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Study of Association of Ankle-Brachial Index in Ischemic Stroke Patients by Using Arterial Doppler Flow

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Abstract

Introduction: Ankle-brachial index (ABI) is a known marker for peripheral arterial disease (PAD), and is also used to assess the severity of ischaemic stroke. This study focuses on evaluating association of ABI in patients of ischemic stroke using Doppler method.

Material methods: 113 diagnosed radiologically by non-contrast head CT (NCCT) head/Magnetic resonance imaging (MRI) and clinically for ischemic stroke were assessed.

Results: Maximum cases belonged to age group interval of $\geq$ 61 years (45.1%). Study revealed male sex predilection with 57% males and 43% females. Majority cases with critical ABI Doppler method (0-0.3) fell under the age group of 61 years (n=4) with female predominance (n=3). ABI was found to be statistically correlated with platelet count and creatinine (P-value = .000; P-value=0.025), while there was no significant correlation with systolic blood pressure(P-value=.473), diastolic blood pressure(P-value=.663), diabetes(P-value=.863), systemic hypertension(P-value=.924) and lipid profile parameters like total cholesterol, high density lipoprotein and low-density lipoprotein (P-value=.069; P-value=.436; P-value=.395 respectively). In conventional method, 66.3% cases had normal ABI whereas in Doppler method, 52.2% had normal levels. In critical cases, 4.4% pertained to Doppler method which was greater than conventional Method (1.8%)

Conclusion: Screening for ABI should be done in ischaemic stroke patients and can aid in planning adequate prevention therapies resulting in a better prognosis

Keywords: Ankle-brachial index (ABI), ischaemic stroke, Doppler

Introduction

The ankle-brachial index (ABI) is the ratio of the systolic blood pressure (SBP) measured at the ankle to that measured at the brachial artery as explained by Winsor in 1950 [1]. Blood pressure (BP) ratios and differences between the four limbs can be simultaneously obtained and calculated with ABI measurement. Among the ratios and differences, ABI difference, systolic inter-ankle blood pressure difference and systolic inter-arm BP difference have been reported to be useful in predicting the prognosis in patients with cardiovascular disease and high-risk populations. This index was initially proposed for the non-invasive diagnosis of lower-extremity peripheral artery disease (PAD) [2]. Later, it was also proved that ABI reflects the severity of systemic atherosclerosis at other vascular sites and can serve as a surrogate prognostic marker for cardiovascular functional impairment, even in the absence of symptoms of PAD and indicate its utility as a predictor of future cardiovascular disease and all-cause mortality [3].

Stroke is defined as a sudden onset of a neurological deficit caused by an acute focal injury to the central nervous system due to a vascular cause. Ischaemic stroke is an acute heterogeneous syndrome caused by several major and some uncommon disorders leading to an occlusion of blood vessels supplying brain tissue [4]. According to the Centre for disease control and prevention (CDC) 2018 report, 1 in every 6 deaths from cardiovascular disease was due to stroke. In 2018, more than 795,000 people in the United States had a stroke. About 610,000 of these are first or new strokes cases. About 87% of all strokes were ischemic stroke according to this report [5]. By 2020 in developed countries, it was predicted that stroke will be accountable for 6.2% of the total burden of illness [6]. The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has quickly spread worldwide, and pandemic outbreak of corona virus disease 2019 (covid-19) potentially increased risk for cerebrovascular diseases. Yaghi et al. reported that in a total 3556 patients with diagnosis of COVID-19, 32 cases (0.9%) experienced an ischemic stroke [7]. Murabito et al. in the Framingham study, the risk of ischaemic stroke was twofold among participants with an ABI< 0.9 [8].

In the etiology, ischaemic stroke caused by arterial occlusion is responsible for the majority of strokes. The events resulting from any subtype of ischemic stroke result in the loss of blood supply, oxygen, nutrients and elimination of metabolic wastes. These resulting changes obstruct normal neuronal functioning. This ultimately results in neuronal death/necrosis from occlusion of the vessel. The brain tissue is exquisitely sensitive to these changes, and the therapeutic window that is needed to prevent reversible ischemia from becoming irreversible infarction is narrow [4]. This concept is especially important to minimizing evolving insult and controlling the propagation of ischemic penumbra. Furthermore, from a therapeutic point of view, this crucial time provides a “window of opportunity” in reversing the neurological symptoms either partly or completely through acute interventional approaches, either invasively or non-invasive [9].

Over the last two decades, a lot of stroke specific structured education, intervention trials, and diagnostic approaches have targeted this time period, resulting in better clinical outcomes with decreased associated mortality and morbidity. The modern stroke field is a fast advancing with an emphasis on endovascular stroke therapy/interventional mechanical devices, and their combined use with thrombolytic agents for better clinical benefits. Management focuses on rapid reperfusion with intravenous thrombolysis and endovascular thrombectomy, which both reduce disability but are time-critical [4]. Accordingly, improving the system of care to reduce treatment delays is key to maximizing the benefits of reperfusion therapies. ABI is simple, non-invasive, convenient, and quick measure that is being increasingly accepted as meaningful clinical indicator and gold standard for

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detecting PAD [10]. However, whether interpretation of ABI is associated to predict risk of ischaemic stroke remains unclear. To address this, we had planned this study to evaluate the association of ABI with Doppler method in patients of ischemic stroke.

Material and methods

This single Centre, hospital based cross-sectional observational study was conducted in department of Medicine at tertiary care hospital located in Central India. 113 patients visiting Medicine OPD with diagnosis of ischemic stroke based on sign symptoms and radiologically confirmed by non-contrast head CT (NCCT) head/ Magnetic resonance imaging (MRI) brain for period of one year from August 2020 to August 2021 were included in this study. Patients suffering from major systemic disease with co-morbidities which might confound the study findings like hemorrhagic stroke, transient ischemic attack, traumatic cerebrovascular disease, space occupying lesions ruled out by computed tomography (CT) head, filariasis or lower limb swelling of any cause that may alter arterial Doppler flow study, patients with known history of vasculitis like buergers disease, deep vein thrombosis, trauma, surgery or amputation involving one or both lower limb were excluded from the study. After explaining the study procedure, written informed consent obtained from all the subjects selected for the study. Data was collected after availing necessary ethical approval from the institution and cases were meticulously looked for various aspects such as name, age, detailed address, education, occupation, monthly income, marital status. The collected data were tabulated and statistically analysed using SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA. Kolmogorove-Smirnove analysis was performed for checking linearity of the data. Pearson correlation analysis was performed to check the correlation between two categorical variables. Chi square test was used to analyse the significance of difference between frequency distribution of the data. P-value <0.05 was considered as statistically significant.

Results

Patients' demographic data showed that the mean age of the patients included in our study population was 58.29 $\pm$ 11.22. Majority of patients belong to the age group more than or equal to 61 that is 45.1%. Gender wise appraisal showed that out of total patients there were 57% Males and 43% Females.

In the present study, maximum number cases with critical ABI Doppler method (0-0.3) fell under the age group of 61 years (n=4) while Lower ABI (0.4-0.8) was observed with age group of 61 years (n=17). Females (n=3) were commonly affected with critical ABI than males (n=2). In lower ABI group, males (n=21) were predominantly affected than females (n=28). There was significant association between ABI and creatinine found in our study (P-value = 0.025). But, no significant association between systolic blood pressure (P-value = .473) as well as diastolic blood pressure and ABI Doppler was established. (P-value = .663). Moreover, we couldn't establish significant statistical association between parameters like diabetes (P-value = .863), systemic hypertension (P-value = .924) and ABI Doppler. In our study, there was significance correlation difference between ABI by Doppler Method and Platelet count (P-value = .000), but we failed to establish significant correlation between ABI and Lipid Profile parameters like total cholesterol, high density lipoprotein (HDL) and low-density lipoprotein (LDL). (P-value =.069; P-value =.436; P-value =.395 respectively). We

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found that most of the patients belonged to the normal levels in both methods but in conventional method 66.3% belonged to normal where as in Doppler methods 52.2% belonged to normal levels. In critical cases 4.4% patients belonged to Doppler method which is greater than conventional Method that is 1.8%.

Discussion

1) Baseline characteristics

In our study, maximum number of patients belonged to the age group more than or equal to 61 years (n=51, 45.1%). Mean age of the patients included in the data was 58.29 (11.22) years.

Saha SK et al., have studied 144 patients of age more than 45 years with ischaemic stroke who reported majority of cases fell under age group 65-74 years (41.67%) with mean age of 63.51±8.096 years [11]. Ratana Korn D et al., have observed the mean age of stroke patients was 63.5±14 years [12]. Johnston KW et al., have reported the mean age as 64.04±12.24 years in patients normal ABI while the mean age was 70.48 ±11.78 years in patients with abnormal ABI [13]. Sharma N et al., reported that maximum patients (14/50) were in 66-75yrs age group. Mean age of patients was 62.68±15.04year while mean age of females was higher than of males [14]. Li et al., have reported mean age of patients with DM and ischaemic stroke as 61.32±9.52 years [15]. Afify H et al., have conducted case-control observational analytical study for 200 patients, 100 patients with ischaemic stroke and 100 patients as control, in which they reported most of cases ranged between 45-83 years with mean age of 63.0±9.8 years [16]. We found males (n=64, 57%) are commonly affected than females (n=49, 43%). Han M et al., have a total of 3822 patients with acute ischemic stroke or TIA were recruited during the study period. A total of 258 (8.9%) patients had PAD. The mean age was 65.4 ± 12.2 years, and 61.8% were men [17]. Afify H et al, have reported that there was male preponderance. (59% males and 41% females) in case group [16]. Li et al., have reported males (n=44) were commonly affected than females (n=18) in diabetic with ischaemic stroke group [15]. Mohammad Salim Sahi et al., also reported the similar results [18]. Lee NK et al (2020) studied 84 cases where there was female predominance (n=50) than male (n=34) [19]. However, Saha SK et al., have reported that females (n=82) are predominantly affected than males(n=62) [11].

2) Age-sex wise distribution of ABI Doppler method

In our study, maximum number cases with Critical ABI Doppler method (0-0.3) fell under the age group of 61 years(n=4) while Lower ABI (0.4-0.8) was observed with age group of 61 years (n=17). Females (n=3) were commonly affected with critical ABI than males (n=2). In lower ABI group, males (n=21) are predominantly affected than females (n=28). Bhat SK et al., studied A total of 39,834 unique patients were included with a median follow up duration of 4.59 years. They observed that males (57.4%) are commonly affected than females (42.6%) with mean age was 69.1±18.0 years [20]. Saha SK et al., have found that most of the patients with PAD (ABI<0.9) had age group of 65-74 years(n=26) and 55-64 years (n=18) [11]. Abboud H et al., observed that 2,637 (77.7%) had ABI ≥0.9 and 757 (22.3%) <0.9. The mean age was 67±11 years and commonly affected males (50.9%) [21]. Lee NK et al., reported the mean age as 66.65 ± 11.32 (46-86) years, predominantly in females in abnormal ABI group [19]. A prospective observational cross-sectional study conducted by Sharma N et al., in 2017 who reported 27 males and 14

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females had ABI less than 0.9 [14]. Gronewold J et al., in their study also found higher percentage of PAD among females as 62.6% and 52.7% respectively [22]. Singh PP et al., studied 2,240 patients in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial and reported mean age as 63.4±8.9 years in low ABI group and 38.8% females were affected [23].

3) Association of ABI Doppler method with other parameters

Most of the cases with SBP (131-190 mm Hg) had normal (n=38), lower (n=27) and critical (n=2) ABI Doppler method, in decreasing order. Maximum number of critical ABI were reported with those with DBP of 70-80mm Hg (n=3) than with 60-70mm Hg (n=2). The most of patients with DBP of 70-80 had lower ABI values (n=19). But there is no significant difference between Systolic blood pressure, Diastolic blood pressure, Hypertension with respect to ABI Doppler. Lee KN et al., did not show any association with SBP and DBP with abnormal ABI [19]. Bhat SK et al., reported hypertension in 79.7% in low ABI with significant association [20]. In a case-control observational analytical study conducted by Afify H et al., have reported that hypertensive cases had lower ABI values, but had no statistically significant [16]. Saha SK et al., have observed that Hypertension was found in 50% cases and difference between mean SBP of upper/lower limbs of both sides were higher in low ABI group which was found to be statistically significant [11]. The similar result was also observed by Abboud H et al., [21]. Sharma N et al., noted similar result in their study as mean systolic BP was significantly different in upper & lower limb on each side. ABI was found to be significantly correlated with difference in systolic BP of upper & lower limb at each side. Mean of difference was significantly higher in low ABI group. (P-value =0.03 at Lt. and 0.02 at Rt.) Systolic BP in each lower limb was significantly different in low & normal ABI group (P-value <0.0001) [14]. The cases with DM had lower ABI (n=14) and critical ABI(n=2) however 17 cases had normal ABI. There no significance difference between DM and ABI Doppler in our study. Similar results have been reported by study conducted by Saha SK et al., They reported 28 cases of ABI less than 0.9 had diabetes, with no significant difference [11]. Sharma N et al., in their study have observed that DM was found in 22 cases those with ABI≤0.9 but had no statistical correlation with ABI [14]. Afify H et al., have reported diabetes was highly significantly associated with abnormal ABI in their case-control observational analytical study [16], similar with studies conducted by Bhat SK et al., [20] and Abboud et al., [21]. Similar results have also been reported by Lee KN et al [19].

There was significance difference between Creatinine and ABI Doppler in our study (P=value = 0.025) Contrary result was reported by study conducted by Abboud H et al., who reported no statistical difference between creatinine levels and ABI values (P-value =0.47) [21].

4) Association of ABI with respect to lipid profile

In our study, there was significance correlation difference between ABI by Doppler Method and Platelet and there was no significance correlation between ABI and Lipid Profile. Bhat SK et al., reported significant association of hyper lipidaemia (66.6%) with low ABI [20]. Saha SK et al., observed that patients with dyslipidaemia were more common in low ABI group and a significant association was found between mean values of LDL, Triglyceride and ABI [11]. Li et al., also studied

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levels of cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, and triglycerides were not significantly different between the diabetes only group and diabetic ischaemic stroke group (P-value > 0.05) [15]. Sharma N et al., have found that Patients with dyslipidaemia were significantly higher in no. in low ABI group but the mean values had no statistical correlation with ABI [14]. Abboud H et al., also did not find a significant correlation between ABI and mean levels of lipid profile [21].

Conclusion

ABI is a simple, non-invasive, convenient and quick modality which being accepted as meaningful clinical indicator and gold standard in diagnosis of peripheral arterial disease. ABI calculation can be used to evaluate atherosclerosis, predictive role for future cardiovascular events and mortality and it can have considered as indirect predictor of recurrent ischemic strokes in future. Different risk factors like hypertension, diabetes mellitus and dyslipidaemia may be associated with both peripheral arterial disease and cardiovascular accidents. Though our inferences are based on a smaller subset of patients, but it suggests that PAD is not very uncommon in ischemic stroke patients in our country and associated risk factors are invariably associated with ABI values. We recommend further studies, so that their correlation can be explored to a great extent. We conclude that screening for PAD by measurement of ABI should be done in acute stroke patients because it has important implication not only for evaluation but also for prognosis of such patients.

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Tables and figures

Table 1: Baseline characteristics of patients included in the study (n=113)

Categorical variables	Percentage
Sex	
Males	57
Females	43

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Age (Years)	
<=40	5.3
41-50	23.9
51-60	25.7
>=61	45.1
Categorical variables Mean age ± SD (years)	58.29 ± 11.226

SD- standard deviation

Table 2: Association between ABI (by Doppler method) and Parameters (n=113)

ABI Doppler Method Cross tabulation					
		ABI Doppler Method			
		Critical	Lower	Normal	P-value
Age	<=40	0	4	2	--
	41-50	0	14	13	
	51-60	1	14	14	
	>=61	4	17	30	
Sex	Female	3	21	25	--
	Male	2	28	34	
SBP	101-110	0	4	8	.473
	111-120	1	5	4	
	121-130	2	13	9	
	131-190	2	27	38	
DBP	50-60	0	1	3	.663
	60-70	2	10	10	
	70-80	3	19	19	
	80-90	0	9	14	
	90-150	0	10	13	
Creatinine	0-1	2	23	34	.025
	1-2	2	25	20	
	2-3	0	1	4	
	3-5	1	0	1	
DM	Yes	2	14	17	.863
	No	3	35	42	
System hypertension	Yes	3	25	30	.924
	No	2	24	29	

ABI- ankle-brachial index, SBP- Systolic blood pressure, DBP- Diastolic blood pressure, DM- diabetes mellitus

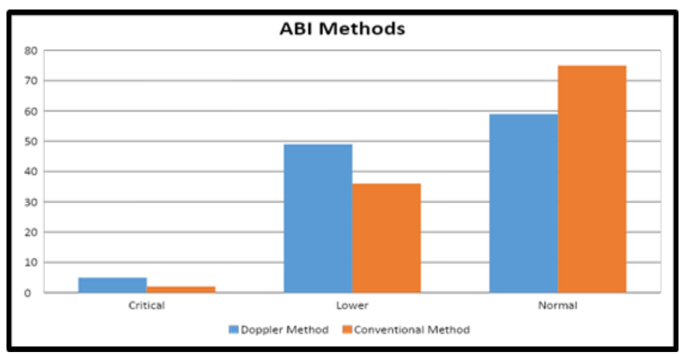
Table 3: Correlation between ABI (by Doppler Method) and Lipid profile (n=113)

Parameter	r	P value
Platelet	-.360	.000**
Total Cholesterol	-.172	.069
HDL	-.074	.436
LDL	-.081	.395

ABI- ankle-brachial index, HDL- High density lipoprotein, LDL- Low density lipoprotein

* P-value <0.05 is considered as statistically significant

Figure 1: Distribution of patients according ABI Methods (n=113)



ABI- ankle-brachial index

* P-value <0.05 is considered as statistically significant

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