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RESEARCH ARTICLE

PREVALENCE OF LOWER LIMB PERIPHERAL ARTERIAL DISEASE IN ANGIOGRAPHICALLY PROVEN CORONARY DISEASE IN KASHMIR REGION

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ABSTRACT

Background: Peripheral artery disease (PAD) is under diagnosed, undertreated, poorly understood, and much more common than previously thought. In primary care practices across the United States, 29% of patients who are older than 70 years or who are older than 50 years with a history of smoking or diabetes have been reported to have PAD. **Objectives:** (i) To assess prevalence of lower limb peripheral arterial disease in patients with angiographically proven coronary artery disease, (ii) to see the relation between severity of coronary artery disease and peripheral arterial disease, and (iii) to study risk factor profile of peripheral arterial vis-à-vis coronary artery disease. **Methodology:** This was a prospective hospital based study conducted in the Department of Cardiology at SKIMS, Soura, Srinagar, Kashmir. All the patients who were taken for coronary angiography in the Department of Cardiology, SKIMS, Srinagar were evaluated in terms of complete relevant history, clinical examination and laboratory investigation. The clinical symptoms like intermittent claudication, resting, pain, feeling of cold or numbness in toes were enquired. To ascertain the presence of intermittent claudication Edinburgh Claudication Questionnaire (ECQ) was administered. **Results:** There were 69 males and 33 females with male female ratio of 2.1:1. Mean age of population was 59.5± 9.1years. Prevalence of peripheral arterial disease was 13.7% as documented by peripheral angiography. Claudication was the only relevant symptom present in two patients (14.3%) with peripheral arterial disease as compared to none without peripheral arterial disease. Hypertensive patients were more likely to have peripheral arterial disease as it was present in 71.4% among patients with peripheral arterial disease. Diabetics were more likely to have peripheral arterial disease as it was present in 42.9% among patients with peripheral arterial disease. Family history of coronary artery disease was equally distributed in both groups. **Conclusion:** Coronary artery disease evaluation should be considered in patients with lower extremity PAD having diabetes, multi-cardiovascular risk factors, or multi-level disease.

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INTRODUCTION

Peripheral artery disease (PAD) is under diagnosed, undertreated, poorly understood, and much more common than previously thought (Hirsch, 2001 and McDermott, 2001). In primary care practices across the United States, 29% of patients who are older than 70 years or who are older than 50 years with a history of smoking or diabetes have been reported to have PAD (McDermott, 1997; Hirsch, 2005 and McDermott, 2002). Not only was the diagnosis of PAD frequently overlooked, but the cardiovascular risk factors were not used as appropriately as in patients with CAD.

Approximately 12% of the adult population has PAD, and the prevalence is equal in men and women (Hiatt, 2001). A strong association exists between advancing age and the prevalence of PAD. Almost 20% of adults older than 70 years have PAD (Regensteiner, 2002). In an elderly hypertensive population from the Systolic Hypertension in the Elderly Program, the prevalence of PAD was 38% in black men, 25% in white men, 41% in black women, and 23% in white women (Newman, 1993). Type 2 Diabetes (T2D) often entails micro- and macrovascular complications. Peripheral arterial disease (PAD) is characterized by reduced blood flow to the lower extremities, which may ultimately require amputation, and has been associated with increased risk of coronary artery disease or stroke. Early diagnosis of PAD may allow for earlier treatment, which could help to prevent or postpone

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complications associated with PAD. T2D patients with PAD are at increased risk of morbidity and mortality from cardiovascular diseases. Furthermore, PAD is an important risk factor of diabetic foot, and is also one of the major reasons for amputation (Boulton, 2004 and Prompers, 2008). It is therefore an urgent task know how to find PAD at an early stage. Diabetic retinopathy (DR), a microvascular complication, which can be screened easily by digital retinal photographs at an early stage, is now the leading cause of blindness in working-age adults¹¹. Generally, DR progresses from non-proliferative diabetic retinopathy (NPDR) to proliferative diabetic retinopathy (PDR). However, diabetes does not necessarily progress to PDR in every patient (Fong, 2004 and Cunha-Vaz, 2005). The incidence of PDR increases as diabetic duration increases from 0 to 15 years. After 15 years, the incidence of developing PDR remains stable (Fong, 2004 and Klein, 1984). Many studies have shown that DR was associated with cardiovascular disease (CVD) (Kramer, 2011 and Reaven, 2008). Moreover, PDR was more strongly associated with CVD than was NPDR (Reaven, 2008 and van Hecke, 2005). PAD has been considered to be one of the subclinical cardiovascular diseases, which implies a possible link between lower extremity PAD and PDR.

Aims and Objectives

- To assess prevalence of lower limb peripheral arterial disease in patients with angiographically proven coronary artery disease in our setup.
- To assess relation between severity of coronary artery disease and peripheral arterial disease.
- To study risk factor profile of peripheral arterial vis-à-vis coronary artery disease.

MATERIALS AND METHODS

This was a prospective hospital based study conducted in the Department of Cardioogy at Sheri-Kashmir Institute of Medical Sciences (SKIMS), Soura, Srinagar, Kashmir. The study population comprised of patients who had angiographically proven significant coronary artery disease who had mean diameter stenosis of >50% diameter reduction of any coronary artery. The study was also designed to evaluate risk factors and clinical characteristics of peripheral arterial disease.

Inclusion Criteria

- All patients with angiographicall proven significant coronary artery disease.
- Informed consent for the study.

Exclusion Criteria

- Lack of informed consent
- Renal insufficiency where dye load was a concern.
- Patients with non-significant coronary artery disease or normal coronaries.
- Any contraindication for arterial puncture like refractory coagulopathy,
- Contrast allergy.

Method of study

All the patients who were taken for coronary angiography in the Department of Cardiology, SKIMS, Srinagar were

evaluated in terms of complete relevant history, clinical examination and laboratory investigation. The clinical symptoms like intermittent claudication, resting, pain, feeling of cold or numbness in toes were enquired. To ascertain the presence of intermittent claudication Edinburgh Claudication Questionnaire (ECQ) was administered. It consisted of six questions:

- Question 1 assesses whether patients get any pain or discomfort on walking.
- Question 2 evaluated whether patients get this pain when they are standing still or sitting.
- Question 3 estimates whether patients get pain when they walk uphill or walk in a hurry.
- Question 4 determines whether get patients get this pain walking at an ordinary pace on level ground.
- Question 5 assesses whether if patients stand still the pain continues for more than 10 min or disappears within 10min.
- Question 6requires whether patients to mark
- On a diagram, where they actually get pain or discomfort.

If these criteria were fulfilled, based on Question6, a patients with definite claudication is one who indicates pain in the calf, regardless of whether the pain is also marked at other sites. A patient with atypical claudication was one who indicated pain in the thigh or buttock in the absence of any calf pain. Subject were not considered to have claudication if pain is indicated in the hamstrings, feet shins, joints or appears to radiate, in the absence of any pain in the calf (Gabriel, 2007). Data regarding cardiovascular risk factors like smoking, diabetes mellitus, hypertension, dyslipidemia and family history of coronary artery disease was collected. Smokers were grouped according to the classification of the patients in smokers at the interview (at least 10 cigarette per day) and non- smokers (those had given up smoking at least two years prior to the interview or those that had never smoked) (Gabriel, 2007). Hypertension was defined as treatment for elevated blood pressure or a systolic pressure greater than or equal to 140mmHg or diastolic greater than or equal to 90mmHg (Chobian, 2003). Patients were considered diastolic when they had prior diagnosis of diabetes or when they reported using insulin or hypoglycemic agents or if blood glucose fasting > 126 mg/dl, symptoms of diabetes with random blood glucose > 200mg.dl, 2 hour post-prandial plasma glucose >200 mg/dl (American Diabetes Association, 2007). Dyslipidemia was defined as treatment for dyslipidemia or serum cholesterol of >200mg/dl or serum triglycerides >150mg/dl (source National cholesterol Education programme-2003). Family history of coronary artery disease was defined present if any of first degree had documented coronary artery disease. Physical examination included body mass index, blood pressure, heart rate, physical signs of atherosclerosis (arcus, xanthelemas, xanthoma) and peripheral pulses, presence of any gangrene or foot ulcers. Lower limb pulses were qualified as present, week or absent. The Body Mass Index (BMI) was calculated as body weight divided by the height squared (kg/m²). Obesity was considered with BMIs greater than 30 kgm².

Statistical Analysis

Data was expressed as mean±SD and percentage. Intergroup comparison was done by using Mann-Whitney U test and further on risk was estimated by Odd's ratio.

RESULTS

This study was Hospital based, prospective study to find prevalence of lower limb peripheral arterial disease in patients with angiographically proven coronary artery disease, to assess relation between severity of coronary artery disease and peripheral arterial disease and to study risk factor profile peripheral arterial disease vis-à-vis coronary artery disease.

Study population consisted of 102 patients who had positive angiography for coronary artery disease and subjected to peripheral angiography for in the same setting. There were 69 males and 33 females with male female ratio of 2.1:1. Mean age of population was 59.5 ± 9.1 years. Prevalence of peripheral arterial disease was 13.7% as documented by peripheral angiography. Most of patients with peripheral arterial disease were > 60 years (71.4%), so peripheral arterial disease was more common in older age. Males (75%) outnumbered females (25%) in peripheral arterial disease group, but the difference was not statistically significant. Claudication was the only relevant symptom present in two patients (14.3%) with peripheral arterial disease as compared to none without peripheral arterial disease. While normal pulse examination did not rule peripheral arterial disease, but abnormalities were strongly associated with peripheral arterial disease. Mean BMI was 23.2 kg/m^2 . There was no statistically significant difference between BMI in patients with and without peripheral arterial disease.

Smoking was equally distributed between patients with and without peripheral arterial disease. Hypertensive patients were more likely to have peripheral arterial disease as it was present in 71.4% among patients with peripheral arterial disease. Diabetics were more likely to have peripheral arterial disease as it was present in 42.9% among patients with peripheral arterial disease. Dyslipidemia was not associated with increased risk of peripheral arterial disease. Family history of coronary artery disease was equally distributed in both groups. Multi-vessel coronary artery disease was present in 92.9% of peripheral arterial disease patients and determined a higher risk.

DISCUSSION

Atherosclerosis is a systemic process with variable expression in different vascular beds²². Coronary artery disease (CAD), carotid artery stenosis (CS) and peripheral arterial based studies have attempted to define the overlap between PAD and CAD. The prevalence of CAD in patients with significant PAD is well defined, with at least a 60% incidence of CAD, and nearly all patients with some degree of CAD²³. The proportion of patients with CAD and PAD is estimated to be between 15% and 40% (Hirsch, 2001; Aronow, 1994; CAPRIE Steering Committee, 1996). In our study, 102 patients were enrolled. The mean age of patients was 59.5 ± 9.1 years similar as reported by Choi *et al* (Choi, 1995).

Table 1. Age and Gender Distribution of Studied Subject

Age (yr)	Male		Female		Total		P value
	N	%	N	%	N	%	
≤ 40	8	11.6	0	0	8	7.8	0.419 (NS)
41 to 50	2	2.9	8	24.2	10	9.8	
51 to 60	25	36.2	12	36.4	37	36.3	
61 to 70	31	44.9	11	33.3	42	41.2	
>70	3	4.3	2	6.1	5	4.9	
Total	69	67.6	33	32.4	102	100	
Mean ± SD	59.4 ± 9.4 (38,78)		59.8 ± 8.5 (45,75)		59.5 ± 9.1 (38,78)		

Table 2. Clinical Symptoms of Studied patients

	No. of Patients	%age
Claudication	2	1.9
Rest Pain	0	0.0
Foot Ulcers	0	0.0

Table 3. Distribution of risk factors in the studied patients

		No. of Patients	%age
Smoking	Present	58	56.7
	Absent	44	43.3
Hypertension	Present	46	45.1
	Absent	56	54.9
Diabetes Mellitus	Present	21	20.6
	Absent		
Dyslipidemia	Present	81	79.4
	Absent	41	40.2
Family History	Present	10	9.8
	Absent	92	90.2

Table 4. Number of Vessel Involved in relation with Peripheral Artery Disease

No of Vessels Involved	CAD with PAD		CAD without PAD		P value
	N	%	N	%	
One	1	7.1	34	38.8	0.000 (sig.)
Two	4	28.6	42	47.7	
Three	9	63.3	12	13.7	
Total	14	13.7	88	86.3	

Mean age was 63.5 ± 9.1 years. Prevalence of lower limb peripheral artery disease by angiography was 13.7%, the result were a nearly similar to the study done by Przewlocki *et al* (Przewlocki, 2009). There were a total of 14 patients in CAD with PAD group and 88 patients in CAD without PAD group. Overall there were 55(53.9%) patients in the group ≤ 60 years and 47 (46.1%) patients in the age group >60 years. In the CAD with PAD group 4 (28.6%) patients were ≤ 60 years of age and 10 (71.4%) patients were in the age group > 60 years, in contrast to the Cad without PAD group wherein 51 (58%) patients were ≤ 60 years of age and 37 (42%) patients were in >60 years age group. The difference between the two age groups (i.e. ≤ 60 and > 60 years) vis-à-vis the PAD was statistically significant with a p value of 0.041. Mean age in CAD with PAD group was 63.6 ± 8.9 years as compared to 58.9 ± 9.1 years in CAD without PAD group. Our result were in similar to Choi *et al.* (Choi, 1995), where mean age was 61.1 ± 9.2 years for years coronary disease patients with peripheral arterial disease compared to 57.5 ± 10.2 years in artery disease patients without peripheral arterial disease. Out of 102, 69 (66.7%) patients were males and 33 (33.3) patients were females with a male female ratio of 2.1:2. In the CAD with PAD group 4 (28.6%) patients were females and 10 (71.4%) patients were males, in contrast to the CAD without PAD group wherein 29 (33%) patients were females and 59 (67%) patients were males. The gender difference was statistically ($p=0.746$). The results were in agreement with the study done by Dieter RS *et al* (Dieter, 2003). Study by Hirsch AT *et al.* (Hirsch, 2001). Revealed less than 6% of newly diagnosed patients and 13% of previously diagnosed patients of peripheral vascular disease presented with classic claudication. In our study out of 102 patients only 2 (1.9%) patients presented with symptoms of limb claudication these 2 patients were in the CAD with PAD group (total of 14 patients) accounting for 14.2% patients in this group who had symptoms of PAD compared to none in CAD without PAD group. Results were similar to Hirsch At *et al* (Hirsch, 2001). Rest pain and foot ulcers were present in none of the patients. Out of 102 patients pulse abnormalities were present in 2 patients.

Dorsalispedis was not palpable in 1 patients on right side and posterior tibial artery was not palpable in other patient on left side. The findings were consistent with study done by Bashir and Aslam³⁰. Both the patients belonged to CAD with PAD group. None of the patients had abnormalities in femoral or popliteal arteries, auscultatory bruits or gangrene. Physical signs of atherosclerosis like xanthelasma and CAD with PAD group with rest 4 (4.9%) patients, 1 (7.1%) patients belonged to CAD with PAD group with rest 4 (4.5%). Patients the difference was statistically insignificant ($p=0.677$). Smoking was the most common risk factor present in 58 (56.7%) patient out of total 102 patients. Smoking was equally distributed in both groups, 8(57.1%) patient in CAD with PAD group as compared to 50 (56.8%) patients in without peripheral arterial disease group. The difference was statistically insignificant ($p=0.982$). our result were similar to study by Choi DH *et al* (Choi, 1995) wherein 35 patients (71.4%) were smokers in peripheral vascular disease group as compared to 83 patients (64.3%) in the group without peripheral vascular disease. The difference was statistically insignificant. In the study conducted by Choi *et al* (Choi, 1995), there were 27 (55.1%) patients with hypertension in peripheral vascular disease group as compared to 47 (36.4%) patients in the group without peripheral vascular disease. The difference was statistically significant ($p=0.024$). In our study out of 102 patients, a total

of 46 (45.1%) patients were hypertensive. 10 (71.4%) patients were hypertensive in CAD with PAD groups as compared to 36 (40.9%) patients in CAD without PAD group. The difference was statistically significant ($p=0.034$). Our results were consistent with the study by Choi *et al.* (Choi, 1995). The likelihood of peripheral arterial disease was 3.6 times more among hypertensive. Dieter *et al.* (Dieter, 2003), studies a total of 100 patients with coronary artery disease. 17 (42.5%) patients were diabetic in peripheral vascular disease group as compared to 11 (18.3%) patients in the groups without peripheral vascular disease. The difference was statistically significant ($p=0.012$). In our study diabetes mellitus was present in 21 (20.6%) patients.

In CAD with PAD group, diabetes was present in 6 (42.9%) patients as compared to 15 (17.1%) patients in CAD without PAD group. The difference was statistically significant ($p=0.027$). Put results were consistent with the study conducted by Dieter RS *et al* (Dieter, 2003). The likelihood of peripheral arterial disease was 3.6 times more among diabetics. Out of total 102 patients studies, dyslipidemia was present in 41 (40.2%) patients, in CAD with PAD group dyslipidemia was present in 5 (35.7%) patients as compared to 36 (40.9%) patients in CAD without PAD group. The difference was statistically insignificant ($p=0.714$). Our results were comparable to study by Choi *et al*²⁷. In their study, there were 10 (20.4%) patients in peripheral vascular disease group as compared to 22 (22.5%) patients in the group without peripheral vascular disease. The difference was statistically insignificant. In our study, positive family history of coronary artery disease was present in 10 (9.8%) patients in CAD with PAD group positive family history was present in 1(7.1%) patients as compared to 9(10.2%) patients in CAD without PAD. The difference was statistically insignificant ($p=0.720$). However, Kafetzakis *et al.* (Kafetzakis, 2001), evaluated 203 patients with positive coronary angiography for coronary artery disease and no symptomatic lower limb arterial disease. A hundred and ten of them had a positive coronary angiography and the presence of occult aorto-iliac disease whereas the remaining 93 patients had only a positive coronary angiography. The positive family history was present in both groups but with a significantly higher prevalence in the patients with occult aorto-iliac disease ($p=0.001$). In our study, out of 102 patients, most had too vessel involvement 46 (45.1%) patients, followed by one vessel involvement in 35 (34.3%) patients and triple vessel involvement in 21 (20.6%) patients. None of the patients had left main coronary artery involvement. Single vessel involvement was in 1 (7.1%) patient in CAD with PAD group as compared to 34 (38.8%) patients in group CAD without PAD. 4 patients (28.6%) had two vessel involvement in PAD group with 42 was more in PAD group with 9 (64.3%) patients as compared to 12 (13.7%) patients in group without PAD. The results were consistent with the study by Basir E Aslam (Bashir, 2001). They studied a total of 200 patients with peripheral arterial disease in 45 patients. Out of 45 patients, 30 (66.7%) patients with evidence of peripheral arterial occlusive disease had triple vessel disease as compared to 13 (28.9%) patients with double vessel disease and 2 (4.4%) patients had single vessel disease. Incidence of PAD among multivessel disease (two and three vessel) in our study was 8.2 times more likely than single vessel disease patients with a marginal significance. Moreover, likelihood of PAD among triple vessel disease patients 11.4 times more than single and double vessel disease that was significant.

Conclusion

We observed a high prevalence of asymptomatic CAD in patients with lower extremity PAD. Furthermore, diabetes, the number of cardiovascular risk factors, and both proximal and distal level involvement of the lower extremities increased significantly with the coexistence of multi-vessel CAD. These findings suggest that CAD evaluation should be performed in hospitalized patients with planned peripheral artery intervention, especially if they have diabetes, multi-cardiovascular risk factors, or multi-level PAD.

REFERENCES

- American Diabetes Association. Clinical practice recommendations 2007. *Diabetes Care* 2007; 30: S4.
- Aronow WS, Ahn C. 1994. Prevalence of coexistences of Coronary artery disease, peripheral arterial disease, and atherothrombotic brain infarction in and women <62 years of age. *Am J Cardiol.*, 74: 64-65.
- Bashir EA, Aslam N. 2001. Peripheral vascular disease in patients with coronary artery disease. *J Coll Physicians Surg Pak.*, 11(10): 614-6.
- Boulton AJ. 2004. The diabetic foot: from art to science. The 18th Camillo Golgi lecture. *Diabetologia.*, 47: 1343-1353.
- CAPRIE Steering Committee. A randomized, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic event (CAPRIE). *Lancet* 1996; 348: 1329-39.
- Chobian AV, Bakris GL, Black HR, et al. 2003. The seventh Report the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report. *JAMMA*; 289: 2560.
- Choi DH, Ha JW, Shim WH, et al. 1995. Peripheral Vascular Disease in Patients with Significant Coronary Artery. *KoreanCirc J.*, 25: 477-487.
- Cunha-Vaz J, Bernardes R. 2005. Nonproliferative retinopathy in diabetes type 2. Initial stages and characterization of phenotypes. *Progress in Retinal and Eye Research.*, 24: 355-377.
- Dieter RS, Chu WW, Paca Nowski JP et al. The significance of lower extremity peripheral arterial disease. *ClinCardiol* 2002; 25: 3-10.
- Dieter RS, Tomasson J, Gudjonsson T, Brown RL, Vitcenda M, Einerson J, et al. 2003. Lower extremity peripheral arterial disease in hospitalized patients with coronary artery disease. *Vasc Med.*, 8: 233-236.
- Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, et al. 2004. Retinopathy in diabetes. *Diabetes Care.*, 27 Suppl 1: S84-87.
- Fowkes F. 1992. The Edinburgh Claudication Questionnaire. An improved version of the WHO/Rose Questionnaire for use in epidemiological surveys. *J ClinEpidemiol.*, 45: 1101-9.
- Gabriel SA, Serafim PH, Freitas CE, et al. peripheral arterial occlusive disease and ankle-brachial index in patients who had coronary angiography. *Rev Bras Cir Cardiovasc.*, 22(1): 49-59.
- Hertzer NR. 1985. Clinical experience with preoperative coronary angiography. *J Vasc Surg.*, 2: 510-14.
- Hiatt WR. 2001. Medical treatment of peripheral arterial disease and claudication. *N Engl J Med.*, 344(21): 1608-1621.
- Hirsch AT, Criqui MH, Treat-Jacobson D et al. 2001. Peripheral arterial disease detection awareness; and treatment in primary care. *JAMA.*, 286: 1317-24.
- Hirsch AT, Criqui MH, Treat-Jacobson D, et al. 2001. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA.*, 286(11): 1317-1324.
- Hirsch AT, Haskal ZJ, Hertzler NR, et al. 2006. ACC/AHA 2005 Practice guidelines for the management of patients with peripheral arterial: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; Trans Atlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation.*, 113(11): e463-e654.
- Kafetzakis A, Giannoukas AD, Kochiadakis G, et al. 2001. Occult aorto-iliac disease in patients with symptomatic coronary artery disease. *IntAngiol.*, 20(4): 295-300.
- Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. 1984. The Wisconsin epidemiologic study of diabetic retinopathy. II. Prevalence and risk of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol.*, 102: 520-526.
- Kramer CK, Rodrigues TC, Canani LH, Gross JL, Azevedo MJ. 2011. Diabetic retinopathy predicts all-cause mortality and cardiovascular events in both type 1 and 2 diabetes: meta-analysis of observational studies. *Diabetes Care.* 34: 1238-1244.
- Liew G, Michaelides M, Bunce C. A comparison of the causes of blindness certifications in England and Wales in working age adults (16-64 years), 1999-2000 with 2009-2010. *BMJ Open.*, 2014; 4: e004015.
- McDermott MM, Hahn EA, Greenland P, et al. 2002. Atherosclerotic risk factor reduction in peripheral arterial disease: results of a national physician survey. *J Gen Intern Med.*, 2002; 17(12): 895-904.
- McDermott MM, Kerwin DR, Liu K, et al. 2001. Prevalence and significance of unrecognized lower extremity peripheral arterial disease in general medicine practice. *J Gen Intern Med.*, 16(6): 384-390.
- McDermott MM, Mehta S, Ahn H, Greenland P. 1997. Atherosclerotic risk factors are less intensively treated in patients with peripheral arterial disease than in patients with coronary artery disease. *J Gen Intern Med.*, 12(4): 209-215.
- Newman AB, Sutton-Tyrrell K, Kuller LH. 1993. Lower-extremity arterial disease in older hypertensive adults. *Arterioscler Thromb.*, 13(4): 555-562.
- Prompers L, Schaper N, Apelqvist J, Edmonds M, Jude E, Mauricio D, et al. 2008. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. *The Eurodiale Study. Diabetologia.*, 51: 747-755.
- Przewlocki T, Kablak-Ziembicka A, Kozanecki A et al. 2009. Polyvascular extra-coronary atherosclerotic disease in patients with coronary artery disease. *Kardiol Pol.*, 67(8): 978-984.
- Reaven, P.D., Emanuele, N., Moritz, T., Klein, R., Davis, M., Glander, K., et al. 2008. Proliferative diabetic retinopathy in type 2 diabetes is related to coronary artery calcium in the Veterans Affairs Diabetes Trial (VADT). *Diabetes Care.*, 31: 952-957.
- Regensteiner, J.G., Hiatt, W.R. 2002. Current medical therapies for patients with peripheral arterial disease: a critical review. *Am J Med.*, 112(1): 49-57.
- van Hecke MV, Dekker JM, Stehouwer CD, Polak BC, Fuller JH, Sjolie AK, et al. 2005. Diabetic retinopathy is associated with mortality and cardiovascular disease incidence: the EURODIAB prospective complications study. *Diabetes Care.*, 28: 1383-1389.