World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

PROSPECTIVE STUDY ON PHARMACOTHERAPEUTIC MANAGEMENT OF HYPERTENSION IN CHRONIC KIDNEY DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL

C. Mohana*[1], G. Likhitha[2], A. K. Sridharan[3], M. Indira[4] and M. Kishore Babu[5], K.R. Manasa Swapna[6]

[1]Assistant Professor, Department of Pharmacy Practice, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh.
[2-4]Pharm.D Intern, Department of Pharmacy Practice, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh.
[5]Principal, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh.
[6]Shadan College of Pharmacy, Hyderabad, Telangana.

Corresponding Author: C. Mohana
Assistant Professor, Department of Pharmacy Practice, Krishna Teja Pharmacy College, Tirupati, Andhra Pradesh.

Article Received on 12/07/2021 **Article Revised on 02/08/2021** **Article Accepted on 22/08/2021**

ABSTRACT

Background: Hypertension is an well-known risk factor for chronic kidney disease and end-stage renal disease. Chronic kidney disease cases have been increasing in worldwide and it is recognized as a global health burden. **Aim:** To study the pharmacotherapeutic management of hypertension in patients of chronic kidney disease at various stages. **Methods:** A Prospective study was carried out in department of Nephrology, SVIMS, Tirupathi. A sample size of 103 patients was participated in the study period. The patients were recruitment was done as per study protocol. The collected data was analyzed and expressed in percentages. **Results and Discussion:** In our study 41-60 years age patients were more 49 (47.5%) as compared to other age patients. Out of 103 patients male patients were more 72 (69.90%) as compared to female patients. In our study hemodialysis male patients were 36 more as compared to females. In our study one treatment regimen patients were more 66 as compared to other treatment regimen patients. **Conclusion:** Chronic kidney disease has been increasing in worldwide and it is recognized as a global health burden. Hypertension is an established risk factor for progression of chronic kidney disease and end-stage renal disease. The more support form physicians and health care professionals to normalize the blood pressure that reduce their cardiovascular and renal risk. Our findings indicate that early detection of CKD stage and its risk factors and continuous lifestyle plan and therapeutic intervention programmes could lower the development of CKD complications.

KEYWORDS: Hypertension, Chronic kidney disease, hemodialysis, cardiovascular disease, and therapeutic intervention programmes.

INTRODUCTION

Chronic kidney disease is defined as altered kidney function or structure where the symptoms persist for more than three months effecting health condition. CKD is characterised by progressive decline in glomerular filtration rate which plays a major role in kidney and diabetes mellitus, family history of kidney disease. The prevalence of CKD is 10–15% in the general adult population in both high- and low-income countries. Individuals with CKD are at risk for developing kidney failure which requires renal replacement therapy.[1-2] The chronic kidney disease stages can be evaluated by as per "National Kidney Foundation" guidelines the stages are classified.

Stages of CKD.

Stages of CKD	GFR
Stage 1	≥90 ml / min / 1.73 m^2
Stage 2	60 – 89 / ml / min /1.73 m^2
Stage 3	30 – 59 ml / min / 1.73 m^2
Stage 4	15 – 29 ml / min / 1.73 m^2
Stage 5	<15 ml / min

Chronic kidney disease (CKD) affects 10–15% of the population worldwide and its prevalence is increasing. CKD is defined as the presence of reduced kidney function (an estimated glomerular filtration rate [eGFR] < 60 mL/ min/1.73 m^2 or kidney damage (often indicated by the presence of proteinuria) for ≥ 3 months duration. Hypertension, defined by the European Society of Cardiology and the European Society of Hypertension

(ESC/ESH) as a blood pressure (BP) of ≥ 140/80 mmHg affects ~ 30% of the general adult population and up to 90% of those with CKD. Hypertension is both a cause and effect of CKD and contributes to its progression.[3-6] As eGFR declines, the incidence and severity of hypertension increase. Additionally, hypertension and CKD are both independent risk factors for cardiovascular disease (CVD). When both exist together the risks of CVD morbidity and mortality are substantially increased. For those with stage 3 (eGFR 30–59 mL/min/1.73 m^2) or stage 4 (eGFR 15–29 mL/ min/1.73 m^2).

Pathogenesis of Hypertension in chronic kidney disease

A number of mechanisms contribute to the development of hypertension in CKD and these influence its management. Increase in sympathetic tone, brought about by afferent signals generated by functionally declining kidneys, contributes to the development of hypertension in CKD. As eGFR declines there is an upregulation of the renin–angiotensin–aldosterone system (RAAS) which promotes salt and water retention. This is compounded by an increased salt sensitivity of BP. Endothelial dysfunction is characteristic of advanced CKD (eGFR < 30 mL/min/1.73 m^2) and its association with hypertension is well-established. Increased arterial stiffness is also seen throughout the spectrum of CKD, is implicated in the development of hypertension, and is an independent risk factor for CVD events. Once hypertension has developed, several factors, including increased oxidative metabolism, with resultant relative renal hypoxia, may drive further progression of BP and CKD. In health, BP demonstrates a nocturnal dip of ~ 10 to 20%. This is controlled by several factors including diurnal variations in autonomic function, salt excretion and the RAAS.[7-9] Dysregulation of these systems in CKD leads to a non-dipping or even rising nocturnal BP, which is associated with increased CVD morbidity and mortality and risk of CKD progression.

Types and causes of hypertension

There are two types of high blood pressure.

Primary hypertension

For most adults, there's no identifiable cause of high blood pressure. This type of high blood pressure, called primary hypertension, tends to develop gradually over many years.

Secondary hypertension

This type of high blood pressure, called secondary hypertension, tends to appear suddenly and cause higher blood pressure than does primary hypertension.[10-11] The secondary hypertension constitutes of 5% patients are affected.

Various conditions and medications can lead to secondary hypertension, including:

- Obstructive sleep apnea
- Kidney disease
- Adrenal gland tumors
- Thyroid problems
- Certain defects you're born with in blood vessels
- Complications of hypertension.
- Certain medications, such as birth control pills, cold remedies, decongestants, over-the-counter pain relievers and some prescription drugs.
- Illegal drugs, such as cocaine and amphetamines.

Pharmacological Treatment

Despite the benefits of non-pharmacological interventions in CKD, antihypertensive medications are usually also required.[10-11] As well as direct BP-lowering effects, certain pharmacological therapies provide additional renoprotective and/or cardioprotective action, which may be independent of their BP-lowering effects.

Renin–Angiotensin–Aldosterone System

RAAS blockade can reduce systolic BP by ~20 mmHg in patients with hypertension and CKD. This is similar to the BP reduction offered by CCBs and diuretics. However, these agents offer a BP independent reduction in proteinuria in both diabetic and non-diabetic CKD and are therefore generally accepted as first-line management of hypertension in patients with proteinuric CKD.

Diuretics

Diuretic therapy can reduce volume expansion and has been shown to improve left ventricular mass index and arterial stiffness in those with CKD. Treatment with a diuretic may also reverse the loss of physiological nocturnal dip in BP described in CKD. Loop diuretics are valuable, although higher doses are often required in those with a lower eGFR as the tubular mechanism of action of these drugs relies first on glomerular filtration. The combination of a loop and thiazide diuretic is particularly powerful, and care should be taken to avoid fluid depletion.[12-16]

Calcium channel antagonists

Dihydropyridine and non-dihydropyridine CCBs are useful in the management of hypertension in CKD. Dihydropyridine CCBs can be used as first-line therapy in non-proteinuric CKD, either alone or in combination. In proteinuric CKD their effect is inferior to RAAS blockade. However, the addition of a dihydropyridine CCB to proteinuric patients with established RAAS blockade improves BP control without worsening proteinuria.[17]

B-Blockers

B-Blockers (β-adrenoceptor antagonists) effectively reduce BP in CKD due to their effect on the dysregulated sympathetic nervous system.[18] The cardioprotective benefits of these drugs are well established and therefore they are particularly advantageous in those with CKD.

α-Blockers

Peripherally acting α-blockers (α-adrenoceptor antagonists; such as doxazosin) are commonly used as

part of combination therapy for the management of hypertension in CKD. This may be due to a pharmacokinetic profile that is undisturbed by declining eGFR in addition to favourable effects on glycaemic control.[19-22]

Aims and Objective

Aim

To study the pharmacotherapeutic management of hypertension in patients of chronic kidney disease at various stages.

Objectives

- To study the usage of Anti-hypertensive drug in terms of different groups, dosages, and frequency of doses, interval of doses, and variety regular/ sustained release and based on the classification of Anti hypertensive such as Monopills and polypills therapy.
- To study the outcomes with the treatment regimen.

METHODOLOGY

Study design

It was Prospective study.

Study site

The study was conducted in Department of Nephrology, SVIMS, Tirupathi, and AP, India.

Study duration

The study was performed for 6 months from December-2020 to June-2021.

Sample size

It was 103 patients.

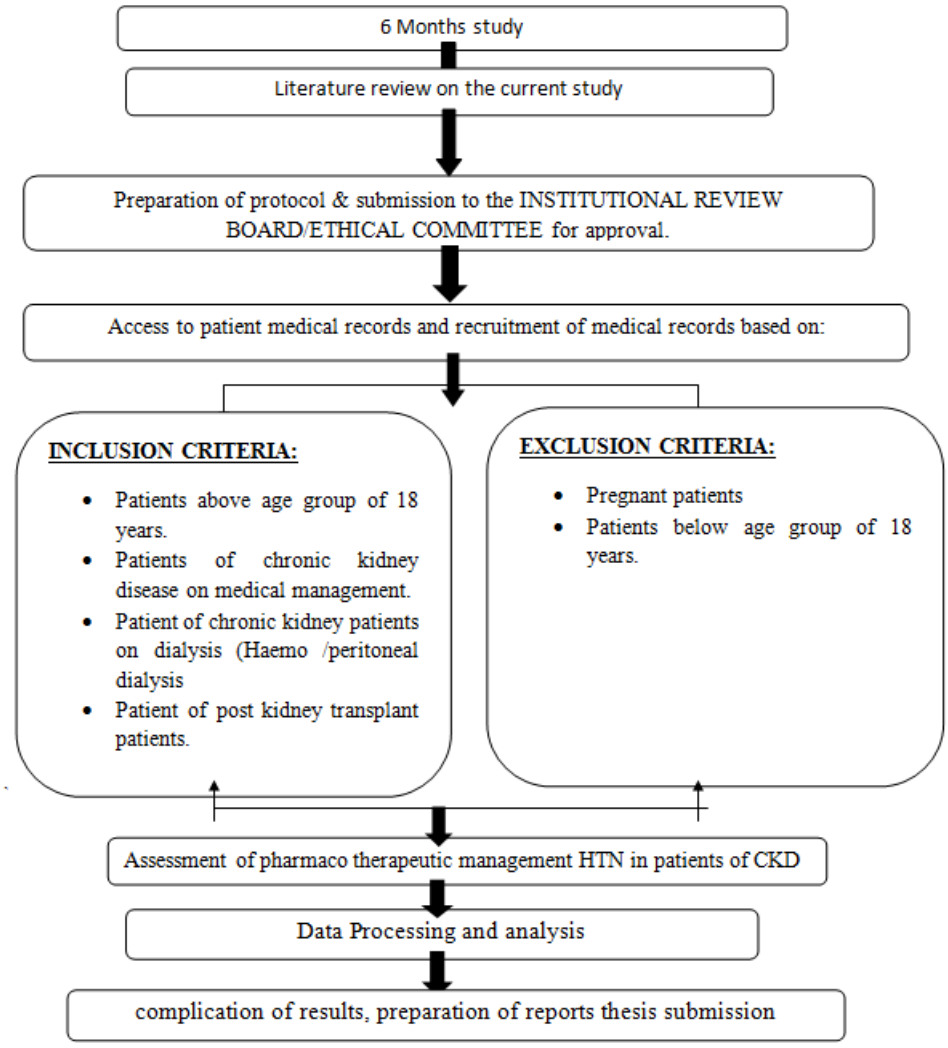
Inclusion criteria

- Patients above age group of 18 years.
- Patients of chronic kidney disease on Medical management.
- Patients of chronic kidney disease on Dialysis both (Hemo dialysis and peritoneal dialysis).

Exclusion criteria

- Pediatric patients.
- Pregnant women.
- Patients Unwilling to participate in the study.

PLAN OF WORK



Data collection

- Baseline clinical and demographic characteristics will be obtained from all patients.
- Data will be collected using a proforma.
- Data collection regarding prescribed medications if any.

Statistical analysis

- Data will be recorded on a predesigned proforma and managed using Microsoft Excel work sheet. All the entries will be double checked for any possible error. Mean will be used to calculate variables. The further data will be assessed and analyzed in the form of percentages or numbers.
- Percentages will be calculated for all categorical variables.

RESULTS

Table 1: Age wise distribution.

S.No	Age (years)	Numbers N=103	Percentage (%)
1.	0 – 20	7	7
2.	21-40	24	23.3
3.	41-60	49	47.5
4.	61-80	23	22.3
Total		103	

In our study 0-20 years age patients were 7(7%), 21-40 years age patients were 24 (23.3%), 41-60 years age patients were 49 (47.5%), 61-80 years age patients were 23 (22.3%).

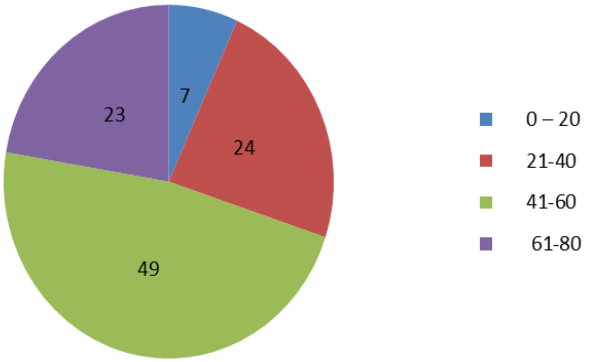


Figure 1: Age wise distribution.

Table 2: Gender wise distribution.

S. NO	Gender	Total N=103	Percentage (%)
1.	Male	72	69.90
2.	Female	31	30.09

Out of 103 patients male patients were 72 (69.90%), and female patients were 31 (30.09%).

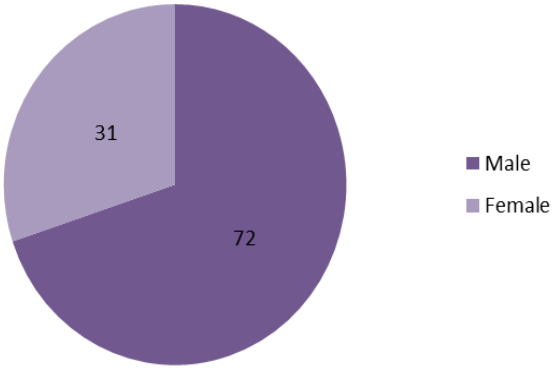


Figure 2: Gender wise distribution.

Table 3: CKD Stages.

S. No.	CKD Stages	Male	Female	Total number of patients
1	5D on MHD	36	14	50
2	CAPD	36	17	53
	Total	72	31	103

In our study 5D on MHD male patients were 36 and female patients were 14. CAPD male patients were 36 and female patients were 17.

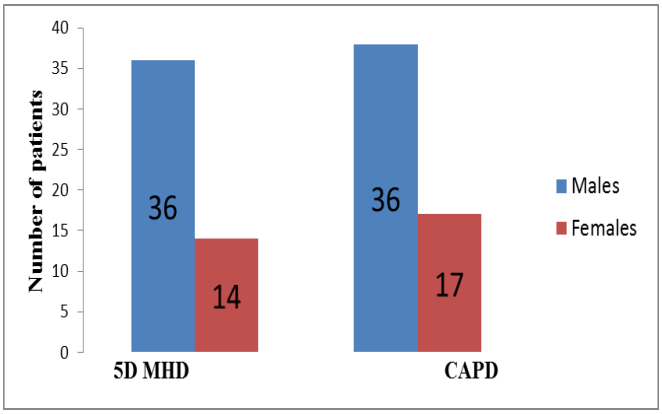


Figure 3: CKD Stages.

Table 4: Type of Dialysis.

Type of Dialysis	Male	Female
HD (Hemo dialysis)	36	14
PD (Peritonial dialysis)	36	17
Total	72	31

In our study hemodialysis male patients were 36 and female patients were 14. Peritonial dialysis male patients were 36 and female patients were 17.

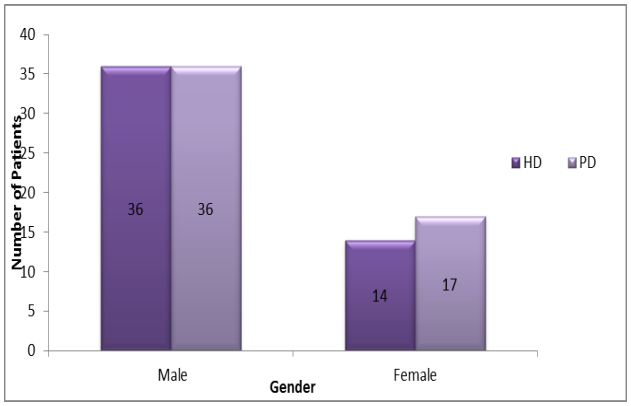


Figure 4: Type of Dialysis.

Table 5: Distribution of treatment regimen.

S. No.	Type of Regimen	Number of Patients
1	1	66
2	2	15
3	3	10
4	4	9
5	5	3
	Total	103

In our study one treatment regimen patients were 66, two treatment regimen patients were 15, three treatment regimen patients were 10, four treatment regimen patients were 9, five treatment regimen patients were 3.

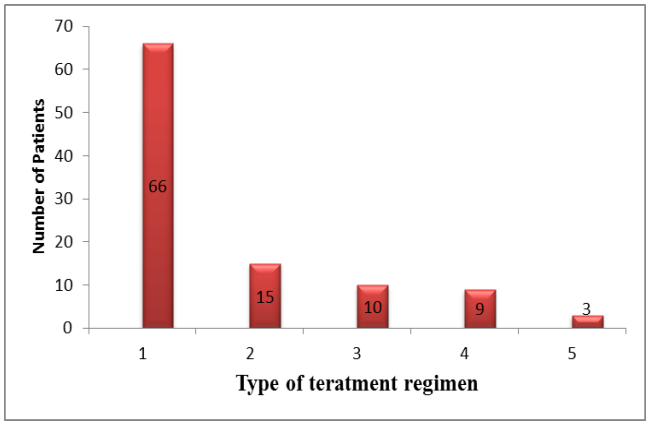


Figure 5: Type of Treatment regimen.

DISCUSSION

A high rate of hypertension awareness and treatment, the combination pharmacotherapy with is needed for management of hypertension.[23-24] The very high prevalence of hypertension in CKD is not unexpected but it is agreement with previous reports from similar cohorts of CKD patients in high-income countries, e.g. Japan, Spain, the U.K., and the U.S. The sociodemographic factors and comorbidities were associated with prevalence rates of uncontrolled hypertension in a statistically significant manner, these effects were generally small, and even the sub-groups with a lower prevalence of hypertension still exhibited a prevalence of uncontrolled hypertension of 90%. While unawareness of hypertension is a well-known obstacle for blood pressure control in the general population, rates of hypertension awareness and treatment were high in the present cohort, as reported in other CKD research studies.[25-27]

In our study 41-60 years age patients were more 49 (47.5%) as compared to other age patients. Out of 103 patients male patients were more 72 (69.90%) as compared to female patients. In our study 5D on MHD male patients were 36 more as compared to females. In our study CAPD male patients were 36 more as compared to females. In our study hemodialysis male patients were more 36 as compared to female patients. Peritonial dialysis male patients were 36 as compared to female patients. In our study one treatment regimen patients were more 66 as compared to other treatment regimen patients.

CONCLUSION

Chronic kidney disease (CKD) has been increasing in worldwide and it is recognized as a global health burden. Hypertension (HTN) is an established risk factor for chronic kidney disease (CKD) and end-stage renal disease (ESRD). The control of blood pressure in patients with CKD and hypertension is a major challenging task.[28] The more support form physicians and health care professionals to normalize the blood pressure that reduce their cardiovascular and renal risk. The better understating of pharmacology of antihypertensive drugs and the tolerability profile is change in advanced CKD. Therefore, regular medication adherence is more useful in advanced CKD. Our findings indicate that early detection of CKD and its risk factors and continuous lifestyle plan and therapeutic intervention programmes could lower the CKD complications.

The study concluded that males (69.9%) are more prone to HTN in CKD patients with age group of 41-60 compare to female patients. In Our study we observed that usage of Anti-hypertensive drug is first line drugs are calcium channel blockers, beta-Blockers, diuretics & ACE-Inhibitors.[29-30] In our study observed that poly pill therapy will more effective as compared to mono pill therapy in control of blood pressure in CKD patients.

REFERENCES

1. Muntner P, Anderson A, Charleston J, Chen Z, Ford V, Makos G, et al. Hypertension awareness, treatment, and control in adults with CKD: results from the Chronic Renal Insufficiency Cohort (CRIC) Study. Am J Kidney Dis., 2010; 55: 441–451.
2. Kestenbaum B, Rudser KD, de Boer IH, Peralta CA, Fried LF, Shlipak MG, et al. Differences in kidney function and incident hypertension: the multi-ethnic study of atherosclerosis. Ann Intern Med, 2008; 148: 501–508.

3. Li Z, Lacson E, Jr, Lowrie EG, Ofsthun NJ, Kuhlmann MK, Lazarus JM, et al. The epidemiology of systolic blood pressure and death risk in hemodialysis patients. Am J Kidney Dis., 2006; 48: 606–615.
4. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, et al. Blood pressure and end-stage renal disease in men. N Engl J Med, 1996; 334: 13–18.
5. Cheung AK, Rahman M, Reboussin DM, Craven TE, Greene T, Kimmel PL, et al. Effects of intensive BP control in CKD. J Am Soc Nephrol, 2017; 28: 2812–2823.
6. Mojon A, Ayala DE, Pineiro L, Otero A, Crespo JJ, Moya A, et al. Comparison of ambulatory blood pressure parameters of hypertensive patients with and without chronic kidney disease. Chronobiol Int., 2013; 30: 145–158.
7. Davis TK, Davis AJ. Ambulatory blood pressure monitoring should be used in the primary care setting to diagnose hypertension. Am J Hypertens, 2013; 26: 1057–1058.
8. Sebo P, Pechere-Bertschi A, Herrmann FR, Haller DM, Bovier P. Blood pressure measurements are unreliable to diagnose hypertension in primary care. J Hypertens. 2014; 32: 509–517
9. Lambers Heerspink HJ, Gansevoort RT, Brenner BM, Cooper ME, Parving HH, Shahinfar S, et al. Comparison of different measures of urinary protein excretion for prediction of renal events. J Am Soc Nephrol, 2010; 21: 1355–1360.
10. Methven S, MacGregor MS, Traynor JP, Hair M, O'Reilly DS, Deighan CJ. Comparison of urinary albumin and urinary total protein as predictors of patient outcomes in CKD. Am J Kidney Dis, 2011; 57: 21–28.
11. Bhandari S, Ives N, Brettell EA, Valente M, Cockwell P, Topham PS, et al. Multicentre randomized controlled trial of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker withdrawal in advanced renal disease: the STOP-ACEi trial. Nephrol Dial Transplant, 2016; 31: 255–261.
12. Bakris GL, Hart P, Ritz E. Beta blockers in the management of chronic kidney disease. Kidney Int., 2006; 70: 1905–1913.
13. Kasiske BL, Anjum S, Shah R, Skogen J, Kandaswamy C, Danielson B, et al. Hypertension after kidney transplantation. Am J Kidney Dis., 2004; 43: 1071–1081.
14. Kithas PA, Supiano MA. Hypertension and chronic kidney disease in the elderly. Adv Chronic Kidney Dis, 2010; 17: 341–347.
15. Wheeler DC, Becker GJ. Summary of KDIGO guideline. What do we really know about management of blood pressure in patients with chronic kidney disease? Kidney international, 2013; 83(3): 377–83.
16. Group SR, Wright JT Jr., Williamson JD, Whelton PK, Snyder JK, Sink KM, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. The New England journal of medicine, 2015; 373(22): 2103–16.
17. Chertow GM, Beddhu S, Lewis JB, Toto RD, Cheung AK. Managing Hypertension in Patients with CKD: A Marathon, Not a SPRINT. Journal of the American Society of Nephrology: JASN, 2016; 27(1): 40–3.
18. Hypertension EETFftMoA. 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension. Journal of hypertension, 2013; 31(10): 1925–38.
19. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). Jama, 2014; 311(5): 507–20.
20. Muntner P, Anderson A, Charleston J, Chen Z, Ford V, Makos G, et al. Hypertension awareness, treatment, and control in adults with CKD: results from the Chronic Renal Insufficiency Cohort (CRIC) Study. American journal of kidney diseases: the official journal of the National Kidney Foundation, 2010; 55(3): 441–51.
21. Wright JT, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glassock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG: Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. JAMA, 2002; 288: 2421–2431.
22. Weiner DE, Tighiouart H, Levey AS, Elsayed E, Griffith JL, Salem DN, Sarnak MJ: Lowest systolic blood pressure is associated with stroke in stages 3 to 4 chronic kidney disease. J Am Soc Nephrol, 2007; 18: 960–966.
23. Rossignol P, Massy ZA, Azizi M, Bakris G, Ritz E, Covic A, et al. The double challenge of resistant hypertension and chronic kidney disease. Lancet, 2015; 386: 1588–1598.
24. Peralta CA, Hicks LS, Chertow GM, Ayanian JZ, Vittinghoff E, Lin F, et al. Control of hypertension in adults with chronic kidney disease in the United States. Hypertension, 2005; 45(6): 1119–24.
25. Landray MJ, Emberson JR, Blackwell L, Dasgupta T, Zakeri R, Morgan MD, et al. Prediction of ESRD and death among people with CKD: the Chronic Renal Impairment in Birmingham (CRIB) prospective cohort study. American journal of kidney diseases: the official journal of the National Kidney Foundation, 2010; 56(6): 1082–94.
26. Martinez-Castelao A, Gorriz JL, Portoles JM, De Alvaro F, Cases A, Luno J, et al. Baseline characteristics of patients with chronic kidney disease stage 3 and stage 4 in Spain: the MERENA

observational cohort study. BMC nephrology, 2011; 12: 53.
27. Imai E, Matsuo S, Makino H, Watanabe T, Akizawa T, Nitta K, et al. Chronic Kidney Disease Japan Cohort study: baseline characteristics and factors associated with causative diseases and renal function. Clinical and experimental nephrology, 2010; 14(6): 558–70.
28. Plantinga LC, Miller ER 3rd, Stevens LA, Saran R, Messer K, Flowers N, et al. Blood pressure control among persons without and with chronic kidney disease: US trends and risk factors 1999–2006. Hypertension, 2009; 54(1): 47–56.
29. Konta T, Ikeda A, Ichikawa K, Fujimoto S, Iseki K, Moriyama T, et al. Blood pressure control in a Japanese population with chronic kidney disease: a baseline survey of a nationwide cohort. American journal of hypertension, 2012; 25(3): 342–7.
30. Thomas G, Xie D, Chen HY, Anderson AH, Appel LJ, Bodana S, et al. Prevalence and Prognostic Significance of Apparent Treatment Resistant Hypertension in Chronic Kidney Disease: Report From the Chronic Renal Insufficiency Cohort Study. Hypertension, 2016; 67(2): 387–96.