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Evaluation of Hemodynamic and Biochemical Parameters to Determine the Severity, Pattern, Location, and Therapeutic Modalities for Subarachnoid Hemorrhage

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Abstract— **Background**: Subarachnoid hemorrhage (SAH) accounts for 50% of hemorrhagic strokes. Very few hemodynamic and biochemical parameters predict the severity, pattern, location, and therapeutic modalities for SAH. This study explores various parameters for predicting SAH. **Material and methods:** A retrospective study of 68 SAH patients admitted to Intensive Care Units (ICUs) of a tertiary care hospital. Patient details were obtained from medical records. Descriptive statistics were used to elaborate on patient-related details. Correlation analyses were used. The first correlation analysis determined the correlation between biochemical and hemodynamic variables with SAH severity, location, and pattern. The second correlation analysis correlated the selection of the treatment modalities and its associated outcomes in terms of SAH severity, location, and pattern. **Results**: The mean age of the participants was 47.84 years and 55.8% were males, indicating that most SAH cases occur in middle-aged males. Few biochemical or hematological parameters, other than creatinine and INR (r=1.25), can differentiate between healthy and SAH patients. However, some parameters, such as fibrinogen levels (r= -0.867), high systolic and diastolic blood pressure (r=0.28 and r=0.38), PT, PTT, and electrolyte levels mediate the pattern, location, and size of aneurysms.**Conclusion:** As per the findings of our study, parameters such as serum sodium, serum chloride, serum phosphate, INR, creatinine, systolic blood pressure, diastolic blood pressure, hemoglobin, and platelet levels all influence SAH.

Keywords: Subarachnoid hemorrhage, Biochemical, Creatinine, INR, Hemodynamic

1. Introduction

Subarachnoid hemorrhage (SAH) is a serious and life-threatening condition resulting from blood accumulation between the arachnoid and the pia mater surrounding the brain. Hemorrhagic strokes are the most commonly reported strokes (20%), followed by intracerebral hemorrhage (10%) and SAH (10%). [1] It is important to treat SAH as a true emergency and treat it promptly. SAH can result from an aneurysmal rupture or a traumatic injury. [2] [3]

Around 80% of non-traumatic SAH cases are attributed to a ruptured secular aneurysm, particularly those located within the Circle of Willis and its branches. Other risk factors that amplify the occurrence of SAH are the presence of anticoagulation disorders, family history

of SAH, sickle cell anemia, bleeding diathesis, amyloid angiopathy, arterial dissections, arteriovenous malformations, and illicit drug use. [4–9] SAH can be divided into two types: traumatic and non-traumatic. Traumatic SAH (tSAH) occurs at the base of the skull at the site of a skull fracture and intracerebral contusion. Non-traumatic SAH is usually described as a burst of saccular and fusiform aneurysms. [10] Patients diagnosed with SAH often complain of a 'thunderclap headache', manifesting as a severe headache that develops within seconds to minutes, with maximal intensity at the onset. [11] Only 10% of patients with 'thunderclap headache' are diagnosed with SAH. Other clinical manifestations are drowsiness, stupor, seizures, neck stiffness, ECG changes, positive Kernig's sign, positive Brudzinski sign, and a history of head injury. [12] Imaging predictors employed at the presentation for SAH are a non-contrast head CT scan and an MRI scan. If done within 6 hours of symptom onset, almost 99% of cases can be picked up on CT. If the patient presents after 6 hours, then a lumbar puncture is indicated. [13–15] Unfortunately, SAH is associated with poorer outcomes. [16]

Knowledge of various biochemical parameters and their clinical correlation is crucial in terms of SAH prevention. [17] This paper presents the changes in biochemical and hemodynamic parameters associated with SAH. The evidence suggests that different biochemical and hemodynamic parameters determine the diagnostics and prognostics of SAH. However, there are very few studies that have evaluated the fluctuations in the biochemical and hemodynamic parameters in terms of severity, location, and pattern of SAH. We, therefore, conducted a retrospective study to analyze various biochemical or hemodynamic parameters that differentiate healthy and SAH individuals.

2. Material and methods

A retrospective study was conducted among patients with Subarachnoid Hemorrhage (SAH) admitted to the Intensive Care Units (ICUs) of King Abdulaziz University Hospital (KAUH). Details of patients admitted were identified from the medical records located at KAUH and were entered into a database by a senior nurse or doctor. Data collected included demographic information and clinical information including age, gender, medical history, medication history, presenting symptoms, a pattern of SAH, and treatment modalities. Using this database, 68 patients were identified between 2015 and 2022.

Descriptive statistics have been used to describe patient details, demographic details, and clinical outcomes. A first correlation analysis was undertaken to evaluate if a specific set of biochemical and hemodynamic variables could signify the severity, pattern, and location of SAH as well as the size of the aneurysm. A second correlation analysis was conducted to identify the correlation between the selection of the treatment modalities and its associated outcomes in terms of SAH severity, location, and pattern. Data analysis was done using SPSS version 21 software. A p-value less than <0.05 was assigned significance in this study.

Given that this was a retrospective study of electronic health records, no permission was required from the study participants. Nevertheless, the study was conducted in line with the Declaration of Helsinki and approved by the Ethics Committee of the Hospital and the

Institutional Review Board of the study site (HA-02-J-008).

3. Results

This retrospective cohort study comprised 68 participants [(Mean age: 47.84 years: Standard deviation: 18.24 years) (Male=38, 55.8%, Female=30, 44.2%), which reflected that most of the cases of SAH occur during middle age and it is more prevalent in males (Table 1).

Table 1 – Patient Demographics and SAH characteristics with treatment outcomes

Parameters	Values n (%)
Age in years (Mean/SD)	47.84 (18.24%)
Gender (n/%)	
Male	38 (55.8%)
Female	30 (44.2%)
Medical history (n/%)	
No	38 (55.8%)
Yes	30 (44.2%)
Medication History (n/%)	
No medication	59 (86.7%)
Anticoagulants	1 (1.5%)
Anti-platelets	8 (11.8%)
Presenting Symptoms (n/%)	
Asymptomatic (mild)	7 (10.3%)
Drowsy	28 (41.2%)
Severe Headache	29 (42.6%)
Stupor	4 (5.9%)
The pattern of SAH (n/%)	
Traumatic SAH (tSAH)	22 (32.4%)
Non-tSAH	46 (67.6%)
• *Aneurysmal SAH (aSAH)*	• 32 (47.1%)
• *Peri-mesencephalic SAH*	• 5 (7.3%)
• *Cortical SAH*	• 1 (1.5%)
• *Undocumented*	• 8 (11.7%)
Treatment Modalities	
Endovascular management	13 (19.1%)
Hematoma Evacuation	2 (2.9%)
No immediate management	43 (63.2%)
Surgical clipping (with and without hematoma evacuation and endovascular management)	10 (14.8%)

Most of the patients (55.8%) had no underlying clinical history. Reported clinical history included diabetes, hypertension, atrial fibrillation, and cancer. The study showed that the risk of SAH is higher in those without a medical history compared to those with a medical history (55.8% versus 44.2%). The involvement of medication history in increasing the risk of SAH seems remote as 86.7% had no medication history, while 1.5% were on anticoagulants and

11.8% were on antiplatelets. The percentage of traumatic and non-tSAH that was depicted was 32.4%, and 67.6%, respectively. The common presenting symptom of SAH in these patients was severe headache (85.3%), and 67.7% of the patients presented these symptoms within 24h of onset of SAH. However, 10.3% of the patients were asymptomatic. Also, a third of the patients (33.3%) presented the symptoms after 24 hours. This highlighted that there is a necessity to evaluate the biochemical and hemodynamic parameters that could ensure the early diagnosis and severity of SAH. The major immediate treatment modalities used in the study were endovascular management and surgical clipping (19.8% and 14.7%). The biochemical and hemodynamic parameters of the patients (n=68) are depicted in Table 2.

Table 2 - Biochemical and hemodynamic parameters of SAH patients (n=68)

Parameters	**Values in Mean (SD)**
Hemodynamic Variables	
Temperature upon presentation (centigrade)	36.39 (0.48)
Heart rate upon presentation (beats/min)	77.04 (12.42)
Systolic blood pressure upon presentation (mmHg)	144 (55.2)
Diastolic blood pressure upon presentation (mmHg)	80 (33.7)
Respiratory rate upon presentation (breaths/min)	20.75 (1.61)
Oxygen saturation upon presentation (%)	96.54 (1.57)
Biochemical Parameters	
BUN mg/dl	6.8 (9.5)
Creatinine mg/dl	139.9 (29.18)
K+ (mEq/L)	3.73 (0.72)
Na+ (mEq/L)	137.26 (6.95)
Cl- (mEq/L)	103.15 (5.72)
Phosphate (mg/dl)	1.15 (0.55)
Magnesium (mEq/l)	2.4 (0.2)
Calcium (mg/dl)	2.09 (0.25)
Random blood sugar (mmol/L)	9.23 (4.22)
PT	12.8 (3.6)
PTT	30.93(7.74)
INR	1.25 (2.75)
Lactic acid mmol/l	3.02 (5.67)
Albumin g/L	35.33 (6.02)
Fibrinogen mg/dl	287.5 (NA)
Hematological Variables	
Hemoglobin (mg/dl)	13.2 (1.68)
White blood cells (WBC) (per microlitre)	12.6 (3.85)
Platelet (per microlitre)	256.25 (69.9)

Most of the hemodynamic variables (except systolic blood pressure (SBP)) such as body temperature, heart rate, diastolic blood pressure (DBP), and hemoglobin levels were within

the normal range, and this signifies that these variables are not diagnostic markers for SAH. However, the mean SBP, respiratory rate, and WBC were mildly elevated, and the mean SPO2 was mildly lower, which again signified that the respective variables are not specific to the diagnosis of SAH.

In terms of the biochemical parameters, the study showed that only mean creatinine levels were mildly elevated, and the International Normalized Ratio (INR) was modest (1.25) in the study population. This indicates that a modest increase in INR is the single and independent predictor for SAH. The INR values were obtained before treatment was initiated. On the contrary, the prothrombin time (PT) and partial thromboplastin time (PTT) were within the normal range. Therefore, the mean values of different biochemical and hemodynamic parameters rarely indicate that there are no specific hemodynamic or biochemical markers for the diagnosis of SAH, except for high creatinine levels and INR.

A correlation analysis was undertaken to evaluate if a specific set of biochemical and hemodynamic variables could signify the severity, pattern, and location of SAH as well as the size of the aneurysm (Table 3). Although the biochemical analysis indicated that there are rarely any hemodynamic variables that differentiate SAH from healthy subjects, it was pertinent to identify if any biochemical variable was related to a pattern of SAH, location of aneurysms, or aneurysm size.

Table 3 - Correlation between biochemical and hemodynamic variables with SAH severity, location, and pattern.

Variables	**Pattern of SAH**	**Location of aneurysm**	**Size (mm)**
Temperature upon presentation	0.068368	-0.16849	-0.17573
Heart rate upon presentation	-0.16586	0.066029	0.242746
Systolic blood pressure upon presentation	0.288523	-0.35116	0.267302
Diastolic blood pressure upon presentation	0.38736	-0.37067	0.238161
Respiratory rate upon presentation	-0.07858	0.256776	0.009672
Oxygen saturation upon presentation	0.077658	-0.12324	0.198446
Hemoglobin	0.145986	-0.11723	-0.41786
WBC	-0.17825	0.306706	0.134549
Platelet	-0.06001	-0.15609	0.394066
BUN	0.126939	0.052954	-0.31622
Creatinine	0.107787	0.104186	-0.17199
K+	0.075783	0.005795	-0.09301
Na+	-0.22444	0.184359	-0.25642
Cl-	-0.23892	0.315254	-0.02791
Phosphate	0.260158	0.00296	-0.24653
Magnesium	-0.0445	-0.2232	0.260729
Calcium	-0.18783	0.105763	-0.04605

Random blood sugar	0.037575	0.171522	-0.00763
PT	-0.07768	0.275193	-0.26593
PTT	0.025993	0.193826	0.371217
INR	-0.0406	0.195674	-0.21338
Lactic acid	0.10191	-0.08423	0.401258
Albumin	-0.14547	-0.05218	-0.12534
Fibrinogen	-0.8667	-0.34364	-1

The pattern of SAH was moderately correlated with high systolic and diastolic blood pressure (r=0.28 and r=0.38). However, the pattern of SAH was weakly correlated with Na+, Cl-, and phosphate levels indicating that the lower the serum level of electrolytes, the more the pattern toward tSAH (tSAH). We found that the pattern of SAH was significantly correlated with fibrinogen levels (r=-0.867), with lower fibrinogen levels being associated with unfavorable outcomes in poor-grade aSAH. Therefore, if the level of fibrinogen is lower, the size of aneurysms will increase as shown (r=-1) because the albumin-fibrinogen ratio would be higher. Our study showed that higher fibrinogen levels are significantly correlated with increased severity of SAH as depicted by both CT and Modified CT (r=0.57 and r=0.36).

The correlation analysis further reflected that the location of the aneurysm is moderately and negatively correlated with both systolic and diastolic blood pressure indicating that low SBP and low DBP are more a feature of SAH location in the anterior communicating artery (r=-0.35 for SBP and -0.37 for DBP). Similarly, both SBP and DBP were weakly and positively correlated with the size of the aneurysm. The correlation analysis further showed that low hemoglobin levels and high platelet levels were associated with an increased size of aneurysms respectively (r=-0.41 and r=0.39). Rather, albumin had a weak and negative correlation with the severity of SAH, and that too was depicted by conventional CT but not for the modified CT.

The correlation matrix (Table 4) shows that the severity of SAH (as depicted by the Modified Fisher CT) is positively but moderately correlated with the selection of treatment modality (r=0.3), and the pattern of SAH is also correlated with the treatment modality (r=-0.22). This finding suggests that surgical management is more solicited in cases of severe SAH or trauma, while endovascular or no immediate management seems appropriate for non-tSAH (such as aSAH).

Table 4 - Correlation between the selection of the treatment modalities and its associated outcomes in terms of SAH severity, location, and pattern.

Parameters	**Modified Fisher CT**	**Pattern of SAH**	**Aneurysm**		**Treatment**
			Location	**Size**	
CT findings					
Modified Fisher CT	1				
Pattern of SAH	-0.08	1			
Location of aneurysm	-0.04	-0.49	1		

Aneurysm size in mm	-0.14	NA	-0.54	1	
Treatment modality	0.35	-0.22	-0.1	0.1	1
Intervention since presentation	-0.21	0.066	-0.19	-0.3	-0.09
External ventricular drain	0.06	-0.15	-0.04	0.11	0.486
Modified Rankin Score (GCS)	0.34	-0.06	0.015	0.65	0.022
Length of hospital stay	-0.04	0.011	-0.19	0.02	0.324

The correlation further showed that if the external drain is applied, the length of stay (LOS) significantly increases. This assumption was supported by the correlation that as the treatment modality shifted to surgical management, the LOS was significantly increased (r=0.32). Table 4 also confirmed that the severity of SAH (in the modified Fisher scale) is associated with mortality, and a Modified GCS ranking score less than 6 was correlated with death (r=0.34). However, as the LOS was insignificantly related to the modified ranking score, it indicated that LOS might not be significantly associated with treatment outcomes.

4. Discussion

We found that the mean age for the incidence of SAH was 47.84 years. This is in accordance with the findings of a meta-analysis conducted by Rooij et al where the mean age for the incidence of SAH was 35 years and for every year increase in mean age, the incidence becomes 1.06 times higher. [1] Gender predisposition towards aSAH was higher among females and for tSAH was higher among males. A similar finding was addressed by Marchis et al in their retrospective cohort study where females outnumbered males among the aSAH patients identified. [18]

In a study conducted by Kralova et al, the authors have elaborated on the importance of assessing serum creatinine values as a predictor for SAH. As per their findings, patients with SAH had significant subnormal creatinine values. [19] This aligns with the findings of our study where creatinine values have slight changes among SAH patients.

The correlation analysis has revealed that lowered levels of serum electrolytes suggest tSAH. In the study conducted by Maysam et al, it was shown that hyponatremia was the most common electrolyte imbalance after an aSAH. As per their findings of all the patients admitted, 15.1%, 22.6%, and 28.3% of patients presented with hyponatremia on the 1st, 3rd – 5th, and 7th – 10th day, respectively. [20] Similarly, Chandy et al have also found that reduced sodium levels were associated with increased occurrence of cerebral vasospasm after an aSAH. [21] Likewise, Sherlock et al, conducted a retrospective study among 316 patients to analyze the role of hyponatremia among patients with aSAH. As per their study, 56% of their patients presented with hyponatremia that caused an increased length of hospital stay. Also, hyponatremia may develop after 7 days following an SAH. [22] Moreover, in a study conducted by Junttila et al, the authors demonstrated that the frequency of hypophosphatemia (70%) was higher during the earlier phase of the hospital stay in patients with non-tSAH. [23] Therefore, in agreement with the previous studies the current study has elaborated on lowered electrolyte (sodium, chloride, phosphate) levels in determining the diagnosis of SAH, possibly tSAH.

Previous studies have suggested that fibrinogen levels less than 2.5 g/L are associated with poor prognostic outcomes in poor-grade aSAH. [24] [25] Previous studies have also suggested that the albumin-fibrinogen ratio is a significant predictor for the severity of SAH as well as prognostic outcomes. [26] A similar finding was seen in our study where low fibrinogen levels had significantly correlated with the pattern of SAH. However, some studies have individually projected high fibrinogen levels to the severity of SAH. The relation between high fibrinogen level and severity is supported by the evidence that fibrinogen could increase platelet aggregation and act as a pro-inflammatory cytokine which increases the chances of vasoconstriction and SAH. [27] Hence, it can be concluded that fibrinogen levels correlate with the pattern and severity of SAH.

Blood pressure regulation is an important aspect of SAH treatment particularly to treat re-bleeding and delayed cerebral ischemia. [28] As per the findings of our correlation analysis, it can be inferred that low SBP and low DBP indicate the location of SAH and weakly affect the size of the aneurysm. In alliance with our findings Subhas et al, have stated in their systematic review that blood pressure variability is an excellent predictor of aSAH prognosis and treatment outcomes. [29] Also, low hemoglobin levels in our study were associated with increased aneurysm size, thus risking hemorrhage. In a study conducted by Andreas et al, the authors concluded that anemic patients are associated with worse outcomes following a SAH. Also, patients with anemia are more likely to be vulnerable to secondary brain injury due to reduced oxygen supply. [30] Similarly, higher platelet activation and inflammation occurring shortly after a SAH are associated with early brain damage, and higher platelet levels may also be utilized as a parameter to guide SAH diagnosis and treatment. [31] Low albumin levels have a weak correlation with the severity of SAH. Despite the weak correlation, high albumin levels could lower the severity of SAH as they act as anti-inflammatory molecules and reduce the risk of vasoconstriction as well as oncotic pressure.

The findings of our study also indicate that treatment and severity of SAH are correlated with the treatment modality. Similarly, to the findings of Sarah et al, the application of an external drain was found to increase the length of hospital stay in our study. [32] However, our findings have also found that the length of hospital stay does not affect the treatment outcomes among SAH patients.

3. Conclusion

There are few biochemicals or hemodynamic parameters, apart from creatinine and INR, that can aid the diagnosis of SAH. However, parameters such as fibrinogen levels and blood pressure, PT, PTT, and electrolyte levels can mediate the pattern, location, and size of aneurysms. Furthermore, the severity of SAH and pattern of SAH significantly correlate with the treatment modality of choice.

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