Assessing ACEI and ARB utilization in Karachi's diabetic nephropathy patients

Faisal Aslam[1], Syed Muhammad Aqeel Abidi[2]*, Syeda Tayyaba Fatima Abidi[3], Faiza Ilyas[2] and Syed Ahsan Ali[2]
[1]The Indus Hospital, Indus Health Network, Korangi Crossing, Karachi, Pakistan
[2]The Aga Khan University Hospital, Karachi, Pakistan
[3]Liaquat National Hospital and Medical College, Karachi, Pakistan

Abstract: **Background**: Diabetes mellitus (DM) is a major global health concern, and its microvascular complication, diabetic nephropathy, is a leading cause of chronic kidney disease and end-stage renal disease. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are proven to delay the progression of diabetic nephropathy; however, their utilization patterns in Karachi, Pakistan, have not been adequately studied. **Objectives**: To assess the prevalence of ACEI and ARB use among patients with diabetic nephropathy in Karachi and to identify demographic and clinical factors influencing their utilization. **Methods**: A cross-sectional study was conducted at Aga Khan University Hospital, Karachi, from September 2021 to August 2022. A total of 118 patients diagnosed with diabetic nephropathy were recruited. Data on demographics, ACEI/ARB usage, creatinine levels, history of ischemic heart disease, and type of treating physician (endocrinologist vs. general physician) were collected. Patients were stratified by age, gender, and ischemic heart disease status. Statistical analysis was performed using chi-square tests, with significance set at $p < 0.05$. **Results**: Of the 118 patients, 53.4% were male and 46.6% female, with a mean age of 62.01 years. Coronary artery disease was present in 66.9% of the cohort. Only 9.3% of patients were under endocrinologist care, and all were prescribed ACEIs. Overall, just 26.3% of patients were receiving ACEIs or ARBs. Females had a slightly higher treatment rate than males (30.9% vs. 22.2%). Patients older than 65 years showed the highest ACEI/ARB utilization (41.9%), indicating an age-associated trend in prescribing patterns. **Conclusion**: The study reveals a substantial underuse of ACEIs and ARBs among diabetic nephropathy patients in Karachi, despite strong evidence supporting their effectiveness. This gap between clinical guidelines and real-world prescribing practices highlights the need for improved physician awareness, enhanced patient education, and strengthened healthcare systems. Addressing these factors could significantly improve renal outcomes and reduce the long-term burden of diabetic kidney disease in South Asia.

INTRODUCTION

Diabetes mellitus is a chronic medical condition characterised by hyperglycemia that necessitates careful and continuing medical care, particularly to prevent the risk of long-term complications. Diabetes mellitus causes a range of complications from microvascular complications (including nephropathy, retinopathy, and neuropathy) to macrovascular complications such as coronary heart disease and stroke (Cade, 2008). The International Diabetes Federation (IDF) estimates that globally, the overall prevalence of diabetes mellitus was 540 million in 2021, and this is expected to rise to 783 million by 2045 (Sun *et al.*, 2022). It is also one of the most common chronic disorders in South Asia (Kanaya, 2024). Diabetic nephropathy is one of the most common microvascular complications that leads to end-stage kidney disease if left untreated. The optimal time for intervention is as early as possible in the course of the disease, involving the use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), coupled with intensive glycemic and blood pressure control (Lim,

2014). The mechanism through which ACEIs and ARBs act is by decreasing intraglomerular pressure, thereby minimizing the progression of, or even preventing glomerular disease (Kobori *et al.*, 2013). Early intervention and treatment for diabetic nephropathy are vital because they not only slow the progression of kidney disease but also lead to improved overall health, reduced healthcare costs, and a better quality of life for individuals with diabetes (Kumar *et al.*, 2023). However, despite the established benefits of ACEIs and ARBs, a study conducted in the United States revealed that only approximately 60% of patients with proteinuria secondary to diabetes were utilizing ACEIs or ARBs, indicating an underuse of these drugs in this population (Yang *et al.*, 2010). Other studies have reported similar trends, underscoring suboptimal utilization of these medications. For instance, a study conducted in the elderly population of Pennsylvania showed that only about half of the population was using ACEI/ARB (Winkelmayer *et al.*, 2005). In another study within the Chinese population, only 39% of individuals were on ACEI/ARB therapy. Multivariate analysis demonstrated that comorbidities, hospital tier, region, physician speciality, and the educational level of

*Corresponding author: e-mail: syed.abidi2@scholar.aku.edu

patients were associated with ACEI/ARB use (Xie *et al.*, 2015). Karachi faces significant challenges in its healthcare infrastructure, particularly concerning diabetes management (Khan *et al.*, 2023). Limited access to healthcare services, disparities in healthcare quality, and a shortage of specialized diabetes clinics pose obstacles to effective diabetes management. Additionally, awareness and education about diabetes prevention and management remain essential in a city where diabetes prevalence is high, making community outreach and education programs vital components of diabetes care in Karachi. Unfortunately, there is no available data from the relevant population regarding the use of these medications. Consequently, this study was undertaken to document the utilization of ACEI/ARB in subjects with diabetes-induced nephropathy in Karachi, Pakistan. The primary objective of this study is to assess the prevalence and factors influencing the utilization of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in patients with diabetes-induced nephropathy in Karachi, Pakistan. The aim to complete this literature gap and provide insights into the extent to which these medications are being used in this patient population and to identify any potential barriers or factors associated with their underuse.

MATERIALS AND METHODS

Study design and duration
This cross-sectional study was conducted from September 2021 to August 2022. Patients were recruited randomly from the inpatient and outpatient departments of Aga Khan University Hospital, Karachi, Pakistan.

Sample size calculation
The sample size was calculated using a predefined formula to ensure adequate power for detecting statistically significant associations (Pourhoseingholi *et al.*, 2013, Roett *et al.*, 2012). A total of 118 patients were included based on this calculation.

Inclusion and exclusion criteria
Inclusion criteria
Diagnosed cases of diabetic nephropathy based on 24-hour urinary protein levels (>30 mg/day) or early morning spot microalbumin levels (≥30 mg/g creatinine) (Persson and Rossing, 2018).

Exclusion criteria
Patients with urinary tract infections, pregnancy, renal artery stenosis, end-stage kidney disease, or hypersensitivity to ACEIs/ARBs.

Data collection
Patients' demographic data, including age, gender, creatinine levels, continuous use of ACEIs and ARBs, and the type of treatment administered (by endocrinologists or general physicians), were meticulously collected and recorded on a pre-designed proforma by the primary investigator.

Statistical analysis
Data were recorded and analyzed using SPSS version 21. Descriptive statistics, including means and standard deviations, were calculated for continuous variables, while frequencies and percentages were determined for categorical variables. Data stratification was performed by age, gender, history of ischemic heart disease, and the type of treatment received to explore potential effect modifiers. The chi-square test was employed to determine associations between categorical variables, with a significance level set at p-value < 0.05.

Study limitations
This study has several limitations, including its single-center design and the potential for selection bias. These factors should be considered when interpreting the findings.

RESULTS

A total of 118 patients were included in this study based on the predefined inclusion criteria. Demographic characteristics, including age (years), gender, usage of ACEIs, ARBs, history of ischemic heart disease, and treatment by endocrinologists or general physicians, were recorded. The study population consisted of 63 males (53.4%) and 55 females (46.6%). The mean age of the included patients was 62.01 ± 13.65 years. Patients were categorised into four age groups: those aged less than 45 years (11.9%), 45 to 55 years (17.8%), 55 to 65 years (32.2%), and those older than 65 years (38.1%) (Fig. 1). The mean age for males was 50.23 ± 11.9 years, whereas for females, it was 52.57 ± 11.56 years. The mean creatinine level was 1.13 ± 0.48 mg/dL, with a range from 0.30 to 2.50 mg/dL. Out of the 118 patients, 79 (66.9%) were diagnosed with coronary artery disease, while 39 (33.1%) did not have coronary artery disease (Table 1).

Table 1: Demographics of the patients

Characteristics	n (%)
Gender	
Male	63 (53.4)
Female	55 (46.6)
Age (years)	
<45	14 (11.9)
45-55	21 (17.8)
55-65	38 (32.2)
>65	45 (38.1)
Mean Age	
Total	62.01 ± 13.65 years
Males	50.23 ± 11.9 years
Females	52.57 ± 11.56 years
Coronary Artery Disease	
Yes	79 (66.9)
No	39 (33.1)
Treatment By Endocrinologists	
Yes	11 (9.3)
No	107 (90.7)
Drug Usage	
ACE Inhibitors	11 (9.3)
ARBs	20 (16.9)
Neither ACEI nor ARBs	87 (73.8)

Stratification according to gender was not statistically significant (p= 0.080) and showed that amongst the 63 male patients, 14 (22.2%) were using ACEI or ARB, while 49 (77.8%) were not. Whereas, among the 55 female patients, 17 (30.9%) were using ACEI or ARB, and 38 (69.1%) were not. A significant association (p= 0.000) was seen between those diagnosed with Coronary Artery Disease and those using ACEI/ARBs, 31 (39.2%) of patients with CAD were also using ACEI/ARBs. On the contrary, no patient who wasn't diagnosed with CAD was using ACEI or ARBs (Table 2).

It was also noted that all of the patients who were under treatment by an endocrinologist were receiving ACEI as treatment and all those under treatment by physicians other than endocrinologists used ARBs as treatment. The results indicate variations in ACEI and ARB utilization based on age and gender within the study population.

DISCUSSION

In our study, a significant finding was the notably low utilization of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), with only 26.2% of eligible patients receiving these critical medications (Fig. 2). These findings are of great concern, especially when considering the well-established fact that diabetic nephropathy is the most prevalent end-organ complication in Type 2 diabetic patients and can progress to chronic kidney disease (CKD). Additionally, it was evident that ARBs were prescribed more frequently than ACEIs, and a higher proportion of females were receiving this therapy compared to males. Numerous studies have demonstrated the increasing prevalence of end-stage renal disease (ESRD) attributable to diabetes over recent decades, making diabetic nephropathy the single most common cause of ESRD in the Western world (Narres *et al*., 2016). Given this alarming trend, timely intervention is paramount. Testing for microalbumin in urine is a simple and cost-effective means of identifying individuals at immediate risk. Early detection of albuminuria can pave the way for treatments that reduce albumin in the urine, ultimately improving renal and cardiac prognosis. Our study found a positive association between those diagnosed with coronary artery disease and the use of ACEI/ARB (p= 0.000), there were no patients who didn't have CAD diagnosed and were using ACEI/ARBs. This could indicate those with CAD were prescribed the medications to help with their heart function (Xiao-Dong *et al*., 2016).

Our study showed that the highest percentage of ACEI/ARBs was being used by those aged 45-55 years (33.3%), whereas those aged 55-65 and >65 years (28.9% for both) trailed behind, and those <45 years weren't using ACEI/ARBs at all (Fig. 3). However, this pattern seems to be random as no significant association was seen (p= 0.120). Still, there is a need to promote the use of ACEI/ARBs early and continue it, unless contraindicated.

The cornerstone of intervention for the prevention and management of diabetic kidney disease lies in the blockade of the renin-angiotensin system (RAS) (Rossing *et al*., 2022). This can be achieved through ACEIs, blockers of the angiotensin type 1 (AT1) receptor, or direct inhibition of the upstream enzyme renin (Scheen, 2004). These RAS blockers have proven effective in ameliorating renal damage in diabetes (Zhang *et al*., 2022). In the case of type 2 diabetic patients with microalbuminuria, these drugs not only stabilize proteinuria but also preserve renal function (Yacoub and Campbell, 2015). Our study found that the frequency of ACEI/ARB use (26.3%) among patients with diabetic nephropathy in Karachi is lower than what has been reported in studies from other regions. For instance, a study in the Chinese population reported a frequency of use of 39.7% (Xie *et al*., 2015). The implications of such underutilization are concerning, as it may predispose diabetic patients to progress towards end-stage kidney disease (ESKD). Research conducted in the United States by Rosen *et al*. reported that only 54% of patients with albuminuria received ACEI or ARB treatment (Rosen *et al*., 2004). Similarly, studies conducted by Gold *et al*. and others in the United States found even lower rates of ACEI or ARB utilization in high-risk groups, ranging from 40% to 45% (Xie *et al*., 2015, Scarsi and Bjornson, 2000, Rosen *et al*., 2004, Dunn *et al*., 1999, Ravid *et al*., 1994). This international trend underscores the need for increased attention to medication utilization in diabetic nephropathy.

The underutilization of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in the management of diabetic nephropathy can be attributed to a complex interplay of healthcare system-related and patient-related factors (Yeh *et al*., 2011). These include limited awareness and education among both healthcare providers and patients, physician practices and adherence to treatment guidelines, inadequacies in healthcare infrastructure, economic considerations affecting medication affordability, guideline variability, demographic disparities in prescription rates, limited access to specialized care, and health literacy challenges etc. As per our findings, all 11 (100%) patients under treatment of an endocrinologist received ACEI or ARBs as treatment. Whereas, only 20 (18.7%) of patients being treated by non-endocrinologists were using ACEI or ARBs as a treatment modality. There was a statistically significant association between the use of ACEI/ARBs and whether treatment was being done by a physician or an endocrinologist (p= 0.000). In our study, there was no significant association (p= 0.120) seen between age and use of ACEI/ARBs. There was no use of ACEI or ARB in those under the age of 45 years, while 7 (33.3%) patients aged between 45 and 55 years were on ACEI or ARB treatment. In the 55 to 65 years age group, 11 (28.9%) patients were using ACEI or ARB. Among patients aged more than 65 years, 13 (28.9%) were on ACEI or ARB treatment (Table 2).

Table 2: Factors associated with the use of ACEI/ ARBs

Variables	Use of ACEI or ARBs		Total	X^2	P value
	Yes N= 31 (%)	No N= 87 (%)			
Under treatment by an endocrinologist					
Yes	11 (100%)	0 (0.0%)	11		
No	20 (18.7%)	87 (81.3%)	107		
Age (years)				5.8289	0.120
<45	0 (0.0%)	14 (100%)	14		
45-55	7 (33.3%)	14 (66.7%)	21		
55-65	11 (28.9%)	27 (71.1%)	38		
>65	13 (28.9%)	32 (71.1%)	45		
Gender				3.0691	0.080
Male	14 (22.2%)	49 (77.8%)	63		
Female	17 (30.9%)	38 (69.1%)	55		
Coronary Artery Disease					20.7569
Yes	31 (39.2%)	48 (60.8%)	79	Yes	
No	0	39 (100%)	39	No	
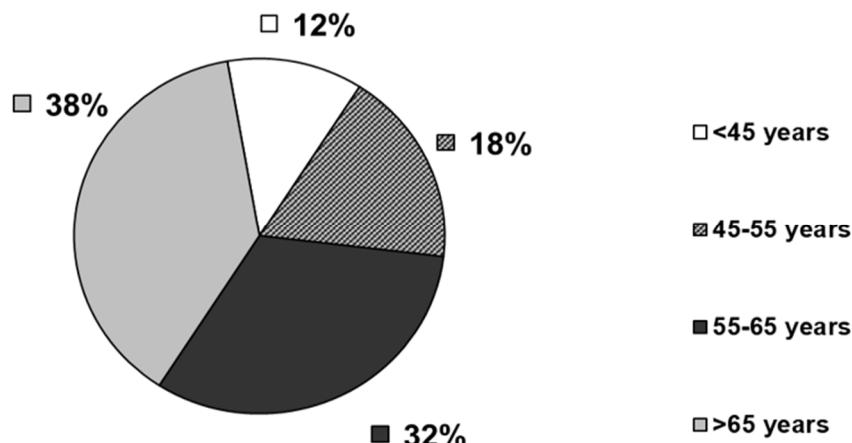
Fig. 1: Distribution of the study population according to age
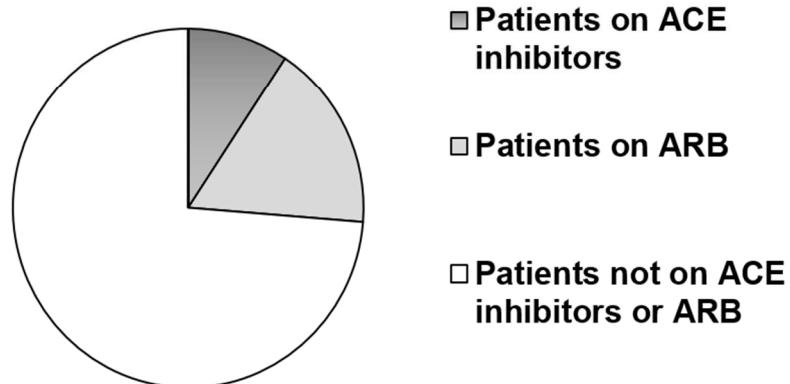
Fig. 2: Distribution of the study population using ACEI or ARB

Pak. J. Pharm. Sci., Vol.39, No.2, February 2026, pp.530-536

533
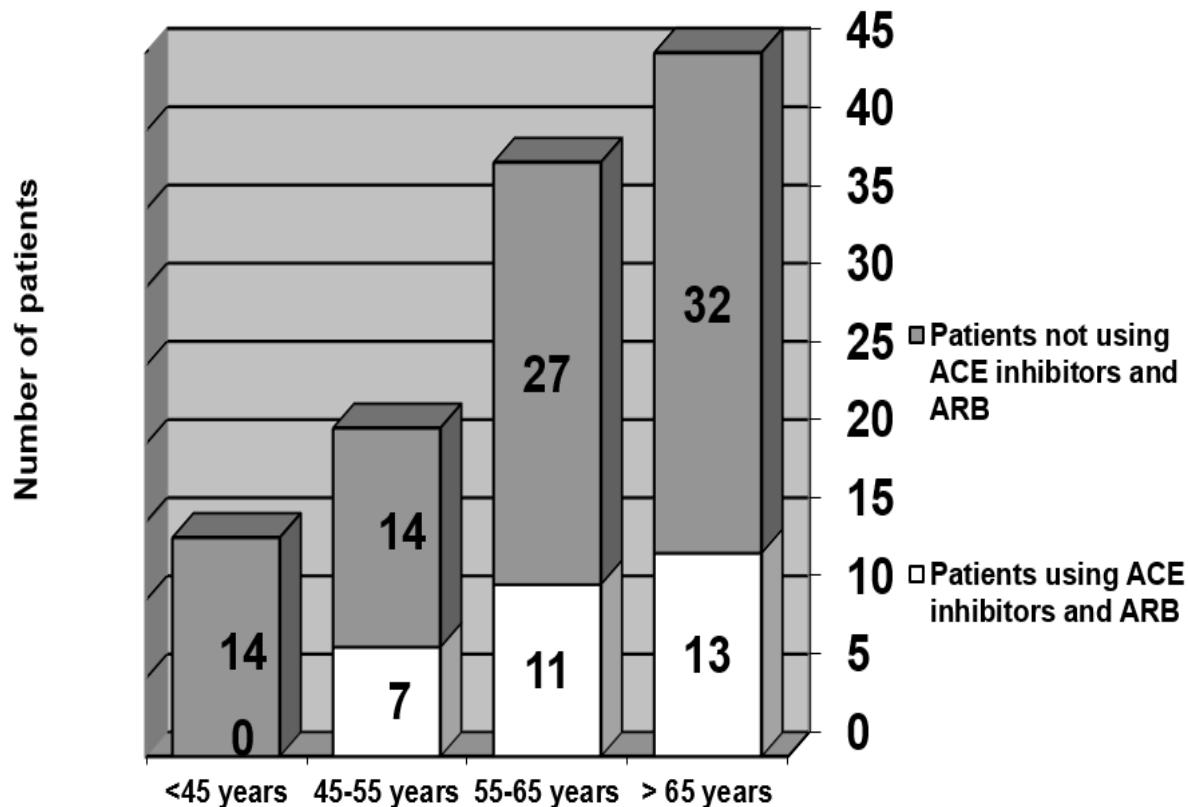
Fig. 3: Frequency of ACEI and ARB use stratified by Age groups (Number of patients)

Our study displayed a significant association (p= 0.000) between the treatment by an endocrinologist and the use of ACEI/ARBs, this shows that endocrinologists do know the significance of incorporating ACEI/ARBs in treatment of patients with diabetic nephropathy. It should be encouraged that patients with diabetic nephropathy consult physicians from the relevant speciality rather than general physicians. However, for those who can't do so for financial, accessibility, or any other reasons the general physician should be well versed in treatment guidelines to make sure maximum benefit reaches to patients.

In light of our findings, it is imperative to consider strategies to address the underuse of ACEIs and ARBs in diabetic nephropathy patients in Karachi and, by extension, South Asia. These strategies may include enhancing physician awareness and adherence to treatment guidelines, facilitating patient education, and improving healthcare infrastructure to ensure equitable access to essential medications. By implementing these recommendations and working collectively to bridge the gap between evidence-based guidelines and clinical practice, we can take significant strides towards reducing the burden of diabetic kidney disease and improving the lives of those affected by diabetes.

Despite these important findings, it is essential to acknowledge the limitations of our study. Firstly, the study was single-centered, which restricts the generalizability of our results to the broader population. Additionally, not all patients visiting this tertiary care centre were consistently followed up, making it challenging to ascertain long-term outcomes. Furthermore, the sample size was relatively small, warranting further large-scale studies, which should consider enrolling physicians to study the multifaceted factors affecting the underuse of ACEIs and ARBs. This study serves as a stepping stone for broader discussions on optimizing diabetes management in South Asia, where the burden of this chronic disease is particularly high. By addressing the underutilization of proven therapies like ACEIs and ARBs, we can potentially mitigate the long-term complications of diabetes and improve the overall quality of life for affected individuals.

CONCLUSION

Our study has unveiled a critical issue in the management of diabetic nephropathy among patients in Karachi, Pakistan. Despite the well-established efficacy of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in slowing the progression of kidney disease, our findings reveal a disconcerting level of underutilization. With only 26.3% of eligible patients benefiting from these essential therapies, a substantial gap exists between evidence-based guidelines and clinical practice.

The significance of our findings cannot be overstated. Diabetic nephropathy remains a prevalent and dire complication of diabetes, often leading to end-stage kidney disease. Timely intervention with ACEIs and ARBs not only preserves renal function but also improves overall patient outcomes, reduces healthcare costs, and enhances the quality of life for those affected by diabetes.

Conflict of interest
The authors declare no conflict of interest related to this research project. They have no financial or personal relationships that could influence the results or interpretation of this study.

Disclaimer
The opinions expressed in this paper are those of the authors and do not necessarily reflect the views of any organization or institution with which they may be affiliated. The information presented in this paper is intended for academic and research purposes only and should not be construed as professional advice or recommendations.

REFERENCES

Cade WT (2008). Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. *Phys. Ther.,* **88**: 1322-1335.

Dunn EJ, Burton CJ and Feest TG (1999). The care of patients with diabetic nephropathy: audit, feedback, and improvement. *Qjm,* **92**: 443-449.

Kanaya AM (2024). Diabetes in South Asians: Uncovering novel risk factors with longitudinal epidemiologic data: kelly west award lecture 2023. *Diabetes Care,* **47**: 7-16.

Khan SJ, Asif M, Aslam S, Khan WJ and Hamza SA (2023). Pakistan's healthcare System: A review of major challenges and the first comprehensive universal health coverage initiative. *Cureus,* **15**: e44641.

Kobori H, Mori H, Masaki T and Nishiyama A (2013). Angiotensin II blockade and renal protection. *Curr Pharm Des,* **19**: 3033-3042.

Kumar M, Dev S, Khalid MU, Siddenthi SM, Noman M, John C, Akubuiro C, Haider A, Rani R, Kashif M, Varrassi G, Khatri M, Kumar S and Mohamad T (2023). The bidirectional link between diabetes and kidney disease: Mechanisms and management. *Cureus,* **15**: e45615.

Lim A (2014). Diabetic nephropathy - complications and treatment. *Int. J. Nephrol. Renovasc. Dis.,* **7**: 361-381.

Narres M, Claessen H, Droste S, Kvitkina T, Koch M, Kuss O and Icks A (2016). The incidence of end-stage renal disease in the diabetic (Compared to the non-diabetic) population: A systematic review. *PLoS One,* **11**: e0147329.

Persson F And Rossing P (2018). Diagnosis of diabetic kidney disease: State of the art and future perspective. *Kidney Int Suppl,* **8**: 2-7.

Pourhoseingholi MA, Vahedi M and Rahimzadeh M (2013). Sample size calculation in medical studies. *Gastroenterol. Hepatol. Bed. Bench,* **6**: 14-17.

Ravid M, Savin H, Jutrin I, Bental T, Lang R and Lishner M (1994). Long-term effect of ACE inhibition on development of nephropathy in diabetes mellitus type II. *Kidney Int. Suppl.,* **45**: S161-164.

Roett MA, Liegl S and Jabbarpour Y (2012). Diabetic nephropathy--the family physician's role. *Am. Fam. Physician,* **85**: 883-889.

Rosen AB, Karter AJ, Liu JY, Selby JV and Schneider EC (2004). Use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in high-risk clinical and ethnic groups with diabetes. *J. Gen. Intern. Med.,* **19**: 669-675.

Rossing P, Caramori ML, Chan JCN, Heerspink HJL, Hurst C, Khunti K, Liew A, Michos ED, Navaneethan

SD, Olowu WA, Sadusky T, Tandon N, Tuttle KR, Wanner C, Wilkens KG, Zoungas S and De Boer IH (2022). KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int,* **102**: S1-S127.

Scarsi KK and Bjornson DC (2000). The use of ACE inhibitors as renoprotective agents in Medicaid patients with diabetes. *Ann. Pharmacother,* **34**: 1002-1006.

Scheen AJ (2004). Renin-angiotensin system inhibition prevents type 2 diabetes mellitus: Part 1. A meta-analysis of randomised clinical trials. *Diabetes Metab,* **30**: 487-496.

Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JCN, Mbanya JC, Pavkov ME, Ramachandaran A, Wild SH, James S, Herman WH, Zhang P, Bommer C, Kuo S, Boyko EJ and Magliano DJ (2022). IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res. Clin. Pract.,* **183**: 109119.

Winkelmayer WC, Fischer MA, Schneeweiss S, Wang PS, Levin R and Avorn J (2005). Underuse of ACE inhibitors and angiotensin II receptor blockers in elderly patients with diabetes. *Am. J. Kidney Dis.,* **46**: 1080-1087.

Xiao-Dong Z, Fei-Fei L, Zhan-Peng W, Xin-Xue L and Zhi-Min D (2016). Renin-angiotensin system inhibitors in patients with coronary artery disease who have undergone percutaneous coronary intervention. *Ther. Adv. Cardiovasc. Dis.,* **10**: 172-177.

Xie Q, Hao CM, Ji L, Hu D, Zhu T, Li X, Qin D and Zhang D (2015). ACEI/ARB underused in patients with type 2 diabetes in Chinese population (CCMR-3B study). *PLoS One,* **10**: e0116970.

Yacoub R and Campbell KN (2015). Inhibition of RAS in diabetic nephropathy. *Int. J. Nephrol. Renovasc. Dis.,* **8**: 29-40.

Yang Y, Thumula V, Pace PF, Banahan BF, 3rd Wilkin NE and Lobb WB (2010). High-risk diabetic patients in Medicare Part D programs: Are they getting the recommended ACEI/ARB therapy? *J. Gen. Intern. Med.,* **25**: 298-304.

Yeh HL, Huang LY, Su S, Yang MC and Wang TC (2011). Underuse of ACE inhibitors and angiotensin II receptor blockers among patients with diabetic nephropathy in Taiwan. *Health Policy,* **100**: 196-202.

Zhang X, Zhou Y and Ma R (2022). Potential effects and application prospect of angiotensin receptor-neprilysin inhibitor in diabetic kidney disease. *J Diabetes Complications,* **36**: 108056.

536

Pak. J. Pharm. Sci., Vol.39, No.2, February 2026, pp.530-536