



**SPONTANEOUS NON-ANEURYSMAL NON-TRAUMATIC
SUBARACHNOID HEMORRHAGE: PATIENT CHARACTERISTICS,
CLINICAL OUTCOME AND PROGNOSTIC FACTORS :- A TERTIARY CARE
CENTRE IN EASTERN INDIA**

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ABSTRACT

Background: Subarachnoid hemorrhage (SAH) is mainly caused by ruptured cerebral aneurysms but in up to 15% of patients with SAH no bleeding source could be identified. Our objective was to analyze patient characteristics, clinical outcome and prognostic factors in patients suffering from non-aneurysmal SAH.

Methods: From 2018 to 2020, data of 62 patients with non-aneurysmal SAH were prospectively entered into a database. All patients underwent repetitive cerebral DSA. Repeat DSA done to all patients. Outcome was assessed according to the modified Rankin Scale (mRS) (mRS 0–2 favorable vs. 3–6 unfavorable). Also, patients were divided in two groups according to the distribution of blood in the CT scan (perimesencephalic and non-perimesencephalic SAH).

Results: Out of 62 patients 02 patients comes to positive in repeat DSA. Out of 60 subjects, 21 (35%) were having nonperimesencephalic hemorrhage and 39 (65%) were having perimesencephalic hemorrhage. GCS grade ≤ 12 was reported among 23.81% of the subjects having non-perimesencephalic hemorrhage. Mean modified Fisher scale grading at admission among the study subjects was 2.92 ± 0.93 and 1.98 ± 0.87 with statistically significant difference as $p < 0.05$. At the end of 6 month, unfavorable outcome was revealed only in one subject (4.8%) having nonperimesencephalic hemorrhage.

Conclusions: Patients suffering from non-aneurysmal SAH have better prognosis compared to aneurysm related SAH and poor admission status was the only independent predictor of unfavorable outcome in the multivariate analysis. Patients with a non-perimesencephalic SAH have an increased risk of a worse neurological outcome. These patients should be monitored attentively.

KEYWORDS : Non-aneurysmal, Aneurysm, Perimesencephalic, Non-perimesencephalic, , Subarachnoid hemorrhage, SAH, DSA

BACKGROUND:-

subarachnoid haemorrhage (SAH) refers to the extravasation of blood into the subarachnoid space. Schematically, a differentiation can be made between primary SAH – bleeding directly into the subarachnoid space – and secondary SAH – the extravasation of blood into the subarachnoid space from a lesion within the brain^[1,2,3]. Spontaneous subarachnoid haemorrhage (SAH) is a lifethreatening condition most commonly caused by the rupture of an intracranial aneurysm [4, 5]. In 20 to 70% of patients with angiography negative SAH the blood distribution is described as perimesencephalic or prepontine [6]. Patients with perimesencephalic SAH are considered to achieve a good outcome and to have a lower risk of rebleeding [6,7]. As there are less or we can say limited study in Indian scenario till date so we wanted to do this study to know prognostic & risk factor and clinical outcome in angiographically negative spontaneous non-aneurysmal subarachnoid hemorrhage in Indian scenario.

METHODS

After exclusion of patients with traumatic SAH we reviewed 62 patients with SAH admitted in the department of neurosurgery, Bangur Institute of Neurosciences Kolkata (BIN) & SSKM Hospital, IPGME & R, Kolkata from December 2018 to December 2020. The study comprised of spontaneous subarachnoid hemorrhage patients diagnosed with initial non-contrast CT followed by CTA/MRA Brain and Digital subtraction angiography brain. Initial NCCT brain suggestive of subarachnoid hemorrhage and initial negative DSA patients can be divided into perimesencephalic and non perimesencephalic pattern.

The data was collected by a preformed structured interviewer-administered questionnaire that was pretested with modifications

made prior to its use in the study. The patients were interviewed that requests for the demographic, medical history and previous history of taking any medications, clinico-radiological status and clinical outcome. We assess the patients on detail history and clinical examinations. After this detail routine blood investigation with viral marker along with radiological investigation in form of NCCT brain, CT/MR angiography & Cerebral DSA. Secondary DSA positive patients excluded from study. Patients of non-aneurysmal spontaneous subarachnoid hemorrhage assessed by initial Hunt & Hess scale, GCS, modified fisher grade, WFNS grade (admission status) and modified Rankin scale for clinical outcome.

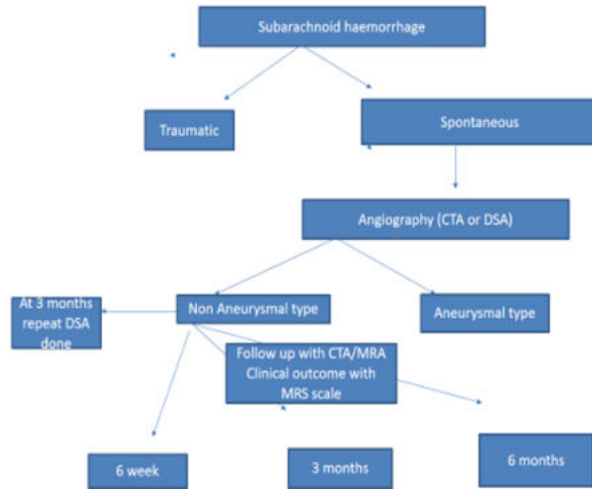
All patients admitted as case of spontaneous subarachnoid in SSKM & IPGME HOSPITAL Kolkata included in study but patients of traumatic SAH, lost to follow up, not giving consent, and diagnosed as structural or radiological aneurysm and AVM Or vascular malformation.

Patients were examined at admission, 6 week, 3 months & 6 months. Clinical outcome is studied with help of Modified Rankin Scale at regular interval 6 week, 3 months & 6 months. AT time of admission patients assess with help of GCS Score, Hunt & Hess scale, WFNS grading and bleeding pattern on Modified fisher grading on NCCT brain. Patients were divided into good grade (WFNS grades I – III) versus (vs.) poor grade (WFNS IV – V) on admission. Outcome was assessed according to the modified Rankin Scale (mRS) and stratified into favorable (mRS 0–2) vs. unfavorable (mRS 3–6) after 6 months.

Ethical clearance:

The study protocol for all procedures was approved by the Institutional Review Board for Ethical Clearance of IPGME, Kolkata and was

performed in accordance with the Code of Ethics of the World Medical Association according to the Declaration of Helsinki of 1975, as revised in 2000. All patients were asked to sign a written consent form prior to commencement of the study.



STATISTICAL ANALYSIS

Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and Fisher Exact Test. The level of significance was set at $p < 0.05$.

RESULTS:-

Patients characteristics :-

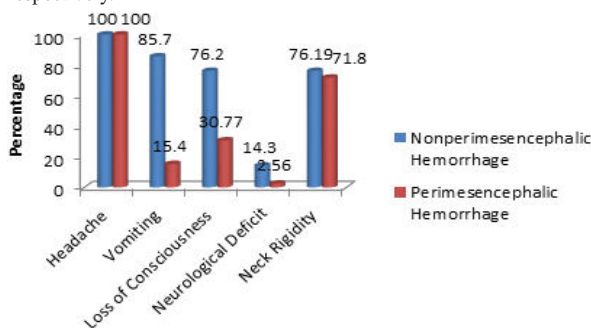
In our study, 61.9% and 69.23% of the subjects were male having nonperimesencephalic and perimesencephalic hemorrhage respectively. Mean age among subjects having nonperimesencephalic and perimesencephalic hemorrhage was 45.67 ± 11.39 and 43.03 ± 15.44 years respectively. In nonperimesencephalic hemorrhage group, maximum subjects were from 51-60 years of age group while in perimesencephalic hemorrhage group, maximum subjects were from 41-50 years of age group.

Misdiagnosis

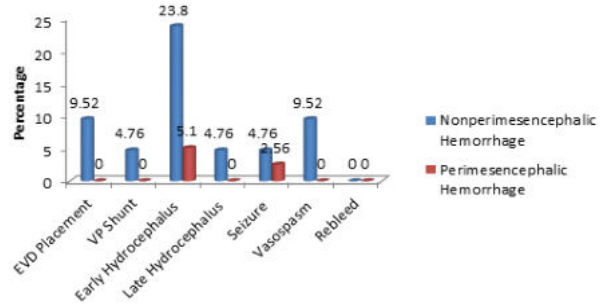
In our study, initially there were 23 subjects having nonperimesencephalic hemorrhage, out of which 2 (8.69%) turned out to be positive on second DSA. None of subjects with perimesencephalic hemorrhage turned out to be positive on second DSA.

Clinical Symptoms

In our study, headache was reported among all the subjects whether suffering from perimesencephalic or non-perimesencephalic hemorrhage. Vomiting and loss of consciousness was comparatively more in non-perimesencephalic hemorrhage group as compared to perimesencephalic hemorrhage with statistically significant difference as $p < 0.05$. Neurological deficit and neck rigidity was comparable among both the groups. Hypertension, diabetes mellitus, antiplatelet & anticoagulant and smoking was found among 52.38%, 42.86%, 19.05%, 23.8% and 43.59%, 30.77%, 0%, 35.9% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively.



Graph 1: Clinical symptoms among the study subjects



Graph 2: Complications among the study subjects

Admission

Hunt & Hess grading 3 and 4 was reported among 9.52%, 4.76% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively. When Hunt & Hess grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically insignificant as $p > 0.05$. In this study, WFNS grading 3 and 4 was reported among 14.3% and 2.56%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively. In our study, GCS grade ≤ 12 was reported among 23.81% of the subjects having non-perimesencephalic hemorrhage. GCS grade 15 was found among 38.09% and 66.67% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively. When GCS grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$. In this study, mean modified Fisher scale grading at admission among the study subjects was 2.92 ± 0.93 and 1.98 ± 0.87 with statistically significant difference as $p < 0.05$. Modified Fisher scale grading 1, 2, 3 and 4 was revealed among 14.29%, 9.52%, 66.67%, 9.52% and 58.97%, 5.13%, 33.3%, 2.56% of the subjects having non-perimesencephalic hemorrhage and perimesencephalic hemorrhage respectively. When modified Fisher scale grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$.

Modified Rankin (MR) Scale at different Intervals

At admission, Moderate and slight disability was found among 3 (14.3%) and 5 (23.8%) subjects having nonperimesencephalic hemorrhage while no moderate/slight disability was reported among subjects having perimesencephalic hemorrhage. Most of the subjects (64.1%) with perimesencephalic hemorrhage didn't have any significant disability. When subjects were compared w.r.t. MR scale at admission among according to nonperimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$. After 6 weeks, 3 months and 6 months; moderate disability was reported among 3 (14.3%), 2 (9.52%) and 1 (4.8%) subjects having nonperimesencephalic hemorrhage respectively. When subjects were compared w.r.t. MR scale at different intervals among according to nonperimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$.

Complications:-

Only 5.1% and 2.56% of the subjects with perimesencephalic hemorrhage were having complications viz. early hydrocephalus and seizure respectively. Complications viz. EVD placement, VP shunt, early hydrocephalus, late hydrocephalus, seizure and vasospasm was revealed among 9.52%, 4.76%, 23.8%, 4.76%, 4.76% and 9.52% of the subjects with nonperimesencephalic hemorrhage respectively. In overall study complication in form of hydrocephalus, need of VP shunt or Need of EVD or Vasospasm was more common among non-perimesencephalic however it comes to be insignificant. No mortality was seen in this study also no case of rebleed was seen among any patients.

DISCUSSION-

Spontaneous subarachnoid hemorrhage (SAH), characterized by bleeding into the subarachnoid space in the absence of trauma, is most often caused by the rupture of an intracranial aneurysm [8,9]

The majority of patients with non-aneurysmal SAH are in good clinical condition at admission [6,10,11,12,13]. perimesencephalic SAH is

often associated with favorable outcome compared to aneurysmal SAH. The present non randomized prospective study was conducted in the department of neurosurgery, Bangur Institute of Neurosciences Kolkata (BIN) & SSKM Hospital, IPGME & R, Kolkata.

In our study, 61.9% and 69.23% of the subjects were male having nonperimesencephalic and perimesencephalic hemorrhage respectively. Hence males were comparatively more as compared to females in the present study. Liang Xu et al [14], Asma Bashir et al^[15] Cody L. Nesvick et al^[16] males were comparatively more as compared to females in the present study. Mean age among subjects having nonperimesencephalic and perimesencephalic hemorrhage was 45.67±11.39 and 43.03±15.44 years respectively. Cody L. Nesvick et al^[16]. Alhoobi, et al^[17]. Akcakaya MO et al^[18] in their study found approximately similar mean age among the study subjects. 2 patients means 8.69% turned out to be positive on second DSA. None of subjects with perimesencephalic hemorrhage turned out to be positive on second DSA. In previous studies, the misdiagnosis rate of the initial DSA in nPMN-SAH patients varied greatly (misdiagnose rate from 4.7% to 45.9%), which is likely due to several factors, as previously mentioned. After pooling all the published studies, the overall misdiagnose rate was 12.5%, which is little higher than the findings at our institution.

In our study, headache was reported among all the subjects whether suffering from perimesencephalic or non-perimesencephalic hemorrhage. Vomiting and loss of consciousness was comparatively more in non-perimesencephalic hemorrhage group as compared to perimesencephalic hemorrhage with statistically significant difference as $p < 0.05$. Neurological deficit and neck rigidity was comparable among both the groups.

In a study by Alhoobi, et al^[17], headache in 73 patients (94.8%), along with vomiting in 24 patients (31.6%) and low level of consciousness in 8 patients 10.4%, all (100%) of them were of NPM. Asma Bashir et al^[15] in their study revealed that seven (9.5%) patients briefly lost consciousness at the time of ictus; among them one (1.4%) had a seizure. Two (2.7%) patients presented with abducens nerve palsy, and one (1.4%) with oculomotor nerve palsy. Hypertension, diabetes mellitus, antiplatelet & anticoagulant and smoking was found among 52.38%, 42.86%, 19.05%, 23.8% and 43.59%, 30.77%, 0%, 35.9% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively in the present study. Liang Xu et al^[19] in their study revealed similar findings.

David P. Bray et al^[20] also noted that 40% patients received antiplatelet drug and associated blood volume is significantly more in nPMN than PMN type SAH.

When Hunt & Hess grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically insignificant as $p > 0.05$. Similarly Asma Bashir et al^[15] in their study reported that HH grades 3 or above were mostly seen in patients with nPMSAH.

When WFNS grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$. Similarly Asma Bashir et al^[15] in their study reported that WFNS grades 3 or above were mostly seen in patients with nPMSAH.

When GCS grading at admission among the study subjects was compared according to non-perimesencephalic and perimesencephalic hemorrhage, it was found to be statistically significant as $p < 0.05$. In a study by Alhoobi, et al^[17], patients with NPM-SAH had initial severe symptoms with low GCS (GCS ≤ 12) as all patients with WFNS Grade IV had NPM SAH, and 3 of them had GCS < 10 as compared to the PM-SAH. In this study, mean modified Fisher scale grading at admission among the study subjects was 2.92±0.93 and 1.98±0.87 with statistically significant difference as $p < 0.05$. Akcakaya MO et al^[16] in their study too reported significant differences in Fisher grades were found between study groups at admission.

At admission, Moderate and slight disability was found among 3 (14.3%) and 5 (23.8%) subjects having nonperimesencephalic hemorrhage while no moderate/slight disability was reported among subjects having perimesencephalic hemorrhage. Most of the subjects (64.1%) with perimesencephalic hemorrhage didn't have any significant disability. Similarly Asma Bashir et al^[15] in their study

found that at discharge 11% of the subjects with non-perimesencephalic hemorrhage were having 3-6 mRS at discharge. Juergen Konczella et al^[21] also reported similar type of finding.

Complications viz. EVD placement, VP shunt, early hydrocephalus, late hydrocephalus, seizure and vasospasm was revealed among patients in study. In a study by Jobyna Whiting et al^[19], hydrocephalus necessitating temporary CSF diversion developed in 22 of these patients (25%); 12 (13%) ultimately required permanent CSF diversion. Clinically significant vasospasm developed in 4 patients (4%), and 2 (2%) had cerebral infarctions. Three patients (3%) died. Good and bad outcome status among the study subjects was found among 76.19%, 23.81% and 100%, 0% of the subjects having non-perimesencephalic and perimesencephalic hemorrhage respectively with statistically significant difference. Juergen Konczella et al^[21] also reported more good grade at admission in perimesencephalic vs. nonperimesencephalic type SAH.

CONCLUSION:-

Perimesencephalic and non-perimesencephalic SAH have similar presentation status. Favorable outcome is achieved in most patients. Poor admission status was the only independent predictor of unfavorable outcome in patients with spontaneous non-aneurysmal SAH. Managing SAH patients with negative initial DSA findings can be challenging. Based on the results of our present study and a review of the pertinent literature, the PMN-SAH subgroup usually has a benign clinical course and a repeat DSA very seldom reveals a ruptured intracranial aneurysm. More importantly, nPMN-SAH patients are associated with higher complication rate and higher incidence of an aneurysm. Therefore, we strongly recommend a repeat DSA in patients with nPMN-SAH pattern on initial imaging.

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