# Transcranial Doppler in Monitoring Management of Patients with Subarachnoid Hemorrhage

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**Abstract**: Cerebral vasospasm remains the most significant and most common complication following subarachnoid hemorrhage (SAH) which is defined as bleeding into the subarachnoid space between the arachnoid membrane and the pia matter surrounding the brain. Transcranial Doppler (TCD) is non invasive tool allowing for bedside monitoring to determine flow velocities indicative of changes in vascular caliber. The true value of this technique as sensitive predictor alone for diagnosing clinical vasospasm, still mater of debate. Aim of the study: was to evaluate the role of TCD in monitoring patients with SAH and early detection of pre symptomatic vasospasm that may help in further early management. Methods: This study was carried out on 30 patients diagnosed to have acute subarachnoid hemorrhage presented within 48 hrs. from onset and confirmed by CT brain. Patients were divided into: Group A; included 15 patients that were monitored by both the usual standard clinical and neurological evaluation and Group B; included the other 15 patients that were subjected in additions to standard clinical evaluation, to continuous non-invasive TCD every 48 hours from day 4 to day 21 of hospital admission. Results: There was 19 females and 11 males with mean age 46.5+11.4 year .Of them, 73.3% were hypertensive and 13.3% were diabetic. Delayed ischemic neurological deficits (DIND) developed in 9 of 30 patients, 6 (40%) pts in group A and only 3 (20%) pts in group B & was not related to the cause of SAH (P: 0.9). There was no significant correlation between Hess and Hunt grading and the occurrence of DIND (P: 0.7). Patients with DIND had a significantly higher peak systolic velocity (PSV)of middle cerebral artery(MCA)in comparison to patients who had no DIND at serial TCD1,2,3 measurements and P values were 0.002, 0.038, 0.026 respectively, but no significance of the difference of percentage of change from the baseline TCD1. Analysis of area under ROC curve revealed, at PSV 172 cm /sec & area under the curve 0.75, sensitivity of 60% & specificity of 88% & the p value was 0.09. ***Conclusion:*** TCD is a useful tool for screening symptomatic vasospasm and for early prediction of DIND in SAH pts.
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**Key words:** DIND: delayed ischemic neurological deficits & TCD: transcranial Doppler & SAH: subarachnoid hemorrhage & cerebral vasospasm. Hess & Hunt grade.

## 1. Introduction:

Cerebral vasospasm remains the most significant and most common complication following subarachnoid hemorrhage. It contributes to high levels of morbidity and mortality and may evolve anywhere between the third and the seventh day following the initial hemorrhage in the neural parenchyma ***(1)***. Some degree of vasospasm develops in almost all patients with significant SAH, and narrowing generally worsens and then reverses over an interval of 1- 2 weeks ***(2).*** Despite confusion over the word "vasospasm" the term refers to the phenomenon of narrowing of arteries seen after SAH. Symptomatic vasospasm and delayed ischemic deficit are considered as synonymous, referring to the clinical syndrome where the narrowing of the arteries is severe enough to cause ischemic symptoms. Angiographic vasospasm refers to the estimation of arterial narrowing by means of a cerebral angiography. Delayed ischemic deficit associated with symptomatic vasospasm usually appears shortly after the onset of angiographic vasospasm, with the acute or sub acute development of focal or generalized symptoms and signs ***(3)***. Trans cranial Doppler ultrasonography is a noninvasive tool, allowing for bedside monitoring to determine flow velocities indicative of changes in vascular caliber. Firstly used by **Aaslid** and his colleagues in **1982**, transcranial Doppler is based on the hemodynamic principle that the velocity of blood flow in a given artery is inversely related to the cross-sectional area of that artery ***(4)***. Transcranial Doppler ultrasonography provides a number of ways to measure the flow patterns of cerebral arteries and can be useful pre, intra and postoperatively, while helping to recognize the development of vasospasm before the onset of its clinical effects ***(5-9)***.

## Aim of the Work:

The aim of this study was to evaluate the role of TCD in monitoring pts with SAH and early detection

of pre symptomatic vasospasm that may help in further early management.

**2. Methods:**

This study was carried out on consecutive thirty patients, diagnosed to have acute subarachnoid hemorrhage presented within 48 hours of hospital admission in the neurosurgical ICU in Kasr El-Aini Hospital, Cairo University in the period between December 2009 to June 2010. The diagnosis of SAH was confirmed clinically and by CT brain.

**Patients were divided into two groups:**

Group A, 15 patients that were monitored by both the usual standard clinical and neurological evaluation stratified by **Hunt and Hess** grading scale ***(10)*** that is normally used in the treatment of SAH. Group B: The other 15 patients subjected to continuous non-invasive Trans –cranial Doppler (TCD) monitoring from day 4 to 21(every 48 hrs) ,to guide for early vasospasm that may require advanced therapeutic intervention. This TCD was done in addition to both clinical and neurological evaluation done daily.

The pts were aged 14 -60 years with traumatic or non –traumatic cause of SAH presented within 48 hours from onset of bleeding. Exclusion criteria were patients with evidence of epidural, subdural or intracerebral hemorrhage, patients with other end organ failure that may interfere with prognosis and outcome such as: congestive heart failure, renal impairment defined as serum creatinine level more than 1.5 mg/dl, end stage liver failure, systemic sepsis and disseminated malignancy.

All 30 patients were subjected to the following: informed consent from the patient or the closest family member, full detailed medical history taken from the patient or a family member with special stress on age , sex & hypertension, diabetes, cardiac disease, full detailed clinical examination with stress on neurological status (according to **Hunt and Hess** scale ***(10);*** electro-cardiogram, chest x ray, all routine LAB investigation, echocardiography, CT scan, CT Or MR Cerebral angiography on admission.

Both groups were given the uniform medical treatment including nimodipine fluid and electrolyte balance and minor analgesic for headache. Strict follow up of sodium and glucose was done to exclude hyponatremia or hypoglycemia as a cause of deterioration in consciousness.

Systolic Doppler indices:

The trans cranial Doppler performed by an experienced Radiologist not involved in the patient care, provides a number of ways to measure the flow patterns of cerebral arteries. The main parameters were mean flow velocity (FVm), peak flow velocity (FVs), and end diastolic flow velocity (FVd). These velocities tend to decrease as age increases. These values were used to calculate the pulsatility index (PI = (FVs - FVd) / FVm) and the resistance index (RI = (FVs - FVd) / FVs) of the vessel.

If deterioration in consciousness occurred, the pt was subjected to control CT brain to confirm diagnosis (by exclusion of re bleeding & hydrocephalus and ischemic stroke). The symptomatic vasospasm was defined as a clinical deterioration in the patient's neurological condition (i.e., insidious onset of confusion, disorientation, or decline in level of consciousness, and focal deficits) later than day 3 after SAH with no evidence of hydrocephalus, hemorrhage, surgical complications, metabolic disturbances, or infection. Two independent investigators directly assessed the patient's neurological status and agreed on symptomatic vasospasm. The angiography was not reliably performed in the presence of clinical vasospasm. Therefore, angiographic criteria were not used for the determination of vasospasm**.**

**Statistics:**

Data were statistically described in terms of range, mean ± standard deviation (±SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of age between the study groups was done using Mann Whitney *U* test for independent samples. For comparing categorical data, Chi square ($X^2$) test was performed. Exact test was used instead when the expected frequency is less than. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

**3. Results**

A total of 30 patients, 11 males (36.7%) and 19 females (63.3%) with mean age 46.5±11.42 years, were prospectively studied. Our results will be presented as follow: demographic and clinical data, frequency and distribution of clinical vasospasm in both groups, correlation between neurological status (HESS & HUNT) and clinical vasospasm in both groups and correlation between trans-cranial Doppler systolic velocity and clinical vasospasm in group B.

**A) Demographic, clinical and management data:**

Basic characteristics of 30 study subjects were comparable between groups. The mean age was 48.2±10.3 years and, 44.7±12.4 in both groups respectively (P value = 0.415). Both groups were

nearly the same as regard sex distribution (the female to male ratio was 9/6 versus 10/5 in group A and B respectively). Hypertension was presented in more than 60%of patients in both groups & while only 13.3% of patients had type 2 diabetes (HTN :10/15&12/15 & DM 2/15 &2/15 respectively in both groups, P value = 0.5).

Spontaneous (non aneurismal) SAH was present in 7 patients in group A and 5 patients in group B & while Aneurysmal SAH was lower in group A compared to group B (6/15 versus 8/15 respectively p value=NS ). The traumatic cause of SAH was the same (2/15 in both groups), (figure 1).

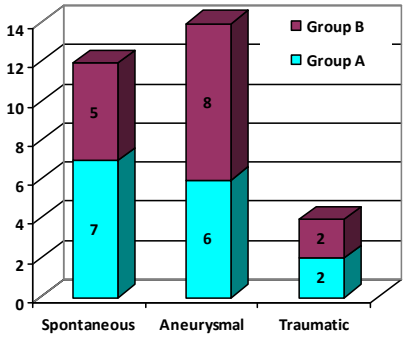


**Fig (1): Causes of SAH in both groups (A & B).**

The surgical intervention was done in 6 pts in group A and 4 pts in group B with no statistical difference in both groups (P value = 0.5). Mechanical ventilation was needed in 4 pts in group A, and 2 pts in group B, with no statistically significant difference (P = value 0.5).

**B) Frequency and distribution of clinical vasospasm in both groups:**

Delayed ischemic neurological deficit (DIND) developed in 9 pts of total population studied (30 pts), 6 pts in group A (40%) and only 3 pts in group B (20 %) (P value = 0.36) (figure 2).

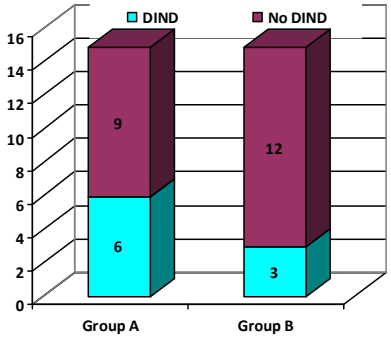


**Fig (2): Delayed ischemic neurological deficit (DIND) occurrence in both groups**

The occurrence of DIND was studied in relation to the cause of SAH in all pts studied (30 pts). Out of 12 pts having spontanous(non aneurysmal) SAH, four pts developped DIND, in comparison to 5 out of 14 pts developped DIND in those having spontanous aneurysmal SAH. with no statistical differerence, P value = 0.9) (fig. 3).

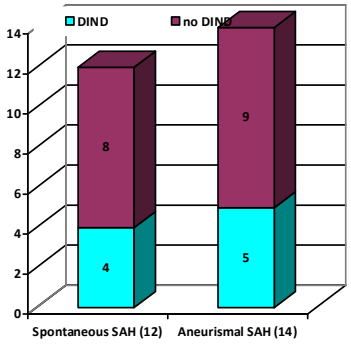


**Fig (3): Correlation between cause of SAH & DIND**

**C) Hess And Hunt evaluation for clinical prediction of DIND:**

According to **Hunt and Hess** evaluation for the whole population studied, neurological clinical evaluation was done for 30 pts on admission (HH0) and daily by HES and HUNT grading scale (10), Hunt & Hess on admission was not significant predictor for DIND and throughout the course of hospitalization as there was no correlation between clinical evaluation and the occurrence of DIND. ***On admission (HH0***) there was 60% (18 pts) class I and 40% (12 pts) class II (figure 4).

Clinical evaluation scale on admission, revealed non significant correlation between H&H grading and occurrence of DIND (table 1).

**Table (1): Correlation between H&H on admission and DIND**

| *H & H0 of admission* | *(18 pts) class 1* | *(12 pts) class 2* | *P value* |
|---|---|---|---|
| DIND | 6 | 3 | 0.7 |
| No DIND | 12 | 9 | |

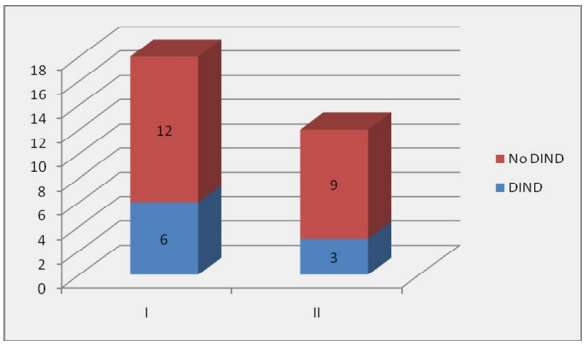


**Fig (4): Correlation between H&H on admission and DIND.**

Daily evaluation of the total 30 pts during hospital stay revealed no significant rise of DIND occurrence with increased H&H class as a sign of more deterioration (table 2).

***Table (2): Correlation between H&H during hospital stay and DIND***

| *During hospital stay* | *DIND* | *No DIND* | *P value* |
|---|---|---|---|
| I | 5 | 9 | 0.5 |
| II | 3 | 11 | |
| III | 1 | 1 | |

**D) TCD monitoring of all group B patients:**

Trans cranial Doppler was done for group B (15 pts), every 48 hrs, (TCD1, TCD 2, TCD3,4,5).An average number of TCD in group B was done for each case was 4.2±0.4, with mean peak systolic velocity of MCA of 109±37.4 msec at TCD1, 147.2 msec at TCD2, 158.8 msec at TCD3, 111.7 msec at TCD4 & 76.4 msec at TCD5 ( table 3, figure 4,5). Maximum PSV recorded was 290 msec and minimal velocity was 39 msec .

***Table (3): Mean peak systolic velocities at TCD 1,2,3 ,4,5 of all pts of group B.***

| | *Mean* | *SD* |
|---|---|---|
| TCD1 | 109 | 37.4 |
| TCD2 | 147.2 | 61.4 |
| TCD3 | 158.8 | 64.2 |
| TCD4 | 111.7 | 64.2 |
| TCD5 | 76.4 | 29.2 |
| Range | 39.9-290 | |

The percentage of change in PSV in TCD evaluation from baseline TCD1 compared to TCD3 and TCD4 was, 23.5±11.2% & 7.7± 8% respectively. **Delayed ischemic neurological defecit developped in only 3 pts during their hospital stay.** Patients with DIND had a significantly higher PSV ofmiddle cerebral artery ( MCA) in comparison to patients who had no DIND at TCD1, 2, 3 ( table 4, figure 4,5), and P values were 0.002, 0.038, 0.026 respectively, but no significant difference of percentage of channge from the baseline TCD1.

**Table (4): Peak systolic velocities in DIND versus non DIND and percentage of change between TCD 1-2 and 2-3.**

| | *Pts with no DIND (12)* | *Pts with DIND(3)* | *P value* |
|---|---|---|---|
| TCD1 | 95.5±27.06 | 163.2±16.3 | 0.002 |
| TCD2 | 124.4±39.4 | 238.36±48 | 0.038 |
| TCD3 | 132.9±34.7 | 262.6±45.6 | 0.026 |
| % change1 | 22.19±7.9 | 28.7±22.07 | 0.6 |
| % change 2 | 7.29±8.5 | 9.3±7.2 | 0.7 |

Peak systolic velocity trend of change in group B patients that developped DIND in comparison to those who did not develop DIND showed non significant correlation (figure 5,6).

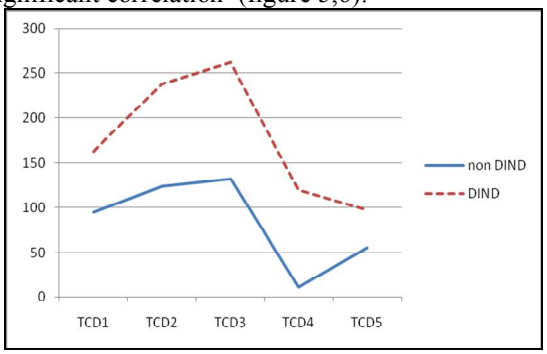


**Fig (5): Trend of change in peak systolic velocities in DIND versus non DIND**

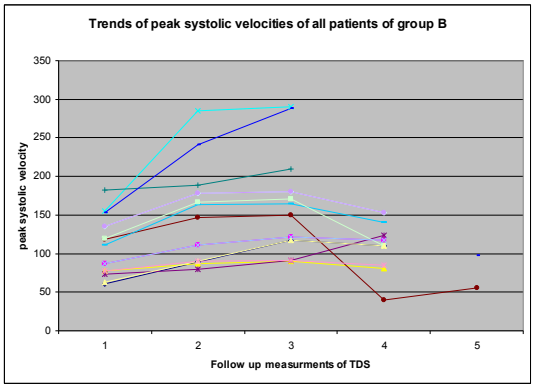


***Fig (6): trend of change in peak systolic velocity of all 15 pts of group B***

***Analysis of area under ROC curve revealed,*** at **PSV** 172 cm /sec &area under the curve 0.75, sensitivity of 60% & specificity of 88% & the p value was 0.09 (figure 7).

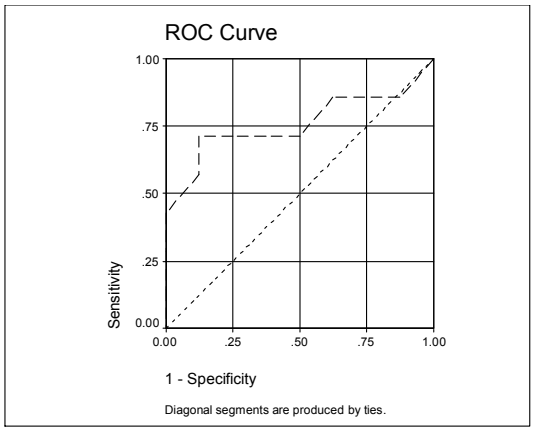


**Fig (7): ROC curve of peak systolic velocity.**

## 4. Discussion

Transcranial Doppler monitoring as a non invasive method to detect flow velocities is useful in almost all patients after onset of subarachnoid hemorrhage to detect early vasospasm and symptomatic ischemia from day 4-21. Peak systolic velocity could be a parameter to detect cerebral vasospasm. In our study, the peak systolic velocity >172 cm/sec was correlated to clinical cerebral vasospasm (delayed ischemic neurological deficit) with a sensitivity of 60% and a specificity of 88% and this implies urgent surgical or aggressive medical measures.

In recent years, considerable investigative interest has been directed at evaluation of frequency of cerebral vasospasm, delayed neurological deficit, clinical implications, predictors and outcome. The clinical vasospasm (DIND) in our study developed in 9 pts with the incidence of 30 % which is nearer to the incidence reported in the study by **Radanovic and Scaff** on 31 pts (36.6%) with SAH ***(11)***. Also, the study reported in 2008 by **Pan Yeal Han** and his colleagues on 40 pts , 30% of their pts developed clinical vasospasm ***(12)***. Nearly the same incidence of vasospasm was reported in pts after SAH, when **Fontanella** and his colleagues studied seven hundred and eighty six cases admitted within 48 hrs after SAH during the period from 1993 till 2005. They reported 27% of pts presented TCD velocities indicative of TCD vasospasm ***(13)***.

The Hunt and Hess scale has two advantages in measurements being relatively easy and widely used in neuroscience community ***(14).*** We assessed our pts on admission and daily by Hunt and Hess grading ***(10)*** scale which was not significant predictor of DIND through the course of hospitalization. There was no correlation between clinical evaluation and occurrence of DIND. **Inagawa *et al.,*** studied 150 patients, 93%with angiographic vasospasm , did not observe significant correlation between clinical status at admission and angiographic vasospasm severity ***(15)***, while **Hijdra *et al.*** using Hunt–Hess grades did not find a statistical correlation with vasospasm" ***(16)***. In similar to our study, **Fontanella *et al.,*** 2008, stated that; no statistical correlation between HESS & HUNT grading scale on admission, and vasospasm diagnosed by TCD ***(13)***.

Transcranial Doppler ultrasonography is based on the hemodynamic principle that the velocity of blood flow in a given artery is inversely related to the cross-sectional area of that artery, first used by **Aaslid** and his colleagues in 1982. In the study by **Rigamonti *et al.,*** 2008, "transcranial Doppler ultrasonography had evolved into an effective bedside tool to follow the progression of vasospasm but it is heavily operator-dependent "***(17)***. In similar, we found that Doppler is useful technique in monitoring clinical vasospasm in patients with SAH.

**Vora *et al.,*** 1999 investigated various TCD parameters including highest velocity, greatest one day increase in velocity before angiography, greatest velocity difference, consecutive number of days of velocity increase, largest right-left velocity difference and they concluded that TCD monitoring was not found to be useful for diagnosing symptomatic vasospasm ***(18)***. Also, in their meta-analysis including twenty-six studies, **Lysakowski *et al.,*** 2001 suggested that there was no evidence for any usefulness of TCD as a diagnostic tool for vasospasm and TCD could not be recommended as a screening method in patient with possible of vasospasm ***(19)***. In contrary and recently **Han *et al.,*** reported in their published study 2008 that ; "transcranial Doppler is useful tool for screening clinical vasospasm and recommended further prospective studies will be needed ***(12)***.

Since, **Aaslid *(15)*** and Lindegaard ***(20)*** have suggested that severe vasospasm was diagnosed by using criteria as mean flow velocity >200 cm/s , many investigators have studied cut-off values for TCD parameter to discriminate between patients with and without vasospasm. However, the optimal threshold of blood flow velocity for the diagnosis of vasospasm has not been clearly determined. In our study, we found that, peak systolic velocity >172 cm /sec, was correlated to clinical cerebral vasospasm (sensitivity 60% & specificity 88%). **Proust *et al.,* 2002** found that diagnostic sensitivity of TCD in vasospasm detection decreased from 83.6% for MCA aneurysm, to 66.6% for ICA aneurysm and 40.6% for anterior communicating arterial aneurysms ***(21)***.

**Aaslid *et al., 1982*** demonstrated an excellent positive correlation between TCD velocities and angiographic Vasospasm on MCA, but no correlation on ACA; the recorded velocity at MCA was already

higher than 120 cm/s ***(5)***. **Sloan *et al., 1989*** found 84% sensitivity and 89% specificity when the spasm segment was the MCA, using a velocimetric VSP threshold value of 130 cm/s ***(22)***.

Similarly color TCD study performed by **Mariak *et al.,*** has shown that the color TCD in the diagnosis of advanced MCA narrowing was very good, but the best-performing parameter was peak systolic velocity of 182 cm/s ***(23)***. TCD peak systolic velocity in our patients with DIND was greater than without. The least recorded velocities in our study was 163+_16.3 m/sec for pts developed DIND. **Sherry et al.,** 2008 found that TCD vasospasm was defined as any peak systolic middle cerebral artery velocity ($PSV_{MCA}$) >200 cm/s ***(24)***.

**Findlay and Vora**, 2000 reported that:" It would be reasonable to expect a positive predictive value (PPV) of at least 80% before undertaking more invasive measures and a negative predictive value (NPV) of at least 90% before repudiating the need to treat or further investigate vasospasm . In their study ,only velocities of <120 cm $s^{-1}$ (NPV = 94%) and ≥200 cm $s^{-1}$ (PPV = 87%) fulfill such criteria and are reliable enough to guide clinical decision-making for individual patients ***(2)***.

**Krejza *et al.,* 2003** studied standardization of flow velocities with respect to age and sex improved the accuracy of transcranial Doppler sonography of middle cerebral artery spasm. They prospectively studied 214 consecutive patients referred for cerebral angiography and demonstrated that"For distinguishing all or moderate to severe vasospasm from lesser grades of vasospasm, peak systolic velocity was the best parameter. Areas under ROC curves for all and moderate to severe middle cerebral artery spasms were 0.83 and 0.92, respectively. After standardization, the ROC areas increased significantly ($p < 0.05$) for all, to 0.86, and only slightly, to 0.93, for moderate to severe spasms. In their study, the optimal efficiency for peak systolic velocity of more than 182 cm/sec corresponds to moderate to severe vasospasm at middle cerebral artery ***(25)***.

In our study, we found that peak systolic velocity > 172cm /sec, was correlated with development of delayed ischemic neurological deficit and implies urgent surgical or aggressive medical measures, but there was no significant difference of percentage of change in peak systolic velocity from the baseline transcranial Doppler measurements.

Considering for discrepancy of absolute flow velocity from person to person in the various clinical settings, the differences of parameters in a serial test still be useful to generalize individual TCD data. **Naval *et al.,*** 2005 reported that relative changes in flow velocity in patient with aneurysmal SAH correlated better with clinically significant vasospasm than absolute flow velocity indices ***(26)***. On the other hand **Pan *yeal Han*** and his **colleagues, *2008*** reported the differences of TCD parameters between base line measurement and successive measurement in successive days. They found that best TCD parameters for the detection of clinical vasospasm were to be differences of blood flow velocities" ***(12)***. In contrary, we found no significance of trend of change in our patients studied with TCD especially in those developed DIND ,when compared to patients did not develop DIND .This could be explained as blood flow may be influenced by various clinical parameters that could influence the blood flow velocity.

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