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Original Research Paper

Radio-Diagnosis

DIGNOSTIC ACCURACY OF ANKLE BRACHIAL INDEX OVER LOWER LIMB ARTERIAL DOPPLER SONOGRAPHY TO EVALUATE PERIPHERAL ARTERIAL DISEASE IN DIABETIC AND HYPERTENSIVE PATIENTS.

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ABSTRACT Peripheral vascular disease (PVD) is a common cause of morbidity and mortality amongst diabetic (DM) and hypertensive (HTN) subjects. PVD can be diagnosed if there is hemodynamically significant obstruction on arterial doppler (AD) ultrasonography, or, if the Ankle Brachial Index (ABI) < 0.9. Though, any PVD can be confirmed by AD, it is, however, time consuming and not always accessible for early screening. ***Objective*** – To assess the diagnostic accuracy of ABI compared with AD for evaluation of severity and duration of PVD in DM and HTN patients. ***Methodology*** - A cross sectional study was conducted among 72 patients (40-75 years) with 21 (29%) having HTN, 24 (33%) having DM and 27 (38%) having both, for suspected PVD assessment by both AD and ABI. Correlation between ABI and AD findings was done after detailed clinical history, physical and local examination, ABI assessment by sphygmomanometer and linear ultrasound probe, AD evaluation of peripheral arteries of lower limbs and other relevant examinations was done as necessitated. ***Result*** - ABI had an accuracy of 80%, a sensitivity of 76.6%, a specificity of 88%, a positive predictive value of 92.3%, and a negative predictive value of 66.6%. DM (81%) and people with both (DM and HTN) (81.3%) were found to have higher sensitivity compared to those with HTN (60%) when evaluated with ABI. It was found that there was a positive correlation between the duration of DM (r=0.86, P=0.00001), HTN (r=0.76, P =0.00006) or both (r=0.64, P=0.003) with the severity of arterial disease as calculated by AD and by ABI (r=0.68, P=0.0002) in DM, (r=0.73, P=0.0001) in HTN, and (r=0.69, P=0.0006) in both. Thus, implying a strong correlation between the duration and severity of PVD involvement as evaluated by ABI and AD. ***Conclusion***- ABI is an effective, non-invasive, early screening tool for PVD.

KEYWORDS : Peripheral Vascular Disease, Arterial Doppler, Ankle Brachial Index.

INTRODUCTION

Diabetes (DM) and hypertension (HTN) are two interconnected and frequently occurring chronic diseases that best illustrates the complexities of India's disease burden. Meanwhile, in developed nations atherosclerotic disease ranks third in terms of mortality after cardiac diseases and cancer. ***[1,2]*** Atherosclerosis often leads to mortality due to critical lower limb ischemia. ***[3,4,5]*** Thus, making it imperative to recognize atherosclerotic changes as early as possible.

The greatest risk factors for lower limb atherosclerotic disease worldwide are DM and HTN. ***[6]*** According to a National Urban Survey conducted in 2000, 12.1% of adults in urban India have DM. ***[2]*** Peripheral neuropathy, peripheral arterial disease (PAD), nephropathy, and retinopathy are common implications associated with DM. Meanwhile, in both urban and rural India, HTN is a major public health menace. The estimated prevalence of HTN worldwide is 7.24%.***[1]*** The bulk of stroke death and death associated with coronary heart disease in India are undeviatingly linked to both HTN and DM.

Though, angiography is regarded as the gold standard; it is, however, an intrusive and expensive diagnostic test which comes with a high risk to patient (mortality risk of 0.16%). ***[7,8,9]*** Thus, for diagnosis and characterization of PAD, amongst non-invasive diagnostic techniques, Arterial Doppler (AD) sonography has a high sensitivity and specificity. ***[10]*** It is simple to execute with no side effects to patient, and has a diagnostic accuracy as being practically identical to that of angiography. Nonetheless, doppler, takes a lot of time and requires significant knowledge and expertise. Therefore, ankle brachial index (ABI), an unsophisticated, reliable, non-invasive test can be readily done within a short time frame without any expensive equipment in a rural or primary health center. Just a stethoscope or a doppler machine can suffice to perform an ankle brachial index (ABI) test.

A study conducted by Carmo et al. comparing the two techniques (AD v/s ABI) came to conclusion that ABI evaluation using a stethoscope and a Doppler probe have similar predictive values. ***[11]*** To our knowledge, there are limited studies published that compares AD sonography with ABI, especially in the background settings of DM and HTN.

The ability of the ABI to foretell PAD has, however, been the subject of numerous investigations. Many have contrasted the results of ABI with those of clinical trials or other physiological tests. ***[4,6,8]*** ABI has the potential to provide further risk stratification in patients with Framingham risk score between 10% and 20% in 10 years. ***[12]*** Thus, mortality due to anticipated cardiovascular events can be prevent by screening people over the age of 70 years or patients between the age of 50 and 69 who already have DM or HTN.

The goal of the current study was to validate the ABI measurement for determining severity of lower limb ischemia due to PAD in DM and HTN along with duration of morbidity to be at par with Doppler sonography. The Doppler probe is used in this investigation to calculate ABI; while, the results from ABI assessment with stethoscope from other studies were extrapolated. Additionally, this studied was conducted to demonstrate ABI can be utilized as a powerful diagnostic tool for screening PVD in DM and HTN.

MATERIAL AND METHOD:

This was an institution based observational study with cross-sectional study design. It was conducted under the

Department of Radio-diagnosis, Bankura Sammilani Medical College and Hospital (BSMCH), Bankura, West Bengal on 72 patients between the age group of 40-75 years with clinical features (intermittent claudication or critical limb ischemia) of lower limb PAD, who were referred for AD evaluation. The same patient was assessed for ABI and AD. So, one particular patient acted as his/ her own control. Hence, there was no need for a separate control group in this study.

The study included three sub-groups - one group having only DM, other group only HTN, and a third subset of patients having both DM and HTN. Suspicious (chronic smokers, raised CRP, dyslipidemia, hyper-viscosity or hypercoagulability, hyper-homocystinemia, DM and HTN) PVD cases were referred from various departments to our radiology department of BSMCH for lower limb AD assessment. Meanwhile, laboratory parameter such as blood glucose, serum creatinine, etcetera; all were recorded along with detailed history about the duration of disease, family history, alcohol consumption and smoking, concomitant medication and other associated ailments; because this invariably helped to segregate patients into 'subset' groups having only DM or HTN or co-existence of both (DM and HTN).

***Inclusion Criteria*:**
All DM and HTN or both with signs and symptoms of PAD of both gender between 40-75 years of age referred to our department of radio-diagnosis BSMCH, Bankura for AD ultrasound of lower limb.

***Exclusion Criteria*:**
- Severely calcific vessel wall at the site of cuff application on the lower limb.
- Patients with cerebrovascular disease.
- Ulcer at the site of application of the cuff.
- Patient not willing to participate in the study or no consent.

***Study Variables*:**
- Interviews
- Scrutiny of previous / current reports.
- Clinical history and examination.
- Imaging investigation – AD and ABI.

METHODOLOGY:
The study was conducted after getting proper ethics approval from the Institutional Ethics Committee of the BSMCH, Bankura, West Bengal. After a brief initial history and entry of patient details from the OPD Card or Bed Head Ticket (if patient was admitted); patients were clinically evaluated along with a Questionnaire Interview (based on a Qualitative Pretest Interview) and record analysis was done for risk factors and duration of morbidity. After that, they were carefully evaluated by Ankle brachial index (ABI)=Highest SBP at ankle/Highest SBP at brachial artery (SBP = Systolic blood pressure). This was followed by arterial doppler (AD) sonography and correlation between ABI and AD.

Whilst explaining the purpose of the study and obtaining the written informed consent, necessary information, including socio-demographic parameters were also gathered from the selected patients and entered into the questionnaire and finally into MS excel sheet using study techniques and tools.

TOOLS:
Equipment: Appropriate size cuff for upper and lower extremities with a properly working sphygmomanometer, ultrasound gel and ultrasound linear probe.

Ankle Brachial Index: Systolic blood pressure (SBP) was measured in both the brachial arteries with the help of BP cuff applied at mid-arm and assessed with 7-12 MHz linear probe on a GE LOGIQ P9 ultrasound machine. Similarly, SBP in arteria dorsalis pedis (ADP) and posterior tibial artery (PTA) was assessed by applying BP Cuff 5 cm above both the ankle joint. It is done in a sequential order of first right arm, then right ankle, followed by left ankle and left arm. Every SBP measurement was taken twice to rule out any discrepancies of > 10 mmHg which could be due to 'white coat effect'. Meanwhile, the highest value was taken into account. ABI Grading: Grade 0 (Normal)- 1.3-0.90, Grade 1 (Minimal)-0.89-0.60, Grade 2 (Mild)-0.59-0.50, Grade 3 (Moderate)- 0.49-0.26, Grade 4 (Severe)- 0.25-0.20 and Grade 5 (very severe)- 0.19-0.00. ***[12, 13] [Figure 1 and 2].***

Figure 1: Measuring the highest systolic blood pressure for ABI with ultrasound linear probe in the right brachial artery.

Figure 2: Measuring highest systolic blood pressure for ABI with ultrasound linear probe in the right posterior tibial artery.

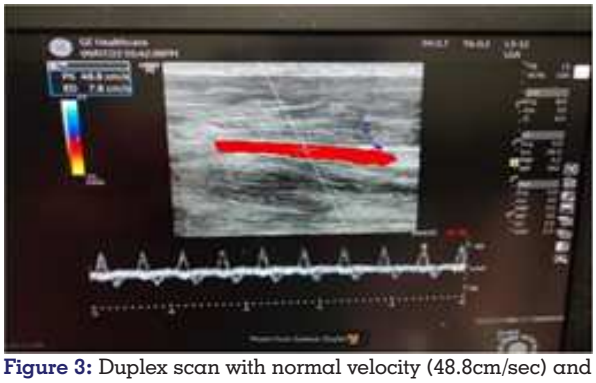

Figure 3: Duplex scan with normal velocity (48.8cm/sec) and flow, along with normal triphasic waveform within the left brachial artery.

Conventional B-mode Ultrasonography: In addition to gray-scale ultrasonography (USG); spectral Doppler USG and color-flow vascular imaging were used to locate vascular stenosis or obstruction, and determine the direction of blood flow. ***[14]*** It was done with 7-12 MHz linear probe, along with AD study in both the limbs for any atherosclerotic changes; like, (iso-to-hyperechoic) plaque formation, aliasing due to

turbulent flow, lumen diameter (for percentage of stenosis), peak systolic and end diastolic velocity, and phasicity of doppler waveform. Doppler Grading: Grade 0 (Normal, Triphasic) – 70 to 100 cm/sec, Grade 1 (<50% stenosis, Triphasic) – 30-100% increase over the proximal segment, Grade 2 (>50% stenosis, monophasic turbulent flow) – >100% increase over the proximal segment, Grade 3 (>75% stenosis, monophasic high velocity bruits maybe heard) - Prestenotic/stenotic ratio > 4.1, PSV >400cm/sec, Grade 4 (occlusion, damped proximal to occlusion) – absent flow, collaterals maybe seen adjacent and Grade 5 (aorto-iliac disease, monophasic throughout) – PSV in Common Femoral artery <45cm/sec. ***[15] [Figure 3].***

Statistical Analysis:

Data was tabulated in Microsoft Excel and was analyzed by appropriate statistical methods. Mean and standard deviation was used to summarize continuous variables. Proportion and percentages were used for categorical variables. Sensitivity, specificity, predictive values were calculated for both ABI and AD. Pearson's/Spearman's Correlation analysis was used. P-value was calculated by the 2-tailed significance and <0.05 was considered significant at 5% precision. Statistical software tool like statistical package for Social Science (SPPSS) version 22 was utilized. Decision criterion - We compare p-value with the level of significance. If $p<0.05$, we accept the null hypothesis that there was no statistically significant difference in duration and severity of PVD by ABI over AD in DM and/or HTN patients.

RESULTS:

In our study, out of 72 cases, 24 patients had only DM (33%), 21 had only HTN (29%) and 27 patients had both (38%). Based on the socio-demographic parameter of age, the age range in our study was 40-75 years with the mean age of 59 years. Meanwhile, the mean age for DM group was 56 years, that of HTN group was 57 years and for both subset group was 58 years. In our study, there was male predominance, 60% (n = 43) [DM =13, HTN = 12 and both =18] given the fact that PVD is more common in males compared to their female (40%, n=29) counterpart [DM =11, HTN = 9 and both = 9].

Data regarding the duration and severity of PVD was collected and entered in the MS-Excel sheet followed by Statistical analysis in SPSS ver. 22. ***[Table 1, 2, 3, 4, 5, 6 and 7]***

Table 1: Duration Of DM/ HTN /both (N=72)

DURATION (IN YEARS)	DIABETICS	HYPERTENSIVES	BOTH
<3	0	0	0
3-5	9	14	18
6-8	13	5	6
9-11	2	2	3
>11	0	0	0

Table 2: Patient Graded For Severity Of PVD Among DM/HTN/both Based On AD. (N=72)

GRADE	DIABETES	HYPERTENSION	BOTH	Total (N=72) (%)
0	8	11	6	25 (35%)
1	4	5	10	19 (26%)
2	10	5	7	22 (31%)
3	2	0	2	4 (5%)
4	0	0	2	2 (3%)
5	0	0	0	0%

Table 3: Patient Graded For Severity Of PVD Among DM/HTN/both Based On ABI. (N=72)

GRADE	DIABETES	HYPERTENSION	BOTH	Total (N=72) (%)
0	10	14	9	33 (46%)
1	6	5	7	18 (25%)
2	7	2	8	17 (24%)
3	1	0	2	3 (4%)
4	0	0	1	1 (1%)
5	0	0	0	0%

Majority of the grade 3 severity patients were having morbidity (DM/HTN/both) or were under treatment for 6 - 8 years. While, a significant proportion of grade 2 severity group was having morbidity for 3-5 years and no case was reported with grade 5 severity. Correlation coefficient was calculated between the duration of DM ($r=0.86$, $P=0.00001$), HTN ($r=0.76$, $P=0.00006$) and both ($r=0.64$, $P=0.0003$) with AD and of DM ($r=0.68$, $P=0.0002$), HTN ($r=0.73$, $P=0.0001$) and both ($r=0.69$, $P=0.0006$) with ABI. ***[Table 8]***

Table 4: Diagnostic Accuracy Of ABI In Recognizing An Abnormal Study In DM With AD As Standard Diagnostic Test. (Grade 0- Normal, Grade ≥1- Abnormal). [N=24]

Parameter	AD (Abnormal)	AD (Normal)	Total
ABI (Abnormal)	13	1	14
ABI (Normal)	3	7	10
Total	16	8	24

Sensitivity – 81.3%, Specificity – 87.5%, PPV – 92.9%, NPV – 70%, Likelihood ration of a positive test – 6.5, Likelihood ration of a negative test – 0.21, Chi-square – 10.37, P-Value – 0.0012.

Table 5: Diagnostic Accuracy Of ABI In Recognizing An Abnormal Study In HTN With AD As Standard Diagnostic Test. (Grade 0- Normal, Grade ≥1- Abnormal). [N=21]

Parameter	AD (Abnormal)	AD (Normal)	Total
ABI (Abnormal)	6	1	7
ABI (Normal)	4	10	14
Total	10	11	21

Sensitivity – 60%, Specificity – 90%, PPV – 85.7%, NPV – 71.4%, Likelihood ration of a positive test – 6.6, Likelihood ration of a negative test – 0.44, Chi-square – 6.1, P-Value – 0.0013.

Table 6: Diagnostic Accuracy Of ABI In Recognizing An Abnormal Study In Both (DM and HTN) With AD As Standard Diagnostic Test. (Grade 0- Normal, Grade ≥1- Abnormal). [N=21]

Parameter	AD (Abnormal)	AD (Normal)	Total
ABI (Abnormal)	17	1	18

ABI (Normal)	4	5	9
Total	21	6	27

Sensitivity – 81%, Specificity – 83.3%, PPV – 94.4%, NPV – 55.6%, Likelihood ration of a positive test – 4.8, Likelihood ration of a negative test – 0.22, Chi-square – 8.6, P-Value – 0.003.

Table 7: Overall Diagnostic Accuracy Of ABI In Recognizing An Abnormal Study In DM/ HTN/ Both With AD As Standard Diagnostic Test. (Grade 0- Normal, Grade ≥1- Abnormal). [N=72]

Parameter	AD (Abnormal)	AD (Normal)	Total
ABI (Abnormal)	36	3	39
ABI (Normal)	11	22	33
Total	47	25	72

Sensitivity – 76.6%, Specificity – 88%, PPV – 92.3%, NPV – 66.7%, Likelihood ration of a positive test – 6.3, Likelihood ration of a negative test – 0.26, Accuracy = 80.5% Chi-square – 27.4, P-Value – <0.00001.

Table 8: Correlation Co-efficient For Duration Of DM, HTN, And Both Between ABI and AD.

	ARTERIAL DOPPLER	
ANKLE BRACHIAL INDEX	r	P
DIABETICS	0.85	<0.0001
HYPERTENSIVES	0.66	0.001
DIABETICS AND HYPERTENSIVES	0.88	<0.0001

Therefore, our study demonstrated that there is a strong positive correlation between the severity and duration of PVD in DM/ HTN/ both as assessed by ABI and AD.

DISCUSSION:

Our research indicates that ABI has an accuracy of 80%, a sensitivity of 76.6%, a specificity of 88%, a positive predictive value (PPV) of 92.3%, and a negative predictive (NPV) value of 66.6% and the study is highly significant in comparison to arterial doppler study (p value<0.00001). ***[Table 7 and 8]*** DM and people with both DM and HTN were found to have higher sensitivity (81.3% and 81%). ***[Table 4 and 6]*** Patients with HTN were found to have lower sensitivity (sensitivity-60%), yet higher specificity (specificity - 90%). ***[Table 5]*** In DM, HTN and both, there was a significant positive correlation between AD and ABI readings. ***[Table 8]***

Our findings were equivalent to those of the Carmo et al study ***[11]***. Comparatively, the calculation PPV (92.3%) of ABI in our study was higher than that of Carmo et al study (PPV-62.5%). However, ABI sensitivity (76.6%), specificity (88%) calculation in our study was lower; in contrast, to high sensitivity (91.2%) and specificity (92%) in study done by Hummel et al. ***[16]***

The second objective of our study was to determine the relationship between abnormal ABI and duration of morbidities like DM and HTN. Results showed that there is a positive correlation between the duration of DM (r=0.86, P=0.00001), HTN (r=0.76, P=0.00006) or both (r=0.64, P=0.003) with the severity of arterial disease calculated by AD and that by ABI (r=0.68, P=0.0002) in DM, (r=0.73, P=0.0001) in HTN and (r=0.69, P=0.0006) in both. Majority of patients with grade 2 or grade 3 severity of ABI had both DM and HTN or either one of them for a period of 6 to 10 years.

Thus, our study showed a strong correlation between the duration and severity of involvement of PVD amongst DM or HTN or those having both (DM and HTN) as assessed by ABI and AD.

The studies done by Fawkes et al, Herch A et al, Van Houtum et al, and Apelquist et al support our finding that the risk of peripheral arterial disease in patients with risk factors like DM/HTN increases with advancing age. ***[17, 18, 19, 20]*** Higher gradings were easily detected by doppler than ABI. In comparison to patients who had either DM or HTN; patients having both (DM and HTN) were found to have more severe arterial involvement.

Nevertheless, ABI is a useful screening tool for detecting peripheral vascular disorders. However, AD should be used in addition to an abnormal ABI if it is available in order to localize the disease, assess flow velocity, resistive index, and spectral pattern, as well as to assess collateral circulation. These are the limits of ABI because it is unable to determine them. ABI thus has a strong diagnostic value but a low therapeutic value. Calculating segmental blood pressure; however, might be useful in determining the location of the lesion.

CONCLUSION:

The study showed that ABI has high specificity (88%) but low sensitivity 76.6% compared to AD. Low sensitivity indicates it might miss some cases with PAD. If ABI is used alone; many patients with stenosis will be diagnosed as normal. But in the view of; the ease of performing and its low cost, ABI is still a good screening tool. It invariably reduces further unnecessary investigations in benign cases along with reduction in the morbidity and mortality associated with the complications of vascular diseases in DM and HTN. The study demonstrated that the length of DM/HTN/both raises the risk of severity of PAD and can be easily assessed by ABI. In summary, the duration of morbidity (like DM/HTN/both) can severely affect the vascular system; thus, mandating the need for early screening of PVD with ABI within a primary health care setting.

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