Original article

The prevalence of peripheral artery disease by using ankle brachial index in hypertensive patients

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Abstract

Introduction: Hypertension is one of the leading causes of global burden of disease. In a study, prevalence of hypertension in India was quoted 13.1% and only 16.7% of the person had achieved BP control of 140/90mm Hg. Peripheral vascular disease (PVD) is a slow and progressive circulation disorder which is characterized by narrowing of the vessels that carry blood to the leg and arm muscles. It is estimated that PAD affects 2 billion people worldwide. It is also estimated that of all the hypertensives at presentation, 2-5% have claudication. Similarly 50-92% of patients with PAD have hypertension. The Ankle-brachial Index (ABI) is the ratio of the systolic blood pressures between the dorsalis pedis and the posterior tibial artery to the higher of the systolic blood pressures in the two brachial arteries. The ABI's sensitivity is 90% and its specificity is 98%. Normal ABI range of 1.00 to 1.40.The patient is diagnosed with PAD when the ABI is ≤ 0.90, ABI Acts as an independent predictor of coronary and cardiovascular morbidity and mortality. ***Materials and methods:*** In this study 100 patients were registered who were suffering from hypertension, which include both indoor and outdoor patients, were studied. These patients were between the age group 45-75 years. In this study 82 were males and 18 were females. .Patients with history of Diabetes, Smoking, Hyperlipidemia, and with other risk factors excluding hypertension were excluded from the study. Ankle Brachial Index (ABI) was measured for the patients. A Doppler ultrasound blood flow detector and a sphygmomanometer (blood pressure cuff) was used to measure ABI. The patient is diagnosed with PAD when the ABI is ≤ 0.90 ***Observation:*** Total number of patients 100. Prevalence rate of peripheral arterial disease in hypertensive patients with age group (45-75) was 7%. The highest prevalence rate was seen in patients in age group 65-75 years. Males had slightly higher prevalence of peripheral arterial disease than females. Prevalence of ECG abnormalities suggesting cardiovascular disease was higher in patients with peripheral arterial disease than patients without peripheral arterial disease. Abnormal ABI (<0.9) was found in significantly higher proportion of patients with clinical evidence of peripheral arterial disease (86%) than in patients without clinical evidence of peripheral arterial disease (1.1%). ***Conclusion****:* The present study shows that ABI is a valuable method for the diagnosis of peripheral arterial disease in patients of Hypertension and should be applied in routine practices which may improve cardiovascular risk prediction

Keywords*:* Hypertension; Peripheral vascular disease (PVD); The Ankle-brachial Index (ABI)

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Introduction

Hypertension is one of the leading causes of global burden of disease. It is common, asymptomatic, readily detectable usually easily treatable and often leads to lethal complications if left untreated. Cardiovascular disease (CVD) is the most common contributor of morbidity and mortality in underdeveloped and developing countries including the South Asian countries (including India and Pakistan)[1]. It has been estimated that 78% of all deaths and 86.3% of all loss of disability adjusted life years are attributable to this cause. Amongst the cluster group of CVDs, Hypertension (HTN) represents the most common cardiovascular risk factor[2]. Several previous studies have clearly shown longitudinal associations between HTN and coronary artery disease, myocardial infarction, stroke, congestive heart failure, and peripheral vascular disease and lowering blood pressure (BP) significantly reduces the cardiovascular morbidity and mortality[3]. Hypertension is defined as systemic blood pressure of 140/90 mmHg or more on two separate occasions measured at least one to two weeks apart[4]. Various studies have been carried out in India to estimate the prevalence of hypertension. In a study, prevalence of hypertension in India was quoted 13.1% and only 16.7% of the person had achieved BP control of 140/90mm Hg. Cardiovascular diseases caused 2.3 million deaths in India in the year 1990; this is projected to double by the year 2020. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India[5].

Peripheral vascular disease (PVD), commonly referred to as peripheral artery disease (PAD) or peripheral artery occlusive disease (PAOD) or peripheral obliterative arteriopathy, refers to the obstruction of large arteries not within the coronary, aortic arch vasculature, or brain. PVD can result from atherosclerosis, inflammatory processes leading to stenosis, an embolism, or thrombus formation. It causes either acute or chronic ischemia (lack of blood supply). Often PVD is a term used to refer to atherosclerotic blockages found in the lower extremity[6].

Peripheral vascular disease (PVD) is a slow and progressive circulation disorder which is characterized by narrowing of the vessels that carry blood to the leg and arm muscles. About 20% of patients with mild PAD may be asymptomatic and symptomatic[7].

Peripheral artery occlusive disease is commonly divided in the Fontaine stages, introduced by René Fontaine in 1954 for chronic limb ischemia[8]:

- Stage I: Asymptomatic, incomplete blood vessel obstruction

Stage II: Mild claudication pain in limb

Stage IIA: Claudication at a distance of greater than 200 metres

Stage IIB: Claudication distance of less than 200 metres

Stage III: Rest pain, mostly in the feet

Stage IV: Necrosis and/or gangrene of the limb

A more recent classification by Rutherford consists of four grades and seven categories[9]:

- Grade 0, Category 0: Asymptomatic
- Grade I, Category 1: Mild claudication
- Grade I, Category 2: Moderate claudication
- Grade I, Category 3: Severe claudication
- Grade II, Category 4: Rest pain
- Grade III, Category 5: Minor tissue loss; Ischemic ulceration not exceeding ulcer of the digits of the foot
- Grade IV, Category 6: Major tissue loss; Severe ischemic ulcers or frank gangrene

  Risk factors contributing to PAD are the same as those for atherosclerosis[10]

Hypertension is a common and important risk factor for vascular disorder, including PVD of hypertensives at presentation, about 2-5% has intermittent claudication, and this prevalence increases with age. Similarly 35-55% of patients with PVD at presentation also have hypertension. Patients who suffer from hypertension with PVD have a greatly increased risk of myocardial infarction and stroke[11].

It is estimated that PAD affects 2 billion people worldwide. It is also estimated that of all the hypertensives at presentation, 2-5% have claudication. Similarly 50-92% of patients with PAD have hypertension[12].

The American Heart Association estimates that as many as 8-12 million Americans have PAD and that nearly 75% of them are asymptomatic[13].An estimated 1 million Americans develop symptomatic PAD every year[14].

The disease spectrum ranges from mild, intermittent claudication resulting in calf pain to severe, chronic leg ischemia requiring arterial bypass, PTA (percutaneous angioplasty)[15].

There are no significant gender differences in the overall prevalence of PAD in the general population. Over a 5-year period 25%-35% of people with PAD will suffer from MI or stroke and additional 25% may die[16].

The history and physical examination are usually sufficient to establish the diagnosis of PAD. An objective assessment of the severity of disease is obtained by noninvasive techniques. These include digital pulse volume recordings, Doppler flow velocity wave form analysis, duplex ultrasonography (which combines B-mode imaging and pulse-wave Doppler examination), Segmental pressure measurement, tanscutaneous oximetry, Stress testing (usually using a treadmill)

The Ankle-brachial Index (ABI)

The ABI is the ratio of the systolic blood pressures between the dorsalis pedis and the posterior tibial artery to the higher of the systolic blood pressures in the two brachial arteries. The ABI's sensitivity is 90% and its specificity is 98% for detecting angiographically defined stenoses of 50% or more. Ankle brachial index is useful in assessing the prognosis in the symptomatic as well as asymptomatic patients in contrast to the variability of pulse assessment and the often non specific nature of information obtained by history and physical examination. The ankle brachial index is a reproducible and reasonably accurate, non invasive measure of detection of peripheral arterial disease and determination of disease severity[17]. Compared to the arm, lower blood pressure in the leg is an indication of blocked arteries (peripheral vascular disease or PVD). The ABI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressures in the arm[18].

The higher systolic reading of the left and right arm brachial artery is generally used in the assessment. The pressures in each foot's posterior tibial artery and dorsalis pedis arteryare measured with the higher of the two values used as the ABI for that leg[19].

$$ABPI_{Leg} = \frac{P_{Leg}}{P_{Arm}}$$

Where P_{Leg} is the systolic blood pressure of dorsalis pedis or posterior tibial arteries

and P_{Arm} is the highest of the left and right arm brachial systolic blood pressure

Upon suspicion of PVD, the first-line study is the ankle brachial pressure index (ABPI/ABI). When the blood pressure readings in the ankles are lower than that in the arms, blockages in the arteries which provide blood from the heart to the ankle are suspected. Normal ABI range of 1.00 to 1.40.The patient is diagnosed with PAD when the ABI is $\leq$ 0.90. ABI values of 0.91 to 0.99 are considered ''borderline'' and values >1.40 indicate noncompressible arteries. PAD is graded as mild to moderate if the ABI is between 0.41 and 0.90, and an ABI less than 0.40 is suggestive of severe PAD. These relative categories have prognostic value[20].

The role of ABI in clinical practice is

(A) To confirm the clinical diagnosis of peripheral arterial disease particularly in patients with atypical symptoms and signs or coexisting musculoskeletal disorder.

(B) Provide semi quantitative assessment of:

1. Severity of peripheral arterial disease, including asymptomatic disease.
2. Progression of peripheral arterial disease with time and progression of disease.
3. Response to therapy

(C)Provide an indication of overall cardiovascular risk. Acts as an independent predictor of coronary and cardiovascular morbidity and mortality[21].

Materials and methods.:

In this study 100 patients were registered who were suffering from hypertension, which include both indoor and outdoor patients, were studied. These patients were between the age group 45-75 years. In this study 82 were males and 18 were females. Study was conducted in Department of Medicine, MMIMSR, Mullana. The study was approved by the Institutional ethics committee.

Patients having history of only hypertension were included, in the study, between the age group of 45-75 years were includedin the study.Patients with history of Diabetes, Smoking, Hyperlipidemia, and with other risk factors excluding hypertension were excluded from the study.

Patient in this study were first evaluated by complete history including age, smoking history, diabetes, history of symptoms of peripheral arterial disease including ,Intermittent claudication, resting extremity pain.

History followed by general physical examination including palpation of all peripheral pulses, bruits and systemic examination. Examination of limbs to look for skin changes, temperature of limb, ulcer of limbs, gangrenous changes.

All the routine investigations like Fasting blood sugar, Blood urea, S.Creatinine, Urine R/E Total Cholesterol, HDL, LDL, VLDL Cholesterol, Triglyceride, and E.C.G

Ankle Brachial Index (ABI)

The ABI is the ratio of the systolic blood pressures between the dorsalis pedis and the posterior tibial artery to the higher of the systolic blood pressures in the two brachial arteries. The ABI's sensitivity is 90% and its specificity is 98% for detecting angiographically defined stenoses of 50% or more. The ABI also helps to differentiate true claudication from pseudoclaudication. Vascular claudication does not occur without a drop in the ABI. Ankle brachial index is useful in assessing the prognosis in the symptomatic as well as asymptomatic patients in contrast to the variability of pulse assessment and the often non specific nature of information obtained by history and physical examination. The ankle brachial index is a reproducible and reasonably accurate, non invasive measure of detection of peripheral arterial disease and determination of disease severity.

Method: The patient was placed supine, without the head or any extremities dangling over the edge of the table as measurement of ankle blood pressures in a seated position will grossly overestimate the ABI.

A Doppler ultrasound blood flow detector and a sphygmomanometer (blood pressure cuff) are usually needed. The blood pressure cuff is inflated proximal to the artery in question. Measured by the Doppler wand, the inflation continues until the pulse in the artery ceases. The blood pressure cuff is then slowly deflated. When the artery's pulse is re-detected through the Doppler probe the pressure in the cuff at that moment indicates the systolic pressure of that artery.

The higher systolic reading of the left and right arm brachial artery is generally used in the assessment. The pressures in each foot's posterior tibial artery and dorsalis pedis arteryare measured with the higher of the two values used as the ABI for that leg.

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Observation:

Table no 1: Gender specific prevalence of peripheral arterial disease in hypertensive patients between the ages 45-75 years.

	No. of patients with peripheral arterial disease	No. of patients without peripheral population arterial disease	Total	Prevalence /1 000 hypertensive Population
Male	5 (6.1%)	77 (93.9%)	82	60.1/1000
Female	1 (5.5%)	17 (94.5%)	18	55/1000
Total	6	94	100	

.Chi –square= 0.21 p=0.64

This shows that males had higher prevalence of peripheral arterial disease than female

Table no 2: Prevalence of peripheral arterial disease in hypertensive patients according to age

Age	Patients	Patients without PAD	Total	Prevalence/1000 hypertensive
45-55	0	15 (100%)	15	0/1000
56-65	0	29 (100%)	29	0/1000
66-75	6(10.7)	50 (89.3%)	56	107/1000

Chi-square=3.30 p=0.06

Table no 3: Prevalence of peripheral arterial disease in patients of hypertension in relation to symptoms (Intermittent Claudication)

Symptoms	Patients with PAD	Patients without PAD	Total
Symptoms of PAD	4 (66.66%)	4 (4.25)%	8
No symptoms of PAD	2 (33.33%)	90 (95.75%)	92
	6	94	100

P=0.0002 (highly significant)
Above data suggests that higher prevalence of peripheral arterial disease is seen in patients with intermittent claudication.

Table no 4: Prevalence of abnormal E.C.G changes in patients of hypertension in relation to peripheral arterial disease.

E.C.G	Patients with PAD	Patients without PAD	Total
Changes suggestive of CAD	4 (66.66%)	18 (19.14%)	22
Changes not suggestive of CAD	2 (33.33%)	76 (80.85%)	78
	6	94	100

Chi-square=4.91 p=0.02 (significant)
This shows that higher prevalence of abnormal E.C.G was found in patients with peripheral arterial disease.

Table no 5: Prevalence of abnormal ankle brachial index in patients of hypertension with peripheral .arterial disease and without peripheral arterial disease on basis of disease severity.

Ankle brachial index	ABI <0.96	ABI 0.81-0.95	ABI 0.51-80	ABI 0.31-0.50	ABI 0.30 or less	Total
Patients with peripheral arterial disease	1(16.66%)	2(33.33%)	2(33.33%)	1(16.66%)	1(16.66%)	7
Patients without peripheral arterial disease	93(93%)	NIL	NIL	NIL	NIL	94
Total	94	2	2	1	1	100

P< 0.001 (significant)
From above data it is clear that patients with peripheral arterial disease had an abnormal ankle brachial index (ABI).

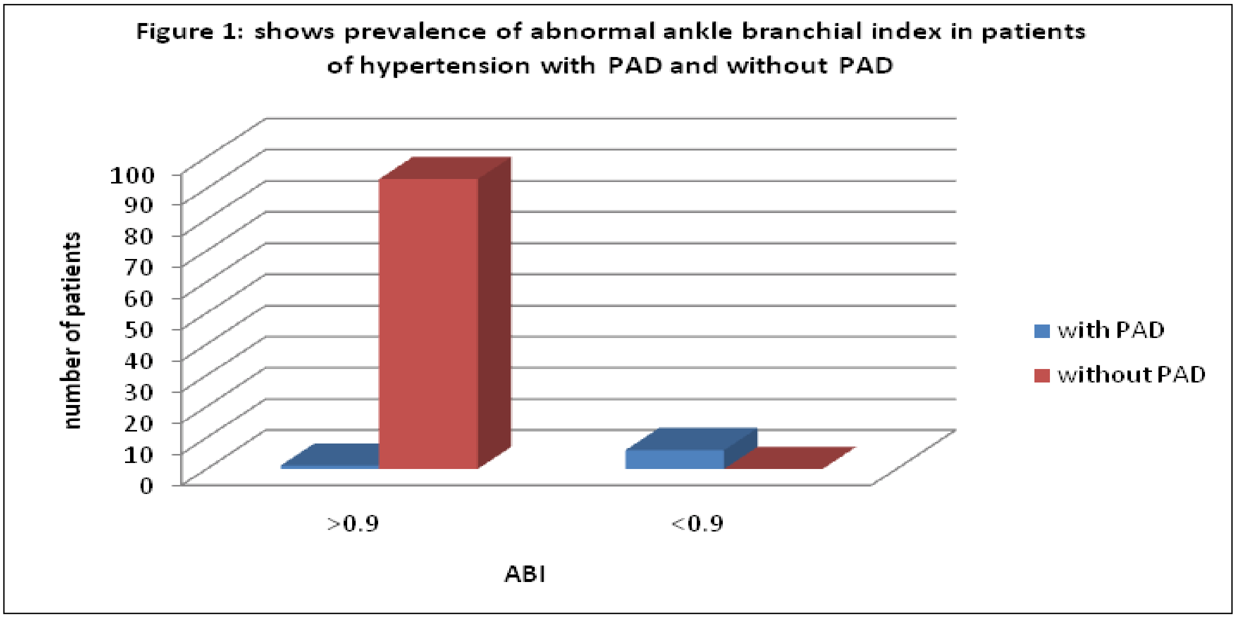
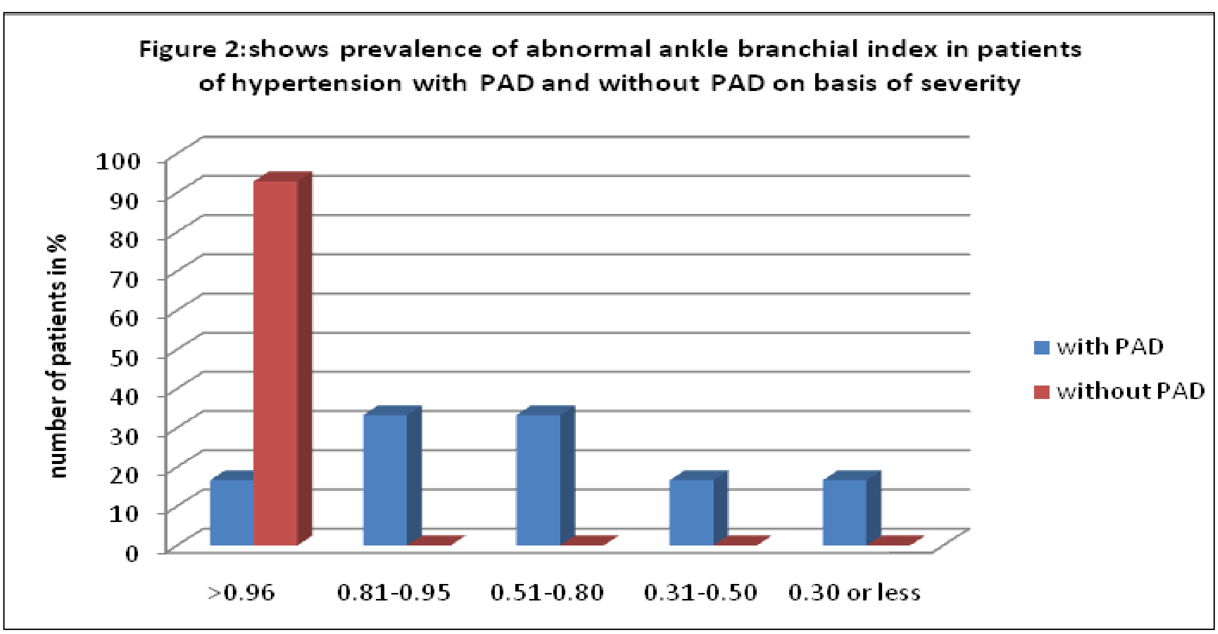


Table no 6: Prevalence of Abnormal ankle brachial index in patients with peripheral arterial disease and without peripheral arterial disease.

ABI	Normal Ankle Brachial Index >0.9	Abnormal Ankle Brachial Index <0.9	Total
Patients of PAD	1 (1.07%)	6 (6.38%)	7
Patients without peripheral arterial disease	93(93%)	0	93
Total	94	6	100

P=0.0001(highly significant)
This suggests that ABI is an important, specific, sensitive and non-invasive diagnostic method for patients with peripheral arterial disease.



Disscussion

In this study 100 patients were registered who were suffering from hypertension, which include both indoor and outdoor patients, were studied. These patients were between the age group 45-75 years. In this study 82 were males and 18 were females. Study was conducted in Department of Medicine, MMIMSR, Mullana. The overall prevalence was found to be 7/100 (7%). The main aim of the study was to determine the prevalence of peripheral arterial disease (PAD) among patients with hypertension. Hypertension is one of the risk factor for developing peripheral arterial disease. Peripheral arterial disease is a slow and progressive circulation disorder. It may involve any blood vessel. These patients mostly present with intermittent claudication, i.e., pain in lower limbs while walking.

Jeffrey I et al (1996) in their studies indicate that up to 5% of men and 2.5% of women 60 years of age or older have symptoms of intermittent claudication due to peripheral arterial insufficiency. The prevalence is at least threefold higher when sensitive non invasive tests are used to make the diagnosis of arterial insufficiency in asymptomatic and symptomatic Individuals[23]. Newman AB et al (1993) evaluated the relationship between ankle brachial index and cardio vascular mortality and morbidity in older adults with systolic hypertension. they concluded that low ABI appears to be an important predictor of morbidity and mortality among older adults with systolic hypertension[22]. Wouter TM WH et al (1998) while conducting the famous Rotterdam study observed that age and sex specific prevalence of PAD in elderly population and observed that prevalence increases with older age[24]. Rhee SY et al (2010) investigated a study to found the prevalence of peripheral arterial disease in hypertensive patients. In 4425 hypertensive patients aged 55 and older were enrolled 982(16.20%) subjects were diagnosed as having PAD by ABI. Patients with PAD had longer duration of hypertension greater than 10 years. PAD screening should be emphasized to every individual who are having risk factor[27].Hypertension is a strong risk factor for cardiovascular disease in both men and women. Longitudinal studies indicate that the risk of atherosclerotic cardiovascular disease is three to four times higher in hypertensive patients than in non hypertensive patients, furthermore patients having peripheral arterial disease are at further risk of coronary artery disease. The annual rate of fatal to non fatal cardiovascular disease among patients with hypertension is 2-4%.Coronary artery disease is the most common cause of mortality among patients with limb artery disease in hypertensive patients. In our study 6 patients had peripheral artery disease, out of which 4 patients had ECG changes suggestive of coronary artery disease. (p=0.02) significant. This shows that there is a higher prevalence of abnormal ECG in patients with peripheral arterial disease. In our study on patients of age between 45-65 years, it was found that prevalence was higher among patients with age greater than 65 years. Makin A et al (2002) in their study on sex prevalence, 512 patients were selected which comprised of equal number of males and females with hypertension. They found that there was a slight increase in number of cases of peripheral arterial disease in males than females. However the prevalence of peripheral arterial disease equals to males after menopause. In our study the data shows that from 6 patients with peripheral arterial disease, males had increased prevalence[16].

One of the study which was taken by Kennedy M, Solomon C et al 2005 on risk factor for declining ankle brachial index in men and women 65 years or older, in which significant number of patients with peripheral arterial diseased were in advancing age[26]. Clement Denis et al (2004) concluded that peripheral arterial disease (PAD) of the lower limbs is associated with a high cardiovascular morbidity and mortality. Intermittent claudication is the most common symptomatic manifestation of PAD, but is in its own value an important predictor of cardiovascular death, increasing it by three-fold, and increasing all cause mortality by two-to-five fold[25]. Hypertension is a risk factor for vascular disorders, including PAD. Of hypertensives at presentation, about 2-5% have intermittent claudication, with increasing prevalence with age. 35¬55% of patients with PAD at presentation also show' hypertension. Patients who suffer from hypertension with PAD have a greatly increased risk of myocardial infarction and stroke.

The aim of this study is to determine the prevalence of PAD in hypertensive patients. The prevalence of PAD is affected by the methods by which the diagnosis is sought. Various methods have been used for the diagnosis of PAD, but the method we have used is Ankle Brachial Index (ABI). It is a non-invasive, easy, cost effective and has sensitivity of 90% and specificity of 98%.

This diagnostic method was applied to the patients in the study, we found that out of 100 hypertensive patients, 6 patients had abnormal ankle brachial index (<9.0) and 96 patients had normal ABI. With this method severity of the disease was also assessed. In this study out of 6 patients 2 (33.3%) patients had mild disease. 2(33.3%) patients had moderate disease. 1(16.6%) had severe disease. 1 (33.3%) had very severe disease. Above all 7 patients had peripheral arterial disease, out of which 6 patients had abnormal ABI (<0.9). 1 patient had normal ABI (>0.9)

All the above observations obtained in the present study indicate that ABI is a simple, non-invasive, easy, specific and highly sensitive method for the diagnosis of peripheral arterial disease (PAD).

Summaray

- Total number of patients 100.
- Prevalence rate of peripheral arterial disease in hypertensive patients with age group (45-75) was 7%.
- The highest prevalence rate was seen in patients in age group 65-75 years.
- Males had slightly higher prevalence of peripheral arterial disease than females.
- Prevalence of ECG abnormalities suggesting cardiovascular disease was higher in patients with peripheral arterial disease than patients without peripheral arterial disease.
- Abnormal ABI (<0.9) was found in significantly higher proportion of patients with clinical evidence of peripheral arterial disease (86%) than in patients without clinical evidence of peripheral arterial disease (1.1%).

Conclusion

The present study shows that ABI is a valuable method for the diagnosis of peripheral arterial disease in patients of Hypertension and should be applied in routine practices which may improve cardiovascular risk prediction.

Conflict of interest: None declared

References

1. Ismail J, Jafar TH, Jafary FH, White F, Faruqui AM, Chaturvedi N. Risk factors for non-fatal myocardial infarction in young South Asian adults. *Heart*.2004**; 90:**259–63.
2. Gupta R, Misra A, Vikram NK, Kondal D, Gupta SS, Agrawal A, Pandey RM.Younger age of escalation of cardiovascular risk factors in Asian Indian subjects. *BMC Cardiovasc Disord.* 2009 Jul **5**;9:28.
3. Stafylas PC, Sarafidis PA. Carvedilol in hypertension treatment. *Vasc Health Risk Manag*. 2008 February;**4**(1):23–30.
4. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JLet al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC report. *JAMA*. 2003; **289**(19):2560-72.
5. Gupta R. Trends in hypertension epidemiology in India. *J Hum Hypertens*. 2004 February;**18**(2):73-8.
6. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal, Curtis W., Creager, Mark A et al. Peripheral Arterial Disease at Merck Manual of Diagnosis and Therapy . *Professional Edition*. 2010; **20**(5):342.
7. Joosten MM, Pai JK, Bertoia ML, Rimm EB, Spiegelman D, Mittleman MA et al. Associations between conventional cardiovascular risk factors and risk of peripheral artery disease in men. *JAMA.* 2012 Oct 24; **308**(16):1660-7.
8. Fontaine R, Kim M, Kieny R (1954). "Die chirugische Behandlung der peripheren Durchblutungsstörungen. (Surgical treatment of peripheral circulation disorders*)". Helvetica Chirurgica Acta (in German)* 21 (5/6): 499–533
9. Norgren L, Hiatt WR, Dormandy JA (2007). "Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)". *Eur J Vasc Endovasc* 2006; **33**(1):111.
10. Price J, Mowbray P, Lee A, Rumley A, Lowe G, Fowkes F: Relationship between smoking and cardiovascular risk factors in the development of peripheral arterial disease and coronary artery disease; Edinburgh Artery

Study Edinburgh Artery Study. *European heart journal* 1999, **20**(5):344-353.

11. Taylor GW, Caloar, Sutton-Tyrell K, Vogt MT, Kuller LH, Fowkes et al. Atherosclerosis of lower limbs. *Dr. med.j* 1979; **1**: 507-510

12. Jamson J, Sherlok H, Sutton-Tyrell K, Vogt MT, Kuller LH. Risk factors of intermittent n claudication with relation to hypertension*: JAMA*. 2000; **82:**1062-1071.

13. Taylor GW, Caloar, Sutton-Tyrell K, Vogt MT, Kuller LH, Fowkes et al. Atherosclerosis of lower limbs. *Dr. med.j* 1979**; 1:** 507-510

14. Jamson J, Sherlok H, Sutton-Tyrell K, Vogt MT, Kuller LH. Risk factors of intermittent n claudication with relation to hypertension: *JAMA*. 2000**; 82**:1062-1071.

15. Meijer WT, Grobee DE, Hoffman A. Determinants of peripheral arterial disease in elderly: the Rotterdam study. *Archives of internal medicine* 2000; **160**(19):2934-2938.447-54.

16. Makin A, Lip GY, Silverman S, Beevers DG. Peripheral vascular disease & hypertension: *J Hum Hypertension* 2002:**15**

17. Felipe E, Cara Vaggie, Screening for peripheral arterial disease. The Cleveland clinic disease management project. 2004;**11**(22):111-113.

18. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal, Curtis W., Creager, Mark A et al. Peripheral Arterial Disease at Merck Manual of Diagnosis and Therapy *Professional Edition*. 2010;**20**(5):342

19. Fontaine R, Kim M, Kieny R. "Die chirugische Behandlung der peripheren Durchblutungsstörungen. (Surgical treatment of peripheral circulation disorders)". *Helvetica Chirurgica Acta* (in German) 1945; **21** (5): 499–533.

20. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al. Jaff MRACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline) a report of the American college of cardiology foundation/American heart association task force on practice guidelines. *Journal of the American College of Cardiology* 2011**; 58**(19):2020-2045.

21. Haliday JR, Estes H. Peripheral vascular disease epidemiology, etiology and diagnosis: *BMJ*. 2000; **124**:36-39.

22. Newman AB, Sutton-Tyrell K, Vogt MT, Kuller LH. Morbidity and mortality in hypertensive adults with low ABI. *JAMA.* 1993 28;**270**(4):487-9

23. Jaffrey, Weitz. MD, Chair, John Byrne MD. Diagnosis and treatment of chronic arterial insufficiency of lower extremities*: Circulation.* 1996**; 94:**3026-3049.

24. Wouter T-Meijer, Armo, Hoes. Peripheral artery disease in Elderly. *Arteriosclerosis, thrombosis and vascular biology*. 1999; **18**,185-192.

25. Clement; Dennis L; DE Buyzere, Marc L. Risk factor and peripheral arterial disease: *Atherosclerosis* 2004;**22(**11) P 3615-3620

26. Kennedy M, Solomon C, Manolio TA, Criqui MH, Newman AB, Polak JF, Burke GL, Enright P, Cushman M: Risk factors for declining ankle-brachial index in men and women 65 years or older. *Arch Intern Med.* 2005 Sep 12;**165**(16):1896-902

27. Rhee SY, stolk RP. Peripheral artery disease and its complications: *Circulation.* 2010; **425**:43-47.