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RESEARCH ARTICLE

PERIPHERAL ARTERIAL DISEASE MORE PREVALENT IN CHRONIC KIDNEY DISEASE PATIENTS (STAGE III-V)

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ABSTRACT

Introduction: Peripheral artery disease in chronic kidney disease patients is commonly reported in Jammu region, especially in patients with concomitant coronary artery disease, attributable to accelerated atherosclerosis. The present study establishes wide prevalence of peripheral artery disease in chronic kidney disease stage III-V. **Material and Methods**: This study is a cross sectional study which was carried out in Department of Nephrology, GMC Jammu during the year 2013-2014. 130 patients were included in the study period and after taking their proper history and medical records, all patients of Chronic kidney disease(stage III-V) were subjected to baseline investigations and their Ankle Branchial index(ABI) was calculated. The GFR was calculated by Cockcroft –Gault equation. **Results**: The mean age of the patients was 52.34±14.42years, 84(64.6%) being male and 46(35.3%) being females. All the patients were known case of CKD (diagnosed or first time evaluated) following Nephrology OPD at Government Medical College, Jammu with mean eGFR of 15.69±9.8 ml/min^{-1}. 12 patients (9.23%) were CKD stage III, (K/DOQI classification), 55(42.3%) were CKD stage IV and 63(48.46%) were CKD stage V. The lower eGFR was independently associated with PAD. **Conclusion**: Our study showed that the PAD is associated with thrice higher mortality than that of the general population and its prevalence is much higher among end-stage renal disease patients i.e. CKD stage III-V.

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INTRODUCTION

Chronic kidney disease (CKD) includes a spectrum of pathophysiological processes leading to kidney malfunction and a progressive decline in glomerular filtration rate (National Kidney Foundation, 2002). Two equations most commonly used for GFR estimation are Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault Equation (Cockcroft and Gault, 1976). Kronenberg (2009) had reported that the normal annual mean decline in GFR with age during the third decade of life is 1 ml/min per year per 1.73m^2 and the mean GFR is lower in women than in men. The clinical and laboratory complications of CKD become more prominent in stage III and stage IV CKD (Kronenberg, 2009). If the patient progresses to stage V CKD, toxic accumulation of metabolic wastes impair daily living and well-being, compromise nutritional status, and water and electrolyte homeostasis, manifesting in the uremic syndrome (Abboud and Heinrich, 2010). Atherosclerosis goes unabated even in the absence of traditional cardiovascular risk factors. The non-traditional risk factors such as inflammation, malnutrition, and oxidative stress, which enhance and accelerate atherosclerosis are also present more in CKD patients. Even minor renal dysfunction influences cardiovascular risk (Mann *et al.,* 2001). The literature on PAD in the lower extremities in patients with CKD is scarce. PAD is associated with thrice higher mortality than that of the general population6 and its prevalence is much higher among end-stage renal disease patients (O'Hare *et al.,* 2014). The most widely used test for diagnosis of asymptomatic PAD is the measurement of the ankle-brachial systolic pressure index (ABI) (Greenlan *et al.,* 2000). PAD is defined as stenosis or occlusion of aorta or the arteries of the limbs. It is traditionally defined by an ankle-brachial index of <0.9, atherosclerosis being the leading cause and intermittent claudication being the most common symptom. The patients without claudication have walking difficulties (Norgren *et al.,* 2007). About 10-50% of patients with intermittent claudication have never consulted a doctor about their symptoms (Kannel *et al.,* 1970). In patients with diabetes, renal insufficiency, or other diseases that cause vascular calcification, the tibial vessels become non-compressible leading to a false elevation of the ankle pressure. Additional non-invasive diagnostic testing using Toe-Brachial Index, pulse volume recordings, transcutaneous oxygen measurements or duplex ultrasound should be employed to evaluate the patient for PAD (Norgren *et al.,* 2007). Risk factors of PAD in general population include non-white (black) ethnicity10, race (non-Hispanic Blacks)6, male gender (Kannel *et al.,* 1970), age more than 70 years1, smoking (Fowkes *et al.,* 1991), diabetes mellitus (Selvin and Erlinger, 2004), dyslipidemia, hypertension,

obesity (ADA, 2003), C-reactive protein (CRP) (Ridker *et al.,* 2001), hyperviscosity and hypercoagulability (Norgren *et al.,* 2007), hyperhomocysteinemia15, chronic renal failure16. For every 1% increase in HbA1c, there is a corresponding 26% increased risk of PAD (Selvin and Erlinger, 2014). Nevertheless, despite its importance, there are few reports of PVD in CRF patients, and most of them, with a few exceptions, have been performed in dialysis patients (O'Hare *et al.,* 2014). PAD in renal patients showed a higher mortality rate than those not affected by PAD (Leskinen *et al.,* 2002). There is paucity of data on peripheral arterial disease in patients with chronic kidney disease from this part of the world. Hence, the present trial was undertaken to study the profile of peripheral arterial disease in chronic kidney disease patients (Stage III-V) presenting to Nephrology Department of Government Medical College, Jammu from November 2013 to October 2014.

MATERIAL AND METHODS

The present work is a hospital-based cross-sectional study that included 130 subjects, 84 being males and 36 females. The diagnosis and staging of CKD was based on history, clinical examination, investigation and according to guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)]. All the patients with Chronic Kidney Disease (Stage III-V) were subjected to baseline investigations. The GFR was calculated by Cockcroft-Gault equation. . All the patients with Chronic Kidney Disease (Stage III-V) were asked Edinburgh Questionnaire of Claudication in PAD. All patients with Chronic Kidney Disease (Stage III-V) were subjected to Ankle Brachial Index (ABI) using sphygmomanometer with standard sized cuffs and a Doppler ultrasound probe with 7.5 MHz frequency. The highest value obtained was used to calculate ABI.

Inclusion Criteria: Patients >18 years who were diagnosed with CKD (Stage III-V)

Exclusion Criteria
Patients of age <18 years
Patients of CKD (Stage I-II)

Statistical analysis: The data obtained was subjected to statistical analysis. Categorical variables were analysed by Pearson chi square test, Fisher exact test and continuous variables were analysed by ANOVA technique along with post- hoc and Kruskall Wallis test. Also, the multivariate analyses like binary logistic regression analysis have been used to analyse the data using SPSS software ver. 20. A p-value less than 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION

The mean age of the patients was 52.34±14.42years, 84(64.6%) being male and 46(35.3%) being females. All the patients were known case of CKD (diagnosed or first time evaluated) following Nephrology OPD at Government Medical College, Jammu with mean eGFR of 15.69±9.8 ml/min^{-1}. 12 patients (9.23%) were CKD stage III, (K/DOQI classification), 55(42.3%) were CKD stage IV and 63(48.46%) were CKD stage V. 31(23.8%) subjects were smokers, 31(23.8%) subjects were ex-smokers and 68(52.3%) subjects were non-smokers. 112(86.15%) patients were hypertensive, 40(30.7%) were diabetics 15(11.5%) had dyslipidemia, 8(6.15%) had been diagnosed with CAD and 3(2.3%) were having history of cerebrovascular accident (CVA) in the past. Intermittent claudication was seen in 16(12.31%) subjects. 19(14.62%) subjects were having PAD with ABI<0.9. Out of 19 subjects with ABI<0.9 (PAD), 9(47.37%) were having history of IC, whereas 10(52.63%) subjects were having asymptomatic PAD. De Vinuesa *et al.* (2005) had reported a mean age (years) 70 ±11, 64% males, estimated GFR of 35 ±12 (range 6-59) ml/min^{-1} and 17% of PAD with CKD had intermittent claudication. De Vinuesa *et al.* (2005) by logistic regression analysis had found male sex and age as independent indicators of PAD risk (De Vinuesa *et al.,* 2005).

Table 1: Risk factor association with PAD

Risk factor	Frequency	p value
Smoking	4(21.05%)	0.046
Hypertension	19(100%)	0.015
Diabetes Mellitus	11(57.89%)	0.017
Dyslipidemia	5(26.32%)	0.05
CAD	6(31.58%)	0.0001
Stroke	1(5.26%)	0.595

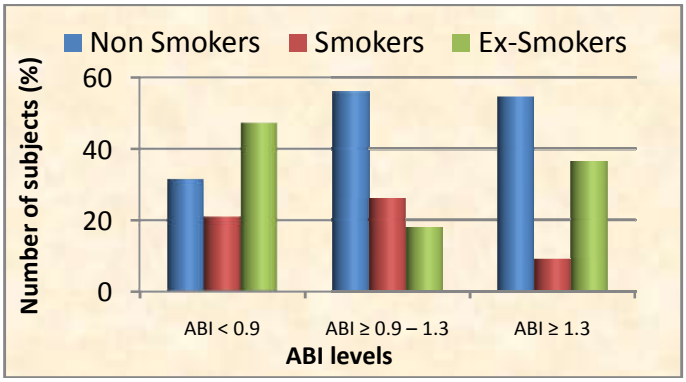

Figure 1. Smoking versus ABI levels

Joachim *et al.* (2009) had similarly found that lower ABI participants were older and more frequently male. Angeles *et al.* (2012) too had reported that PAD affects significantly more males subjects (P = 0.001). Angeles *et al.* (2006) had reported 19% prevalence of PVD in patients with CKD stages IV and V, a mean age of 58 ± 15 years and estimated GFR of 18.6 ± 6.1ml/min^{-1} (Angeles *et al.,* 2006). Shlipak *et al.* (2002) had reported PVD prevalence of 12%, 24%, 13% and 15.9% respectively in CKD stages IV and V patients. They had reported that lower eGFR was independently associated with PAD (Shlipak *et al.,* 2002). Mean eGFR in these studies was higher compared to Angeles *et al*. (2012) and our study. This can be explained by the fact that our study population is relatively small in epidemiologic terms, which suggests that there may not have been sufficient numbers of patients representing the whole range of renal function deterioration. In our study, no association was found between BMI and prevalence of PAD (p-value 0.521). Our results are similar to that observed by Angeles *et al.* (2006). Joachim *et al.* (2009) too reported that lower ABI participants had a higher prevalence of hypertension, diabetes and tobacco use and had more risk of having dyslipidemia (Joachim *et al.,* 200). Binary logistic regression analysis showed significant association of CAD with PAD (p-value 0.041). Angeles *et al*. (2012), by multivariate risk factor analysis, had reported that a previous clinical record of coronary heart disease increases the risk of developing PAD as both condition share same pathogenesis and risk factor profile resulting in accelerated atherosclerosis[19].

Conclusion

PAD is associated with thrice higher mortality than that of the general population and its prevalence is much higher among end-stage renal disease patients. Aggressive screening for risk factors and early risk factor modification should be done in CKD patients in a pursuit to reduce the PVD, CAD and CVD.

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