FREQUENCY AND CLINICAL PROFILE OF PATIENTSWITH INTRADIALYTIC HYPERTENSION ON MAINTENANCE HEMODIALYSIS IN A TERTIARY CARE CENTER

ABSTRACT

Aims- to estimate frequency of intra-dialytic hypertension in indian maintenance hemdialysis patients. to describe the clinical profile of patients with intra-dialyticypertension.

Study Design: observational descriptive study

Place and Duration of study: dialysis unit father muller medical college hospital, mangalurukarnataka state india from 1st august 2022 to 31stjuly 2023.

Methodology a minimum of 71 patients age 18 - 85 years on maintenance hemodialysis for more than 3 months previously diagnosed with hypertension - pre-dialysis blood pressure >140/90 mmhg or post-dialysis blood pressure >130/80 who are at target dry weight enrolled. weight blood pressure of each patient measured before dialysis and immediately after dialysis termination before removing dialysis access needles during six consecutive dialysis sessions. data analyzed as percentage for categorical variables and mean and standard deviation for continuous variables. proportions compared using chi-square test and means compared using student t test. all analysis done using spss software

Results-prevalence of intradialytic hypertension is 59.2 %.

occurrence of idh is significantly associated with hem dialysis frequency, calcium channel blocking medication use, inter-dialysis serum potassium level, post-dialysis mean systolic blood pressure, post dialysis mean diastolic blood pressure occurrence of idh is not significantly associated with gender, type 2 diabetes mellitus, age, hem dialysis vintage, pre- dialysis weight, intra-dialysis weight loss, dry weight, post-dialysis weight, pre-dialysis mean systolic blood pressure, pre-dialysis mean diastolic blood pressure.

Conclusion:intradialytic hypertension is multifactorial. nitrogen balance, sodium ion, water movement between intracellular, extracellular and intravascular compartments. inter-dialytic weight gain, pre-dialysis weight intra-dialytic weight loss post dialysis weight dry weight endothelial dysfunction, vasocontrsictor, vasodilalation, changes in diastolic lv filling, changes in systolic function, compliance with oral antihypertensive medication use, frequency of non dialysable oral antihypertensive medications use and other unknown factors might be operating to cause this phenomenon.

Keywords:*INTRADIALYTIC HYPERTENSION MAINTENANCE HEMODIALYSIS*

1. INTRODUCTION

The prevalence of Intradialytic Hypertension (IDH) is estimated to be around 5 to 15% in the Hemodialysis (HD) population (1). Intra-dialytic hypertension has been associated with increased risk for short-term (6 months) and long-term (2 years) morbidity and mortality (1).Indian data on Intradialytic hypertension is sparse (3).We plan to estimate the

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frequency of IDH in Maintenance Hemodialysis [MHD] Patients and describe the clinical profile of Maintenance Hemodialysis Patients [MHD] with intradialytic hypertension [IDH].

1.2 REVIEW OF LITERATURE

In patients with end-stage renal disease, hem dialysis decreases blood pressure in most hypertensive patients, but some hypertensive patients show an increase in blood pressure during hem dialysis. (1). Occurrence of increase in BP pre- to post-dialysis has been identified in up to 15% of maintenance HD patients (1). In earlier studies, participants with intra-dialysis hypertension were older, had lower dry weight, had lower inter-dialysis weight gain, had lower serum albumin levels, and were prescribed a greater number of anti-hypertensive medications (1). Patients with Intra-dialysis Hypertension had an increased risk of hospitalization or death compared with patients with SBP which decreased with Hem dialysis (1). Intra-dialysis hypertension is managed with volume management by decreasing dry weight, inhibition of the sympathetic nervous system with beta-adrenergic antagonist drugs etc. (1)

Intra-dialytic hypertension, IDH refers to increase in blood pressure (BP) from pre- to post-hem-dialysis HD. Accepted definitions are not there for IDH. Inrig JK, Oddone EZ, Hasselblad V, et al [75]adapt definition systolic BP SBP rise 10mmHg or more, Inrig J, Van Buren P, Kim C, Vongpatanasin W, Povsic T, Toto R et al[34] adapt definition SBP increase 10mmHg or more in 4 out of 6 HD sessions,Amerling R, Cu G, Dubrow A, et al[68] , Prabhu RA et al [60] adapt definition mean arterial pressure MAP rise 15mmHg or more, Cirit M, Akcicek F, Terzioglu E, et al[66] adapt definition BP that is higher at the session end than at the session onset in 50 or more percent sessions, Gunal AI, Karaca I, Celiker H, Ilkay E, Duman S et al[12]adapted definition BP that exceeds initial values during 4 HD sessions in a row, Chou KJ, Lee PT, Chen CL, et al[21] adapt definition 15 mmHg mean BP increase occurring in 8 or more of the 12 most recent hemodialysis sessions. Chen J, Gul A, Sarnak MJ et al[20] adapted definition intradialytic hypertension is hypertension occurring during or immediately after the dialysis procedure that appears resistant to ultra filtration UF. Charles Chazot**,** Guillaume Jean et al[4], opine any sustained BP rise during dialysis session with BP values during and at the end of session exceeding BP values at dialysis onset without having to frame this definition with strict numbers and also patient can be normotensive at the start of dialysis but the BP rise during haemodialysis session makes the patient hypertensive during and at the end of session.Inrig JK, Oddone EZ, Hasselblad V, et al[75] adapt IDH definition SBP 10 or more pre to post dialysis holds same significance in heart failure patients as in other dialysis patients.

Inrig JK.et al[31], Kalainy S et al[44] Prevalence IDH 15% to 30% of patients treated with HD,Charles Chazot**,** Guillaume Jean et al[30] IDH occursin 10% of HD patient. Amerling R et al [67] found IDH in 8% patients, DorhoutMeesEJ[68] et al found IDH in 5- 15 % patientsInrig JK, Patel UD, Toto RD, Szczech LA et al[28] found IDH in 12.2 % large cohort patients. IDH systolic BP 10 mmHg or more from pre to post HD occurred in at least once in 90 % of the patients over the course of 6 months in one study (Van Buren PN, Kim C, Toto R, Inrig JK et al[2], Van Buren PN, Kim C, Toto R, Inrig JK et al [35]) half of the patients had IDH in 18% or less of the total HD sessions over the 6 months study period while the another half of the patients had IDH in 18 % or more of the total HD sessions over the 6 month study period. 9% patients had mean increase in systolic BP 10mm or more. This mean is calculated from sessions over 6 months. In Park J, Rhee C, Sim J,[40] et al study

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of 1 hundred thousand patients over 5 years, mean SBP increase 10 mmHg or more occurred in 10% patients.

Intra-dialysis hypertension is associated with increased morbidity and mortality in maintenance hem dialysis patients. Zager PG, Nikolic J, Brown RH, et al[8] found increased mortality if IDH systolic BP SBP is over 180 and or diastolic BP DBP is over 90 mmHg Flythe J, Inrig J, Shafi T, et al[41] large variations in Blood pressure BP during HD is risk factor for increased mortality., , Inrig JK, Oddone EZ, Hasselblad V, et al[75] found increased risk of hospitalization death.Inrig J, Oddone EHV, Gillespie B, et al.[25] IDH patients after 6 months had higher hospitalization, mortality. Inrig J, Oddone EHV, Gillespie B, et al.[25]Inrig J, Patel U, Toto R, Szczech L. et al[28] Park J, Rhee C, Sim J, et al[40]IDH patients have poor outcomes. Charles Chazot**,** Guillaume Jean et al[4],IDH increases hospitalization mortality. Charles Chazot**,** Guillaume Jean[4], observed survival of patients with Intra dialytic hypotension of mean systolic BP decrease of 14 mmHg is more than either 30mmHg mean systolic BP SBP decrease or any SBP increase. Charles Chazot**,** Guillaume Jean[4],observed heart failure patients can have low blood pressure SBP rise 10 mmHg or more, and this low BP rise increases mortality in heart failure patients whose pre-dialysis SBP is less than 120 mmHg. Foley R.N.HerzogC.A.Collins A.J.et al[13]Robinson B.M.TongL.Zhang J.et al[39]JheeJ.H.ParkJ.Kim H.et al[52])pre- and post- dialysis SBP DBP correlation to mortality in HD patients follows either U or J shaped curve.Van Stone J, Bauer J, Carey J et al[64] observed low dial sate sodium 7% lower than serum causes more extracellular volume(measured using dilution techniques)removal than total fluid removed, more fluid moves from extracellular space to intracellular space- causes intra-dialytic hypotension. High dial sate sodium removed fluid from both intracellular and extracellular space such that overall extracellular fluid reduction was much lower than with hypotonic or isotonic dial sate. Bazzato G, Coli U, Landini S, et al[65] found captopril efficient in preventing BP rise in IDH patients. dynamic changes in cardiac output with end diastolic volume reduction during HD increase BP. (Cirit M, Akcicek F, Terzioglu E, et al66], Gunal A, Karaca I, Celiker H, Ilkay E, Duman S.et al[12]) decreasing post dialysis body weight decreased pre dialysis bp and make IDH disappear(Cirit M, Akcicek F, Terzioglu E, et al[66]), prolonging ultra filtrate [UF] time and UF rate normalized the BP, increased cardiac index and ejection fraction between the start of the dialysis session and the bp zenith and then decreased at the end of session (Gunal AI, Karaca I, Celiker H, Ilkay E, Duman S et al[12]). Erythropoietin Epo triggers endothelin synthesis (Bode-Böger SM, Böger RH, Kuhn M, Radermacher J, FrölichJC:et al[6] large sodium intake in dialysis patients modified endothelium metabolism decreasing nitric oxide NO and increasing ADMA asymmetrical dimethyl arginine in the same way shear stress forces applied on endothelium had similar effect (Osanai T, Saitoh M, Sasaki S, Tomita H, Matsunaga T, Okumura K et al [14]. Although high dial sate sodium concentration improves dialysis tolerance it increases sodium diffusion and exposes patient to high intra dialytic sodium load (Locatelli F, Covic A, Chazot C, Leunissen K, Luno J, Yaqoob M et al[16,], Moret K, Hassell D, Kooman JP, et al[11] Song JH, Lee SW, Suh CK, Kim MJ et al[10])positive sodium balance is the mechanism causing extracellular fluid overload and hypertension in dialysis patients (Locatelli F, Covic A, Chazot C, Leunissen K, Luno J, Yaqoob M et al[16,]K/DOQI Workgroup: K/DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Am J Kidney Dis 2005[19]lower circulating endothelial progenitor cell levels measured prior to dialysis Werner N, Kosiol S, Schiegl T, et al.[18]) mechanism of

positive dial sate to plasma sodium gradient in IDH unknown (Chen J, Gul A, Sarnak MJ et al[20]),increased vessel resistance pre- to post- hem-dialysis in IDH patients (Chou K, Lee P, Chen C, et al.[21]) with progressive UF removal, lesser rise in Hematocrit in IDH group compared to non IDH group Chou KJ, Lee PT, Chen CL, et al[21] positive and large sodium gradient between dial sate and plasma can be mechanism causing IDH can be put forward as hypothesis (Chou KJ, Lee PT, Chen CL, et al[21]) no difference between IDH and control groups in potassium and calcium variations (Chou KJ, Lee PT, Chen CL, et al[21]) heart rate variability as measured by holter monitor recording absent in IDH patients whereas present in control subjects, Chou KJ, Lee PT, Chen CL, et al,[21] Chou KJ, Lee PT, Chen CL,[21] et al found increased peripheral vessel resistance in IDH patients. In the same patients whose vessel resistance increased, sympathetic nervous system SNS activity(assessed by plasma catecholamines), renin angiotensin aldosterone RAS system activity did not increase Chou KJ, Lee PT, Chen CL, et al[21].In IDH patients, plasma epinephrine, non epinephrine, renin did not increase (Chou KJ, Lee PT, Chen CL, et al[21] ., Gunal AI, Karaca I, Celiker H, Ilkay E, Duman Set al[12] , Raj D, Vincent B, Simpson K, et al. et al[9], El-Shafey E, El-Nagar G, Selim M, El-Sorogy H, Sabry A.et al[26]) raj et al[9]found Endothelial cell derived mediators et-1 higher levels in , lower levels vasodilator nitric oxide in idh. also found low et 1 levels in intra dialytic hypotension subjects.

cultured endothelial cells stiffen associated with nitric oxide synthesis down-regulation in high sodium concentration medium (Oberleithner H, Riethmüller C, Schillers H, MacGregor GA, de Wardener HE, Hausberg M et al[22] high extracellular sodium concentration impairs nitric oxide release, investigator hypothesized high extracellular sodium might decrease nitric oxide and increase et-1.(Oberleithner H, Riethmuller C, Schillers H, MacGregor G, de Wardener H, Hausberg M. et al[22]) more serum to dial sate sodium gradient removed less intracellular fluid as measured with whole body bioimpedance spectroscopy (Sarkar S, Wystrychowski G, Usvyat L, Kotanko P, Levin N.et al [24])in HD patients sodium balance becomes positive when sodium intake exceeds sodium removal during dialysis (Chazot C et al [**27]**) Reassessing target weight (Agarwal R, Alborzi P, Satyan S, Light RP et al[29]) dry weight probing over several weeks in dry weight reduction in hypertension hemodialysis patients DRIP study lowered intra-dialytic BP slope and ambulatory BP (Agarwal R, Light R.et al[32] ,),.Chazot g jean et al [30] Opined maintaining sufficient plasma volume at all times throughout dialysis procedure prevent clinically significant cardiac output reduction. Author also opined the need to study if any correlation exists between higher dial sate sodium and vasoconstriction and whether higher dial sate sodium causes vasoconstriction, and if vasopressin is the one that mediates this higher dial sate sodium causing vasoconstriction which is causing IDH. Author also opined the need to study whether dial sate sodium that is higher than serum sodium is causing IDH. IDH patients can be fluid overloaded hemodynamic changes(Charles Chazot**,** Guillaume Jean[30])(patients with IDH can be volume overloaded.(Charles Chazot**,** Guillaume Jeanet al [30]) (Van Buren PN, Inrig JK et al[48] Van Buren PN.et al[38] antihypertensive drugs removal by dialysis treatment(Charles Chazot**,** Guillaume Jeanet al[30]) vasodilator nitric oxide levels did not change in between IDH and control HD patients (Charles Chazot**,** Guillaume Jean[30] opined when renin levels did not increase in IDH patients, efficiency of captopril to prevent IDH may not be due to renin angiotensin converting inhibiting mechanism but may be due to general vasodilator action of captopril. Inrig JK et al[31] observed IDH occurs more

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frequently in patients who are older, have lower dry weights, are prescribed more antihypertensive medications, and have lower serum creatinine levels Lower flow mediated vasodilatation measured on a non haemodialysis day is observed in IDH patients. In this study et-1 levels not different between groups, nitric oxide levels not measured (Inrig J, Van Buren P, Kim C, Vongpatanasin W, Povsic T, Toto R et al [34]), Carvedilol changing Et-1 from pre- to post- haemodialysis is not different between IDH and non-IDH patients in the pilot study. Carvedilol significantly decreased change in ET-1 from pre- to post- haemodialysis in IDH patients , decreased ambulatory BP, improved FMD fibro muscular dysplasia, decreased the overall percentage of dialysis sessions in whom IDH occurs (Inrig J, Van Buren P, Kim C, Vongpatanasin W, Povsic T, Toto R et al [37] blood pressure is high throughout dialysis in high dial sate sodium (pre dialysis serum sodium +5) compared to low dial sate sodium (pre- dial sate sodium -5) . (Inrig J, Molina C, D'Silva K, et al.[42]),higher ratio of extracellular water to total body water is seen in patients whose bp increased during dialysis (Nongnuch A, Campbell N, Stern E, El-Kateb S, Fuentes L, Davenport A.et al[43]). ratio of extracellular water ECW to total body water TBW was significantly higher in the increased blood pressure group, particularly post dialysis group(nongnuch A et al [43]) endothelial stiffness, volume excess, sympathetic nervous system SNS, renin angiotensin system RAS (Inrig J.K et al[31], GeorgianosP.I.SarafidisP.A.Zoccali C.et al[46] , subclinical pre dialysis fluid overload as measured by bioimpedance spectroscopy BIS is significantly associated with IDH, in this study mean ultra filtrate UF volume is not different between IDH and non-IDH group (Sajith Sebastian, ChristelleFilmalter, Justin Harvey, Mogamat-YaziedChothia,et al[47]) changes in endothelial cell function, (Van Buren PN, Inrig JK.[48]) association between dial sate to serum sodium gradient and IDH.(Van Buren PN, Inrig JK.[48]), carvedilol decreases IDH and improves endothelial cell dysfunction. (Van Buren Peter N , Toto Robert , InrigJula [35],Van Buren Peter N , Toto Robert , InrigJula [48]) older patients, less haemoglobin, less npcr, less urine output, less serum bicarbonate level, higher carotid femoral pulse wave velocity and carotid augmentation index, correlated with IDH. Less urine output UO patients had increased sodium level and pulse pressure. Less bicarbonate level correlated with higher carotid femoral pulse wave velocity (Raikou, Vaia D., Kyriaki, Despina,et al[50]) Pre dialysis SBP, post-dialysis ECW/TW left ventricle volume is significantly associated with IDH Ren, H., Gong, D., He, X., Jia, F., He, Q., Xu, B. and Liu, Z.et al [53], excess ultrafiltrate volume significantly associated with IDH and less nitric oxide levels , less nitric oxide levels significantly associated with IDH in this study endothelin 1 levels and ADMA level not associated with IDH (Kandarini, Yenny, SuwitraKetutWidiana, Raka et al [54]. Pratik shete et al[55] diabetes mellitus , CKD duration, HD vintage pre- and post- HD SBP and DBP, serum cholesterol level, significantly correlated with IDH. age gender previous history of hypertension Frequency of HD Serum creatinine, haemoglobin, not associated with IDH. IDH prevalence higher could be because poor compliance antihypertensive drugs HD frequency two times weekly, and small sample size. Wajedmogal et al [56] pre- dialysis Systolic BP, after adjusting for gender, diabetes mellitus, HD vintage HD frequency, IDWG, serum cholesterol, types of anti-hypertensive drugs is significantly associated with HD. Bilateral renal artery stenosis cause of refractory IDH in a case report.Wolfmueller, Z., Goyal, K. & Prasad, B. et al[57] target weight has to kept above dry weight [flythe 58] age, duration of HD, ESA,amount of antihypertensive drugs not associated with IDH, while dry weight gain, UF goal volume statistically significantly associated with IDH D.P. Mulia, R.

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Irawan, M. Shanty, I. Trikandiani, F. Ariyanti, S. Sugihartono, F. Fahrizal, A. Permana, I. Effendi, Z. Ali, N. Suhaimi, S. Suprapti,et al [59]. Prabhu RA et al[60] observed type2 diabetes mellitus, undernourishment, inter-dialytic weight gain greater than 3 kg, dialysis vintage greater than 3 years significantly associated with IDH. Prasad B, Hemmett J, Suri R. et al[61] observed IDH Tend to occur in older age, lower serum albumin, lower kt/v, lower body mass index, greater use of antihypertensive medication. Prasad B, Hemmett J, Suri R.et al[61] observed IDH is seen in normal, low and high –volume status, Prasad B, Hemmett J, Suri R.et al [61] opined could be because greater refilling from interstitial space in fluid overloaded patients.[61]. Factors that increase total peripheral resistance especially in those with vessel stiffness cause IDH.[61]. Carvedilol can inhibit the release of ET-1 in endothelial cell cultures.(Saijonmaa O, Metsarinne K, Fyhrquist F et al [7]) intra dialytic hypotension associated with inadequate dialysis dose FlytheJ.E.XueH.Lynch K.E.et al.[45]Chang T.I.PaikJ.Greene T.et al[36].Shoji T.TsubakiharaY.Fujii M.et al[15]

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

2.1SOURCE OF DATA AND STUDY SETTING

Patients on Maintenance Hemodialysis in Dialysis Unit, Father Muller Medical College Hospital, Mangaluru, Karnataka State, India.

2.2SAMPLE SIZE CALCULATION

The sample size for estimation of prevalence is calculated using

$$n \geq \frac{z2^{\frac{1-\alpha}{2}} p(1-p)}{d}$$

$Z_{1\text{-alpha}/2}$ = 1.96 with 95% confidence Interval

P= Prevalence from Reference Study (2) =5%

d= margin of error =5%

n=71

A minimum of 71 patients will be included in the study.

2.3INCLUSION CRITERIA

Age 18 - 85 years

Patients on dialysis for more than 3 months

Previously diagnosed with Hypertension - Pre-Dialysis Blood Pressure >140/90 mmHg or Post-Dialysis Blood Pressure >130/80

Patients at target dry weight

2.4EXCLUSION CRITERIA

Oral/intra-venous antibiotic treatment within the past one month.

Active Malignancy

Not willing to participate.

2.5STUDY DESIGN AND DURATION

Cross-sectional Observational Study of Hypertensive Maintenance Hem dialysis patients who fulfill the inclusion criteria undergoing Hem dialysis for 6 consecutive treatment sessions in the hem dialysis unit.

A minimum of 71 patients in between August 1, 2023 to July 31, 2023 enrolled in this study

2.6 METHODOLOGY

Patients satisfying the inclusion criteria, on arrival to the Hem dialysis Unit, seated comfortably in a chair and questioned about the pertinent clinical history and the same

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recorded. Latest available laboratory parameters entered in the data sheet. The weight of the patient is then recorded using an electronic weighing scale. The blood pressure measured by staff nurse/dialysis technician or a doctor.The patient is then made to lie down supine in bed. Manual BP measured and recorded using a mercury sphygmomanometer before insertion of dialysis access needles on patients on dialysis through A V Fistula.On completion of Hem dialysis, before removing access needles, post HD Blood Pressure is measured and recorded while the patient is in the supine position.The patient is allowed to stand and Post Hem dialysis Weight is checked by making the patient stand on the electronic weighing scale.For each patient, this procedure routine is repeated during the next 5 consecutive hem dialysis sessions. STATISTICAL ANALYSISData analyzed as percentage for categorical variables and mean and standard deviation for continuousvariables. Proportions compared using chi-square test and mean compared using student t test. All analysis done using SPSS software

3. RESULTS AND DISCUSSION

3.1RESULTS

Results of 71 patients were analyzed.

Frequency percentage distribution analyzed for Categorical variables

Table1 Categorical variables -frequency distribution percentages

Gender	female	23	male	48
HD sessions frequency/week	three	33	two	38
Loop Diuretic use yes/no	no	53	yes	18
Intra-dialysis hypertension in 4 out of 6 consecutive session IDH yes/no	no	29	yes	42
Type2 diabetes mellitus yes/no	no	42	yes	29
Htn hypertension yes/no	no	06	yes	65
Hypothyroidism yes/no	no	70	yes	1
IHD ischemic heart disease yes/no	no	63	yes	8
Compliance with Oral anti hypertension medication use before dialysis session yes /no	no	64	yes	7
Alpha–adrenergic receptor blocker use yes/no	no	63	yes	8
Beta adrenergic receptor blocker use yes/no	no	55	yes	16
Alpha plus beta adrenergic receptor blocker use yes/no	no	50	yes	21
RAS Renin Angiotensin System inhibitor-Angiotensin converting enzyme inhibitor	no	-	yes	-
RAS Renin Angiotensin System inhibitor - angiotensin receptor blocker ARB use yes/no	no	70	yes	1
Central sympatho-lytic Clonidine or Moxonidine use yes/no	no	40	yes	31
calcium channel blocker use yes/no	no	22	yes	49
Diltiazem use yes/no	no	70	yes	1
Direct acting vasodilator Minoxidil use yes/no	no	70	yes	1
Direct acting vasodilator Hydralazine	no	70	yes	1

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excluding Isolazine use yes/no				
Direct acting vasodilator Hydralazine including Isolazine use yes/no	no	63	yes	8
Isosorbidedinitrate – hydralazine combination tablet use Isolazine use yes/no	no	64	yes	7

Association of categorical variable intra dialytic hypertension to other parametric categorical variables analyzed using chi-square test, to non parametric variables using Fischer exact test.

Table 2 Association of each categorical variable with IDH Chi-square test /Fischer's exact test

Table 2		
Categorical variable	value	***P***
Gender male vs female	0.686	.41
Type 2 diabetes mellitus yes/no	1.295	.26
Hypertension yes/no	1.410	.24
Hypothyroidism yes/no	1.309	.25
IHD ischemic heart disease yes/no	3.6	.06
HD frequency/week two sessions vs three sessions	4.79	.03
Compliance Oral anti hypertension medication use before HD session compliance yes/no	2.724	.1
Alpha beta adrenergic receptor antagonist yes/no	0.093	.76
RAS inhibitor- Angiotensin converting enzyme inhibitor	-	-
RAS inhibitor - angiotensin receptor antagonist ARB	1.309	.25
Beta adrenergic receptor antagonist yes/no	0.787	.36
Central sympatho-lytic Clonidine or Moxonidine use yes/no	1.679	.19
Loop diuretic use yes/no	2.473	.12
Alpha adrenergic receptor antagonist use yes/no	0.313	.58
Calcium channel blocker use yes/no	6.853	.009
Direct acting vasodilator Hydralazine use yes/no	0.313	.58
Direct acting vasodilator Minoxidil use yes/no	0.786	.38
diltiazem	0.786	.38
IsosorbideDinitrate-hydralazinehydrochlorideIsolazine use yes/no	0.719	.4

Table 3 Mean and standard deviations are calculated for continuous variables.

Table 3		
Continuous numerical variable	Mean	Standard deviation
Age in years	57.034	13.1930
Hemoglobin level in g/dl	10.404	1.8222
Albumin llevelin g/dl	3.823	.4867
Hemodialysis Vintage in months	48.69	41.001
Serum Creatinine level in mg/dl	9.828	2.8836
serum sodium level in mEq/L	138.32	3.541
K serum potassium level in mEq/L	5.013	.8108

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Serum Bicarbonate level in mg/dl	20.455	4.0580
Serum Calcium level in mg/dl	8.203	.8457
Serum Phosphorus level in mg/dl	5.855	1.8335
Alkaline phosphotase level in mg/dl	144.69	90.206
Dry weight in Kgs	54.631	11.4019
Pre-dialysis weight in Kgs	58.4532	11.88017
post dialysis weight in Kg	55.1870	11.62593
Intra-dialysis weight loss in Kg	3.2361	0.95275
Pre- dialysis mean systolic BP in mmHg	-	-
Pre- dialysis mean diastolic BP in mmHg	-	-
Post- dialysis mean systolic BP in mmHg	-	-
Post- dialysis mean diastolic BP in mmHg	-	-
Post dialysis systolic BP minus pre-dialysis systolic BP in mmHg	4.8826	19.81727
Post-dialysis diastolic BP minus pre-dialysis diastolic BP in mmHg	1.1737	6.08403

Association of each continuous parametric variable to categorical variable intra-dialysis hypertension IDH yes or no- analyzed using student t- test

Table4. Association of IDH with Numerical variables analyzed using student t-test.

Table 4		
Continuous numerical variable	Student t test value	***P***
Age in years	0.166833267000971	.87
Vintage in months	1.43571992207052	.16
Inter dialysis Hemoglobin level in g/dl	1.64650142096256	.10
Inter dialysis Albumin level in g/dl	0.665233254254108	.51
Inter dialysis Serum Creatinine level	0.173203437951382	.86
Inter dialysis Serum total calcium level	1.29624655909213	.2
Inter dialysis Serum phosphorus level	1.83525993326298	.07
Inter dialysis Serum alkaline phosphotase level	0.71744277853745	.48
Inter dialysis Serum bicarbonate level	-0.277366373997268	.78
Inter dialysis Serum sodium level	-0.229889568163969	.82
Inter dialysis Serum potassium	2.11487715207016	.04
Dry weight	1.87735000996512	.06
Pre-dialysis weight	1.79674649800867	.08
Post- dialysis weight	1.8616572180599	.07
Intra-dialysis weight loss IDWL =UF	-0.33883631060996	.74
Pre- dialysis mean Systolic BP mmHg	-0.80832883701688	.42
Pre- dialysis mean Diastolic BP mmHg	-0.226245641661444	.82
Post- dialysis mean Systolic BP mmHg	-7.98672327422955	.001
Post dialysis mean Diastolic BP mmHg	-5.17947095990307	.001

3.2DISCUSSION

frequency of IDH occurrence is 59.2 % in this maintenance hemodialysis [MHD] study population,while another recent single center study from south India showed prevalence

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57%Prabhu RA et al [60]. IDH occurrence is not correlating with gender in this study while also not correlating with gender in Pratik shete et al study [55], D.P.Mulia et al study [59], and Mujtaba F et al [63] study. IDH is significantly associated with dialysis frequency number of sessions two/three per week in this study while Pratik shete et al study [55] found IDH is not significantly associating with dialysis frequency. IDH occurrence is not associating with type2 diabetes mellitus in this study population while Pratik shete et al [55], Prabhu RA et al [60] found type2 diabetes mellitus significantly associating with IDH. VajedMogal et al study [56] and also Mujtaba F et al [63] study not found correlation between IDH and type 2 diabetes mellitus occurrence. IDH occurrence is not associating with hypertension in this study population while IDH occurrence is not correlating with hypertension occurrence in Pratik shete et al [55], VajedMogal et al study [56], D.P.Mulia et al study [59], and Mujtaba F et al [63] study. IDH occurrence is not correlating with Ischemic heart disease IHD occurrence in this study population while IDH occurrence is not correlating with IHD in VajedMogal et al study [56], Mujtaba F et al [63] study. While Mujtaba F et al [63] study found 85.5 % study population compliant with oral anti hypertensive medication, only 9.9 percent of our study population was using oral anti hypertensive medication before hem-dialysis session while the rest of them were not using. Compliance was checked by interviewing the patients. This method of checking compliance may have recall and response bias. Intra-dial tic hypertension occurrence is significantly correlating with Calcium channel blocking drug use in this study. Hem-dialysis may not remove CCBs which are among non dialyzable oral anti-hypertensive medications and therefore CCB use is able to correlate with IDH occurrence in our study while VajedMogal study [56] did not find significant association between calcium channel blocker use and IDH. IDH occurrence is not correlating with alpha plus beta adrenergic receptor blocking drug use in this study while IDH occurrence is correlating with non dialyzable beta blockers [alpha plus beta adrenergic receptor blocking drug use in Van Buren PN, Toto R, Inrig JK et al [37] study IDH occurrence is not correlating with alpha adrenergic receptor blocking drug use in this study while IDH occurrence is not correlating with alpha adrenergic receptor drug use in VajedMogal et al [56] study, Mujtaba F et al [63] study IDH occurrence is not correlating with beta adrenergic receptor blocking drug use in this study while beta adrenergic receptor blocking drug use is not associated with IDH in VajedMogal et al study [56], Mujtaba F et al [63]study. IDH occurrence is not correlating with loop diuretic use in this study while study where correlation between IDH occurrence with loop diuretic use is lacking. IDH occurrence is not correlating with central sympatho-lytics clonidine, moxonidine use in this study while IDH occurrence is not correlating with central sympatho-lytic use clonidine, moxonidine use in VajedMogal et al [56] study. IDH occurrence is not correlating with hydralazine use in this study while IDH occurrence is correlating with vasodilator use in Mujtaba F et al [63] study. Correlation of IDH occurrence with Angiotensin converting enzyme inhibiting drug use Angiotensin receptor blocking drug use cannot be assessed in this study as only one patient is using this drug among our study subjects. While IDH not correlating with ACE inhibitors / ARB use in Mujtaba F et al [63] study Correlation of MRA mineral corticoid receptor antagonists on IDH occurrence is not able to study as none of our study patients are using this class of drugs. Correlation of thiazide diuretics and IDH occurrence could not be studied as none of this study patients are using this class of drugs. Correlation of minoxidil on IDH occurrence could not be analyzed for statistical significance in this study because only one patient in this study

population is using this drug. While Mujtaba F et al [63] study found IDH occurrence is not correlating with vasodilator use.

Among numerical continuous variables, IDH occurrence is significantly correlating with post dialysis mean Systolic BP in our study and Pratik shete et al study [55] IDH occurrence is significantly correlating with post dialysis mean diastolic BP in this study and Pratik shete et al study.[55] IDH occurrence is not correlating with age in this study and Pratik shete et al study[55], D.P.Mulia study[59], while Mujtaba F et al [63] study found is correlating with age. IDH occurrence is not correlating with hem dialysis vintage in this study, Pratik shete et al study[55],also Mujtaba F et al, [63]study found IDH is not correlating with vintage. IDH occurrence is not correlating with inter dialysis serum creatinine level in our study while and Pratik shete et al study [55] study also found not correlating with serum creatinine level. IDH occurrence is not correlating with serum albumin level while Zou LX, Sun L et al [72] found study found IDH correlating with serum albumin level. Grangé S et al [73] studied serum albumin level in MHD patients and opined the need to define intra dialysis hypertension IDH definition. IDH occurrence is not correlating with Hemoglobin level in this study while Zou LX, Sun L et al [72] found hemoglobin level is correlating with IDH. Pratik shete et al [55] study found IDH not correlating with hemoglobin level. Grangé S et al [73] studied hemoglobin level and opined the need to define IDH hypertension definition. IDH occurrence is found not correlating with serum sodium level in this study while Van Buren PN, Inrig JK et al [70] study found difference from dial sate to serum sodium level is correlating with IDH. IDH occurrence is found significantly correlating with serum potassium level in this study while Choi CY, Park JS, Yoon KT, Gil HW, Lee EY, Hong SY..et al [71]study found IDH mortality correlating with low serum potassium level. IDH occurrence is not correlating with serum bicarbonate level in this study while Grangé S et al [73] study serum bicarbonate level opined the need to define hypertension IDH. IDH is found not correlating with serum total calcium level while Grangé S et al [73] studied serum calcium level and opined the need to define hypertension in hem dialysis patients. IDH is found not correlating with Serum Phosphorus level in this study while Grangé S et al [73] study serum phosphorus level and opined the need to define hypertension IDH. IDH is not correlating with ideal weight in this study while Zou LX, Sun L et al [72] found dry weight is correlating with IDH. D.P.Mulia et al [59] study found is correlating with dry weight gain UF goal volume. IDH is not correlating with pre dialysis weight while Ren H, [53] et al study found proportion of extracellular water to total body weight (extra-cellular water ECW/ total body water TW), as evaluated by bio-impedance analysis [BIA], was significantly higher in the IDH group than in the other three groups both in pre-and post-dialysis. IDH is not correlating with post dialysis weight in this study while Zou LX, Sun L et al [72] study found IDH is correlating with post dialysis weight. Mujtaba F et al [63] study found inter-dialysis weight gain is not correlating with IDH. Zou LX, Sun L et al [72] found higher IDWG, % post dialysis body weight is correlating with IDH ,Prabhu RA et at study [60] found IDWG more than 3 kg is found significantly associated with IDH. IDH is not correlating with pre dialysis Systolic BP in this study while Pratik shete et al study[55], found IDH is correlating with pre dialysis systolic BP, VajedMogal et al [56] also found pre dialysis systolic BP is found significantly associated with IDH Mujtaba et al[63] study found IDH is not correlating with pre dialysis systolic BP. IDH is not correlating with pre dialysis diastolic BP in this study , while Pratik shete et al study[55] found IDH is correlating with pre dialysis systolic BP,

LIMITATIONS

Small sample size is limitation in this study. many patients not using oral anti-hypertensives before dialysis session is limitation in this study.

CONCLUSION

Intradialytic hypertension is multi-factorial. occurrence of IDH in this study is not significantly associated with gender, type 2 diabetes mellitus, age, hem dialysis vintage, serum creatinine level, pre dialysis weight, Intra dialysis weight loss, pre dialysis mean systolic BP, pre dialysis mean diastolic BP, IDH occurrence of IDH in this study is significantly associated with post dialysis mean BP, post dialysis mean diastolic BP, inter-dialysis serum potassium level and calcium channel blocking drug use.nitrogen balance, sodium ion movement, water movement between intracellular, ecf and intravascular compartments inter-dialytic weight gain, pre-dialysis weight intra-dialytic weight loss post dialysis weight dry weight endothelial dysfunction, vasoconstriction influence, vasodilatation influence, changes in diastolic lv filling, changes in systolic function, compliance with oral antihypertensive medication use, frequency of non dialysable oral antihypertensive medications use and other unknown factors might be operating to cause this phenomenon**.**

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COMPETING INTERESTS

Author has declared that no competing interests exist.

CONSENT

Authordeclares that 'written informed consent was obtained from the patient for publication of this original research article.

ETHICAL APPROVAL

The research study approved by the institutional review board at father muller institutional ethics comittee, number fmmciec/ccm/537/2022, dated 28.07.2022.

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DEFINITIONS, ACRONYMS, ABBREVIATIONSDEFINITIONS

INTRADIALYTIC-HYPERTENSION: Intra-dialysis-Hypertension is defined as the increase in Systolic Blood Pressure greater than 10mmHg from Pre- Hem dialysis to Post-hem dialysis in hypertensive maintenance hem dialysis patients in at least four of out six consecutive hem dialysis treatments.

DRY WEIGHT: Dry weight is defined as the level below which further fluid removal would produce hypotension, muscle cramps, nausea, and vomiting. This weight will be decided by the treating nephrologists.

HYPERTENSION IN DIALYSIS: Hypertension in dialysis patients is defined as a midweek median intra-dialysis blood pressure greater than 140/80 mmHg

ABBREVIATIONS

LV left ventricle
BP-Blood pressure
IDH Intradialytic Hypertension
HD hemodialysis
MHD maintenance Hemodialysis
SBP Systolic Blood Pressure
DBP Diastolic blood pressure
NO Nitric Oxide
ADMA asymmetric di methyl arginine
ECW extra-cellular water
ICW Intra- cellular water
TW total body water
TBW total body water
IDWL intradialytic weight loss
IDWG interdialytic weight gain
BIA bio impedance analysis
BISbioimpedance spectroscopy
RAS renin angiotensin system
ACE angiotensin converting enzyme
ACEI angiotensin converting enzyme inhibitors
ARB angiotensin receptor blocking medication

APPENDIX

UNDER PEERREVIEW