005). However, there was no significant difference was found between mean values of hemoglobin, serum creatinine, sodium, potassium, calcium, phosphorus, uric acid, serum albumin, bicarbonate level. ($p > 0.05$)(Table 2)

Mean pre- HD systolic BP was 150.52 (±14.05) and mean post- HD systolic BP was 159.52 (±14.99) for IDH group and mean pre- HD systolic BP was 133.14 (±12.68) and Mean post- HD systolic BP was 135.33 (±17.22) for non-IDH group. Mean pre- HD diastolic BP was 89.00 (±8.36) and mean post- HD diastolic BP was 88.39 (±9.8) for IDH group and mean pre- HD diastolic BP was 81.55 (±9.58) and mean post- HD diastolic BP was 82.26 (±6.43) for non-IDH group.In our study, pre and post HD systolic and diastolic BP were higher in IDH group compared with non-IDH group. This difference was statistically significant. ($p < 0.001$)(Table 3)

We assessed the anti-hypertensive requirement in both IDH & non-IDH groups. Percentages of patients on Calcium channel blockerss in both groups were almost similar.(94.20% in non-IDH group & 100% in IDH group) Percentage of patients on α-blocker(31.88% in non-IDH group & 70.90% in IDH group), β-blocker (62.3% in non-IDH group & 87% in IDH group) and central sympatholytics (5% in non-IDH group & 32.25% in IDH group) were significantly more in IDH group. ($p < 0.05$) (Table 1)

Multivariate regression analysis was performed to find out independent risk factors for IDH. It was found that Pre-HD SBP was an independent risk factor (p-0.000) for IDH after adjusting for gender, diabetes mellitus, HD vintage, cholesterol, IDWG, frequency of HD and types of anti-hypertensive drugs (CCB, α blocker, β blocker, CS). (Table 4)

IV. Discussion

The present study is a prospective observational study of the incidence of IDH in CKD patients undergoing maintenance hemodialysis. A total of 100 CKD patients were studied over a period of 18 months. In our study, incidence of IDH is 31%, which was greater than the incidence found in western studies by Stidley et al[6], Mees D et al[7], in which it was found to be 5-15%.

A recent study by Sebastian S et al[8] from South Africa showed that IDH may affect as many as 28% of the dialysis population. One study from South India by Darimireddi SK et al [9] found the incidence of IDH to be 49% in 100 patients studied. This supports our finding that the incidence of IDH is higher in Indian population.

In this study, no relation was found between the incidence of IDH and the age or gender of the patient. No previous studies demonstrated a statistically significant difference among males and females. According to a study by Inrig et al [5] on 32,295 patients, incidence of IDH was more in the elderly patients. We found that the mean age was not different in IDH group (40.84 ± 15.99) & non-IDH (42.90 ± 14.15) groups.

The proportion of diabetes patients was more in IDH groups compared to non-IDH groups which was statistically significant. (p-0.005) No comparable data for association of diabetes mellitus and IDH was found in previous studies. No previous study assessed the association between previous hypertensive status & IDH. Even in our study, the percentage of previous hypertensive patients was comparable in IDH & non-IDH groups.

Patients who are on less frequent hemodialysis have more interdialytic weight gain and are more prone for intradialytic hypertension. Our study showed slightly greater percentage of IDH in patients with twice a week HD than in patients taking thrice a week HD. However, it did not reach statistical significance.

To assess the relation between HD vintage and intradialytic hypertension (IDH), we compared these parameters in both groups. The proportion of patients with greater HD vintage was higher in IDH groups. It will be important to investigate the role of dialysis related inflammation and vascular changes in IDH. In none of the previous studies reviewed, HD vintage was taken into consideration.

As fluid status plays an important role in hypertension in patients on hemodialysis, we compared the interdialytic weight gain (IDWG) in both IDH and non-IDH groups. This factor has probably not been emphasized previously as an association with IDH. However, in our study IDW was significantly higher in IDH group. This emphasizes the role of fluid volume in hypertension in IDH patients.

When we compared the target dry weight in both groups, it showed no statistically significant difference. The IDH was probably related to the incremental change in fluid volume status in interdialytic period than absolute dry weight.

We assessed the anti-hypertensive requirement in both IDH & non-IDH groups. Patients on CCBs in both groups were almost similar. Percentages of patients on α-blocker, β-blocker and Central sympatholytics (CS) were significantly more in IDH group. This could be due to the higher requirement of anti-hypertensive drugs in IDH group.

It is also proposed that removal of anti-hypertensive medications is one of the mechanism for IDH. Chou et al [10] reported that RAAS and sympathetic over-activity were unlikely to play a role in the genesis of IDH.

When biochemical parameters were compared in IDH & non IDH group, there was no statistically significant difference found between mean values of hemoglobin, serum creatinine, sodium, potassium, calcium, phosphorus, uric acid, serum albumin, bicarbonate level. ($p > 0.05$)

However, serum cholesterol was significantly higher in IDH group. None of the previous studies reviewed, revealed cholesterol level among the biochemical parameters. Interdialytic weight gain and cholesterol are modifiable risk factors with appropriate measures, so these observations can potentially guide us to prevent IDH in dialysis patients. A follow up interventional study targeting lower IDWG and rigid control of cholesterol would help in confirming the role of these factors in IDH.

Pre and post HD systolic and diastolic BP were higher in intradialytic HTN group compared with non-IDH group. This difference was statistically significant. It would be interesting to see whether more aggressive control of BP would be helpful in reducing prevalence of IDH.

In the multivariate regression analysis, Pre-HD SBP was found to be an independent risk factor for IDH after adjusting for gender, diabetes mellitus, HD vintage, cholesterol, IDWG, frequency of HD and types of anti-hypertensive drugs (CCB, α blocker, β blocker, CS).(Table 4) These factors were not associated with the previous studies reviewed. Better control of pre-HD systolic blood pressure may help in reducing incidence and severity of IDH.

V. Conclusion

Incidence of IDH in our study was 31% which was higher than what was found in the other studies. This suggests that prevalence of IDH is more in Indian population. We found a statistically significant relation between prevalence of IDH and diabetes mellitus, IDWG, type of anti-hypertensive drugs, cholesterol level & pre and post HD systolic & diastolic blood pressures.

However, no significant relation was found between incidence of IDH and factors like age, gender, hypertension, frequency of HD, TDW, and other biochemical parameters. Interdialytic weight gain and cholesterol are modifiable risk factors. Pre-HD SBP was independent risk factor for IDH. Patients with higher overall BP burden are more likely to have IDH.

Limitations of this cross-sectional study is a smaller study population.. An interventional longitudinal study with more sample size and longer follow up duration would be helpful in assessing the benefits of controlling IDWG, cholesterol level and pre-HD systolic blood pressure. This study would also be helpful in assessing the impact of these factors on IDH and overall morbidity & mortality in HD population.

Table: 1: Demographic details and Baseline Characteristics all subjects**:**

Parameters	**Non-IDH Group**	**IDH Group**	**P Value**
Age, Year	42.90 (±14.15)	40.84 (±15.99)	0.52
Males %	49 (71%)	26 (84%)	0.17
D.M.	18 (26%)	18 (58%)	**0.0052**
HTN %	65 (94%)	30 (97%)	0.58
IHD %	09 (13%)	3 (10%)	0.63
HD vintage	9.75 (±8.87)	15.19 (±16.96)	**0.001**
ACCESS			
•AV Fistula%	22 (32%)	14 (45%)	0.42
•Cuffed Tunnledcath%	67 (54%)	14 (45%)	
•UncuffedNontunnledcath %	10 (14%)	3 (10%)	
Frequency of HD per week			
•Twice	44 (64%)	16 (51%)	

•Thrice	25 (36%)	15 (49%)	0.25
TDW	52.26 (±10.94)	52.22 (±11.17)	0.98
IDWG	1.65 (±0.73)	2.14 (±0.83)	**0.004**
CCB (n=96)	65 (94.20%)	31 (100%)	0.17
α –blocker (n=44)	22 (31.88%)	22 (70.90%)	< **0.001**
β –blocker (n=70)	43 (62.3%)	27 (87%)	**0.01**
CS (n=14)	4 (5%)	10 (32.25%)	**0.03**

Table: 2: Laboratory parameters in IDH and non-IDH groups :

Laboratory parameter	**Non- IDH Group**		**IDH Group**		**P value**
	Mean	**SD (±)**	**Mean**	**SD(±)**	
Hemoglobin	8.01	1.24	7.64	0.92	0.10
Creatinine	7.64	1.86	8.25	2.03	0.66
Sodium	136.0	3.84	135.7	3.25	0.66
Potassium	4.44	0.56	4.38	0.48	0.46
Calcium	8.44	0.39	8.39	0.43	0.55
Phosphorus	4.62	1.29	4.60	1.20	0.96
Uric acid	5.71	1.64	5.63	1.89	0.86
S. Albumin	3.17	0.41	3.21	0.38	0.63
S. Bicarb	20.60	2.12	20.45	2.02	0.74
Cholesterol	188.3	32.62	205.7	35.7	**0.001**

Table 3: Comparision of Pre and Post HD SBP & DBP in IDH and non-IDH groups:

Parameters	**Non-IDH Group**		**IDH Group**		**P value**
	Mean	**SD**	**Mean**	**SD**	
Pre HD Systolic BP Diastolic BP	 133.14 81.55	 12.68 9.58	 150.52 89.00	 14.05 8.36	 <**0.001 (S)** <**0.001 (S)**
Post HD Systolic BP Diastolic BP	 135.33 82.26	 17.22 6.43	 159.2 88.39	 14.99 9.8	 <**0.001 (S)** <**0.001 (S)**

Table 4 : Regression Analysis:

Predictors / Risk factors for Intradialytic Hypertension (IDH) :

	Unstand- Coefficients		Stand- Coefficients	t	p-value
	B	Std. error	β		
(Stable)	-2.816	0.524		-5.370	0.000 (S)
Gender	0.075	0.092	0.070	0.812	0.419
DM	0.080	0.095	0.078	0.839	0.404
HD Vintage	0.003	0.003	0.090	0.993	0.323
CHO	0.003	0.001	0.213	2.532	0.01 (S)
IDWG	0.037	0.056	0.063	0.652	0.516
Frequency of HD	0.126	0.085	0.134	1.490	0.140
Pre HD SBP	0.015	0.003	0.489	5.564	0.000 (S)
CCB	-0.110	0.211	-0.047	-0.520	0.604
α - blocker	0.206	0.105	0.222	1.973	0.05 (S)
β -blocker	-0.003	0.105	-0.003	-0.032	0.975
CS	0.056	0.147	0.037	0.384	0.702
Dependent Variable: IDH					

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