



ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF INTERNAL MEDICINE

**THESIS ON “PREVALENCE OF INTRADIALYSIS HYPERTENSION AND
THE ASSOCIATED RISK FACTORS IN PATIENTS WITH HYPERTENSION
AND ESRD UNDERGOING MAINTENANCE HEMODIALYSIS IN THREE
HEMODIALYSIS CENTERS AT ADDIS ABABA : A RETROSPECTIVE
CROSS SECTIONAL STUDY“**

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**A THESIS TO BE SUBMITTED TO ADDIS ABABA UNIVERSITY,
COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, AND
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PARTIAL FULFILLMENT OF THE REQUIREMENT FOR A SPECIALTY
CERTIFICATE IN INTERNAL MEDICINE**

ABBREVIATIONS

IDH (Intradialysis hypertension)

MHD (maintenance hemodialysis)

HD (hemodialysis)

UF (ultra filtration)

DM (diabetes mellitus)

T2DM (type 2 diabetes mellitus)

HTN (hypertension)

ESRD (end stage renal disease)

RAAS (renin-angiotensin-aldosterone system)

EPO (erythropoietin)

ABSTRACT

BACKGROUND: Intradialytic hypotension is an established, common, and risky complication of hemodialysis.⁽¹⁾ However, hypotension is only 1 component of the abnormal hemodynamic response to ultra filtration dialysis; the opposite phenomenon, that is, paradoxical rise in blood pressure (BP) during or immediately after dialysis, intradialytic hypertension is equally common and associates with adverse cardiovascular outcomes. (1, 2) IDH affects 5-15% of patients. (1) The pathophysiologic of IDH is complex and not fully understood, but several factors are thought to play a role, including volume overload, RAAS activation, endothelial dysfunction, and sympathetic over activity. (1)

OBJECTIVE: the aim of the study is to assess prevalence of Intradialysis hypertension (IDH) and the associated factors with it in three private HD centers

Secondary objective: to assess the prevalence of Intradialysis hypotension

DESIGN: Retrospective cross sectional study

METHODOLOGY: study population was all ESRD patients on maintenance hemodialysis aged 18 and above who meet inclusion criteria and were willing to participate in the study. Blood pressure was recorded for all patients at pre-dialysis, 1st, 2nd, 3rd and post dialysis time for the last consecutive 6 sessions. Blood pressure records are by the HD machine and if unexpectedly high it will be confirmed by manual BP device (sphygmomanometer). Demographic and other clinical data were collected from patient charts and by interviewing patients. Data analysis was done by SPSS26. The factors associated with IDH will be researched using a univariate logistic regression model. The significance threshold for all statistical tests has been set at 5%. A P value of less than 0.05 is considered significant.

RESULT: our study included 156 patients and analyzed 936 HD sessions over three week's period. Close to half of the patients (49.4%) are between 40-60 years of age. Males accounted for 65.4%, females 34.6%. Diabetes mellitus was present in 28.2% (44) of the patients. Majority of the participants were on MHD for more than a year (1-2 years (30.8%), \geq 2 years (34.6%). 69.9% (109) of the participants underwent twice per week of MHD while 27.6% (43) underwent thrice per week of MHD. A single session of HD lasts for 3.5hrs in 75% of the cases and the rest for 4hrs. Mean ultra-filtration rate of \geq 13ml/kg/hr was prevalent in 42.3%. The mean pre HD SBP of 140-160mmhg accounted for 41% and SBP $>$ 180 in 7.7%. 42.9 % (67) of the participants were on dual antihypertensive.

Prevalence of IDH was 27.6 % (43) and intradialytic hypotension was found in 648 sessions out of 936 sessions of HD (69.2%). The single factor affecting IDH was ultra filtration rate.

CONCLUSION: our study showed that IDH is very prevalent in our set up and it is more common in those with lower ultra filtration rate. The prevalence of higher ultra filtration rate is very high close to half of patients had rate of \geq 13ml/kg/hr.

KEY WORDS: intradialytic hypertension, intradialytic hypotension, end stage renal disease, maintenance hemodialysis

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1- INTRODUCTION

Intradialytic hypotension is an established, common, and risky complication of hemodialysis.¹ However, hypotension is only 1 component of the abnormal hemodynamic response to ultra filtration dialysis; the opposite phenomenon, that is, paradoxical rise in blood pressure (BP) during or immediately after dialysis, intradialytic hypertension is equally common and associates with adverse cardiovascular outcomes. During HD, blood pressure (BP) changes occur frequently and large variability in BP is a risk factor for increased mortality in these patients. Although the phenomenon of BP rise during hemodialysis is recognized for several years, there are no accepted criteria to define intradialytic hypertension. The current agreed upon definition is a rise in SBP of 10mmhg or more from pre to post HD time.(1,2)

Effective peri-dialysis blood pressure and other cardiovascular function control is necessary for the delivery of an adequate dialysis dose and attainment of optimal clinical outcome.

A prevalence of \approx 5% to 15% is reported from western data whereas higher numbers (from 20-48%) are reported from studies done in Africa.(6,7,8,9) IDH is associated with increased cardiovascular events and death(US Renal Data System Dialysis Morbidity and Mortality Wave II cohort reported that each 10–mm Hg rise in SBP from pre to post dialysis underlies a 12% excess risk for all-cause mortality during a mean follow-up of 2 years (hazard ratio [HR], 1.06; 95% CI, 1.01–1.12).(2)

Possible pathophysiologic mechanisms include:

- (i) Fluid overload,
- (ii) Renin Angiotensin Aldosterone System (RAAS) and sympathetic nervous system over activation,
- (iii) Removal of antihypertensive medications during dialysis,
- (iv) Endothelial dysfunction,
- (v) Electrolyte imbalance involving dialysate sodium, calcium or potassium,
- (vi) Treatment with erythropoietin.

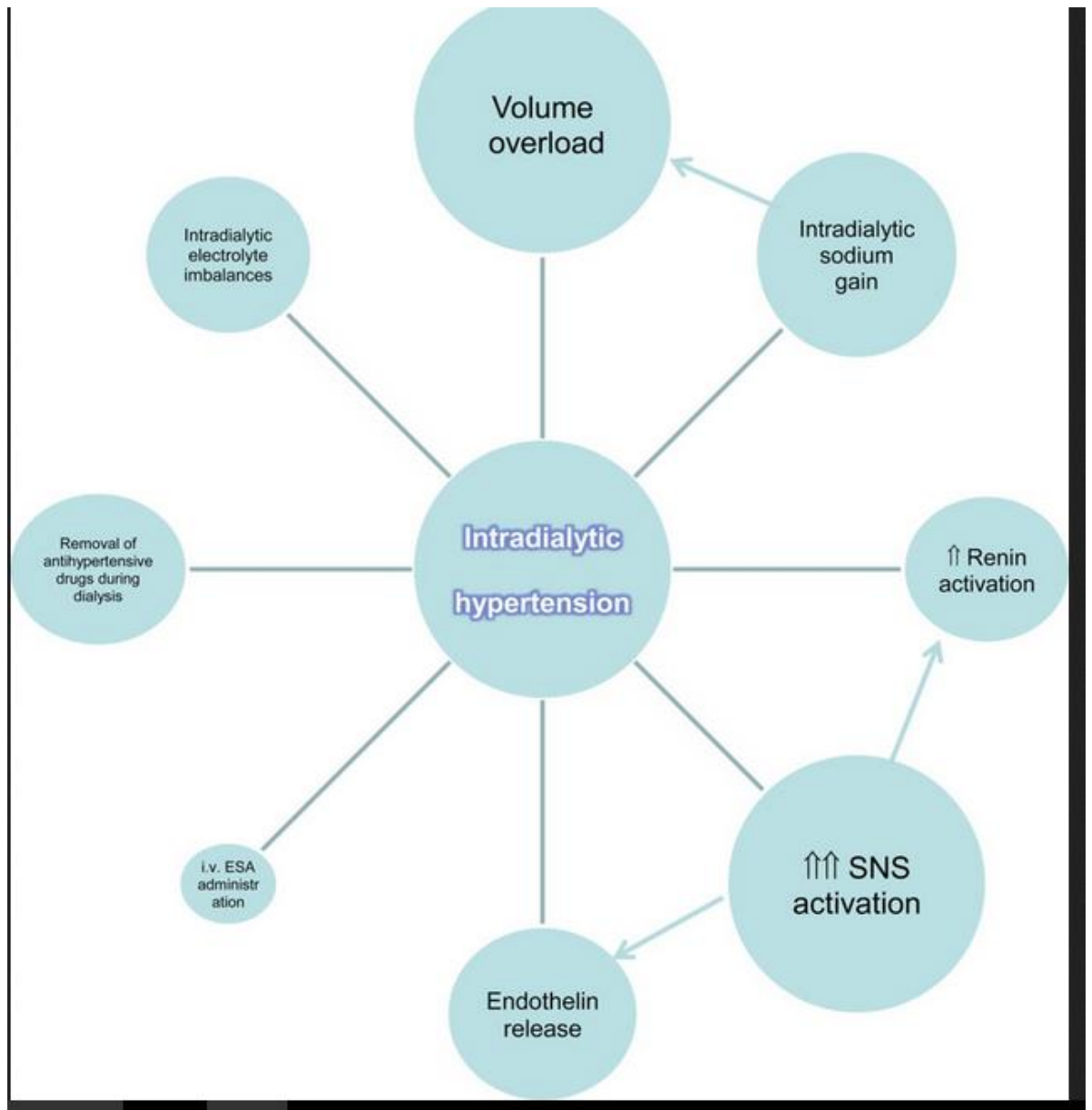


FIGURE 1; PATHOPHYSIOOLOGY OF IDH(1)

1.1 SIGNIFICANCE OF THE STUDY:

Despite its high prevalence and association with adverse cardiovascular outcomes data on this entity is nonexistent in our country. Thus the aim of this study is to assess the prevalence and associated factors of IDH in ESRD who are hypertensive and undergoing MHD.

Table 1: Association between IDH and cardiovascular outcomes(4)

Table 2. Prospective Observational Studies Associating Intradialytic Hypertension With Increased Risk of Mortality					
Study ID	Patients	Follow-Up	Predictor	Outcome	Risk
Inrig et al ⁹ <i>Kidney Int</i> 2009	438 dialysis patients participating in the CLIMB study	6 mo	Δ SBP from pre to post dialysis ≥ 10 mm Hg	Combined end point of non-dialysis-related hospitalization or all-cause mortality	OR, 2.17; 95% CI, 1.13–4.15
Inrig et al ³ <i>AJKD</i> 2009	1748 hemodialysis patients participating in the USRDS Dialysis Morbidity and Mortality Wave II study	2 y	Δ SBP from pre to post dialysis	All-cause mortality	HR, 1.12; 95% CI, 1.05–1.21 per 10 mm Hg increase in SBP during dialysis
Yang et al ¹² <i>BMC Nephrol</i> 2012	115 prevalent dialysis patients	4 y	Δ SBP > 5 mm Hg from pre to post dialysis	All-cause mortality	HR, 3.925; 95% CI, 1.410–10.846
Park et al ¹³ <i>Kidney Int</i> 2013	113 255 prevalent dialysis patients	2.2 yr	Δ SBP from pre to post dialysis	All cause mortality Cardiovascular mortality	Intradialytic reduction in SBP > 30 mm Hg and any rise in SBP during dialysis were both associated with increased risk of all-cause and cardiovascular mortality

Δ SBP indicates change in systolic blood pressure; CI, confidence interval; CLIMB, Critic-Line Intradialytic Monitoring Benefit study; HR, hazard ratio; OR, odds ratio; and USRDS, US Renal Data System.

2- METHODS

2.1 OBJECTIVES

2.1.1 General objectives

- To assess prevalence and risk factors for IDH in ESRD patients with hypertension.

2.1.2 Specific objectives

- 1- To determine the prevalence of IDH
- 2- To assess risk factors for IDH
- 3- To assess comorbidities in ESRD patients
- 4- To assess how prevalent Intradialysis hypotension is

2.2 STUDY SETTING: our study is done on three private HD centers

- 1) Ethio Tebib general hospital- is one of the private hospitals in Addis Ababa delivering multispecialty services both inpatient and outpatient. It has a dedicated HD unit having 10 machines (one dedicated to medical ICU). Currently it has enrolled 88 patients on MHD + cases of AKI (variable number based on cases).
- 2) Yerer general hospital: is one of the private hospitals in Addis Ababa delivering multispecialty services both inpatient and outpatient. It has a HD unit equipped with 08 HD machines. Currently it enrolls around 75 MHD patients + cases of AKI
- 3) Tom HD center: is one of the largest private owned dedicated HD center. It has close to 25 HD machines working in 2-3 shifts. currently it has enrolled close to 90 patients. All of the centers had trained HD nurses, GP and nephrologists.

2.3 STUDY POPULATION: all adults above the age of 18 years with ESRD + hypertension on MHD attending the 3 HD centers.

2.3.1 Inclusion criteria:

- Age \geq 18 years
- Willing to participate in the research
- diagnosed to have hypertension
- On MHD for $>$ 1 month

2.3.2 Exclusion criteria:

- not willing to participate in the research
- patients with acute kidney injury
- patients hospitalized recently over the last 1 month

2.4 OPERATIONAL DEFINITION:

IDH- increase in systolic blood pressure by at least 10mmhg from pre to post-hemodialysis readings in a minimum of four out of 6 consecutive HD sessions.

Intradialysis hypotension- a decrease in systolic blood pressure \geq 20 mmHg or a decrease in mean arterial pressure by 10 mmHg

MHD: on HD for at least 1 month

Sample size: convenient sampling was used so all eligible patients were included.

2.5 DATA COLLECTION: after getting ethical clearance from the ethical board of AAU data was collected from January 10th to February 20th 2024. Socio-demographic data (including age, sex, address and educational status): comorbidities (diabetes mellitus, hypertension, cardiac, stroke, RVI, other): duration on HD: frequency of HD per week, ultra filtration volume and rate, pre HD weight & weight gained between HD sessions: number & type of antihypertensive with their doses, timing of antihypertensive on the day of HD: EPO use, frequency and dosage: transfusion during the 6 sessions if any.

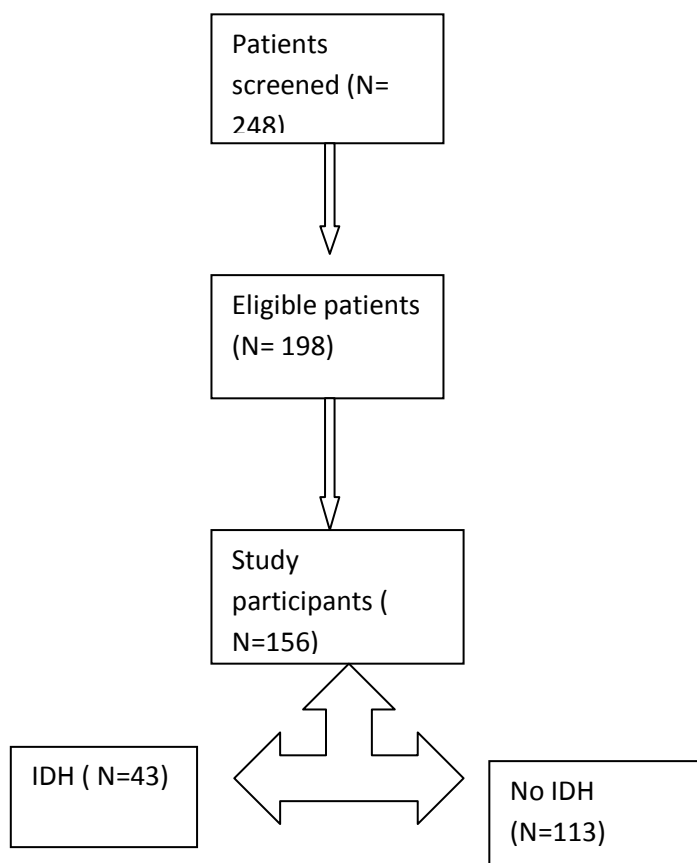
At each session BP was measured on the arm without vascular access using an automatic manometer supplied with the dialysis generators, if needed confirmed by manual measurement. The first measurement was performed five to ten minutes before the beginning of the session, after a resting period of at least fifteen minutes and before the needle insertion. The measurements were then made every hour and the last one at the end of the session and after completion of the session. The pre-HD and maximum and minimum SBP were tabulated on the questionnaire.

2.6 STATISTICAL ANALYSIS: Data was collected by general practitioners working in the respective units using standardized questionnaires.

All data was accounted for and analyzed using SPSS version 26. Categorical data was analyzed and displayed as frequencies and proportions. While continuous data was analyzed and displayed as mean and standard deviation. Chi square test was used to test the association between IDH and selected characteristics. Initial association was looked for using bivariate analysis with each independent variable and those variables with p value < 0.05 were again analyzed using multivariate analysis. Prevalence of IDH was analyzed using the aforementioned definition I.e. four or more of the six sessions showing rise in SBP \geq 10mmhg.

Mean of the pre dialysis SBP, ultra filtration volume, ultra filtration rate and weight gained between dialysis sessions was used for analysis.

FIGURE 2: FLOW CHART



3. RESULT:

A total of 165 patients were recruited but 9 were excluded from final analysis because of incomplete data. So 156 patients were included in the final analysis. Males accounted for 65.4 % (102/156) and females for 34.6 % (54/156). Almost half were between the ages of 40-60 (49.4 % (77/156)), 31.4% between 18-40 years and 19.2% are above 60 years of age. Most of the patients were residents of Addis Ababa (91%), the rest 9 % (14/156) were from different parts of the country. Diabetic patients accounted for 28.2% (44/156). Only one patient had RVI diagnosis.

More than 2/3rd of patients were undergoing twice per week of HD (69.9%, 109/156), 27.6 % (43/156) were undergoing thrice per week of HD and 2.6 % (4/156) underwent once per week. In 75% (117/158) of the patients the HD was lasting 3.5hrs and the remainder 25 % (39/156) for 4 hrs. The duration of HD lasted for <6months in 13.5 % (21/156), 6months- 1year (21.2%, 33/156), 1-2 years (30.8%), >= 2 years 34.6%). In more than 2/3rd of patients(67.9%, 106/156) the mean UF volume was more than the mean weight gained between HD sessions, 10.9%(17/156) had equal mean UF volume and weight gained between HD sessions and the remainder 21.2% (33/156) had under filtration (lower mean UF volume compared with mean weight gained). Mean ultra filtration rate of 13ml/kg/hr or more was present in 42.3 % (66/156).

No antihypertensive was being taken in 9.6% (15/156) of the patients, single antihypertensive 38.5 % (60/156), dual 42.9 % (67/156), triple 7.7 % (12/156) and quadruple 1.3 % (2/156). Seventy patients (44.9%) were not taking antihypertensive on the day of HD at all whereas the rest 55.1 % (86/156) do take the antihypertensive. Of those who took antihypertensive the commonest time

was after HD 75.6%, followed by both before and after HD (15.1%) and some were taking before HD session 9.3%.

Erythropoietin was being given in just 16 % (25/16) of the patients. Of those who took EPO most were taking it once per week (40%, 10/25), followed by thrice weekly 36 % (9/25), lastly twice per week in 24% (6/25).

No RBC transfusion during the study period.

The most common pre dialysis SBP was 140-160mmhg accounting for 41 % (64/156) followed by equal contribution 120-140 and 160-180mmhg each accounting for 22.4% (35/156 each).

The prevalence of **IDH** is **27.6% (43/156)**. **The only factor affecting IDH was UF rate of < 13ml/kg/hr (RR 3.69 95% CI (1.595- 8.54) p value 0.002).**

Intradialysis hypotension was seen in 648 sessions out of 936 sessions of HD (69.2%). **The only association was with duration of HD 4hrs having lower risk as compared to 3.5hrs (0.245 95% CI (0.084- 0.719) p value of 0.01).**

TABLE 2: SUMMARY OF DEMOGRAPHIC DATA

Variable		Frequency	Percentage (%)
Age distribution	18- 40	49	31.4
	40-60	77	49.4
	>60	30	19.2
Sex	Male	102	65.4
	Female	54	34.6
Place of residentship	Addis Ababa	142	91%
	other	14	9%
Educational status	Elementary	23	14.7
	High school	59	37.8
	Diploma	24	15.4
	Degree	42	26.9
	Masters/P HD	1	.6
	not educated	7	4.5
Comorbidities	Diabetes	44	28.2
	Stroke	2	1.3
	RVI	1	0.6

FIGURE 3: AGE

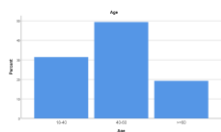


FIGURE 4: GENDER

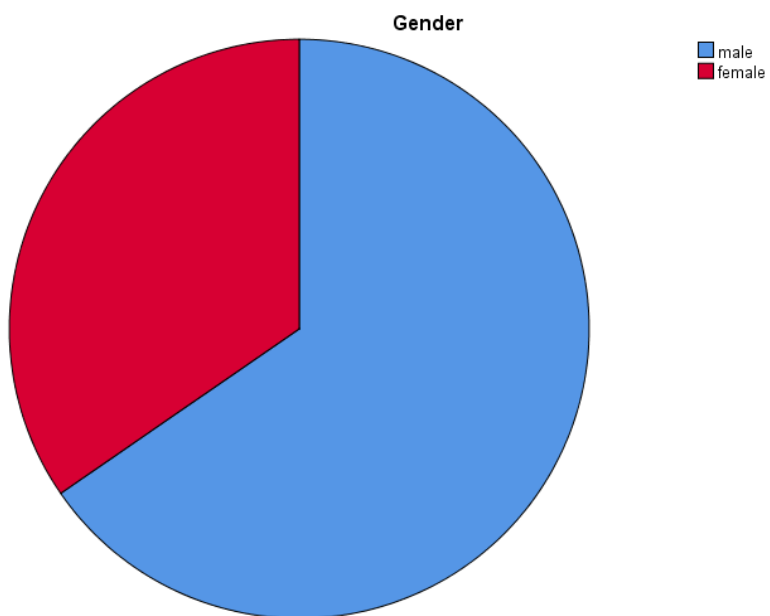


FIGURE 5: FREQUENCY OF DIALYSIS

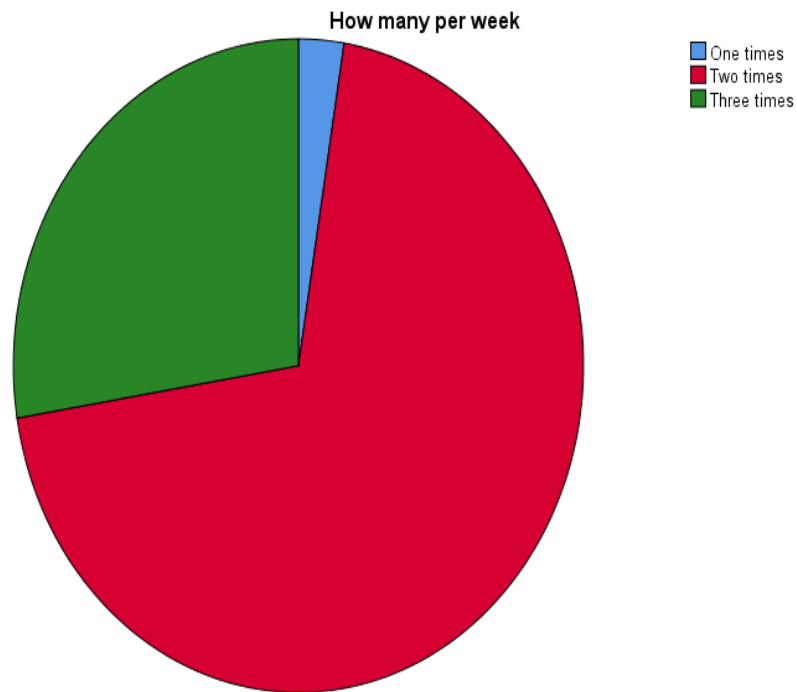


FIGURE 6: ULTRAFILTRATION RATE

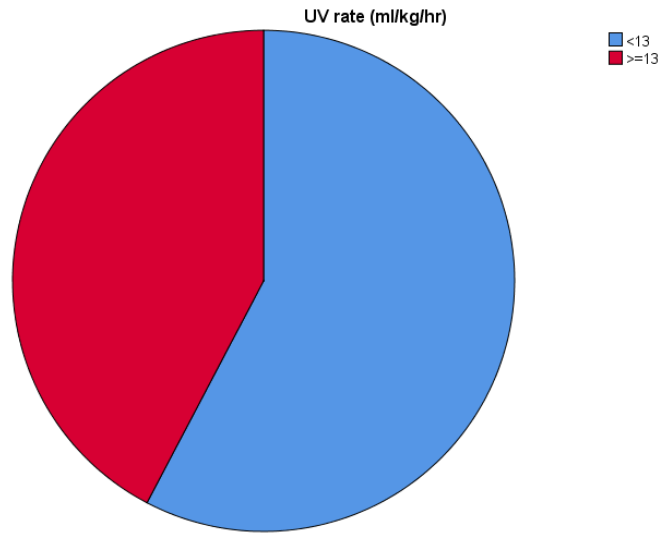


FIGURE7: NUMBER OF YEARS ON DIALYSIS

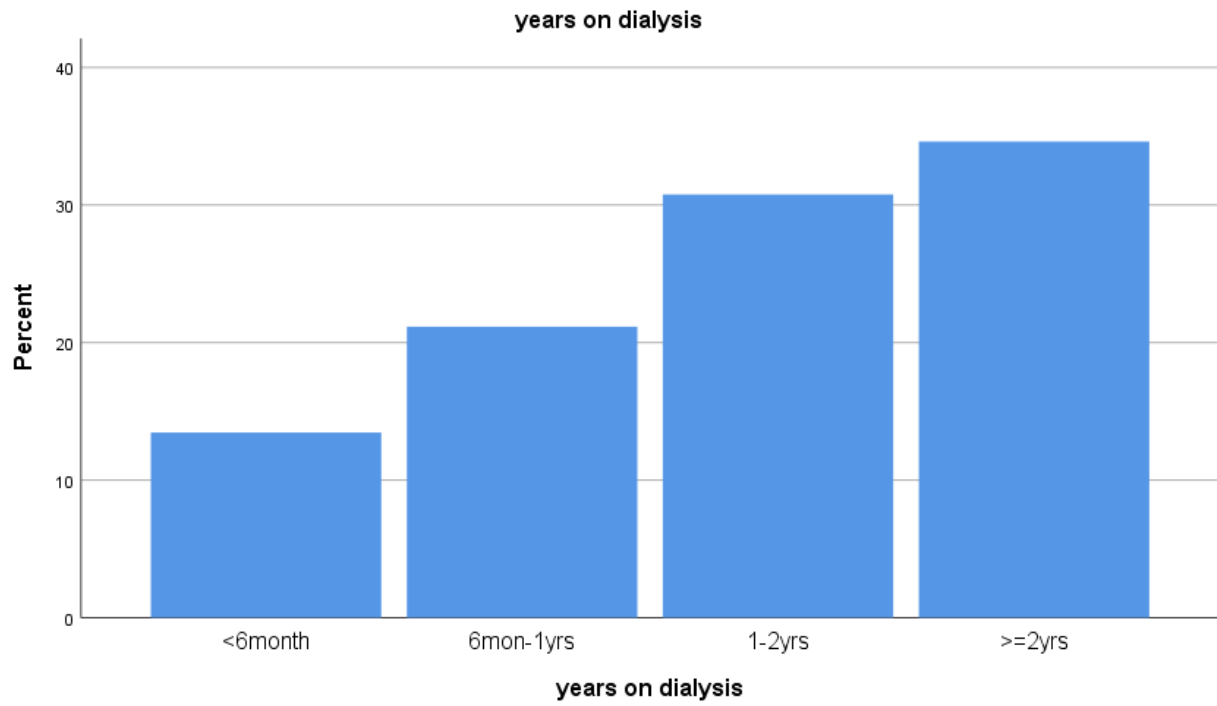


FIGURE 8: HOW MANY OF THE PATIENTS TAKE THE ANTIHYPERTENSIVE ON THE DAY OF HD

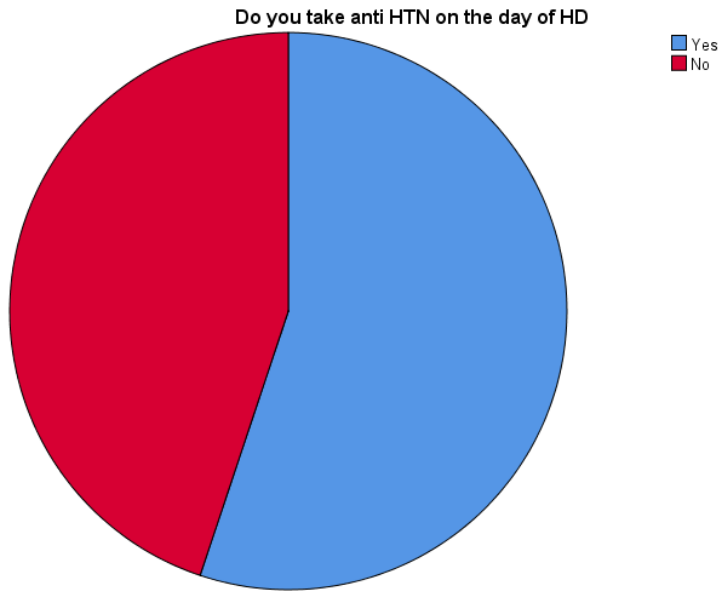


FIGURE 9: NUMBER OF ANTIHYPERTENSIVE

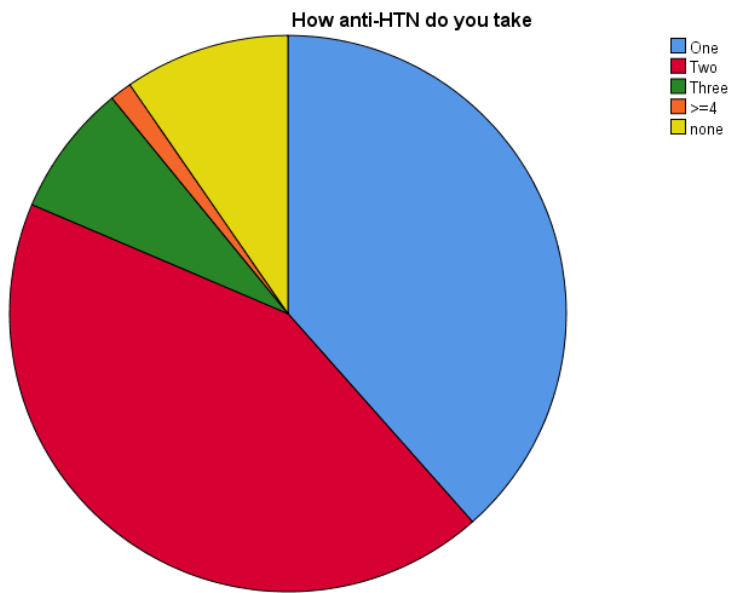
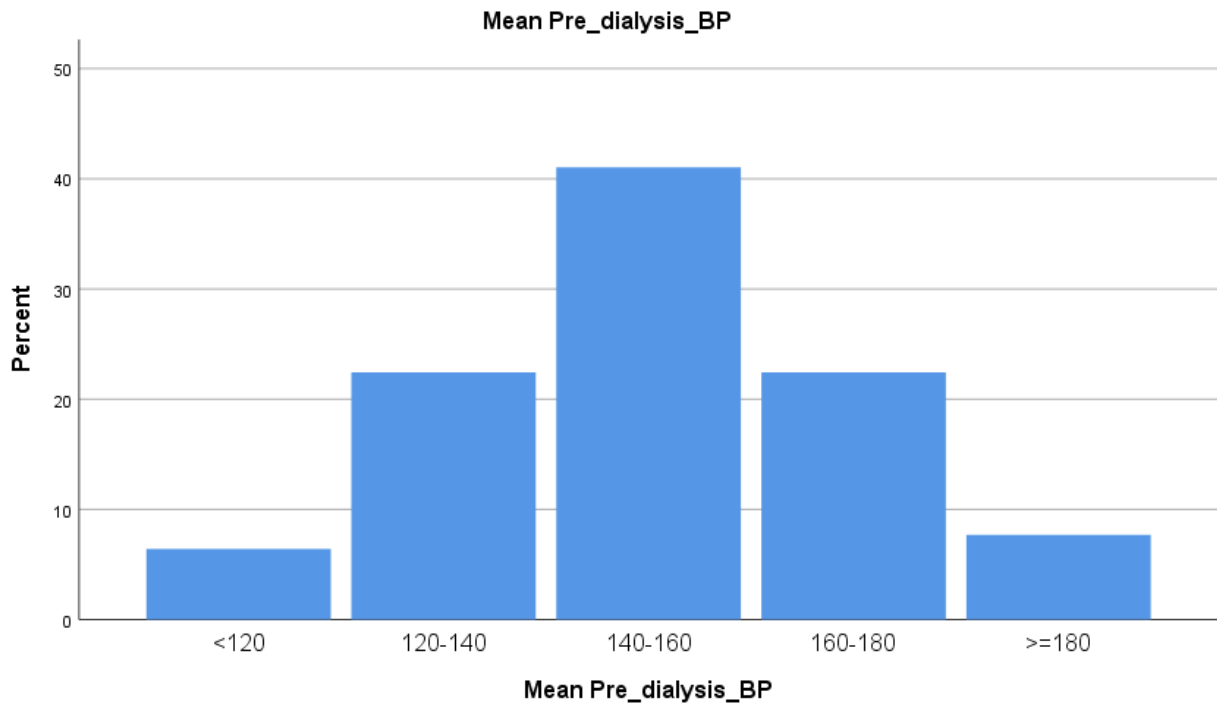


FIGURE 10: MEAN PRE DIALYSIS SBP



4. DISCUSSION

In our study middle aged males between the age of 40-60 predominate. The prevalence of IDH was 27.6% in our study which is comparable to some of the studies done here in Africa like Nigeria(24.4%), Senegal (22.6%), South Africa (28.4%) but much lower than those done in Cameroon(48.3%) and Kenya(51.2%).(6,7,8,9)

The definitions used to define IDH were the same as ours in the Senegalese, South African and Kenyan study but not to that of Nigerian and Cameroonian studies which defined it merely by increase in SBP by >10mmhg without restraining it to number of HD sessions. The higher prevalence seen in the Cameroonian and Kenyan study could be attributed to the lesser frequency of HD sessions per week (it was twice per week). (6,7,8,9)

Although the prevalence of IDH is comparable to most studies done in Africa and lower than some countries it is much higher than what is reported in the USA. The initial report came from the CLIMB study (Crit-Line Intradialytic Monitoring Benefit) done by Inrig et al. which showed prevalence of 13.2%.(1) In a subsequent analysis from the US Renal Data System Dialysis Morbidity and Mortality Wave II cohort, Inrig et al showed that 213 of 1718 patients (12.2%) experienced intradialytic hypertension, defined as increase in SBP >10 mm Hg from pre to post dialysis.(2) Another retrospective study, including data from 22 995 dialysis treatments for a 6-month follow-up, showed that 22.3% of dialysis sessions were complicated by intradialytic increase in SBP >10 mm Hg. However, in this study, persistent (i.e., consistent over time) intradialytic hypertension was observed only in 8% of participants. (3)

A single center experience in Indonesia whereby patients were undergoing twice per week of HD lasting for 5hrs each. The prevalence of IDH was 33.1%. Diabetes was prevalent in 28.6% and ACEi/ARB was used in 41.4% of the subjects.(10)

Lots of corroborating evidences support the increased cardiovascular events and mortality associated with IDH. In the CLIMB study above, intradialytic hypertension was associated with 2.17-fold increased risk for a combined end-point including all-cause mortality and non-vascular access-related hospitalization (odds ratio, 2.17; 95% confidence intervals [CI], 1.13–4.15).

(1)Another analysis performed in the US Renal Data System Dialysis Morbidity and Mortality Wave II cohort reported that each 10–mm Hg rise in SBP from pre to post dialysis underlies a

12% excess risk for all-cause mortality during a mean follow-up of 2 years (hazard ratio [HR], 1.06; 95% CI, 1.01–1.12)(2)

The only factor significantly affecting the prevalence of IDH in our study was lower UF rate (RR 3.69 95% CI 1.595-8.54). This was seen in the Cameroonian study whereby UF rate of > 800ml/hr decreased IDH prevalence by 29% (RR 0.71 95% CI 0.6-0.81).

TABLE 3: USA STUDIES (4)

Table 1. Prevalence of Intradialytic Hypertension Among Hemodialysis Patients			
Study ID	Patients	Definition	Prevalence Estimates
Inrig et al ⁹ <i>Kidney Int</i> 2009	438 hemodialysis patients participating in the CLIMB study	Rise in SBP ≥10 mm Hg from pre to post dialysis	13.2% of patients met the definition of intradialytic hypertension
Inrig et al ³ <i>AJKD</i> 2009	1748 hemodialysis patients participating in the USRDS Dialysis Morbidity and Mortality Wave II study	Rise in SBP >10 mm Hg from pre to post dialysis, averaged from 3 consecutive dialysis sessions	12.2% of patients were classified as intradialytic hypertensives
Van Buren et al ¹¹ <i>Int J Artif Organs</i> 2012	362 hemodialysis patients receiving treatment in the USA	Rise in SBP >10 mm Hg from pre to post dialysis, averaged for the total number of dialysis treatments performed during 6 months of follow-up	22.3% of dialysis treatments were complicated by intradialysis hypertension. Persistent intradialytic hypertension was noted in 8% study participants
CLIMB indicates Critic-Line Intradialytic Monitoring Benefit study; SBP, systolic blood pressure; and USRDS, US Renal Data System.			

TABLE 4: AFRICAN STUDIES

Study	Number of patients	Definition	Prevalence estimates
Sajith S 2016 (South Africa)	190	SBP increase ≥ 10 mmHg from pre- to post-hemodialysis in at least 4/6	28.4%
Halle Marie Patrice 2018 (Cameroon)	176	SBP increase ≥ 10 mmHg from pre- to post-hemodialysis	48.3%
Mouhamadou Moustapha 2018 (Senegal)	93	SBP increase ≥ 10 mmHg from pre- to post-hemodialysis in at least 4/6	22.6
Kakai E 2021 (Kenya)	86	SBP increase ≥ 10 mmHg from pre- to post-hemodialysis in at least 4/6	51.2%

ULTRAFILTRATION RATE - the rate of fluid removal during hemodialysis is strongly associated with adverse cardiovascular outcomes, and such findings are supported by plausible physiologic rationale. Potential mechanistic pathways include ultra filtration-related ischemia to the heart, brain, and gut, and volume overload-precipitated cardiac stress from reactive measures to ultra filtration-induced hemodynamic instability.

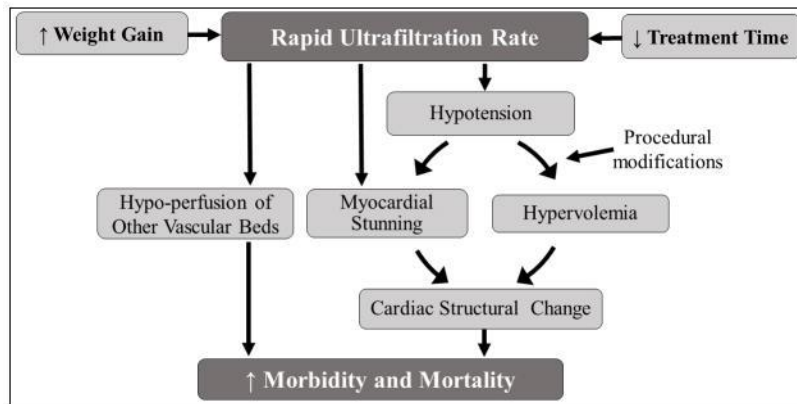
What is the ceiling UF rate? An Italian study in which Movilli *et al.* demonstrated that for every 1 ml/h/kg increase in ultra filtration rate, there was a 22% increase in mortality risk ($P < 0.01$).⁽¹¹⁾ In secondary analyses, authors identified an ultra filtration rate of 12.4 ml/h/kg as the most discriminatory cut-point for predicting 2-year mortality.

In a post-hoc analysis of the Hemodialysis (HEMO) study, Flythe *et al.* employed an ultra filtration rate threshold of 13 ml/h/kg, finding that patients with ultra filtration rates above 13 ml/h/kg had a 59% increased risk of all-cause mortality and 71% increased risk of cardiovascular mortality ($P < 0.001$ for both).⁽¹²⁾

One of the largest evidence came from a retrospective study done in North Carolina university whereby 118,394 hemodialysis patients dialyzing in a large dialysis organization, from 2008 to 2012, were included in the study and they found out that 21,735 (**18.4%**) individuals had ultra filtration rates $> 13\text{mL/h/kg}$ and 48,529 (**41.0%**) had ultra filtration rates $> 10\text{mL/h/kg}$. Median follow-up was 2.3 years, and the mortality rate was 15.3 deaths/100 patient-years. Compared with ultra filtration rates $\leq 13\text{mL/h/kg}$, ultra filtration rates $> 13\text{mL/h/kg}$ were associated with greater mortality (adjusted HR, 1.31; 95% CI, 1.28-1.34). Compared with ultra filtration rates $\leq 10\text{mL/h/kg}$, ultra filtration rates $> 10\text{mL/h/kg}$ were associated with greater mortality (adjusted HR, 1.22; 95% CI, 1.20-1.24).⁽¹³⁾

Compared to this study the prevalence of UF rate $\geq 13\text{ml/kg/hr}$ was much higher in our study 42.3%. This could be because of relatively shorter duration of HD time (3.5hr in 3/4th of the patients), lower frequency of HD per week which puts them at risk to have fluid retention and higher UF volume removal per session(twice per week HD accounted for 69.9%) and the relatively lower mean weight of our patient population.

FIGURE 11:PATHOGENESIS OF ULTRAFILTRATION RATE



The association of higher UF rate and lower incidence of IDH could be explained by greater removal of fluid and better control of fluid status hence lower intradialytic rise in BP.

Other factors were not significantly associated with IDH.

Erythropoietin use was lower than in other studies like the Senegalese study it was 20.4%, in the Cameroonian study 23.86% but better than the Kenyan study (4%, 4/86 patients).

Our low rate could be because of stock out of EPO from government pharmacies during the study period and inflation of the EPO price in private pharmacies.

Our study tried to assess prevalence of intradialytic hypotension as secondary outcome defining it as drop in SBP by 20mmhg or more and was prevalent in 648 sessions out of 936 sessions of HD (69.2%). The earlier Nigerian study reported a prevalence of 19.4%. Another Cameroonian study reported prevalence of 11.6%. The higher prevalence in our study is likely because of the loose definition we used without any accompanying need for intervention or associated symptoms which were used in the above studies. Because our main target was not assessing Intradialysis hypotension we did not ask for further information so our result needs confirmation by another dedicated study.

5-CONCLUSION: our study showed that IDH is very prevalent in our set up and it is more common in those with lower ultra filtration rate. The prevalence of higher ultra filtration rate is very high close to half of patients had rate of ≥ 13 ml/kg/hr.

6-LIMITATIONS OF THE STUDY

- Retrospective nature of the study
- Assessment of volume status was based on weight gained between HD sessions only, other studies tried to use more objective evidence like bioimpedance spectroscopy
- Longer period of study to see the persistence of IDH more than 6 sessions

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