ROLE OF COLOR DOPPLER ULTRASONOGRAPHY IN EVALUATION OF EXTRACRANIAL CAROTID ARTERY IN STROKE PATIENTS: A PROSPECTIVE STUDY

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ABSTRACT

Introduction

Stroke is life threatening & debilitating neurological disease, defined as focal neurological deficit of sudden onset lasting >24 hours & vascular in origin. Significant association between ischemic type of stroke with carotid artery disease seen, more prevalent with carotid artery stenosis.

Objectives

This study was done to show association between extracranial carotid artery disease & cerebrovascular accidents (CVAs) with the help of Color Doppler Sonography (CDS). The association between carotid artery disease with associated risk factors were also assessed.

Methodology

In this ethically approved prospective study, carotid CDS was done in 79 consecutive patients with diagnosis of acute ischemic stroke (AIS). The various parameters studied included peak systolic velocity (PSV) of internal carotid artery (ICA) & common carotid artery (CCA), ICA/CCA PSV ratio & plaque characteristics. The data collected was analyzed with appropriate statistical test of significance was calculated.

Results

Total 79 patients with AIS included out of which 53 were males & 26 were females. The most common presenting complains were hemiparesis (30.4%) & most commonly associated risk factors included hypertension (62.02%). Right sided strokes were most common (44.3%) & middle cerebral artery was most commonly involved vascular territory. Significant stenosis (≥50%) of carotid artery was seen in 27 patients with ICA most common site (45.8%) for plaque formation. Bilateral carotid artery involvement (52.1%) with hypoechoic echotexture of atheromatous plaques (46.6%) was most responsible for significant stenosis & increased intima media thickness. Increased value of PSV & EDV was seen in the stenotic area in the proportion of stenosis with increased PSV ICA/CCA ratio of more than three indicates >60% stenosis.

Conclusion

The present study showed well documented role of carotid doppler in detection of site & extent of carotid artery stenosis due to atheromatous plaques of various characteristics playing critical role in thromboembolic phenomenon responsible for development of stroke.

KEYWORDS

Carotid artery, color doppler ultrasonography, stenosis, stroke
INTRODUCTION

Stroke is third leading cause of death worldwide after malignancies and cardiac disease and is defined as focal neurological deficit of sudden onset lasting for more than 24 hours with cause being vascular origin. About one third cases are severe & prolonged or irreversible disabilities seen in survivors. Transient ischemic attack (TIA) occurs for less than 24 hours. About 80-85% of strokes are thromboembolic in origin leading to ischemic cerebral infarct & ischemia with atherosclerotic plaques involving both extracranial & intra cranial carotid arteries acting as source of thrombus. Hemorrhagic causes of stroke include subarachnoid hemorrhage & intra cranial hemorrhage accounting of 15-20% of total stroke cases. It is seen that within three months of TIA, there is chance of major stroke and about 20% major stroke was preceded by TIA. Severe stenosis of carotid artery, large artery lesions, diabetes mellitus, asymptomatic atherosclerotic plaques or combinations of these risk factors are causes for large artery involvement in stroke.

Grey scale and color doppler ultrasonography (CDUS) of extra cranial carotid artery is popular, safe, noninvasive, accurate & cost-effective high-resolution imaging procedures which can accurately detect hemodynamically significant stenosis of carotid arteries in patients who may benefit from surgical intervention. High resolution grey scale ultrasound B-mode imaging allows detailed anatomical details of carotid artery including intima media thickness (increased intima media thickness (IMT) is surrogate marker for early development of plaques) & detection of small nonstenotic atheromatous plaques. Color Doppler Ultrasonoaphy is replacing Carotid angiography in the evaluation of extracranial carotid artery atherosclerotic disease & severity of carotid artery stenosis so that early intervention & endarterectomy can be done to prevent further development of stroke. The gold standard test for diagnosis of severity of carotid artery stenosis is conventional angiography however it is an invasive and expensive procedure with risk of contrast medium related complications & some degree of morbidity. With recent use of Magnetic resonance angiography, similar or better evaluation of carotid disease can be done besides flow quantification. It is however time consuming and of higher cost. Ultrasonography will calculate the extent & degree of carotid artery stenosis besides plaque characterization. Plaques having intra plaque hemorrhage which is precursor for plaque ulceration which can be further source of thrombus can be detected using high-resolution ultrasound. The brain is having anterior circulation supplied by two internal carotid arteries (ICAs) and posterior circulation supplied by the two vertebral arteries. This study was done to assess the carotid arteries with the help of color Doppler sonography and to correlate cerebrovascular accidents (CVAs) with extracranial carotid artery status. The association between carotid artery disease with risk factors like diabetes mellitus, hypertension, hyperlipidemia, smoking and age also assessed.

METHODOLOGY

After institutional ethical committee approval, this prospective study was done in all patients with features of stroke presenting in one of the tertiary care hospitals of eastern region of Nepal from February 2020 to July 2020. After obtaining informed consent from the patients, information's about clinical features, risk factors (Diabetes mellitus, Hypertension, Smoking, Hyperlipidemia & Family history) & general physical examination were carried out in all patients with stroke meeting the inclusion criteria. The inclusion criteria included patients presenting with history, clinical features & imaging findings of acute ischemic stroke. Patients with hemorrhagic stroke, stroke of greater than one-week duration, features of primary & secondary brain tumors, traumatic brain injury & vertebralbasilar insufficiency were excluded from the study. All patients underwent noncontrast computed tomography (NCCT) of brain using 64 slice MDCT scanner (Somatom Perspective, Siemens, Erlangen, Germany) to see the area of brain & vascular territory involved before doing color doppler ultrasonography of carotid arteries.

Carotid Doppler ultrasonography Technique:

Color doppler ultrasonography was performed using high end Voluson S10 ultrasound machine (GE Healthcare, USA) with linear array transducer of 7-12MHz frequency. Information regarding grey scale imaging features of carotid artery was done prior to the doppler study. Patients were placed in supine position with neck extended & tilted for better exposure of neck with head rotated to opposite side being examined & ipsilateral shoulder being dropped down as far as possible. Longitudinal & axial views of carotid arteries were examined by same operator standing on right side of the patient with all examinations performed at doppler angle of 60 degree.

On grey scale images [Figure 1 (A) & (B)], intima media thickness is measured (>0.08cm is abnormal). Information regarding presence or absence of plaque, location of plaque, number of plaque & plaque characterizations including echotexture (hypoechoic, calcified, moderately echogenic & echogenic), calcification, plaque ulceration & intraplaque hemorrhage. Hypoechoic plaques are pathological which contain lipid & cholesterol deposits which can ulcerate and can lead to thromboembolic events. Calcified plaques are commonly seen in asymptomatic individuals & give posterior acoustic shadowing while echogenic plaques may be pathological & contains dense fibrous & connective tissue. On Doppler study (Figure 2), peak systolic velocity (PSV) & end diastolic velocity (EDV) of internal carotid artery (ICA) & common carotid artery (CCA), ICA/CCA PSV ratio were evaluated in normal within 2cm from the CCA bifurcation & stenosed portion in addition to information regarding color flow & spectral wave pattern. Criteria used for stenosis in our study was ICA/CCA PSV ratio>PSV ICA/CCA ratio of >1.5 suggests stenosis of ≥50%, ratio of >1.8 suggests stenosis of >60% & ratio of >3.7 suggests stenosis of >80%) & residual lumen diameter at the site of most stenosis (>50% luminal narrowing significant stenosis).
**Statistical Analysis:**

Data was analyzed using SPSS 20.0 version software & results were expressed in mean ± standard deviation for continuous data & median for noncontinuous data. Results were also presented in Tables, graphs, Figures & diaphragm where necessary with Chi-Square test, Fisher's Exact test, Pearson's & Spearman's correlation, Independent sample T-test & odd ratio for risk estimate were calculated. P values less than 0.05 were considered statistically significant.

**RESULTS**

A total of 79 consecutive patients with diagnosis of acute ischemic stroke were included in this study, out of which 53 (67.1%) were male & 26 (32.9%) were female with mean age of 60.3±10.5 years & 62.3±12.4 years for males & females respectively. The most common presenting complains were hemiparesis with other complains were shown in table 1. Most common risk factors associated were hypertension was seen in 49 (62.02%) patients followed by diabetes in 32 (40.5%) patients, smoking in 25 (31.6%), hyperlipidemia in 21 (26.6%) & family history in 11 (13.9%) patients.

<table>
<thead>
<tr>
<th>Table 1: The clinical complains with which patients presented</th>
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<tr>
<td><strong>Complains</strong></td>
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<td>----------------</td>
</tr>
<tr>
<td>Hemiparesis</td>
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<tr>
<td>Hemiplegia</td>
</tr>
<tr>
<td>Giddiness</td>
</tr>
<tr>
<td>Slurring of Speech</td>
</tr>
<tr>
<td>Unconsciousness</td>
</tr>
<tr>
<td>Others</td>
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<tr>
<td><strong>Total</strong></td>
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</table>

Out of 79 patients, 35 (44.3%) patients had right sided stroke, 32 (40.5%) patients had left sided stroke, 5 (6.3%) patients had bilateral involvement while 7 (8.9%) patients had TIA. Middle cerebral artery (MCA) was the most commonly involved vascular territory seen in 35 (44.3%) patients found on NCCT scan (Figure 3) shown in Table 2.

Significant stenosis (≥50%) of carotid artery on color doppler was seen in 27 patients (34.2%) while normal carotid artery seen in 31 (39.2%) patients & non-significant stenosis (<50%) seen in 21 (26.6%) patients. Calculation of PSV & EDV of ICA & CCA with estimation of ICA/CCA ratio were made in all patients.

Out of 27 patients with significant stenosis, right sided involvement was seen in 15 (55.6%) patients followed by left sided involvement in 9 (33.3%) patients & bilateral involvement in 3 (11.1%) patients. Among the patients with significant stenosis, 15 (55.6%) patients had 50-69% stenosis, 7 (25.9%) patients had 70-89% stenosis, 2 (7.4%) patients had >90% stenosis while in 3 (11.1) patients, complete occlusion of carotid artery seen where no flow seen on color doppler study and PSV ratio was not applicable.

The correlation of PSV and EDV in the area of stenosis was made showing increased PSV & EDV in the proportion of stenosis with increased PSV ICA/CCA ratio (Table 3).

<table>
<thead>
<tr>
<th>Table 2: Findings of NCCT scan in stroke patients</th>
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<tr>
<td><strong>CT Findings</strong></td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Right MCA</td>
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<tr>
<td>Left MCA</td>
</tr>
<tr>
<td>Right ACA</td>
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<tr>
<td>Left ACA</td>
</tr>
<tr>
<td>Right PCA</td>
</tr>
<tr>
<td>Left PCA</td>
</tr>
<tr>
<td>AICA/PICA</td>
</tr>
<tr>
<td>Lacunar Infarct</td>
</tr>
<tr>
<td>≥2 arteries</td>
</tr>
<tr>
<td>Normal CT scan</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
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MCA- Middle Cerebral Artery, ACA- Anterior Cerebral Artery, PCA- Posterior Cerebral Artery, AICA- Anterior Inferior Cerebellar Artery, PICA- Posterior Inferior Cerebellar Artery

<table>
<thead>
<tr>
<th>Table 3: Range of Spectral velocities in the region of stenosis with PSV ICA/CCA ratio</th>
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<tr>
<td><strong>Stenosis (%)</strong></td>
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<td>-------------------</td>
</tr>
<tr>
<td>&lt;50</td>
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<tr>
<td>50-69</td>
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<tr>
<td>70-95</td>
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<tr>
<td>&gt;95 (Near complete occlusion)</td>
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PSV- Peak systolic velocity, EDV- End diastolic velocity, ICA- Internal carotid artery, CCA- Common carotid artery

The main factor responsible for extracranial carotid artery occlusion was atheromatus plaques due to atherosclerotic changes seen in 48 (60.8%) patients while 31 (39.2%) patients showed no atherosclerotic changes. Most common involvement of atheromatus plaques was bilateral carotid artery involvement seen in 25 (52.1%) patients followed by right sided carotid artery involvement in 12 (25%) patients & left sided carotid artery involvement in 11 (22.9%) patients. ICA was most commonly involved site followed by carotid bifurcation & CCA. Along with ICA, CCA was also involved in 2 patients bilaterally, 1 patient on right side & 1 patient on left side (Table 4).
ICA- Internal Carotid Artery, CCA- Common Carotid Artery

Total 75 atheromatous plaques seen in 48 patients on grey scale ultrasound images for plaques characterization. Most common type of plaques are hypoechoic type in 35 (46.6%) followed by hyperechoic type in 17 (22.7%), calcified type 15 (20%) & moderately echogenic in 8(10.7%) (Figure 4).

Diabetes mellitus, smoking & Hypertension were more significant & prevalent risk factors associated with ischemic stroke & atheromatous plaques formation seen in this study. Out of 32 diabetic patients, 15 (46.8%) showed significant stenosis of >50%. Out of 49 patients with hypertension, 18 (36.7%) showed significant stenosis of >50%. Among 21 patients with hyperlipidemia, 9 (42.9%) showed significant stenosis while 25 patients with history of chronic smoking, 11 (44%) patients showed significant stenosis. Out of 11 patients with family history of stroke, 4(36.3%) showed significant stenosis. There is statistically significant relation of diabetes with significant stenosis of carotid artery with p value <0.05. The patients with diabetes mellitus have 2.57 times risk (odd ratio) of having significant carotid artery stenosis (95% confidence interval: 0.99-6.69). Patients with history of chronic smoking also showed statistically significant relation with significant carotid artery stenosis at P value <0.02 & odd ratio of 3.1(95% confidence interval: 1.15-8.36).

Intima media thickness of more than 0.08cm was considered abnormal (Figure 5) & associated with increased risk of atheromatous plaque formation. The mean of abnormal IMT was 0.13±0.065cm in male which is higher than mean value of IMT 0.10±0.042cm in female & the results were statistically significant (P-value <0.009). There is statistically significant difference of abnormal increased intima media thickness in patients with diabetes mellitus (P value <0.004) than nondiabetic patients. Increased abnormal intima media thickness seen in patients with chronic smoker than non-smoker patients & the difference was statistically significant (P value <0.02). Also, the patients with hyperlipidemia showed statistically significant difference of IMT then patients with normal lipid profile (P value <0.03). The patients having family history of stroke showed statistically significant difference of IMT than in patients with no family history at P value <0.03. Hypertensive patients showed higher intima media thickening than normotensive patients however the difference was not statistically significant (p value >0.05).
DISCUSSION

Atherosclerotic disease of extracranial carotid arterial system occurring within 2cm of carotid bifurcation & ICA is mainly responsible for stroke in majority of the population (30-60%). High-resolution CDUS timely allow adequate detection, diagnosis & characterization of atheromatous plaques having great value in selection of proper medical & surgical therapy for patients having critical stenosis (≥70%) carrying greater risk for the development of cerebral infarction (Figure. 6 & 7). Carotid lesions causing stenosis <70% were treated with medical therapy causing inhibition of aggregation of platelet & formation of thrombus noted by Moneta et al while surgical intervention like endarterectomy should be option for the patient with carotid artery stenosis more than >70% as suggested by North American Symptomatic Carotid Endarterectomy Trial (NASCET). Chambers & Norris noticed that even subcritical carotid stenotic lesion may play role in the pathogenesis of cerebral thromboembolism. Carotid angiography is gold standard diagnostic modality for the carotid arterial system and is replacing the color doppler study for the same purpose however with proper & experienced use of color doppler study for impending surgical intervention in absence of angiography should be encouraged & recommended. So, this study was done to see the role of color doppler study in evaluation of extracranial carotid artery in stroke patients.

In our study, all the 79 patients undergone CDUS for accurate detection, interpretation & diagnosis of extracranial carotid arterial disease. High frequency linear probe provides better resolution & adequate penetration for adequate field of view as carotid arterial system is superficially located which is also used by Kreb & Giyani et al, Sehrawat et al, Samrin Haq et al & Fernandes M et. The incidence of stroke cases increases with increasing age after 60 years which was also seen in our study. In our study, most of the stroke cases were seen in the age group 61-70 years (25 patients out of 79) followed by 50-60 years (23 patients out of 79) which was also seen in the study done by Sehrawat et al, Samrin Haq et al, Fernandes M et & Febris et al. In this study, 53 (67.1%) were male & 26 (32.9%) were females showing similarity with study done by Sehrawat et al, Samrin Haq et al & Fernandes M et. The findings of this study were well correlated with study done by NASCET which also showed 72% patients were male & 28% patients were female while only 2.5% patients were female in study done by Lemolo et al.

In our study, majority of the patients presented with complaint of hemiparesis with right sided stroke seen in 35 patients, left sided stroke in 32 patients & bilateral involvement was seen in five patients. Stroke involving anterior circulation was seen more frequently in our study than posterior circulation stroke with MCA was most commonly involved vascular territory. These findings were similar to study done by Samrin Haq et al & Fernandes M et while it was different from study done by Baidya OP et al where most of the lesions involving left side of brain.

In this study, most common risk factors seen were hypertension
present in 62.02% patients followed by diabetes in 40.5% patients, smoking in 31.6% & hyperlipidemia in 26.6% & family history in 13.9% patients. Due to continuous trauma to endothelium of blood vessels in hypertension leads to development of atherosclerosis resulting into formation & growth of plaque responsible for cerebral thromboembolism. In our study, 18 patients out of 49 hypertensive patients had significant stenosis of >50%. The abnormal increased IMT was also seen in hypertensive patients than normotensive patients. With the control of hypertension, there is significant reduction in risk of stroke shown by Ladeola et al. Diabetes mellitus was another most important & documented risk factor for atherosclerosis & stroke. There was significant association of levels of plasminogen activator antigen & plasminogen activator inhibitor-1 in diabetic patients with history of ischemic stroke. In our study, 32 patients out of 79 patients presenting with ischemic stroke had diabetes mellitus out of which 46.8% (15 patients out of 32 diabetic patients) had significant stenosis of >50% with two patients having complete luminal narrowing. These findings were similar to study done by Samrin Haq et al, Fernandes M et al & Sethi SK et al. About two third cases of all types of ischemic stroke cases had diabetes mellitus on admission shown by Lindberg Pertu & Roine Risto in their study. Most important risk factor responsible for stroke was chronic smoking & there was positive relationship between smoking & risk of stroke. Chronic Cigarette smoking was strong predictor of severe extracranial carotid artery atherosclerotic disease according to Whisnant et al & was responsible for stroke in 22% of cases. In our study, 25 patients (31.6%) out of 79 patients had history of smoking out of which 11 (44%) had significant stenosis which is similar to study done by Sehrawat et al. Hyperlipidemia was another risk factor responsible for atherosclerosis & stroke due to formation of plaque which is main culprit for the development of cerebral thromboembolism. In our study, hyperlipidemia was seen in 26.6% of patients, out of which 9 (42.9%) patients showed significant stenosis. In this study, 11 (13.9%) patients had family history of stroke out of which 4(36.3%) showed significant stenosis which is similar to study done by Fernandes M et al & Schulz et al where family history was seen in 14% & 23% of cases respectively.

Abnormal intima media thickening (IMT) is earliest representation of atherosclerosis & >0.08cm is considered abnormal. In our study, there is statistically significant difference of IMT seen between male & female at p-value <0.05 which similar to the study done by Sehrawat et al & Samrin Haq et al. The increased IMT was seen more in male sex, patients with history smoking & diabetic patients in our study showing similarities with study conducted by Sun, Cheng-Huai et al, Jhadav & Kadam. The main factor responsible for extracranial carotid artery stenosis is atheromatous plaques within 2cm vicinity of CCA bifurcation & ICA in 30-60% of patients & seen in 48 (60.8%) patients while normal in 31 (39.2%) patients out of total 79 patients. Majority of the patients showed bilateral carotid artery involvement by plaques in 25 (52.1%) patients followed by right sided carotid artery involvement in 12 (25%) patients & left sided carotid artery involvement in 11 (22.9%) patients. ICAs was most commonly involved site followed by carotid bifurcation & CCA. These findings were similar to study conducted by Sehrawat et al while carotid bulb was most common site involved in study done by Samrin Haq et al, Sethi SK et al & Petrovic S et al. Carotid ultrasonography showed location & morphology of atheromatous plaques along with its characteristic & majority of the plaques in our study is hypoechoic type in 35 (46.6%) followed by hyperechoic type in 17 (22.7%), calcified type 15 (20%) & moderately echogenic in 8(10.7%). Plaque surface ulceration was seen in three patients while intraplaque hemorrhage with surface ulceration was seen in two patients in our study. Most of the plaques were hypoechoic in study done by Sehrawat et al similar to our study while echogenic in study done by Samrin Haq et al. Characterization of atheromatous plaques, primary pathology of carotid artery by grey scale ultrasonography was important as there is more chance of ulceration in hypoechoic plaques responsible for nidus formation for platelet aggregation which may migrate into cerebral circulation causing TIA or cerebral ischemia. Normal color doppler spectral wave form of CCA was shown in figure 2 showing normal arterial flow with forward diastolic flow with normal value of PSV & EDV. The main doppler parameters used in different study to determine the clinically significant carotid stenosis were PSV, EDV & PSV ICA/CCA ratio, out of which PSV ICA/CCA is best due to physiological variability from patients to patients. Endarterectomy showed long term benefits over medical treatment either in symptomatic or asymptomatic patients with ICA stenosis of 60% or 70% in trials conducted by NASCET & European Carotid Endarterectomy trail. The patients were classified into different groups with degree of stenosis & presence of symptoms in our study & degree of stenosis in our study was done according to the extent of area reduction. PSV ICA/CCA ratio of >1.5 suggests stenosis of ≥50%, ratio of >1.8 suggests stenosis of >60% & ratio of >3.7 suggests stenosis of >80%. It was seen in most of the study that ratio is more accurate than PSV. In our study, PSV ICA/CCA ratio of 1.3-1.7 seen in stenosis of <50% in 21 patients, ratio of 1.8-2.9 suggested 50-69% stenosis (Figure 7) in 15 patients while ratio of 3.1-4.9 seen in stenosis of 70-95% (Figure 6 & 7) in 9 patients. Complete occlusion was seen in three patients with echogenic thrombus within the lumen or atheromatous plaque completely obliterating the lumen with loss of arterial pulsation, subnormal size of vessel & no flow across stenosed segment on color doppler with inapplicable PSV ICA/CCA ratio (Figure 8). Normal carotid artery with no stenosis seen in 31 patients out of total 79 patients. The similar results were also seen in study done by Sehrawat et al & Samrin Haq et al. PSV and EDV in our study were increased in the region of stenosis & increment was according to the extent stenosis showing similarities with the study done by Grant et al & Staikov et al.
CONCLUSION
Majority of the patients presented with complaints of hemiparesis with right sided stroke was more common & MCA was most commonly involved vascular territory. Atheromatous plaque was more common obstructing lesion of carotid arterial system responsible for stenosis. ICA was most commonly involved site. Hypoechoic plaque was more common with bilateral involvement. Hypertension, Diabetes mellitus & smoking were most common associated risk factors. The present study showing the importance of CDUS in evaluation of extracranial carotid arterial system for detection of stenosis as ultrasonography is cheap, easily available, more accurate, noninvasive & less time-consuming modalities.

LIMITATIONS
Limitations of study include difficulty in examination of carotid arterial system in case of high position of carotid bifurcation & obscuration of field of view due to posterior acoustic shadowing in case of large calcified atheromatous plaque. Other limitations of our study were a smaller number of sample size.

ACKNOWLEDGMENTS
We would like to acknowledge study participants & Institutional Review Committee of Birat Medical College & Teaching Hospital. We would like to thank Dr. Surya B. Parajuli (Assistant Professor, Department of Community Medicine), Dr Dilip Choudhary (Lecturer, Department of Dermatology), Dr Rajeev Shah (Assistant Professor, Department of Otolaryngology) & Dr Nabaraj Koirala (Professor, Department of Psychiatry) for their immense contribution in data management & guiding us for manuscript preparation.

FINANCIAL SUPPORT AND SPONSORSHIP
None

CONFLICTS OF INTEREST
None

REFERENCES


