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ASSESSMENT OF WHOQOL BREF DOMAINS AND ANTIHYPERTENSIVES PRESCRIPTION PATTERN IN HEMODIALYSIS PATIENTS

Nephrology

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ABSTRACT

Background: ESRD is considered as an important cause of mortality worldwide. Patients with CKD on Hemodialysis treatment is very complex requires additional importance in prescribing antihypertensives and also patients on Hemodialysis have effects on functional state and quality of life (QOL). **Objectives:** The study aimed to assess prescribing pattern of antihypertensives and to demonstrate QOL in different domains of patients with ESRD underdoing hemodialysis. **Materials and Methods:** Study comprised of 85 patients with ESRD under hemodialysis conducted in multi-speciality hospital between September 2019 to February 2020.The data was collected from the records and by interviewing patients. **Results:** The mean age of the study population was 54.76±14.32, 72% were males, hypertension is the common cause of ESRD. Calcium channel blockers are the most commonly prescribed drugs followed by alpha blockers, diuretics, beta blockers, vasodilators etc. Comparing the four domains of ESRD patients, environmental domain was the highest with a mean score of 64.56±19.86while the physical health domain was the lowest with a mean score of55.6±12.60. **Conclusion:** Calcium channel blockers and alpha blockers are most commonly prescribed antihypertensives. The four domains were significantly and positively interrelated with moderate to strong relationships.

KEYWORDS

Hemodialyis , Quality of life , End stage renal disease , Chronic kidney disease , Antihypertensives ,prescribing pattern.

INTRODUCTION

Chronic kidney disease (CKD) is a heterogeneous disorder affecting kidney structure and function [1]. CKD on HD (hemodialysis) is associated with poor outcomes due to a high burden of comorbidity. It affects multiple organ systems in the human body and is associated with a markedly increased risk of cardiovascular morbidity and mortality [2]. The three common comorbidities associated with CKD are hypertension (HTN), diabetes, and hyperlipidemia . The Prevalence of hypertension in CKD ranges from 60 to 90 % based on the stage of CKD. Uncontrolled hypertension is also associated with higher risk for cardiovascular morbidity and mortality [3]. Patients with end stage renal failure (ESRD) can undergo either renal replacement therapy or kidney transplantation. Renal replacement therapy includes hemodialysis and peritoneal dialysis [4]. Dialysis should be initiated when the benefit from relieving uremic signs and symptoms is thought to outweigh its risk and associated effect on quality of life. Hemodialysis can help your body to control blood pressure and maintain the proper balance of fluid and various minerals such as potassium and sodium in your body. In general, hemodialysis begins well before your kidneys have shut down to the point of causing life-threatening complications [5].

There is a periodical connection between CKD and HTN. There is strong evidence that HTN accelerates the progression of renal disease. The prevalence of HTN in CKD patients are very high, which may progress to high cardiovascular risk in CKD patients [6, 7]. Hence, maintaining target blood pressure(BP) in CKD patient is very essential. According to Kidney Disease Improving Global Outcomes (KDIGO), individualization of BP targets and drugs must be chosen according to age, co-existent cardiovascular disease and other co-morbidities, risk of progression of CKD and tolerance of treatment should be considered while selecting a drug to treat HTN in CKD patient [8].

CKD is considered to be an important cause of morbidity and mortality worldwide. Individual, social, and economic consequences of CKD are enormous. Patients with CKD on hemodialysis have to bear significant physical, psychological, and economic challenges [9].Not only patients but also their families must change lifestyles to adapt to the rigor and frequencies of hemodialysis sessions, which can be multiple times a week. In addition to that, specific dietary regimens and associated health problems also adversely affect QOL of these patients. Thus, in patients with CKD on hemodialysis, there is a considerable effect on functional state and QOL [10]. QOL is a significant parameter that needs to be addressed in chronic diseases like CKD. Evaluation of QOL of patients with CKD not only helpful to assess the quality of dialysis program but also help nephrologists to develop better interventions and plans of care for the future [11]. Therefore, we conducted a prospective observational study to determine the drug utilisation pattern by comparing the antihypertensive prescription trends with standard guidelines and quality of life was assessed in patients undergoing hemodialysis in a Tertiary care hospital.

MATERIALS AND METHODS

Study Design

This was a single-center, prospective observational study carried out at Tertiary care hospital, Secunderabad over a period of six months. This protocol was approved by the Ethics Committee at our institution. Between September 2019 and February 2020 all consecutive patients with the following criteria were recruited: a) Patients undergoing haemodialysis are considered; b) Male and Female age group between 19 to 80 years are considered; c) Both Inpatients and Outpatients are considered. The following criteria were excluded: a) Pregnant and lactating women are excluded; b) Other types of dialysis like Peritoneal dialysis subjects are excluded; c)Psychiatric patients are excluded; d) Pediatric patients are excluded.

Data Collection

Ethical clearance has been obtained from Institutional Ethical Committee prior to the initiation of study. Patients who met the inclusion criteria were enrolled for the study. Informed consent was obtained from the patient or attenders of patient. The patient's demographic details, medical and medication history, clinical data such as diagnosis, clinical illness, drugs details such as name of the drug, dosage, route, frequency and other relevant details were collected by reviewing their prescriptions, medical records and by interviewing the patients and/or care takers were documented in a suitably designed individual case record form. In order to assess the QOL, WHOQOL- BREF was used.

WHOQOL-BREF questionnaire consists of 26 items. First and second items assess individual's overall perception of QOL and health then the remaining items are categorized under physical, psychological, social, and environmental domains. Each item is rated by a 5-point Likert scale. The responses were scaled in a positive direction. The mean score of each domain was used to calculate the raw score. Raw scores were then transformed to a 0–100scale using a transformation formula.

Higher score reflects a better QOL. Lower score indicates a poor QOL.WHOQOL-BREF questionnaire has been validated for assessing QOL in patients with ESRD in different settings and has been used to assess QOL by a number of studies elsewhere [12].

STATISTICALANALYSIS

Using the Statistical Package for Social Service (SPSS) 20 version, the results were analyzed by t test and pearson's correlation. A *p* value less than 0.05 were considered as statistically significant at 5% level of significance with confidence interval 95%.

RESULTS

Demographics

A total of 85 patients were included in the study based on inclusion criteria. Table 1 shows the characteristics of study population. Age parameter reveal that 35% of patients were found between 61-70 years followed by 22% of patients between 51-60 years, 12% between 41-50 years, 11% between 21-30 years and 71-80 years then 9% between 31-40 years. The mean age of the study population was found to be 54.76±14.32.Of all the patients, 72% were male and 28% were female. Body mass index (BMI) data showed that 48% of patients belong to normal category followed by 21% of overweight patients, 20% of underweight patients and 11% of obese patients. Common comorbidities observed in this population were hypertension, DM, CAD and hypothyroidism.

Table 1: Demographic characteristics of the Study Population

Parameter	Number	Percentage
Age (years)		
21-30	9	11
31-40	8	9
41-50	10	12
51-60	19	22
61-70	30	35
71-80	9	11
Gender		
Male	61	72
Female	24	28
BMI		
Underweight	17	20
Normal	41	48
Overweight	18	21
Obese	9	11
Comorbidities		
Hypertension	59	69
DM	29	34
CAD	8	9
Hypothyroidism	12	14
Others	34	40

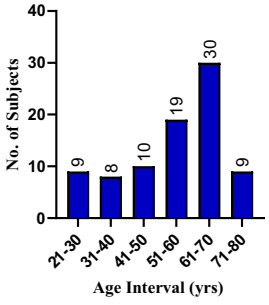


Figure 1:Age wise distribution of patients

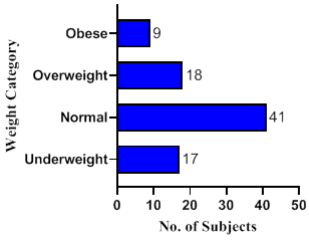


Figure 2: Distribution of patients according to weight

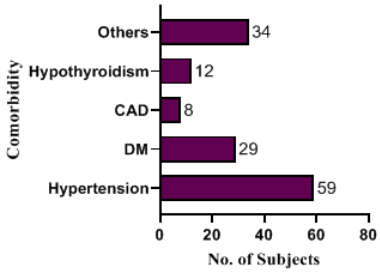


Figure 3:Distribution of patients according to comorbidities

Drug utilization pattern

Antihypertensive drugs used in the study population were identified and categorized. It is shown in Table 2 which depict that 27%calcium channel blockers (CCBs), 24% alpha blockers, 20% diuretics, 17% beta blockers, 7% vasodilators,1% angiotensin receptor blockers (ARBs)s. The most commonly prescribed CCBs in this study was nifedipine followed by amlodipine, cilnidipine , benidipine and diltiazem.

Table 2: Drug utilization of Anti-hypertensive Agents

Category	N	%
Calcium channel blockers(27%)		
Nifedipine	25	12%
Amlodipine	14	7%
Cilnidipine	13	6%
Benidipine	3	1%
Diltiazem	1	1%
Beta Blockers(17%)		
Metoprolol	24	12%
Carvedilol	10	5%
ARBs(1%)		
Olmesartan	1	1%
Alpha blockers(24%)		
Prazosin	16	8%
Moxonidine	15	7%
Clonidine	11	5%
Midodrine	4	2%
Tamsulosin	3	1%
Silodosin	1	1%
Vasodilators(7%)		
ISDN + Hydralazine	4	2%
ISDN	2	1%
Hydralazine + Minoxidil	2	1%
Minoxidil	2	1%
Nicorandil	1	1%
Hydralazine	1	1%
Diuretics(20%)		
Torsemide	31	15%
Metolazone	8	4%
Furosemide	3	1%

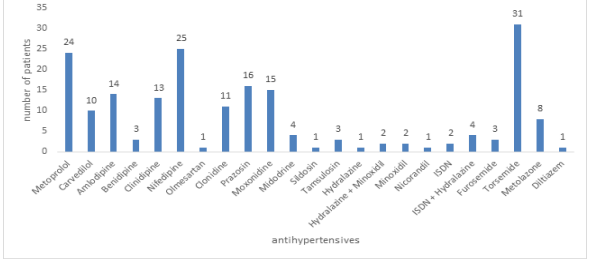


Figure 4: Frequency of individual antihypertensives prescribed in patients with hemodialysis

The average number of antihypertensives prescribed to the patients is found to be 2 antihypertensives.

In this study multiple classes of antihypertensives were prescribed the average number of antihypertensives per patient is found to be two drugs and among the patients (17%) were prescribed with a single class of antihypertensive, (36%) were prescribed with two

antihypertensives, (25%) were prescribed with three antihypertensives, (15%) were prescribed with four antihypertensives, and remaining (4%) were prescribed with more than four classes of antihypertensives.

In patients with monotherapy Calcium channel blockers are the most prescribed followed by diuretics in double therapy the combination of Calcium channel blockers + Diuretics are the most prescribed followed by combination of Beta blockers + Alpha antagonists and the triple mostly included Calcium channel blockers, Beta blockers, Diuretics in combination with other classes of antihypertensives.

Assessment of laboratory parameters

Various laboratory parameters were monitored in this study population. The mean and SD values of each parameter is given in Table 4. The mean blood urea nitrogen and creatinine level were found to be increased. Hemoglobin level was decreased. Sodium and potassium level were normal.

Table 4: Laboratory Parameters

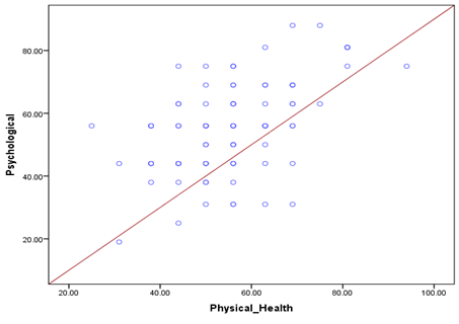
Parameter	Mean ± SD
Hemoglobin (g/dl)	9.68±1.50
Blood urea nitrogen (mg/dl)	88.38±23.07
Sodium (mEq/L)	139.3±4.10
Potassium (mmol/L)	4.71±0.71
Creatinine (mg/dl)	7.86±1.94

QOL scores and correlation among various domains

The QOL scores of various domains are mentioned in the table 5. Details of Pearson's correlations among various domains in Figure 5 to 10. Analysis of the strength of correlation among various domains showed moderate inter domain correlation (Pearson's r>0.3 and <0.5) in Figure 1 and 4then strong inter domain correlation (Pearson's r>0.5) in Figure 2, 3, 5 and 6.

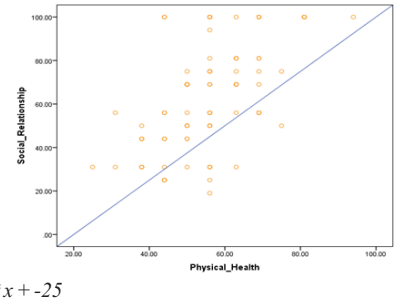
Table 5: WHOBREF- QOL

Domain	Minimum	Maximum	Mean ± SD
Physical Health	25	94	55.6±12.60
Psychological	19	88	55.75±14.81
Social Relationship	19	100	63±23.99
Environment	19	100	64.56±19.86



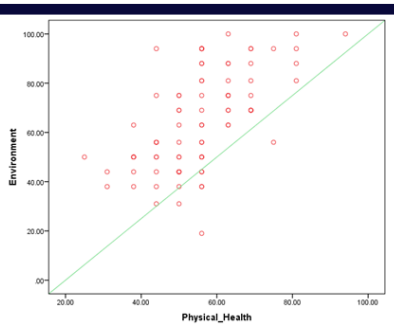
*y= 1*x + -10*
r= 0.496

Figure 5: Correlation Between Physical Health and Psychological Domain



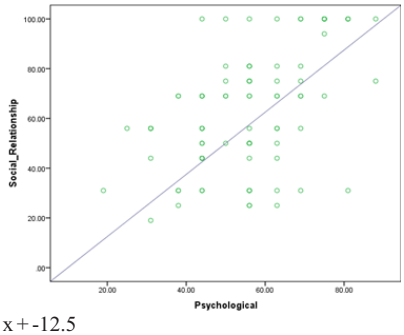
*y= 1.25*x + -25*
r= 0.567

Figure 6: Correlation Between Physical Health and Social Relationship



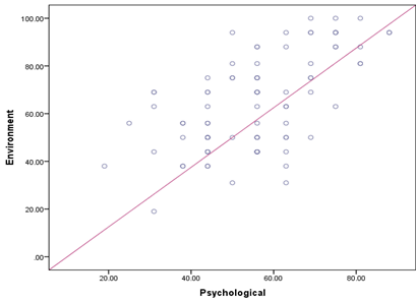
*y= 1.25*x + -25*
r= 0.607

Figure 7: Correlation Between Physical Health and Environment



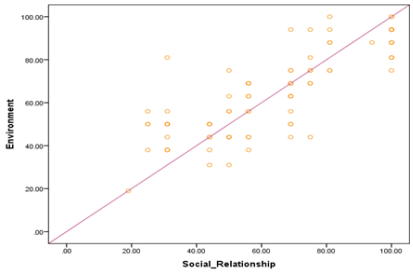
y= 1.25* x + -12.5
r= 0.496

Figure 8: Correlation Between Psychological and Social Relationship



*y= 1.25*x + -12.5*
r= 0.596

Figure 9: Correlation Between Psychological and Environment



*y= 1*x + 0*
r= 0.802

Figure 10: Correlation Between Social Relationship and Environment

LIMITATIONS: The major limitation of this study is the sample size.

DISCUSSION

In the present study, 85 patients were enrolled. More number of this patients belonged to the age group 61 to 70 years since the older one is the likelihood for ESRD which is similar to the study reported by Neethu J, et al. Our study showed that male preponderance with

corresponds to results showed in another study [13]. In addition to this, findings also revealed that prevalence of ESRD was more in male than female. Men are at increased risk of reaching kidney failure sooner than women due to factors like higher testosterone level and unhealthier lifestyles [14]. Only 41 patients were fall into normal BMI category, while the rest of the population resided in other categories of BMI like underweight, overweight and obese. Being overweight increases the risk for diabetes and hypertension which in turn are the two main causes of kidney disease [15]. Cardiovascular disease is considered as the number one cause of morbidity and mortality in patients with ESRD. Diabetes mellitus is the greatest contributor to ESRD. Hypertension, DM, CAD and hypothyroidism were repeated comorbidities seen in this study with similar to findings reported by Pranavi D, et al [16].

Hypertension and CKD are closely interlinked pathophysiologic states. Persistent hypertension worsens kidney function and progressive decline in kidney function can conversely lead to worsening blood pressure (BP) control [17]. This study revealed that 69% of patients which is almost three fourth of the study population were suffering with hypertension, which is similar to the findings reported by Lee YB, et al [18]. The first step to treat HTN in ESRD patient is to start with non-pharmacologic therapy like dietary interventions and life style modifications.

The Sympathetic over activity is observed in ESRD patient compared to the hypertensive patients with normal renal functions and Increased risk of cardiovascular mortality upto 30% higher than normal patients, the selection of anti-hypertensive regimen in ESRD should be individualised and aimed at preserving Residual Renal Function and considering Associated comorbid conditions, Inter and Intra dialytic blood pressure, Proteinuria.

According to KDIGO and JNC- 8 guidelines for treatment of hypertension in ESRD patients undergoing hemodialysis, RAAS inhibitors are considered first-line antihypertensive agents since they possess cardioprotective and renoprotective properties which add benefits to the patients, when compared to ACEI based therapy ARB based therapy lead to decreased increase in creatinine levels in patients with ESRD as found in a Systematic Review and Meta-Analysis by Kanran Wang et al [19]

Calcium channel blockers are non dialyzable antihypertensives used as second line therapy in ESRD patients prescribed either alone or in combination. Dihydropyridines CCB's have similar benefits as ARB or ACEI in reducing oxidative stress and RAAS inhibitors are considered as third-line antihypertensives in dialysis according to Panagiotis 1 Georgianos et al[20]

In beta blockers Carvedilol and Metoprolol are commonly prescribed drugs in ESRD patients. Beta blockers are preferred choice of drug in patients with cardiovascular complications associated with ESRD.A cohort study conducted by shafi T et al[21] on antihypertensive regimens containing Renin-angiotensin system blocking drug alone, Beta-blocker alone and a combination of both Renin-angiotensin system blocker + Beta blocker found no difference in cardiovascular hospitalizations between antihypertensive regimens.A Systemic review and Meta-analysis study by Jingjing jin et al[22] found evidence that Beta blockers reduced all-cause mortality, cardiovascular events, and hospitalizations in Randomised controlled trials as well as relative reduction of all cause mortality in observational studies in dialysis patients. In another observational study by Assimon M et al[23]found that carvedilol initiation was associated with higher 1-year all cause and cardiovascular mortality than metoprolol initiation which supports the higher use of metoprolol than carvedilol in our study.

In alpha blockers the most prescribed drug was prazosin, most of the patients on haemodialysis were on multiple antihypertensive medications along with alpha antagonists(prazosin) so to reduce the risk of hypotension prazosin is also given in specialized forms like GITS (gastrointestinal therapeutic system) and OPS (osmotic pump drug delivery system).Rajan P Nerukar[24] studied novel formulations alpha blockers found that prazosin(GITS) are more safe and effective . As sympathetic activation is common in ESRD alpha and beta blockers are the rational approach.

The most prescribed drug in diuretics are torsemide followed by metolazone , mostly diuretics are prescribed on non HD days .Diuretics are considered as third line antihypertensives in ESRD .Metolazone was found to be effective than thiazide diuretics at low GFR levels. Patients were prescribed torsemide more than furosemide because of compliance with the number of doses ,Se Won Oh et al [25] studied use of loop diuretics in clinical practice found that torsemide is safe and effective than furosemide in ESRD patients.

Vasodilators mostly prescribed in patients who are diagnosed with coronary artery diseases and among vasodilators the combination of Isosorbide dinitrate and Hydralazine is common followed by Isosorbide dinitrate, a combination of Hydralazine and Minoxidil, Minoxidil, Nicorandil, Hydralazine. The Vasodilators aid in normalising blood pressure by reducing Total peripheral resistance.

Assessment of QOL has become an essential outcome measure for patients with CKD and end stage renal disease (ESRD) in order to evaluate the influence of the disease on patients and the type of renal replacement therapy they require. The different interdomain correlation helps in the provision of better quality of life by considering the relation-ship between quality of life domains as a part of team caring especially in the dialysis units, and the individualised care as a part of Renal replacement therapy decreases the overall health related burden in the End stage renal disease patients undergoing hemodialysis . This study demonstrates QOL in different domains (Physical health, Psychological, Social relationship and Environment) of patients with CKD undergoing hemodialysis. The mean score of all domains (Physical health- 55.6; Psychological -55.75; Social relationship -63; Environment -64.56) suggests that study population have moderate quality of life which is alike to the study reported by [26]. Comparing the four domains of ESRD patients, environmental domain was the highest with a mean score of 64.56±19.86while the physical health domain was the lowest with a mean score of55.6±12.60.The four domains were significantly and positively interrelated with moderate to strong relationships. Moderate inter domain correlation was noticed between physical health and psychological domain then psychological and social relationship domain which is shown in Figure 5 and 8. Strong inter domain correlation was noted among rest of the domains which are shown in Figure 6,7,9 and 10.

CONCLUSION

ESRD has been recognized as a leading public health problem worldwide. In order to treat ESRD, it is important to treat comorbidities as well especially hypertension since hypertension and ESRD are related to each other. Our study provides an insight into Antihypertensive drug prescription in the dialysis dependent ESRD patients who are vulnerable , compliance of drug utilization in our study with standard guidelines is highly variable with mixed results and further long-term antihypertensive drug studies are necessary in dialysis dependent ESRD patients. Domain specific individual care is necessary in Hemodialysis units and importance should be given to strongly correlating domains for optimising Health-related quality of life.

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DISCLOSURE

The authors report no conflicts of interest in this work.

ABBREVATIONS:

CKD : Chronic kidney disease**, ESRD**: End stage renal disease , **HD** : Hemodialysis , **QOL**: quality of life .

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