Prevalence of Peripheral Arterial Disease (PAD) in End Stage Renal Disease (ESRD) Patients on Hemodialysis: A Study from Central Nepal.

Ghimire M[1], Pahari B[1], Das G[1], Sharma SK[2], Das GC[1]

[1]Department of Nephrology

[2]Department of Cardiology

College of Medical Sciences Teaching Hospital

Bharatpur, Nepal

Corresponding Author

Madhav Ghimire

Department of Nephrology

College of Medical Sciences Teaching Hospital

Bharatpur, Nepal

Email: madhavghimirenp@yahoo.com

Citation

Ghimire M, Pahari B, Das G, Sharma S K, Das GC. Prevalence of Peripheral Arterial Disease (PAD) in End Stage Renal Disease (ESRD) Patients on Hemodialysis: A Study from Central Nepal. *Kathmandu Univ Med J* 2014;47(3):181-4.

ABSTRACT

Background

Peripheral arterial disease is a common condition in the hemodialysis population with an estimated prevalence ranging from 17-48%. Many studies have been conducted to know the prevalence of peripheral vascular disease in hemodialysis population. However no such study has been conducted so far in Nepal.

Objective

This study was carried out with an objective to assess the prevalence of Peripheral Arterial Disease in End Stage Renal Disease Patients on Hemodialysis.

Method

Fifty patients with a diagnosis of End Stage Renal Disease (irrespective of the underlying cause), and those who were on hemodialytic support for more than 3 months were studied over a period of one year. Peripheral arterial disease was diagnosed on the basis of the ankle –brachial index, which was the ratio of the resting systolic blood pressure in the arteries of the ankle to that of the brachial artery, measured by using a standard mercury manometer with a cuff of appropriate size and the Doppler ultrasound. Patients with ankle –brachial index ≤0.9 were considered positive for peripheral arterial disease.

Result

A total of 50 End Stage Renal Disease patients were analyzed. The mean age of the patient was 49.81±12.63 years. The age range was from 18- 79 years. Majority of them were males 64% (n=32). Peripheral arterial disease defined by ankle –brachial index ≤0.9 was present in 30% (n=15) of patients. The three major cause of End Stage Renal Disease in the study population was Chronic Glomerulonephritis 40 % (n=20), Type 2 Diabetes Mellitus 28 % (n=14) and Hypertension 24 % (n=12). Type 2 Diabetes Mellitus was the commonest cause 53% (n=8) of End Stage Renal Disease in patients with peripheral arterial disease followed by hypertension 33% (n=5). On univariate analysis, peripheral arterial disease was found to be significantly associated with age >40 years (p value= 0.003; OR=14.8; CI=1.75-125.27), Type 2 Diabetes Mellitus (p value= 0.009; OR=5.4; CI=1.44-21.14), parasthesia of lower limbs (p value= 0.001; OR=10; CI-2.31-43.16), and intact PTH >300 ng/ml (p value =0.006; OR=5.7; CI=1.55-21.50). However on multivariate analysis only parasthesia of lower limbs and intact PTH >300 ng/ml were significantly and independently associated with peripheral arterial disease, while other variables were not significant.

Conclusion

Peripheral arterial disease was common occurrence in End Stage Renal Disease patients on hemodialysis. Ankle –brachial index needs to be included as a routine assessment in End Stage Renal Disease patients to detect peripheral arterial disease at its earliest.

KEY WORDS

Ankle–brachial index, end stage renal disease (ESRD), hemodialysis peripheral vascular disease

INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem in Nepal. It is estimated that the prevalence of CKD is around 10.6% in urban areas of Nepal and the three most common causes of End Stage Renal Disease (ESRD) in Nepal are believed to be Diabetes Mellitus, Glomerulonephritis and Hypertension.[1] Majority of people with ESRD need renal replacement therapy and hemodialysis is the most popular and widely used renal replacement therapy, worldwide. In Nepal, Hemodialysis service was first started in Bir Hospital in 1987 and in our center it was started in 2007.[2] Majority of ESRD patient in our center are also in hemodialysis.

Peripheral Arterial Disease (PAD) is a common problem in Chronic Kidney Disease. Moreover, its prevalence is seen to be much higher among hemodialysis patients than in the general population with an estimated prevalence ranging from 17% and 48%.[3,4] Knowledge of the PAD in patients with CKD (Chronic Kidney Disease) is limited because of a lack of routine evaluation and detection. The prevalence of PAD appears to be higher among ESRD (End Stage Renal Disease) patients than in the general population due to dialysis or uremia-associated risk factors.[3] It is also known that peripheral arterial disease (PAD) is a strong predictor of Coronary artery disease and this is of particular interest to Nephrologists because the risk for PAD is increased in CKD but it is unfortunate that PAD is often overlooked as a source of morbidity and as a cardiovascular risk factor in ESRD population.[5]

Early detection of PAD identifies a group of patients who would benefit from aggressive cardiovascular risk factor modification and prevent the adverse outcomes like pain at rest, risk of tissue necrosis, and even amputation of legs.[6-8]

Many studies have been conducted to know the prevalence of peripheral arterial disease in hemodialysis population. However no such study had been conducted so far in Nepal. This study was carried out with an objective to assess the prevalence of Peripheral Arterial Disease in End Stage Renal Disease (ESRD) Patients on Hemodialysis from central Nepal.

METHODS

This hospital based cross sectional study was carried out at Hemodialysis Unit of College of Medical Sciences Teaching hospital over a period of one year; from October 2010 to September 2011, where 50 cases of hemodialysis patients were prospectively analyzed. Patients with a diagnosis of ESRD (End Stage Renal Disease), irrespective of the underlying cause and who were on maintenance Hemodialysis for more than 3 months were included in the study. ESRD was defined when there was irreversible loss of GFR of ≤5 ml/min on the basis of Cock-Croft and Gault Equation.[9,10] All the patients included in the study were explained about the nature of the study and a written consent was taken. The Institutional Review board has given the ethical clearance for the study.

Patient with documented diagnosis of peripheral arterial calcification, patient with bilateral arteriovenous fistula and patient with non-compressible upper and or lower limb vessels were excluded from the study. Non Compressible vessel was defined as an ankle- brachial index (ABI) > 1.30 or an apparent lower extremity systolic pressure above 300 mmHg.[11]

An ultrasound Doppler (TOSHIBIA XARIO, SSA-660A) machine with 7.5 MHZ transducer was used to look for and document the Peripheral arterial disease and to rule out the possibility of Medial arterial calcification. The highest systolic blood pressure in Posterior tibial artery or dorsalis pedis artery (whichever was high) was taken and then divided by the systolic blood pressure in the brachial artery from the upper limb to calculate the ABI. Patients with ABI ≤0.9 was considered positive for peripheral arterial disease.[7] Tests of inter observer and intra observer variability revealed excellent reproducibility in the readings. ESRD (End stage renal disease) was defined by e-GFR ≤ 5 ml/min, which was calculated by using Cock Croft and Gault equation.[9,10] Intact PTH was estimated by mid-region radioimmunoassay technique in the random blood sample. Data was carefully entered on MS XP sheet and then the data was converted to SPSS PC+ 16 version for statistical analysis. Chi square (X^2) test was used to examine the association between ABI groups (ABI ≤0.9 and ABI>0.9). Ratio, mean and standard deviation were calculated for descriptive data.

RESULTS

The mean age of the patient enrolled in the study was 49.81 years ± 12.63 years and the mean age of the patient who had PAD was 58.27 years ± 13.11 years. The majority of the cases in our hemodialysis population were > 40 years, accounting up to 62% (n=31). Similarly in the PAD group, (n=14) were of age > 40 years and only (n=1) was of age ≤40 years. Majority of the Patients in the study were males 64% (n=32) and 36 % (n=18) females. Out of patients who had PAD, (n=10) majority were males approximately (n=10) and (n=5) were females. Peripheral arterial disease was present in 30% (n=15) of patients. Symptomatic PAD (ABI ≤0.9) was present in (n=12) patients and asymptomatic PAD present in (n=3) patients. However none of the patient had classical symptom of PAD in the form of intermittent leg claudication and or the rest pain. The three major causes of ESRD in the study population on hemodialysis were Chronic Glomerulonephritis 40 % (n=20) followed by Type 2 DM (n=14) and then Hypertension (n=12). Out of 20 cases with CGN, (n=2) had PAD. Similarly, out of 14 cases with Type 2 DM, (n=8) had PAD and out of 12 hypertensive patients (n=5) had PAD. Out of 49 Hypertensive patients, (n=15) of patients had PAD. Similarly, out of 14 Type 2 DM, (n=8) had PAD and out of 14 CCF patients (n=5) had PAD. On statistical analysis, Type 2 DM was significantly associated with PAD. Twelve cases (n=12) in PAD group were symptomatic and the predominant symptom was parasthesia of lower limbs. None of the patients in the study group had classical history suggestive of PAD, in the

form of rest pain in leg or intermittent claudication of limbs except parasthesia of lower limb, skin color changes in lower limbs and generalized weakness, which again have multi factorial etiology other than PAD. Out of 22 cases who have parasthesia of lower limbs, (n= 12) had PAD.

On univariate analysis, PAD was found to be significantly associated with age >40 years (p value= 0.003; OR=14.8; CI=1.75-125.27), Type 2 DM (p value= 0.009; OR=5.4; CI=1.44-21.14), parasthesia of lower limbs (p value= 0.001; OR=10; CI=2.31-43.16), skin changes in lower limbs (p value= 0.01; OR=8.2; CI=1.38-49.21), and intact PTH >300 ng/ml (p value= 0.006; OR=5.7; CI=1.55-21.50). However on multivariate analysis only parasthesia of lower limbs and PTH >300 ng/ml were significantly and independently associated with PAD, while other variables were not.

Table 1. Demographic characteristics of patients with and without the diagnosis of PAD

Variables	PAD Present (ABI ≤ 0.9)	PAD Absent (ABI>0.9)	P Value
Age (>40 years)	14	17	0.003(OR=14.8) CI=1.75-125.27
Male	10	22	0.797

Table 2. Clinical characteristics of patients with and without the diagnosis of PAD

Variables	PAD Present (ABI ≤ 0.9)	PAD Absent (ABI>0.9)	P Value
Etiology			
Chronic Glomerulonephritis	2	18	0.01(OR=0.14) CI=0.028-0.74
Type 2 DM	8	6	0.009(OR=5.4) CI=1.44-21.14
HTN	5	7	0.312
Comorbidity			
HTN	15	34	0.508
Type 2 DM	8	6	0.009(OR=5.5) CI=1.44-21.14
Symptoms			
Parasthesia of Lower Limbs	12	10	0.001(OR=10) CI-2.31-43.16
Skin changes in Lower Limbs	5	2	0.01(OR=8.2) CI=1.38-49.21
Sign			
Evidence of Peripheral Neuropathy	10	11	0.02(OR=4.3) CI=1.20-15.83
Investigation			
PTH >300 ng/ml	10	9	0.006 (OR=5.7) CI=1.55-21.50

DISCUSSION

Our study is the first of its kind in Nepal, to evaluate the prevalence of Peripheral Arterial Disease in hemodialysis patients using ABI. Different studies had come with different prevalence of PAD in hemodialysis population.[12-14] The difference in prevalence between different series could be because of difference in study methodology and design.

Our study showed a 30% prevalence of PAD, which is a higher prevalence of PAD in hemodialysis patients. This is in accordance with the data published in series like DOPPS.[15] PAD is usually seen in older people in general populations.[16] However, in hemodialysis patients; even younger patients can have a high prevalence of PAD because of uremia and dialysis associated factors. But our study showed the prevalence of PAD being higher in older people. The reason for not finding younger patients with PAD in our study may be because of the fact that majority of our patients, 62 % (n= 31) were of advanced age i.e. age > 40 years and majority of them were in hemodialysis for less than one year duration. The prevailing notion is that peripheral arterial disease is common in males in general population.[17-19] This notion was maintained even in our study. However the frequent association of male gender with PAD in ESRD population is still unknown.

In terms of symptomatology, twelve (n=12) of PAD patients were clinically symptomatic in our study which was similar to a study done by Ogata et al in which 240 (76.4%) of 315 hemodialysis patients were symptomatic.[20] Majority of patients, 56 % (n=28) in our study were asymptomatic. These data suggest that clinicians who utilize a classic history of claudication alone to detect PAD were more likely to miss the diagnosis. To strengthen this fact in some studies it was shown that 85% to 90% of the PAD diagnoses were missed when classic history of claudication alone was utilized to detect PAD.[17-19] Hence the diagnosis of PAD may be missed unless if not looked for by using some tools.

In PAD cohort of our study, the major comorbidity was HTN which was present in all the patients followed by Type 2 DM present in (n=8) of cases. The prevalence of PAD in patients with CKD (Chronic Kidney Disease) and Type 2 DM is two to four fold greater than that of normal population.[21,22] Therefore, it may be logical to propose that CKD/ESRD also further predisposes patients with diabetes to the development of PAD. There was a significant association of Type 2 Diabetes Mellitus with PAD in our study (p value = 0.009). Although hypertension is a risk factor for PAD among patients without ESRD.[23] An association of hypertension with PAD among hemodialysis patients has not been reported yet. Similar negative association of PAD with hypertension was also shown in other studies.[24-28] No significant association was observed between HTN and PAD in our study as well.

In PVD group of our study, 67.7% (n=10) cases had elevated intact PTH level with a cut off value of > 300 ng/ml. On analysis, this finding was of important significance. It was found that there was a significant association between elevated intact PTH level and PVD. On multiple logistic regression analysis also intact PTH value>300 ng/ml was significantly and independently associated with PVD. This significant association between elevated intact PTH and PVD is a unique finding in our study. Previous studies like DOPPS had failed to show the significant association

of intact PTH and PVD.[15] This contradictory finding in our study needs further analysis with a larger sample size and randomized controlled trials.

CONCLUSION

The present study demonstrated the high prevalence of Peripheral Arterial Disease in CKD patients on hemodialysis. Type 2 DM Mellitus was the commonest cause of End Stage Renal Disease in patients with Peripheral Arterial Disease. The significant association between elevated intact PTH and Peripheral Arterial Disease is a unique finding in our study. Previous studies had failed to show the significant association of intact PTH and Peripheral Arterial Disease. This unique finding in our study warrants further analysis with a larger sample size.

ACKNOWLEDGEMENT

We would like to thank Dr. P.K. Deka (Professor and Head, Department of Radiology), Dr. Ashok Tayal (Associate Professor Department of Radiology), Dr. Pramod Kumar Chhetri (Associate Professor Department of Radiology), for their constant help, guidance and encouragement throughout the study period. We also would like to thank PG Residents of Department of Radiology and all the Patients and Nursing staffs of Nephrology Department, who were directly and indirectly involved in the study.

REFERENCES

1. Sharma SK, Karki P, Baral N, Perico N, Perna A, Remuzzi G, et al. A community screening for chronic kidney disease, hypertension, diabetes and their management in Dharan, Nepal. World Congress of Nephrology, Rio de Janeiro, Brazil. 2007 April 21–25;415.
2. Chhetri PK, Satyal PR, Kafle R, Khakurel S, Pradhan BR. Experience of hemodialysis in Bir Hospital. *Nepal Med Coll J* 1999; 1: 99-101.)
3. O'Hare AM, Johansen KL. Lower-extremity peripheral arterial disease among patients with end-stage renal disease. *J Am Soc Nephrol* 2001; 12: 2838-47.
4. O'Hare AM, Hsu CY, Bacchetti P, Johansen KL. Peripheral vascular disease risk factors among patients undergoing hemodialysis. *J Am Soc Nephrol* 2002; 13: 497-503.
5. Stephanie S, DeLoach E, Mohler R. Peripheral Arterial Disease: A Guide for Nephrologists. *Clin J Am Soc Nephrol* 2007; 2: 839–46.
6. Guerrero A, Montes R, Muñoz-Terol J, Gil- Peralta A, Toro J, Naranjo M, et al. Peripheral arterial disease in patients with stages IV and V chronic renal failure. *Nephrol. Dial Transplant* 2006; 21: 3525–31.
7. Ono K, Tsuchida A, Kawai H, Matsuo H, Wakamatsu R, Maezawa A, et al. Ankle-brachial blood pressure index predicts all-cause and cardiovascular mortality in hemodialysis patients. *J. Am. Soc. Nephrol* 2003; 14 (6):1591-8.
8. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, Browner D. Mortality over a period of 5 years in patient with peripheral arterial disease. *N Engl J Med* 1992; 326: 381-6.
9. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39:S1.
10. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from kidney disease: Improving global outcomes (KIDIGO). *Kidney Int'l* 2005; 67(6): 2089-100
11. Brass EP, Adler S, Sietsema KE, Amato A, Esler A, Hiatt WR. Peripheral Arterial Disease Is Not Associated with an Increased Prevalence of Intradialytic Cramps in Patients on Maintenance Hemodialysis. *Am J Nephrol* 2002; 22: 491-6.
12. O'Hare AM, Glidden DV, Fox CS, Hsu CY. High prevalence of peripheral arterial disease in persons with renal insufficiency: Results from the National Health and Nutrition Examination Survey 1999-2000. Circulation 2004; 109:320-3.
13. Mostaza JM, Suarez C, Manzano L, Cairols M, García-Iglesias F, Sanchez-Alvarez J, et al. MERITO Study Group: Relationship between ankle-brachial index and chronic kidney disease in hypertensive patients with no known cardiovascular disease. *J Am Soc Nephrol* 2006; 17[Suppl 3]: S201–S205.
14. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001; 286: 1317–24.
15. Rajagopalan S, Dellegrottaglie S, Furniss AL, Gillespie BW, Satayantum S, Lameire N, et al. Peripheral arterial disease in patients with end-stage renal disease; observations from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Circulation 2006; 114:1914-22.
16. Diehm C, Schuster A, Allenberg JR, Darius H, Haberl R, Lange S, et al. High prevalence of peripheral arterial disease and comorbidity in 6880 primary care patients: cross -sectional study. *Atherosclerosis* 2004; 172(1):95-105.
17. Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. *Vasc Med* 1997; 2:221-6.
18. Aronow WS, Ahn C. Prevalence of coexistence of coronary artery disease, peripheral arterial disease, and atherothrombotic brain infarction in men and women 62 years of age. *Am J Cardiol.* 1994; 74: 64-5.
19. Kannel WB, Skinner JJ Jr, Schwartz MJ, Shurtleff D. Intermittent claudication. Incidence in the Framingham Study. *Circulation.* 1970; 41:875-83.
20. Ogata H, Kumata Maeta-C, Shishido K, Mizobuchi M, Yamamoto M, Koiwa F, et al. Detection of Peripheral Artery Disease by Duplex Ultrasonography among Hemodialysis Patients. *Clin J Am Soc Nephrol* 2010; 5: 2199–206.
21. Leskinen Y, Salenius JC, Lehtimaki T, Huhtala H, Saha H. The prevalence of peripheral arterial disease and medial arterial calcification in patients with chronic renal failure, requirements for diagnostics. *Am J Kidney.* Dis 2002 Sep; 40(3):472-9.
22. Walters DP, Gatling W, Mullee MA, Hill RD. The prevalence, detection, and epidemiological correlates of peripheral vascular disease: A comparison of diabetic and non-diabetic subjects in an English community. *Diabet Med* 1992; 9:710-5.
23. Newman AB, Siscovick DS, Manolio TA, Polak J, Fried LP, Borhani NO, Wolfson SK. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. *Circulation* 1993; 88:837-45.
24. Schroll M, Munck O. Estimation of peripheral arteriosclerotic disease by ankle blood pressure: measurements in a population study of 60-year-old men and women. *J Chron Dis* 1981; 34(6): 261-9.
25. Cheung AK, Sarnak MJ, Yan G, Dwyer JT, Heyka RJ, Rocco MV, et al. Atherosclerotic cardiovascular disease risks in chronic hemodialysis patients. *Kidney Int* 2000; 58: 353–62.
26. Newman AB, Sutton-Tyrrell K, Rutan GH, Locher J, Kuller LH. Lower extremity arterial disease in elderly subjects with systolic hypertension. *J Clin Epidemiol* 1991; 44: 15-20.
27. Bulpitt CJ. Blood pressure. In: Fowkes FGR, ed. Epidemiology of Peripheral Vascular Disease. New York, NY: Springer-Verlag; 1991: 181-6.
28. Marcus EB, Curb JD, MacLean CJ, Reed DM, Yano K. Pulmonary function as a predictor of coronary heart disease. *Am J Epidemiol.* 1989; 129: 97-104.