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Research article

PREVALENCE AND PROGNOSTIC SIGNIFICANCE OF RESISTANT HYPERTENSION IN DIALYSIS AND NON DIALYSIS CKD PATIENTS

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ABSTRACT

Objectives: To evaluate the risk of morbidity and hospitalization of patients with resistant hypertension. To assess the progression of CKD to ESRD and cardiovascular co- morbidities with resistant hypertension. **Background:** In CKD and ESRD, uncontrolled hypertension is a major risk factor, but no study has properly investigated the role of RH. **Methods:** We prospectively studied 187 patients and out of which 24 patients were excluded from the study due to insufficient data (or) patients who are not interested to share the data. In remaining patients of 163, 81patients were ESRD and undergo dialysis periodically are categorized into one group, and 82 patients were CKD are categorized into another group Endpoints of survival analysis were renal (end-stage renal disease or death) and cardiovascular events (fatal and nonfatal cardiovascular event). **RESULTS:** A total of 163 patients were included in study in which 74.8% (n=121) of the patients were male. Majority of the patients 54.6% (n=89) were in age-group of 40-59 years and the mean age was 47.2 years.. In the dialysis patients (66) males are having normal hypertension and (47) males are having resistant hypertension (11) females are having normal hypertension and (8) females are having resistant hypertension. In the non-dialytic CKD patients (54) males are having normal hypertension and (9) males are having resistant hypertension; (9) females are having normal hypertension and (6) females are having resistant hypertension. About 50% of patients had CKD of unknown etiology. Diabetes mellitus accounted for 38.03% (n=62) of the cases. Patients having glomerulonephritis accounts for 30.6% (n=50). Whereas hypertension in 85.8 % (n=140), adpkd in 11.04% (n=18). About 37% (n =3) of the patients were on thrice weekly dialysis and 61.7% (n =50) were on twice-weekly dialysis. CAD accounts 0.08% (n=7) in non-dialysis, whereas in dialysis 0.13% (n=11)LVD accounts 0.045% in non-dialysis, 0.25 in dialysis patients. 17.8 %, 66.2 %of pts having resistant hypertension in CKD, Dialysis respectively. **Conclusions:** In conclusion, we found that individuals with CKD and RH as well as ESRD with RH were at higher risk for coronary heart disease mortality and incident stroke. In this study, the presence of CKD did not appear to amplify the risks for the occurrence of these 2 disease entities associated with RH, whereas progression of CKD to ESRD is rapid. But the presence of ESRD may amplify the risk for the of cardiovascular co morbidities with RH but no evidence of enhancing the lethality of cardiovascular disease.

Key Words: - CKD (Chronic kidney disease), Hypertension, Prognosis, Risk factors.

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INTRODUCTION

The American Heart Association defines apparent treatment-resistant hypertension (ATRH) as the requirement of 3 or more medications (1 preferably a

diuretic) to adequately control blood pressure to 140/90[Calhoun, D. A. *et al*., 2014]. As defined, resistant hypertension includes patients whose blood pressure is controlled with 4 or more medications[Daugherty, S. L. *et al*, 2014]. If tolerated, medications should be titrated to 50% or more of their maximal dose[Muntner, P. *et al*., 2014].

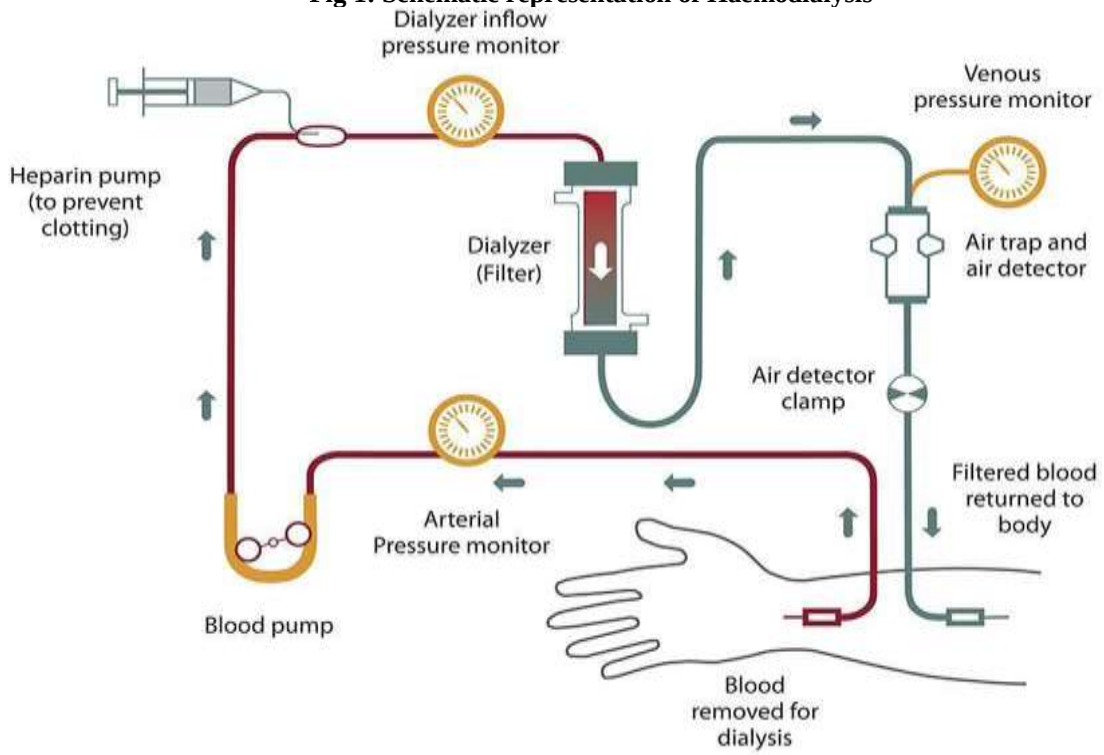
Chronic kidney disease (CKD) is a condition characterized by a gradual loss of kidney function over time. Chronic kidney disease includes conditions that damage kidneys and decrease their ability to keep healthy by doing the jobs listed[De Nicola, L. *et al*, 2013]. If kidney disease gets worse, wastes can build to high levels in your blood and make you feel sick. patient may develop complications like high blood pressure, anemia (low blood count), weak bones, poor nutritional health and nerve damage[Thomas, G. *et al*., 2016].

Other conditions that affect the kidneys are[Egan BM, *et al*, 2011]:

- Kidney's filtering units. These disorders are the third most common type of kidney disease[Parikh NI, *et al*, 2006].
- Inherited diseases, such as polycystic kidney disease, which causes large cysts to form in the kidneys Glomerulonephritis, a group of diseases that cause inflammation and damage to the and damage the surrounding tissue[Coresh J, *et al*, 2001].
- Malformations that occur as a baby develops in its mother's womb. For example, a narrowing may occur that prevents normal outflow of urine and causes urine to flow back up to the kidney. This causes infections and may damage the kidneys[Muntner P, *et al*, 2010].
- Lupus and other diseases that affect the body's immune system.
- Obstructions caused by problems like kidney stones, tumors or an enlarged prostate gland in men.
- Repeated urinary infections.

Normally, the kidneys filter blood, removing harmful waste products and excess fluids and turning these into urine to be passed out of the body[Abdel-Kader K, *et al*, 2012]. If kidneys aren't working properly for example, because patients have advanced CKD (kidneys failure) – the kidneys may not be able to clean the blood properly[D. A. Calhoun *et al*, 2008]. Waste products and fluids can build up to dangerous levels in the body[De Nicola L, *et al*, 2011]. Left untreated, this can cause a number of unpleasant symptoms and eventually be fatal. Dialysis filters out unwanted substances and fluids from the blood before this happens[J. P. Garg *et al*, 2005].

Fig 1: Schematic representation of Haemodialysis



N= number of patients, %= percentage for number of patients

AIM :

To Evaluate the occurrence of cardiovascular complications like Left Ventricular Hypertrophy (LVH), Left Ventricular Disfunction (LVD), Coronary Artery Disease (CAD), Cardiovascular Accident (CVA) in ESRD patients and morbidity in dialysis patients and CKD patients with resistant hypertension.

OBJECTIVES :

- ✓ To evaluate the risk of morbidity and hospitalization of patients with resistant hypertension.
- ✓ To assess the progression of CKD to ESRD and cardiovascular co- morbidities with resistant hypertension.

MATERIALS & METHODS:

Study Site: The study was carried out in outpatient department and in dialysis unit of Vedanta Hospital, Guntur, .AP., under the guidance of Dr.CH. Ramakrishna (MD., DM., Nephro) and Asst. prof. Dr. D. Rispa (pharm-D).

Study Period: The patients was observed during the study period of six months from October-2018 to April 2019.

Study Design: It is a comparative cross sectional study, A comparative cross sectional study was conducted between two groups. This study represents the comparative analysis of prevalence, mortality and morbidity in CKD and ESRD patients caused by resistant hypertension[D. P. Papadopoulos and V. Papademetriou,2006].

SELECTION CRITERIA:

Inclusion criteria:

- ✓ Patients with age group 18-60 years.
- ✓ Patients of both genders.
- ✓ Patients with chronic kidney disease.
- ✓ Patients who have undergone investigations of renal function tests, urine analysis.
- ✓ The patients who met the study criteria along with the other co-morbidities were enrolled in the study.

Exclusion criteria:

- ✓ Patients not willing to participate in the study.
- ✓ Patients of age below 18 years.
- ✓ Patient who are in gestational period.

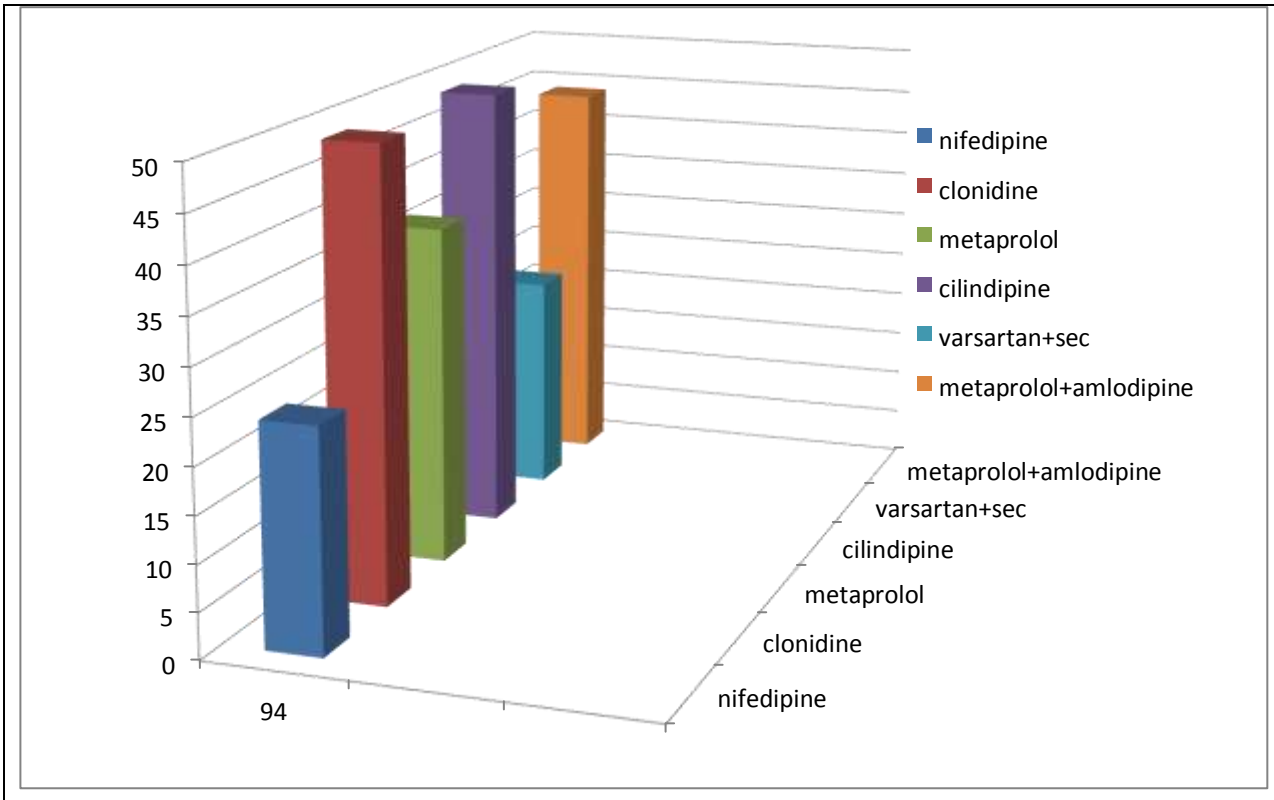


Fig 2: HTN Management in CKD

About 61% of patients acquired Hypertension after kidney disease.

Table 1: Cardiovascular Complications In CKD And Dialysis

Cardiovascular complications	Frequency (no.of Patients)	Percent	Cumulative frequency	Cumulative percent
CKD	9	10.84	82	98.80
DIALYSIS	24	28.92	82	98.80

Table 2: RR ASSESSMENT

• **Relative risk**: ratio of risk rate of cardiovascular complications in dialysis to risk rate in non-dialysis.

Cardiovascular Complications	Present	Absent
Dialysis (ESRD)	24	57
Non dialysis (CKD)	9	72

RR=(A/A+B)/(C/C+D)=2.6; Therefore RR is 2.6; It means, dialysis patients have 2.6 times more risk of cardiovascular complications than nondialytic CKD patients.

Table 3. OR ASSESSMENT

ODDS RATIO:

Cardiovascular Complications	Present	Absent
Dialysis (ESRD)	24	57
Non Dialysis (CKD)	9	72

OR= A/C X B/D=3.3

- An Odds ratio >1 implies that cardiovascular complications is more likely in dialysis patients
- Resistant hypertension is more predominant in dialysis patients when compared to non-dialytic CKD patients.
- 17.8 %, 66.2 %of pts having resistant hypertension in CKD, Dialysis respectively

Table 4: Resistant HTN in CKD And Dialysis

(Rest. HTN)	Frequency (No.of PTS)	Percent	Cumulative Frequency	Cumulative Percent
CKD	15	17.86	82	97.62
Dialysis	55	66.27	81	97.59

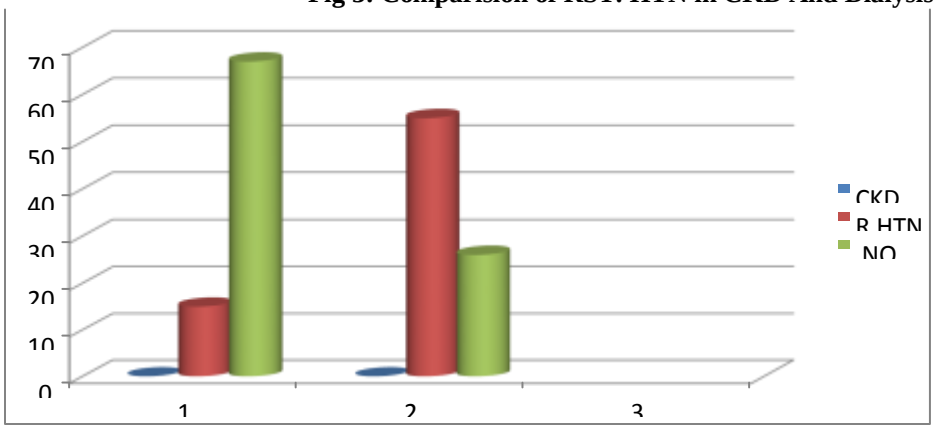
P Value for Resistant Hypertension

Mean	95% CI Mean		Std Dev	95% CI Std Deviation	
0.1605	-Infty	0.2288	0.3694	0.3199	0.4370

Table 5: t-Test for Resistant Hypertension

DF	T Value	PR < T
80	-117.92	<.0001

Fig 3: Comparision of RST. HTN in CKD And Dialysis Patients



Comparison Graph For Resistant Hypertension: 1=CKD PATIENTS
2=DIALYSIS PATIENTS

Table 6: Predialytic BP

The mean pre dialytic systolic and diastolic blood pressures were 154 &109 mmHg respectively.

- While mean post dialysis systolic and diastolic blood pressures were 152 &109 mmHg respectively.

Predialytic BP	No.of Patients	Percent
130/90	2	2.44
140/90	6	7.32
150/90	16	19.51
160/100	12	14.63
170/100	11	13.41
180/110	3	3.66

Tab 7: Postdialytic BP

Postdialytic BP	No.of Patients	Percent
130/90	8	9.76
140/90	18	21.95
150/90	16	19.51
160/100	5	6.10
170/100	4	4.88
180/90	3	3.66

Out of 163 pts, 74 % (n=120) of pts having HTN. Most commonly used antihypertensives among Dialysis and Non-dialytic pts are : toresemide -57.2%(n=94); Nifedipine – 20.8%(n=24); clonidine – 30% (n=49); cilindipine - 30% (n=49); Metaprolol – 21% (n=37); Valsartan + secubotril – 14.7%(n=24); metaprolol +amlodipine – 26.9%(n=44)

Fig 4: Therapy Of Resistant Hypertension

TREATMENT FOR RESISTANT HYPERTENSION GRAPH

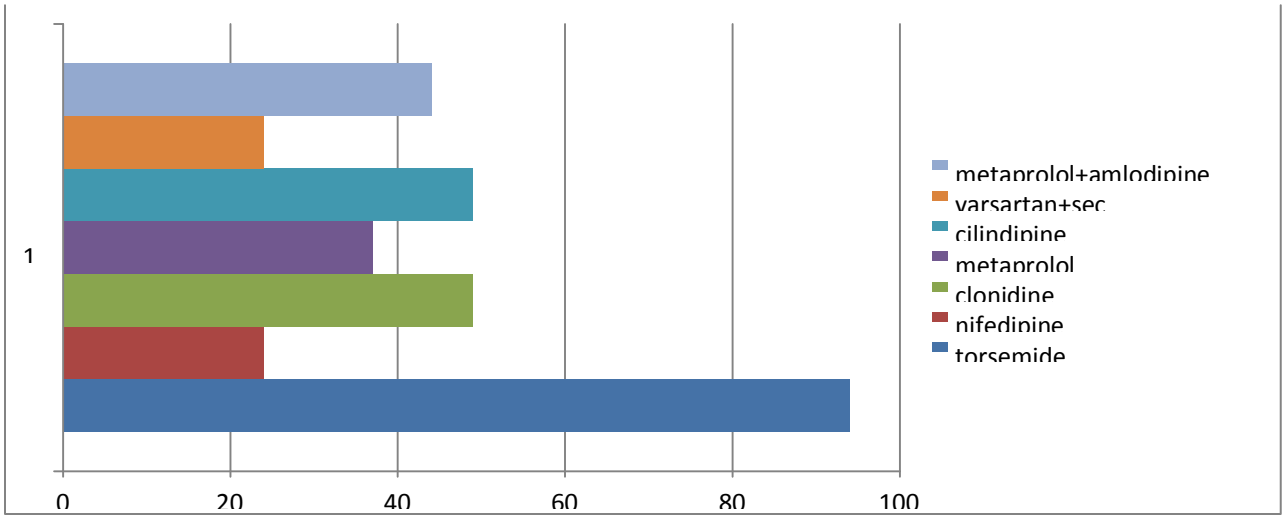


Table 8: RR Assessment of Resistant HTN

Relative risk: Ratio of risk rate of resistant Hypertension in dialysis to risk rate in nondialysis

Resistant hypertension	Present	Absent
Dialysis	55	26
Non-dialysis	15	66

RR= (A/A+B)/(C/C+D)=8.8 , Therefore RR is 8.8. It means, dialysis patients have 8.8 times more risk of resistant hypertension than non dialytic CKD patients.

Table 9: OR Assessment of Resistant HTN

ODDS RATIO:

Resistant hypertension	Present	Absent
Dialysis	55	26
Non-dialysis	15	66

- OR= A/C X B/D =9.3

Table 10: Salt-Intake

An Odds ratio >1 implies that resistant hypertension is more likely in dialysis patients.

An average daily intake of salt is upto 2 grams reported.

Salt Intake	Frequency (no.of Patients)	Percent	Cumulative Frequency	Cumulative Percent
CKD	46	55.42	82	98.80
DIALYSIS	50	60.98	81	98.78

DISCUSSION:

About (66.2%) of the dialysis and (17.8%) of the non-dialytic CKD patients had uncontrolled blood pressure. Our study found that (95%) of the patients on HD were hypertensive and (45%) of them had persistent elevation of BP, despite being on one or more anti-hypertensive medications. Most patients were on calcium channel blockers, angiotensin receptor blockers, diuretics and other anti-hypertensive medications. The etiology of the kidney disease may be hypertension which was not controlled, prolonged diabetes, non- adherence to medication, non-compliance to medication, social history, gene abnormalities and unknown etiologies[P. A. Sarafidis and G. L. Bakris, 2008].

In our study some patients are having the Autosomal Dominant Polycystic Kidney Disease [ADPKD] which is a gene abnormality and some are having the family history of kidney disease. In rare conditions some may develop the contrast induced nephropathy may occur due to increased dose of fluorescent dye which is used during the Coronary Angiogram.

The other co morbidities in the patients of dialysis includes the cardiovascular problems, cerebrovascular problems, gout, asthma and other respiratory tract problems. In the ultrasonography impression states that almost every patient is having the renal parenchymal changes in both the categories. In our study we observed the serum creatinine levels, blood urea nitrogen levels in order to treat the both categories of patients. The etiology of hypertension before and after Kidney disease was found to be(61%) of the non-dialytic CKD patients.

Medication adherence usually refers to whether patients take their medications as prescribed as well as whether they continue to take a prescribed regimen. Taking medicine as prescribed or medication adherence is important for controlling chronic conditions, treating temporary conditions and overall long term health and well-being.

Morisky medication adherence scale was used to calculate the medication compliance which contains 8 questionnaires and the information was gathered during the patient counselling. This scale is used in our study to know the significance of medication adherence. programs, as these patients do not demonstrate proteinuria or hypertension for early detection and management.

OPTIMAL BP IN HEMODIALYSIS PATIENTS

There are three ways in which we can assess the level of BP in hemodialysis patients. Blood pressure can be obtained before, during and after hemodialysis, by the dialysis staff. This can be done at home by the patient, or by an automatic ambulatory BP monitor. Optimal blood pressure is defined when pre and post–dialysis BP is < 150/90 mmHg without therapy or the ambulatory day BP monitoring < 135/85 without therapy or the ambulatory nigh time BP monitoring < 120/80 without therapy[M. H. Alderman, 2008].

HTN MANAGEMENT IN PATIENTS WITH CKD

SALT RESTRICTION

The available evidence supports a large component of salt sensitivity to HTN in patients with CKD. Therefore, educating patients with CKD on a low salt diet is critical to achieving BP control while maintaining a simple BP medication regimen. A modest dietary sodium restriction can enhance the effects of antihypertensive medications like angiotensin converting enzyme inhibitors or angiotensin receptor blockers when treating HTN in CKD.

Importantly, low dietary salt intake also augments the antiproteinuric effect of diuretics and renin-angiotensin-aldosterone blocking drugs. The combination of a low salt diet and hydrochlorothiazide reduced proteinuria by 70% from baseline. Conversely, a high salt diet offsets the efficacy of diuretics and renin-angiotensin-aldosterone blockers to both reduce BP and proteinuria. In proteinuric patients with diabetes mellitus,

reductions in mean baseline proteinuria were increased from 30% to 55% with the addition of a low salt diet to losartan monotherapy.

Concerns have been raised about potential risks from overlying restricting dietary sodium higher levels of sodium intake were associated with higher risk of cardiovascular disease.

MINERALOCORTICOID ANTAGONIST USE IN CKD

Impressive reductions in BP for individuals receiving 3 or more antihypertensive medications have made mineralocorticoid antagonists an important fourth-line BP agent in the treatment of resistant HTN[M. Moser, *et al*, 2006]. However, risks of hyperkalemia and acute kidney injury have limited mineralocorticoid antagonist use in advanced CKD. spironolactone effectively reduces both BP and urine protein levels However, caution is advised with starting spironolactone in patients who have a baseline serum potassium greater than 4.6 mEq/L. Spironolactone is contraindicated in patients with acute kidney injury and creatinine clearances less than 10 mL/min. Eplerenone, a more selective mineralocorticoid antagonist, is contraindicated for use when creatinine clearance falls less than 30 mL/min[J. Amar, 2007].

CONCLUSION:

The reasons include inadequate dialysis, dietary salt intake, and non compliance to the medication. If left untreated in these patients may leads to frequent hospitalizations and leads to mortality. So measures are taken to control the hypertension include short daily haemodialysis, nocturnal dialysis, daily salt and fluid restriction.

Incidence of Cardiovascular complications in non dialytic CKD patients with resistant hypertension is 10% where as in dialysis population with resistant hypertension is 30%. Salt intake of <2 grams is beneficial in the dialysis patients where the intradialytic weight gain is between 1-2 Kgs among these patients and rarely >2 Kgs is observed.

In conclusion, we found that individuals with CKD and RH as well as ESRD with RH were at higher risk for coronary heart disease mortality and incident stroke. In this study, the presence of CKD did not appear to amplify the risks for the occurrence of these 2 disease entities associated with RH, whereas progression of CKD to ESRD is rapid. But the presence of ESRD may amplify the risk for the of cardiovascular co morbidities along with RH but cannot rule out that it may enhance the lethality of cardiovascular disease.

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