

**Article History** 

## **Original** Article

# Asymptomatic Peripheral Arterial Diseases in Acute Ischemic Stroke Patients in Sualimani City-Iraq

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## ABSTRACT

Background: Peripheral arterial disease is an atherosclerotic syndrome in which the lumen of the arteries in the extremities becomes progressively obstructed by plaque. Received: 01 Mar 2016 Few studies focus on the relationship between low ankle-brachial index and acute Revised: 04 Mar 2016 ischemic stroke. Accepted: 08 Mar 2016

> Aims: To find out the prevalence of asymptomatic peripheral arterial diseases in patients with acute ischemic stroke in Sulaimani city-Iraq.

> Patients & Methods: A cross sectional study carried out in the Neurology Department of Sulaimani Teaching and Shar Teaching hospitals in Sulaimani city between 1st of December, 2014 to 30th of May, 2015on a convenient sample of 118 patients with stroke. The data was collected by the researcher through direct interview and filling a prepared questionnaire.

> Results: Prevalence of PAD among stroke patients was 19.5%. A significant association was observed between elderly age patients and PAD (p<0.001). There was an apparent association between female gender and PAD (p=0.05). There was an obvious association between ex-smokers and PAD (p<0.001). There was a noticeable association between DM and PAD (p<0.001). A conspicuous association was observed between each of uncontrolled DM (≥ 7%) and IHD with PAD (p<0.05). There was seeming association between patients with no CATH and PAD (p<0.001).

> Conclusions: The prevalence of PAD among patients with ischemic stroke was within the accepted range.

**KEYWORDS:** Ischemic stroke, IHD, Peripheral arterial diseases.

#### **INTRODUCTION**

Stroke is a major cause of death and a subversive disorder that puts a large burden on health care systems. It occurs particularly in the elderly. Most studies on the incidence of stroke have focused on persons aged younger than 85 years and limited data exist on the occurrence of stroke in the very old. Since populations are growing older in Kurdistan region of Iraq, an increase in the burden of stroke is expected in coming decades. A challenge for medical research is the question whether and how this devastating disease can be prevented. This requires identification of modifiable risk factors that are amenable to intervention. Moreover, it requires possibilities to recognize those who may benefit most from preventive interventions<sup>1</sup>.

The main risk factor for stroke is atherosclerosis, which accumulates with age. Several non-invasive measures of atherosclerosis exist. Despite research that has been done in this field, the strength and nature of the relation between measures of atherosclerosis and stroke subtypes

is not yet fully understood. Further, it is not clear whether other risk factors are related to stroke through unrelated mechanisms, or that they trigger the presence or progression of atherosclerosis. In addition to atherosclerosis, there are other putative risk factors for stroke such as sex hormones and genetic factors<sup>2</sup>.

Peripheral artery disease (PAD) is under-diagnosed, undertreated, poorly understood, and much more common than previously thought. The term peripheral artery disease was used to denote vascular diseases caused by atherosclerosis of the abdominal aorta, iliac, and lower-extremity arteries leading to stenosis or occlusion. 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. Not only was the diagnosis of PAD frequently overlooked, but the cardiovascular risk factors were not treated as appropriately as in patients with CAD<sup>3</sup>.

\*Correspondence to: Dr Kosar M. Ali Department of Medicine /School of Medicine – University of Sualimani, IRAQ kjwanrowy@hotmail.com Patients with cerebrovascular disease are at substantially higher risk of mortality than the general population, primarily from cardiovascular disease.<sup>4</sup>

Peripheral arterial disease (PAD) is an atherosclerotic syndrome in which the lumen of the arteries in the extremities becomes progressively obstructed by plaque. Recent epidemiological studies estimate a prevalence of PAD of 11% to 16% in the population aged $\geq$  55 years<sup>5</sup> and prevalence as high as 20% to 30% in specific high-risk populations<sup>6</sup>. Several prospective and cross-sectional studies have shown that PAD is a marker for arterial disease in other vascular beds and is associated with a 6-fold increase in fatal and nonfatal myocardial infarction<sup>7</sup>.

An ankle-brachial index (ABI) less than 0.9 is broadly acknowledged to indicate peripheral arterial disease (PAD) of the lower limbs<sup>8,9</sup>. Stroke patients with PAD may have a higher risk of recurrent cardiovascular events and poorer outcomes<sup>10</sup>. Few studies focus on the relationship between low ABI and acute ischemic stroke<sup>11,12</sup>.

Previous studies which surveyed relatively stable subjects in the outpatient setting showed conflicting results in predicting stroke risk by a low ABI<sup>13-16</sup>. The association of low ABI with stroke was less significant after adjusting for traditional vascular risk factors<sup>13</sup> or became statistically insignificant in multivariable regression analysis<sup>14</sup>.

A recent worldwide registry showed that patients with both stroke and PAD have very high risk for recurrent vascular events, and require aggressive optimized vascular risk-reduction strategies<sup>17</sup>. PAD is underdiagnosed and under-treated worldwide<sup>18</sup>. Better understanding the clinical course and outcomes in patients with acute ischemic stroke and PAD helps in determining the benefit of programmed screening ABI in stroke patients and optimizing therapeutic interventions.

## Epidemiology

Atherosclerotic peripheral vascular disease (PVD) is an under diagnosed, undertreated, age-dependent disease that profoundly impacts patient quality of life, and is an independent predictor of mortality. On average the mortality rate of claudicated patients is 2.5 times higher than non-claudicated patients. Atherosclerosis is a ubiquitous process of chronic low grade inflammation with superimposed acute thrombotic events that affects the entire arterial tree in the coronary, cerebral, visceral, and upper and lower extremity circulation. Patients with PVD are at increased risk of cardiovascular and cerebrovascular events, including death, MI, and stroke. clinical continuum of PVD ranges The from asymptomatic stenosis to limb-threatening ischemia.

Intermittent Claudication (IC) is defined as ischemic limb pain in one or both legs that occurs with exertion and is alleviated with rest. IC is associated with marked limitations in walking ability, which translates into a considerable negative impact on occupational, social, and leisure activities<sup>19</sup>.

## **Risk factors**

The most common risk factors associated with PAD are increasing age, diabetes, and smoking<sup>20</sup>.

- Age: Persons aged 65 years or older in the Framingham Heart Study and persons aged 70 years or older in the National Health and Nutrition Examination Survey (NHANES) were at increased risk for the development of PAD<sup>3</sup>.
- **Smoking:** Is the single most important modifiable risk factor for the development of PAD. It is unknown why the association between PAD and smoking is about twice as strong as that between PAD and CAD<sup>3</sup>.
- Diabetes: Increases the risk of developing symptomatic and asymptomatic PAD by 1.5- to 4fold and leads to an increased risk of cardiovascular events and early mortality<sup>21</sup>.
- **Hyperlipidemia:** In the Framingham Study, an elevated cholesterol level was associated with a 2-fold increased risk of claudication; more than 60% of patients with PAD had hypercholesterolemia, whereas in the PARTNERS program, the prevalence of hyperlipidemia in patients with known PAD was 77%<sup>22</sup>.
- Hypertension: Almost several studies have shown a strong association between hypertension and PAD, and as many as 50% to 92% of patients with PAD have hypertension<sup>24</sup>.
- Non-traditional risk factors: Other risk factors that are associated with an increased prevalence of PAD include race and ethnicity (African Americans and those of Hispanic origin are at higher risk), chronic kidney disease, the metabolic syndrome, and levels of C-reactive protein, B2-microglobulin, cystatin C, lipoprotein(a), and homocysteine<sup>3</sup>.

## Clinical presentation of PAD<sup>2,3</sup>

- Classic claudication: Pain, discomfort, aching, heaviness, tiredness, tightness, cramping, or burning in the calf, thigh, hip, and buttocks that is reproducible with a similar level of walking from day to day, disappears after several minutes of standing, and occurs at the same distance once walking has resumed<sup>2,3</sup>.
- Atypical leg pain: Lower-extremity discomfort that is exertional but does not consistently occur at the same distance walked and may require a longer period of time to resolve or require the patient to sit down or change body position<sup>2,3</sup>.
- **Asymptomatic:** Without obvious symptoms, but usually associated with functional impairment on formal testing<sup>2,3</sup>.

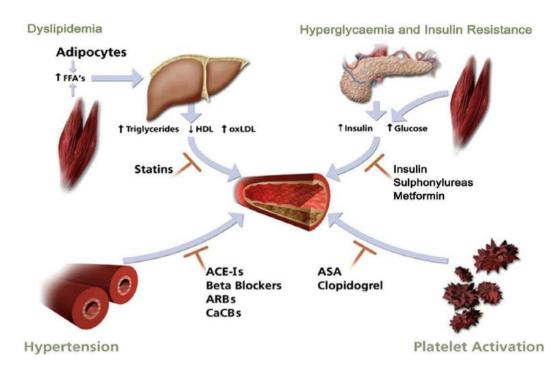


Fig1: Effect of dyslipidemia and DM on PAD<sup>23</sup>

#### Table 1: Therapy for PAD<sup>2</sup>.

Decrease Cardiovascular events	Improve symptoms	
Smoking cessation	Smoking cessation	
Statin-goal LDL-C <70mg/dl	Supervised exercise program	
ACE inhibitor-goal BP<130/80mmHG	Cilostazol	
Anti-platelets therapy	Percutaneous Endovascular therapy	
Diabetes treatment	Surgical revascularization	

#### **Diagnostic evaluation**<sup>3</sup>

- Duplex Ultrasonography.
- Exercise Treadmill Testing and ABI.
- Magnetic Resonance Angiography.
- Computed Tomographic Angiography.
- Digital Subtraction Angiography.

## Treatment

The two primary treatment goals in patients with PAD are to decrease cardiovascular morbidity and mortality and to improve limb-related symptoms (claudication) and quality of life (Table 1)<sup>2</sup>.

## AIMS

The aim of the present study is to find out the prevalence of asymptomatic peripheral arterial diseases among elderly patients with acute ischemic stroke in Sulaimani city.

## PATIENTS AND METHODS

A cross sectional study was carried out in the Neurology department of Sulaimani Teaching and Shar Teaching hospitals in Sulaimani city between 1st of December, 2014 to 30<sup>th</sup> of May 2015.

All patients with acute stroke and/or transient ischemic attack (TIA) were admitted to the Neurology department of Sulaimani Teaching and Shar Teaching hospitals in Sulaimani city where the population of the study.

#### **Inclusion criteria**

- 1. Acute stroke.
- 2. TIA.
- 3. Age range of patients were 65 years and above.

#### Exclusion criteria

- 1. Hemorrhagic stroke.
- 2. Previous rheumatologic disorders.
- 3. Previous leg surgery.
- 4. Disc prolapsed.
- 5. Cancer, limb ischemia, diabetic foot.

A convenient sample of 118 patients with stroke was taken after consideration of inclusion and exclusion criteria.

The data was collected by the researcher through direct interview and filling a prepared questionnaire. Patients were diagnosed as stroke and/or TIA by a specialist physician in the Neurology department approved by CT scan. History was taken from the patients, if they were unable to give information; history was taken from relatives and patient chart. Investigations were carried out by the researcher by collecting 5 ml of blood from the patients. The vascular risk factors were defined as follows: arterial hypertension, on antihypertensive treatment or blood pressure ≥140/90 mmHg at two readings before stroke or >5 days after stroke; diabetes mellitus, on anti-diabetic treatment or elevated hemoglobin A1c > 7 percent; and hyperlipidemia, on lipid-lowering medication or total cholesterol > 200 mg/dL or triglycerides > 200 mg/dL or LDL> 150 mg/dL before or after stroke. The patients were classified as non-smokers, ex-smokers and smokers. The pre-existing ischemic heart disease was diagnosed according to the following documented history: previous angiogram showing significant occlusive disease; history of myocardial infarction; previous coronary artery bypass surgery or angioplasty. The type and size of stroke was diagnosed by the specialist and taken from chart of the patient. Patients received standard treatment based on the local guidelines and the judgment of attending physicians. Management was not delayed nor altered by participation in this study.

PAD could be determined with high sensitivity and specificity using the ABI, a simple, noninvasive procedure<sup>25</sup>. The systolic blood pressure was measured on the right arm (brachial artery) and both ankles (posterior tibial and dorsalis pedis arteries). The researcher measured the systolic pressure after taking 10 minutes rest using hand helddopplex (MD2; HUNTLEIGH) and patient in supine position.

If the participant had a condition associated with the right arm that would interfere with measurement, the left arm was used for brachial pressure measurement. Systolic blood pressure was measured twice at each site for participants aged  $\geq 60$  years. Left and right ABI measurements were obtained by dividing the mean systolic blood pressure in the right and left ankle by mean blood pressure in the arms. The PAD was defined as an ABI <0.90 in either leg<sup>8,26</sup>.

#### Ethical considerations:

- Verbal consent was taken from each patient and/or their relatives to be enrolled in the study.
- Confidentiality was taken into consideration.
- The researcher was responsible with other colleagues in providing full examination and treatment of the patients

#### Data collection and analysis

All the patients' data was collected using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 17 was used. Descriptive statistics presented as (mean  $\pm$  standard deviation) and frequencies as percentages. Kolmogorov Smirnov analysis verified the normality of the data set. Multiple contingency tables conducted and appropriate statistical tests performed, The Chi-square was used for categorical variables (Fishers exact test was used when expected

variables were less than 5) an independent t-test was used to compare the means values. The Binary logistic regression analysis was used to find the predictive variable. In all statistical analysis, the level of significance (p value) set at  $\leq 0.05$  and the result presented as tables were and/or graphs. The Statistical analysis of the study was made by the community medicine specialist.

## RESULTS

A total of 118 stroke patients were included in this study with mean age  $74\pm9$  years, age group 70-79 years was a prevalent. The male patients (56.8%) were more than the female patients (43.2%) with a male to female ratio 1.3:1. The occupation of studied patients was distributed as 43 housewives, 22 free workers while 53 patients were retired. The Urban residents (58.5%) among the stroke patients were prevalent, (Table 2).

More than two thirds of the studied patients were nonsmokers, only 4 patients were current smokers and 26 were ex-smokers. Mean duration of smking for the exsmokers was  $27\pm6$  years who had ceased smoking befor $7\pm3$  years. (Table 3)

Approximately, two thirds of the studied patients had stroke and one third had TIA. The stroke types distributed as 53.1% of them had left type, 40.7% right where as 6.2% both. 87.7% of stroke size was small while 12.3% was big in size. (Table 4)

Seventy five stroke patients had HT, 58.7% of them had good HT control while 41.3% had poor HT control, In addition, 74.7% of them were taking monotherapy as HT treatment, 17.3% were taking dual therapy, 5.3% were taking triple treatment and 2.7% were only on diet therapy, (Table 5).

More than half of the studied patients (56.7%) had DM with mean duration  $12\pm5.8$  years, 58.2% of diabetic patients had DM duration more than 10 years. Mean HbA1c level was  $8.1\pm2.2\%$ , about two thirds (67.2%) of stroke diabetic patients had HbA1c level  $\geq 7\%$ , (Table 6).

Seventy four stroke patients in the present study were diagnosed as hyperlipidemia. Of them, 35% had high Tg, 59.5% had high cholesterol and 86.5% had high LDL, (Table 7)

Less than half of the studied patients (40.5%) had history of IHD, 50% of those IHD had history of catheterization and 54.2% did CATH in duration of more than 5 years, (Table8).

The left brachial systolic BP mean was 134.8,the left dorsalis pedis systolic BP mean was 136,theleft posterior tibial systolic BP mean was 136.1, right brachial systolic BP mean was 134.9, right dorsalis pedis systolic BP mean was 134.4 and the right posterior tibial systolic BP mean was 134.4. (Table 9)

The prevalence of PAD among the stroke patients was 19.5%, the prevalence of left leg PAD among stroke

patients was 11.9% and the prevalence of right leg PAD was 14.4%, (Table 9 and Figure 9). Fourteen patients had ABI < 0.9 in the left leg and 17 patients had ABI

<0.9 in the right leg, on the other hand, 7 patients had ABI >1.2 in the left leg and 3 patients had ABI >1.2 in the right leg. (Table 10)

Variable	No.	%
	110.	70
Age		
Mean±SD (74±9 years)		
65-69 years	40	33.9
70-79 years	51	43.2
80-89 years	18	15.3
$\geq$ 90 years	9	7.6
Total	118	100.0
Gender		
Male	67	56.8
Female	51	43.2
Total	118	100.0
Occupation		
Housewife	43	36.4
Free works	22	18.6
Retired	53	44.9
Total	118	100.0
Residence		
Urban	69	58.5
Rural	49	41.5
Total	118	100.0

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Table 2: Sociodemographic character	islics of stroke datients.

Table 3: Distribution of smoking and durations of ex-smoking.

Table 5. Distribution of smoking and durations of ex-smoking.		
Variable	No.	%
Smoking		
Non-smoker	88	74.6
Current smoker	4	3.4
Ex-smoker	26	22.0
Total	118	100.0
Duration of smoking for ex-smoker	'S	Mean±SD
Duration since smoking cessation for	or ex-smokers	Mean±SD

Table 4: Distribution of stroke, TIA, types and size among studiedpatients.

Variable	No.	%
Stroke		
Yes	81	68.6
No	37	31.4
Total	118	100.0
TIA		
Yes	37	31.4
No	81	68.6
Total	118	100.0
Stroke type		
Left	43	53.1
Right	33	40.7
Both	5	6.2
Total	81	100.0
Stroke size		
Big	10	12.3
Small	71	87.7
Total	81	100.0

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Variable	No.	%
HT		
Yes	75	63.6
No	43	36.4
Total	118	100.0
HT control		
Good	44	58.7
Poor	31	41.3
Total	75	100.0
HT treatment		
Monotherapy	56	74.7
Dual therapy	13	17.3
Triple therapy	4	5.3
Diet therapy	2	2.7
Total	75	100.0

## Table 6: Distribution of DM and its duration among the studied patients.

Variable	No.	%
DM		
Yes	67	56.7
No	51	43.3
Total	118	100.0
DM duration Mean±SD (12±5.8 yea	rs)	
$\leq 10$ years	28	41.8
>10 years	39	58.2
Total	67	100.0
HbA1c level Mean±SD (8.1±2.2%)		
< 7%	22	32.8
$\geq 7\%$	45	67.2
Total	67	100.0

Table 7: Distribution of lipid profile among the stroke patients.		
Variable	No.	%
Hyperlipidemia		
Yes	74	62.7
No	44	37.3
Total	118	100.0
Triglycerides Mean±SD (164	±49 mg/dl)	
High	26	35.0
Normal	48	65.0
Total	74	100.0
Cholesterol Mean±SD (212.4	±36.5 mg/dl)	
High	44	59.5
Normal	30	40.5
Total	74	100.0
LDL Mean±SD (128.9±58.2)	ng/dl)	
High	64	86.5
Normal	10	13.5
Total	74	100.0

Variable	No.	%
IHD		
Yes	48	40.5
No	70	59.5
Total	118	100.0
History of cardiac catheteriza	tion (CATH)	
Yes	24	50.0
No	24	50.0
Total	48	100.0
Duration since CATH Mean±SD (5.6±1.2 years)		
$\leq$ 5 years	22	45.8
> 5 years	26	54.2
Total	48	100.0

Table 8: Distribution of IHD among the studied patients.

Table 9: Mean systolic blood pressures of left and right brachial and legs.

Variable	Mean	SD
Left brachial systolic BP	134.8	20.9
Left dorsalis pedis systolic BP	136	27.1
Left posterior tibial systolic BP	136.1	24.9
Right brachial systolic BP	134.9	20.1
Right dorsalis pedis systolic BP	134.4	26.1
Right posterior tibial systolic BP	134.4	26.8

Table 10: Distribution of PAD among the stroke patients.

Variable	No.	%
Left PAD mean±SD of left ABI (1.	02±0.11)	
PAD	14	11.9
No PAD	104	88.1
Total	118	100.0
Right PAD mean±SD of right ABI	(1.01±0.11)	
PAD	17	14.4
No PAD	101	85.6
Total	118	100.0
PAD mean±SD of average ABI (1.01±0.1)		
PAD	23	19.5
No PAD	95	80.5
Total	118	100.0

Table 11: Distribution of sociodemographic characteristics according to the presence of PAD.

Variable	P	PAD		PAD	$\chi^2$	Р
	No.	0⁄0	No.	%		
Age					65.4*	<0.001
60-69 years	1	2.5	39	97.5		
70-79 years	3	5.9	48	94.1		
80-89 years	10	55.6	8	44.4		
$\geq$ 90 years	9	100.0	0	-		
Gender		3.6	0.05			
Male	9	13.4	58	86.6		
Female	14	27.5	37	72.5		
Occupation		3.2	0.1			
Housewife	12	27.9	31	72.1		
Free works	4	18.2	18	81.8		
Retired	7	13.2	46	86.8		
Residence					1.4	0.2
Urban	16	23.2	53	76.8		
Rural	7	14.3	42	85.7		

A considerable association was observed between elderly patients and PAD (p<0.001). There was a seeming association between female gender and PAD (p=0.05). No marked differences were observed between patients with PAD and those without regarding occupation and residence (p>0.05). (Table 11)

There was a apparent association between the exsmokers and PAD (p<0.001). No manifest differences were observed between patients with PAD and those without regarding HT and its control and treatment (p>0.05). (Table 12)

There was a perspicuous association between DM and PAD (p<0.001). A trenchant association was observed between each of uncontrolled DM ( $\geq$  7%) and IHD with PAD (p<0.05). No pointed differences were observed between patients with PAD and those without regarding hyperlipidemia (p=0.6). There was significant association between patients with no CATH and PAD

(p<0.001), (Table 13)

No clear differences were observed between patients with PAD and those without regarding stroke characteristics (p>0.05), (Table 14).

There was significantly higher mean of age associated with PAD patients (p<0.001). A obvious longer duration of smoking for ex-smokers was associated with PAD patients (p=0.05). The duration was manifested longer among patients with PAD (p<0.001). The mean LDL was marked higher among the PAD patients (p<0.001). The lt. ankle systolic BP was significantly lower among PAD patients than those without PAD (p=0.002). The rt. ankle systolic BP was seeming lower for PAD patients than those without PAD (p=0.002). The rt. ankle systolic BP was seeming lower for PAD patients than those without PAD (p=0.001). The brachial systolic BP was not significantly different according to PAD presence (p=0.6). The means of ABIwere noticeable lower among the patients with PAD (p<0.001). (Table 15)

Variable	PAD		No	PAD	$\chi^2$	Р
	No.	%	No.	%		
Smoking					44.8*	<0.001
Non-smoker	6	6.8	82	93.2		
Current smoker	0	-	4	100.0		
Ex-smoker	17	65.4	9	34.6		
НТ					1.5	0.2
Yes	12	16.0	63	84.0		
No	11	25.6	32	74.4		
HT control					0.001	0.9
Good	7	15.9	37	84.1		
Poor	5	16.1	26	83.9		
HT treatment					2.3*	0.5
Monotherapy	11	19.6	45	80.4		
Dual therapy	1	7.7	12	92.3		
Triple therapy	0	-	4	100.0		
Diet therapy	0	-	2	100.0		

Table 12: Distribution of smoking and HT of	characteristics according to the presence of PAD.
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\*Fishers exact test.

Table 13: Distribution of DM, lipid profile and IHD characteristics according to the presence of PAD.

Variable	PAD		No PAD		χ²	Р
	No.	%	No.	%		
DM					19.6*	<0.001
Yes	23	34.3	44	65.7		
No	0	-	51	100.0		
HbA1c level					4.9	0.01
< 7%	3	13.6	19	86.4		
$\geq 7\%$	20	44.5	25	55.5		
Hyperlipidemia					27.9	0.6
Yes	16	21.5	58	78.5		
No	7	15.9	37	84.1		
IHD					27.2*	<0.001
Yes	21	43.7	27	56.3		
No	2	2.8	68	97.2		
History of CATH					14.1	<0.001
Yes	5	20.8	19	79.2		
No	18	75.0	6	25.0		

Variable	PAD		No PAD		$\chi^2$	Р	
	No.	%	No.	%			
Stroke					0.8	0.3	
Yes	14	17.3	67	82.7			
No	9	24.3	28	75.7			
TIA					0.8	0.3	
Yes	9	24.3	28	75.7			
No	14	17.3	67	82.7			
Stroke type					1.04*	0.5	
Left	9	20.9	34	79.1	I		
Right	4	12.1	29	87.9			
Both	1	20.0	4	80.0			
Stroke size					0.05	0.8	
Big	2	20.0	8	80.0			
Small	12	16.9	59	83.1			

 Table 15: Distribution of age, smoking duration and systolic BP means according to presence of PAD.

Variable	PAD		No PAD		$\chi^2$	Р
	No.	%	No.	%		
Stroke					0.8	0.3
Yes	14	17.3	67	82.7		
No	9	24.3	28	75.7		
TIA					0.8	0.3
Yes	9	24.3	28	75.7		
No	14	17.3	67	82.7		
Stroke type					1.04*	0.5
Left	9	20.9	34	79.1		
Right	4	12.1	29	87.9		
Both	1	20.0	4	80.0		
Stroke size					0.05	0.8
Big	2	20.0	8	80.0		
Small	12	16.9	59	83.1		

Table 16: The binary logistic regression analysis for variables associated with PAD.							
Variable	В	S.E.	Р	OR			
Age	1.1	10.4	0.001	0.2			
Gender	3.02	1.8	0.09	0.04			
Smoking	2.9	0.9	0.003	0.5			
DM	1.3	8.7	0.002	1.1			
IHD	0.3	1.4	0.6	0.3			
Lt. ankle sys. BP	-0.01	0.03	0.6	0.9			
Rt. ankle sys. BP	-0.06	0.03	0.1	1.06			
Constant	14.5	5.8	0.01	19.2			

#### Multiple regression analysis

The binary logistic regression analysis for factors associated significantly with PAD revealed that age, smoking and DM were significant predictors for PAD among the stroke patients (p<0.05). (Table 16)

### DISCUSSION

Peripheral arterial disease proved to be a marker for atherosclerosis in different vascular beds of the body. The ankle brachial index is a non-invasive and effective screening tool for the diagnosis of PAD. The prevalence of asymptomatic PAD among patients with atherothrombotic cerebral infarction and TIA was found to be high. The ankle brachial index was shown to be lower in patients with ischemic stroke and was considered as a predictor for stroke recurrence<sup>27</sup>.

In our study the mean age of stroke patients was a  $74\pm9$  year with the predominance of male gender, unemployment and urban residence. These sociodemographic characteristics are consistent with results yielded by Al-Mahdawi  $(2002)^{28}$  and Alvariz-Sabin et al.  $(2009)^{29}$ . One third of the stroke patients had

a history of smoking and TIA with prevalent HT, DM and an abnormal lipid profile. These findings are similar to the results of Hasan et al. (2011)<sup>30</sup>, Fahimfar et al. (2012)<sup>31</sup> and Li Cy et al. (2012)<sup>32</sup>. The risk factors for ischemic stroke include aging, hypertension, diabetes, smoking, history of cardiovascular diseases (CVD), atrial fibrillation, and left ventricular hypertrophy<sup>33</sup>. The interstroke study, involving 22 countries demonstrated that ten risk factors account for 90% of the population attributable risks for stroke events. However, not all potential risk factors were considered in interstroke study.<sup>34</sup> More than half of the studied patients in present study had left stroke and small stroke size which was consistent with results of Al-Tameemi et al. (2012)<sup>35</sup>.

The prevalence of PAD among patients with stroke was 19.5%. This prevalence is close to the prevalence of PAD reported by Hoshino et al.  $(2013)^{36}$  as (18.8%). The PAD prevalence in present study is lower than that reported by Sen et al.  $(2009)^7$  as (26%) and El-Jafaary et al.  $(2015)^{27}$  as (31%), on the other hand, this prevalence of 19.5% is higher than that reported by Al-Sheikh et al.  $(2007)^{37}$ . This variation in PAD prevalence might be attributed to the difference in sample size, in addition to the different inclusion and exclusion criteria between different studies.

In a survey of Scottish men and women aged 55 to 74 years, 4.5% had claudication and 9.0% had a low ABI (defined as < 0.9). In a similar survey of individuals free of clinical cardiovascular disease, 10.9% had a low ABI, increasing with age, deprivation, and female sex<sup>38</sup>.

These previous studies have tended to concentrate on the prevalence of asymptomatic PAD, claudication, and stable PAD. Unlike acute CAD and acute stroke/TIA, there are few population based data on the incidence or outcome of acute PAD events. In the Oxford Vascular Study (OXVASC), they could provide reliable data on the epidemiology of different acute PAD events within the same population over the same period, 9% of all acute vascular deaths were due to acute PAD (compared with 45%, 42%, and 4% due to cerebrovascular, coronary, and unclassifiable deaths). The incidence of acute PAD events was therefore lower than for CAD and stroke/TIA (0.52, 1.91, and 2.27 per 1000 population per year, respectively), but case fatality proved higher<sup>39</sup>. A recent worldwide registry showed that patients with both stroke and PAD have a very high risk for recurrent vascular events, and require aggressive optimized vascular risk-reduction strategies7.

PAD is under-diagnosed and under-treated worldwide<sup>40</sup>. Better understanding the clinical course and outcomes in patients with acute ischemic stroke and PAD helps in determining the benefit of programmed screening ABI in stroke patients and optimizing therapeutic interventions<sup>32</sup>.

The present study revealed that patients with PAD were significantly associated with elderly age (p<0.001). This

finding is consistent with results of Savji et al. (2013)<sup>41</sup>, which concluded association of PAD with advancing age. Vascular dysfunction has been shown to increase with age because of decreased compliance<sup>42</sup>, angiogenesis<sup>43</sup>, endothelial antithrombotic property<sup>44,45</sup>, and increased inflamation<sup>42</sup>, possibly due to vascular endothelial cell senescence<sup>46</sup>, which also increases with age.

The female patients in our study were significantly associated with PAD (p=0.05). Those with PAD were found to be more functionally impaired than men and had lower rates of revascularization of the lower extremities<sup>47</sup>. Also, women who did undergo revascularization procedures had more adverse outcomes than men<sup>48</sup>. However, the PAD related mortality rates were comparable among both genders<sup>49</sup>. This finding of female gender is inconsistent with the results of many previous studies like Alvariz-Sabin et al. (2009)<sup>29</sup> and Li et al. (2012)<sup>32</sup> which reported the prevalent male gender of PAD patients.

This inconsistency might be attributed to few reasons; a} elderly age patients are more commonly associated with female gender, b} HT, DM and hyperlipidemia are more common among females, c} difference in sample size of different studies.

The main risk factors that are significantly associated with PAD in the present study were smoking, DM, poor glycemic control and hyperlipidemia (p<0.05). These findings agreed with results of Banerjee et al.  $(2010)^{50}$  and Olin et al.  $(2010)^3$ .

In population-based studies such as the Framingham Heart Study and the Edinburgh Artery Study, the relative risk of developing PAD increases by 1.5 to 4 times in patients with diabetes<sup>51-53</sup>. This data shows the impact of diabetes on the progression of the atherosclerotic process. Smoking was evident in PAD in the present study, It was also apparent in other studies<sup>53</sup>. Whereas the impact of dyslipidemia was highly marked in PAD (the present study and others)<sup>54</sup>. In agreement with our results hypertension was more common in PAD<sup>52</sup>. In the present study, high proportion of studied cases was hypertensive that led to no statistical marked association between PAD and HT.

Smoking duration, DM duration and LDL seemed higher among patients with PAD in our study. This finding agreed with results of Al-Menyar et al. (2013)<sup>55</sup> which clarified hazardous effect of LDL, DM duration and smoking duration on PAD. Similarly, epidemiological studies have found that smoking increases the risk of lower extremity PAD by 2 to 6 folds and the risk of intermittent claudication by 3- to 10-fold<sup>56</sup>. More than 80% of the patients with lower extremity PAD are current or former smokers<sup>54</sup>. In other studies, the total cholesterol levels are generally higher in patients with intermittent claudication than in those without lower extremity PAD<sup>57</sup>. The Communities Study has shown that the risk associated with a low ankle-arm index diminish after adjustment for cardiovascular risk factors including systolic blood pressure, antihypertensive medication, diabetes, smoking, pack years smoking, LDL cholesterol, HDL-cholesterol and prevalent coronary heart disease. Therefore, it is doubtful whether assessment of ankle-arm index has prognostic ability beyond the traditional risk factors in the prediction of stroke<sup>58</sup>.

Logistic regression analysis revealed that the elderly, DM and smoking were significant predictors of PAD (p<0.05). This finding is similar to results of Savji et al.  $(2013)^{41}$  and Al-Zahrani et al.  $(2014)^{59}$ . Diabetes increases the risk of developing symptomatic and asymptomatic PAD by 1.5- to 4-fold, and leads to an increased risk of cardiovascular events and early mortality<sup>60</sup>. In NHANES,<sup>61</sup> 26% of participants with PAD were identified as having diabetes, whereas in the Edinburgh Artery Study, the prevalence of PAD was greater in participants with diabetes or impaired glucose tolerance (20.6%) than in those with normal glucose tolerance  $(12.5\%)^3$ .

## CONCLUSIONS

The study draws the following conclusions

- Prevalence of PAD among patients with ischemic stroke was within accepted range.
- Elderly age, female gender, smoking with its long duration, DM with poor glycemic control and hyperlipidemia were significant risk factors for PAD.
- Elderly age, smoking and DM were significant predictors for PAD.

## LIMITATIONS OF STUDY

- As other cross sectional studies, temporal relationship cannot be assessed.
- Small sample size.
- Recall bias.

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