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ORIGINAL RESEARCH **INTENSIVE CARE**

Mortality among patients with subarachnoid hemorrhage: a retrospective study

Anees A. Sindi[1], Ibrahim Abushoshah[2], Diyaa H. Bokhary[3], Sultan M. Banser[4], Wejdan H. Bedaiwi[5], Khalid M. Bajuneid[6], Haifa M. Algethamy[7]

Authors' Affiliation:

1. Anees A. Sindi, Associate Professor of Anesthesia and Critical Care, Faculty of Medicine, King Abdulaziz University / Pulmonary & Critical Care Consultant, International Medical Center, Jeddah, Saudi Arabia; E-mail: asindi2@kau.edu.sa; ORCID {0000-0002-5854-6298}
2. Ibrahim Abushoshah, Department of Anesthesia and Critical Care, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; E-mail: Iabushoshah@kau.edu.sa
3. Diyaa H. Bokhary, Senior Resident, Department of Emergency Medicine, King Abdulaziz University Hospital, Jeddah, Saudi Arabia; E-mail: diyaabokhary@gmail.com;
ORCID iD: {0000-0002-7374-3329}
4. Sultan M. Banser, Medical Student, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; E-mail: Sultan.ban50@gmail.com
5. Wejdan H. Bedaiwi, Medical Student, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; E-mail: wbedaiwi@stu.kau.edu.sa
6. Khalid M. Bajunaid, Department of Surgery, Faculty of Medicine, University of Jeddah, Jeddah, Saudi Arabia; E-mail: Kbajunaid@uj.edu.sa; ORCID {0000-0002-7925-5959}
7. Haifa M. Algethamy, Associate Professor, Faculty of Medicine, King Abdulaziz University / Consultant, Anesthesia & Critical Care Department, King Abdulaziz University Hospital, Jeddah, Saudi Arabia; E-mail: Halgethami@kau.edu.sa; ORCID {0000-0003-1381-521X}

Correspondence: Anees A. Sindi, E-mail: ansindi@imc.med.sa / asindi2@kau.edu.sa

ABSTRACT

Background & Objective: Subarachnoid hemorrhage (SH) accounts for 50% of hemorrhagic strokes. Few individuals present with 'thunderclap headaches', resulting in delayed diagnoses of aneurysmal SH (aSH). We conducted this retrospective study to explore factors for predicting the risk, severity and mortality patterns of aSH and traumatic SH (tSH).

Methodology: A retrospective study was conducted on 68 SH patients admitted to Intensive Care Units (ICUs) of a Middle East tertiary care hospital. Medical history, demographics, risk factors, outcome and the type of SH were evaluated.

Results: The mean age of the patients was 47.84 ± 18.24 y, and 38 (55.8%) were males, showing most SH cases occur in middle-age and in males. Majority 59 (86.7%) of the patients presented with risk factors such as trauma (35%), hypertension (37%), anti-thrombotic use (15.25%), alcoholism (3%) and smoking (1.5%). The regression model showed age and risk factors significantly influence the type and severity of SH ($P < 0.05$). The mortality was significantly higher in those suffering from traumatic SH compared to non-traumatic SH (84.6% versus 10.5%, $P < 0.0061$).

Conclusion: Age, male gender and risk factors predispose the type and severity of SH. Mortality rates are higher among traumatic SH in comparison to non-traumatic SH patients.

Abbreviations: SH - Subarachnoid Hemorrhage; aSH - Aneurysmal Subarachnoid Hemorrhage; tSH - Traumatic Subarachnoid Hemorrhage; WFNS - World Federation of Neurological Surgeons; MRI - Magnetic resonance imaging

Key words: Subarachnoid hemorrhage; Risk Factors; Severity; Classification; WFNS

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1. INTRODUCTION

Subarachnoid hemorrhage (SH) is a serious and life-threatening condition that results from the accumulation of blood between the arachnoid and the pia mater surrounding the brain. Typically, 20% of the strokes reported are hemorrhagic, out of which 10% are intracerebral hemorrhages and the other 10% are SH.[1] It is important to treat SH as a true emergency and treat it promptly. SH can result from an aneurysmal rupture or a traumatic injury.[2,3]

Around 80% of non-traumatic SH are attributed to a ruptured saccular aneurysm, particularly those located within the Circle of Willis and its branches. Other risk factors that amplify the occurrence of SH are the presence of anticoagulation disorders, family history of SH, sickle cell anemia, bleeding diathesis, amyloid angiopathy, arterial dissections, arteriovenous malformations, and illicit drug use.[4–9] SH can be divided into two types: traumatic and non-traumatic. Traumatic SH occurs at the base of the skull at the site of a skull fracture and intracerebral contusion. Non-traumatic SH is usually described as a burst of saccular and fusiform aneurysms.[10] Patients diagnosed with SH often complain of a 'thunderclap headache' that manifests as a severe headache that develops within seconds to minutes and with maximal intensity at onset.[11] Unfortunately, only 10% of patients with 'thunderclap headache' are diagnosed with SH. Other clinical manifestations are drowsiness, stupor, seizures, neck stiffness, ECG changes, positive Kernig sign, positive Brudinski sign, and a history of head injury.[12] Imaging predictors employed at the presentation for SH are a non-contrast head CT scan and an MRI scan. If done within 6 h of symptom onset, almost 99% of cases can be picked up on CT. If the patient presents after 6 h, then a lumbar puncture is indicated.[13–15] Unfortunately, SH is associated with a poor outcome.[16]

Knowledge of preventable risk factors is crucial in terms of SH prevention.[17] We, therefore, conducted a retrospective study to analyse the various risk factors for the predisposition to SH, the common presenting symptoms, CT findings, and the location of the aneurysm, the desired tool for severity assessment and the mortality / discharge outcome. The main aim of the study was to compare the mortality rate among those suffering from traumatic SH with non-traumatic SH.

2. METHODOLOGY

A retrospective study was conducted among patients with subarachnoid hemorrhage (SH) admitted to the Intensive Care Units (ICUs) of a tertiary care hospital in the Middle East. Given that this was a retrospective study from 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).

Details of patients admitted were identified from the medical records located at King Abdulaziz University Hospital (KAUH) and entered into a database by a senior nurse or a doctor. Demographic and clinical information was collected, including the history of medical illness like diabetes, hypertension, congestive cardiac failure, atrial fibrillation, etc., history of trauma, risk factors, and medication history including anticoagulants, antiplatelet drugs, etc. The presenting symptoms, time of onset of symptoms, and CT scan findings were noted. The length of hospital stay, mortality outcomes and mortality rates were also noted. Based upon these criteria, 68 patients were identified between 2015 and 2022 and included in the study.

We estimated the power of the study considering 2.4% of Saudi Arabians, out of the total population of 36,000,000 (as of now) suffer from SAH/year. Thus, the

Table 1: Baseline characteristics of the patients

Parameters	Values
Age in years (Mean ± SD)	47.84 ± 18.24
Gender	
Male	38 (55.8)
Female	30 (44.2)
Presence of Risk Factors	
No	9 (13.3)
Yes	59 (86.7)
Risk factors (n = 59)	
Hypertension alone	22 (37.3)
Hypertension with trauma	3 (5.1)
Hypertension with smoking	1 (1.7)
Trauma	21 (35.6)
Smoking	1 (1.7)
Alcoholism	2 (3.4)
Anti thrombotics	9 (15.2)
Comorbidity (n = 20)	
Diabetes	13 (65)
Cancer	2 (10)
Atrial fibrillation	3 (15)
Congestive heart failure	2 (10)
Medication History	
No medication	59 (86.7)
Antiplatelet / Anticoagulant drugs	9 (13.2)
Anticoagulant	1 (1.4)
Antiplatelets	8 (11.7)

Data presented as n (%)

Table 2: Presentation and the outcome of the patients (n = 68)

Parameter		n (%)
Time to onset of symptoms to the presentation	< 24 h	46 (67.64)
	Between 24 to 72 h	15 (22)
	>72 h	7 (10.2)
Presenting symptoms (Hunt and Hess Grade Classification)	Asymptomatic (mild)	7 (10.3)
	Drowsy	28 (41.2)
	Severe Headache	29 (42.6)
	Stupor	4 (5.9)
CT scan findings	SH without Midline Shift	58 (85.2)
	SH with Midline Shift	9 (13.2)
	Hydrocephalus	1(1.4)
Modified Fischer Grade CT appearance	Grade 1: Thin SH with no IVH	32 (47)
	Grade 2: Thin SH with IVH	1(1.4)
	Grade 3: Thick SH with no IVH	8 (11.7)
	Grade 4: Thick SH with IVH	5 (7.3)
Pattern of SH	Traumatic SH (tSH)	22 (32.6)
	Non-Traumatic SH	46 (67.6)
	○ *Aneurysmal SH (aSH)*	32 (47)
	○ *Peri-mesencephalic SH*	5 (7.3)
	○ *Cortical SH*	1 (1.4)
	○ *Undocumented*	8 (11.7)
Location of aneurysms (n = 32)	Anterior Communicating Artery	17 (53.1)
	Internal Carotid Artery	2 (6.2)
	Middle Cerebral Artery	5 (15.6)
	Right Internal Carotid Artery	1 (3.1)
	Right Middle Cerebral Artery	1 (3.1)
	V4 of Left vertebral artery	1 (3.1)
	Not documented	5 (15.6)
Mortality outcomes (n = 68)	Death	8 (11.7)
	Discharge from Hospital	60 (88.3)
Mortality as per Traumatic (n = 26) and Non-Traumatic SH (n = 38)	Traumatic SH (tSH)	6/22 (27.27)
	Non-traumatic SH including aSH	2/46 (4.34)
Length of stay (Days in hospital) (Mean ± SD)		21.72 ± 19.52

Data presented as n (%)

sample size required for the study was 36 patients or more to give the power of the study to 95%. Our sample size is 68, so the power is more than 95%.

SH was defined by the presence of bleeding in the subarachnoid space, confirmed by either imaging or by sampling of the CSF examination.[2] SH was divided into traumatic (tSH) and non-traumatic SH (aSH) based on the history of trauma. Traumatic SH occurs at the base of the skull at the site of a skull fracture and intracerebral contusion. Non-traumatic SH is usually described as a burst of saccular and fusiform aneurysms.[10] Co-morbidities like hypertension, diabetes, etc. were diagnosed based on the standard procedure.

Statistical analysis

Descriptive statistics have been used to describe the patient details, demographic details, and clinical outcomes. Correlation analysis was done to evaluate the predisposing factors for the severity, pattern, and location of SH that ranged from demographics and clinical parameters as well as the clinical outcomes driven by the severity, pattern, and location of SH. Logistic regression analysis was done with the severity of SH (CT) as the dependent variable, and age, gender, onset of symptoms, type of symptoms, medical history, medication history, and ethnicity (nationality) as the independent variables to identify the risk factors. A second regression analysis was also done to evaluate if the severity of SH significantly influenced mortality outcomes. Data analysis was done using SPSS version 21 software. P value less than <0.05 was assigned significant in this study.

3. RESULTS

During this 7-year retrospective cohort study 68 patients were identified with SH. The baseline demographic data of the patients are given in Table 1, which reflect that most of the cases of SH occur during middle age and it is more prevalent in males. Patients presentation patterns at the time of admission and the final outcome of the patients are presented in Table 2.

In our study, 9 (13.3%) of the patients had no risk factors, while 59 (86.7%) of the patients presented with the risk factors such as trauma 21(35%), hypertension 22 (37%), smoking 1 (1.5%), alcoholism 2 (3%), and antithrombotic drugs 9 (15.25%). The involvement of medication history in increasing the risk of SH seems remote as 59 (86.7%) patients presenting with SH did not exhibit any medication history, while one patient was on anticoagulants and 8 were on antiplatelets.

Figure 1: Hospital mortality in traumatic and non-traumatic SH groups

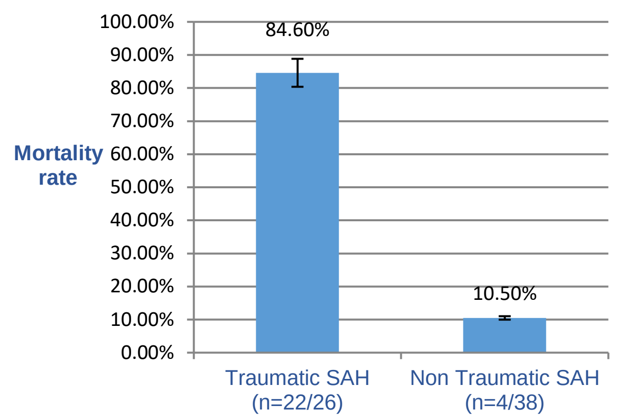

Figure 1: Comparative mortality in two types of SH

The common presenting symptom of SH in these patients was severe headache (85.2%), and 67.64% of the patients presented these symptoms within 24 h of onset of SH. However, 7 patients were asymptomatic. The CT scan findings depicted the severity of SH, which showed that 58 (85.2%) of the patients presented with SH without midline shift, while the modified Fischer Grade CT assessment showed that 32 (47%) of the patients exhibited Grade 1 SH.

The percentage of traumatic and non-traumatic SH was calculated in the study to be 32.6% and 67.6%, respectively. The most common non-traumatic SH in the study was aneurysmal SH (n = 32/68; 47%). The prevalence of the aneurysm was more in the anterior communicating artery and V4 of the left vertebral artery; 53.1%, and 10.2%, respectively.

The outcome analysis showed that the overall mortality was 11.8%, while 88.2% (60/68) of the patients were discharged successfully from the hospital. The mortality was significantly more in patients admitted with traumatic SH (6/22) than in the non-traumatic SH (2/46) patients (84.6% versus 10.5%; P < 0.0061) (Figure 1).

The correlation analysis (Table 3) showed that age positively and significantly correlated with the severity of SH as depicted for conventional CT findings (r = 0.23) and Modified Fischer Grade CT (r = 0.24). However, age is weakly correlated with the pattern and location of SH. Gender was positively and significantly correlated with the pattern of SH (r = 0.24), with males being more predisposed to peri-mesencephalic tSH while females were more predisposed to non-traumatic aSH. The correlation analysis further showed that medical history weakly but significantly (r = 0.2) influenced the pattern of SH but not the severity (r = 0) nor location of SH (r = 0). However, the number of risk factors was negatively related to SH severity (r = -0.1) with CT but significantly with modified Fischer CT (r = -0.4). Medication history was only weakly correlated with the location of SH (aneurysm) (r = 0.2). The onset of symptoms was negatively correlated with the presenting symptoms. Presenting symptoms significantly and positively correlated with the severity of SH (r = 0.2) and location

Table 3: Correlation analysis

	Age	*Gender*	*Medical history*	*Risk factors*	*Medication history*	*Presenting symptom*	*Time from Onset*	*CT finding*	*Modified Fisher*	*Pattern of SH*	*Aneurysm location*	*Hospital outcome*
Age	1											
Gender	-0	1										
Medical history	0.59	0.09	1									
Risk factors	-0.3	0.18	-0	1								
Medication history	0.37	0.1	0.6	-0	1							
Presenting symptoms	-0.2	0.07	-0	0.51	-0.1	1						
Time from Onset	0.08	0.01	0.3	-0.2	0.1	-0.3	1					
CT findings	0.23	0.04	0	-0.1	-0.1	0.2	0.1	1				
Modified Fisher grade =	0.24	-0.07	0	-0.4	-0.1	-0	0.1	0.5	1			
Pattern of SH	0.15	0.24	0.2	-0.2	-0	-0.1	0	0	-0.1	1		
Location of aneurysm	-0.2	-0.01	-0	0.77	0.2	0.51	-0.1	0.2	-0	-0.5	1	
Hospital outcome?	0.01	-0.04	0.1	0.04	0.04	0.23	0.2	0.3	0.4	-0.1	0.2	1
Length of hospital stay	0.15	-0.15	0.3	-0.3	-0	-0.2	0	0	-0	0.01	-0	-0

Table 4: First logistics regression analysis

Regression statistics						
Multiple R	0.497915					
R Square	0.24792					
Adjusted R Square	0.145943					
Standard Error	0.339815					
Observations	68					
ANOVA	***df***	***SS***	***MS***	***F***	***Significance F***	
Regression	8	2.245861	0.280733	2.431135	0.024154	
Residual	59	6.812962	0.115474			
Total	67	9.058824				
	Coefficients	***Standard Error***	***t Stat***	***P-value***	***Lower 95%***	***Upper 95%***
Intercept	1.351135	0.296085	4.563329	2.6E-05	0.75867	1.943601
Age	0.007227	0.002971	2.432983	0.018025	0.001283	0.013171
Gender	0.057809	0.085779	0.673925	0.502991	-0.11384	0.229453
Past medical history	-0.05092	0.067186	-0.75788	0.451541	-0.18536	0.08352
Risk factors	-0.0607	0.037198	-1.63193	0.10802	-0.13514	0.013728
Past medication history	-0.11255	0.109337	-1.02942	0.307483	-0.33134	0.106229
Presenting symptoms	0.347079	0.115049	3.016794	0.003766	0.116866	0.577291
Time from onset of symptoms to presentation	0.080755	0.064187	1.258114	0.213307	-0.04768	0.209194

Table 5: 2nd Logistic regression model

Regression Statistics						
Multiple R	0.374965					
R Square	0.140599					
Adjusted R Square	0.127578					
Standard Error	0.303174					
Observations	68					
ANOVA	***df***	***SS***	***MS***	***F***	***Significance F***	
Regression	1	0.992464	0.992464	10.79768	0.00163	
Residual	66	6.06636	0.091915			
Total	67	7.058824				
	Coefficients	***Standard Error***	***t Stat***	***P-value***	***95% CI (Lower)***	***95% CI (Upper)***
Intercept	0.814732	0.099245	8.209314	1.12E-11	0.616584	1.012881
Modified Fisher grade = CT appearance severity	0.103508	0.0315	3.285982	0.00163	0.040617	0.1664

of an aneurysm (aSH) (r = 0.51), which was predominantly the anterior communicating artery. This altered or loss of consciousness was implicated more with tSH than with non-traumatic aSH, which correlated more with a headache. Contrastingly, the timing of onset was positively correlated with mortality outcomes, which means that the more delayed the onset of symptoms, the more the risk of death in patients presenting with SH (r = 0.2).

The CT findings were positively and significantly correlated with Modified Fisher CT which suggested that

Table 6: Correlation between subjective and objective measures for assessing SH severity

	Hunt and Hess grade	WFNSG	CT	Fischer	Modified Ranking
Hunt and Hess grade	1				
WFNSG	0.63550661	1			
CT	0.125288383	0.234896735	1		
Fischer	0.260412206	0.316011701	0.472387	1	
Modified Rankin	0.269457289	0.496015182	0.116727	0.341678	1

WFNSG - World Federation of Neurological Surgeons grade

both could be interchangeably used to diagnose SH severity (r = 0.5). The correlation further showed that the location of SH significantly influenced its severity (r = 0.2), while the severity of CT significantly and positively correlated (r = 0.3) with mortality (hospital outcome, coded as 1 = healthy discharge and 2 = death). These findings suggested that the severity of SH influenced mortality, which was confirmed by the correlation of Modified Fischer CT with hospital discharge (r = 0.4). The correlation analysis further showed that the location of an aneurysm (SH) influenced mortality (r = 0.2) but the pattern of SH did not (r = 0.1). On the contrary, the pattern of SH significantly and negatively influenced the location of SH (LOS). The correlation also showed that the severity of SH increases mortality, so the LOS reduces (negative correlation). Therefore, the first logistic regression analysis was conducted with the severity of SH (CT) as the dependent variable and age, gender, onset of symptoms, type of symptoms, medical, medication history, and ethnicity (nationality) as the independent variables (Table 4).

The regression analysis (Table 4) exhibited a coefficient of determination (R^2) value of 49.5%, which indicated the moderate goodness-of-fit of the model. The regression analysis was highly significant (F = 2.4, df = 67, P = 0.02) and it concluded that age and risk factors, either alone or in combination, significantly influenced the severity of SH. However, the significance level of the beta-coefficients of the independent variables indicated that age and presenting symptoms (type of symptoms) significantly influenced SH severity as the P-values for both these variables were less than 0.05.

The 2nd logistic regression model (Table 5) showed that the severity of SH (as depicted by Modified Fischer CT) significantly predicted mortality (F = 10.79, df = 67, P = 0.001) (Table 6).

4. DISCUSSION

The advancement of living conditions has resulted in an increase in the population over 50 y of age, with associated age-related diseases. The advancement in science and technology has also resulted in an increase in the accidents and trauma. Both of these factors have enhanced the frequency of both types of SH, tSH as well as aSH, especially in the developed countries. We found that the mean age for the occurrence of SH was 47.84 y. This is in accordance with the findings of a meta-analysis conducted by Rooij et al., where the mean age for SH was 35 y and for every year of increase in mean age, the incidence became 1.06 times higher.[1] Although, as per our findings, age was a strong predictor for the severity of SH, it did not have much influence over the pattern and location of SH. Furthermore, the findings of our study indicate that the severity of SH was a strong predictor of mortality. Gender predisposition towards aSH was higher among females and the tSH was higher among the males. A similar finding was documented by Marchis et al. in their retrospective cohort study where females outnumbered males among the aSH patients.[18]

Our study showed the involvement of various predisposing risk factors in SH. Trauma carried the highest risk for SH among the individuals in our study. On the contrary, smoking and alcoholism were associated with aSH, which is in line with Sundstrom et al. who reported that smoking had a greater risk for SH.[19] Our study further showed that more than one pre-defined risk factor influences the severity of SH, while the type of risk factor determines the classification of SH. This is an important finding because various studies have suggested that the number of risk factors points towards the severity of SH.[20–23] Also, altered consciousness was more likely in patients presenting with delayed onset, while headache was more common with those presenting with early onset. Although, our study has analyzed the various risk factors that influences the severity of SH, the mortality rate was higher among tSH in comparison to aSH. This highlights that both, the severity and pattern of SH, have an effect on the mortality.

The first logistic regression model showed that age and pre-existing risk factors were significantly associated with the severity of SH. In accordance with the findings of our study, Pahl et al. also concluded that ageing is a risk factor for poor outcomes in patients with ruptured or unruptured intracranial aneurysms.[24] The model also showed that the intercept was significant too, which implicated that there could be other independent variables than those included in this model which could predispose the occurrence of SH. There are several systems for the classification of SH. The given study has utilized Modified Fischer CT scale,[25] as the objective assessment tool for SH severity as its correlation with the outcome is higher than for conventional CT. Table 6 depicts that the subjective measures, such as Hunt and Hess grade,[26] and World Federation of Neurological Surgeons (WFNS) grade,[27] also correlated with the outcomes (Modified Rankin) but the later was more correlated than the former. The WFNS exhibited a higher correlation with outcomes compared to Modified Fischer scale, but as the objective assessment of SH severity is more specific, it was used as the dependent variable in this study. Therefore, it can be recommended that WFNS have a higher sensitivity as shown by its correlation with outcomes and it could be used as a diagnostic or screening measure for assessing SH severity in resource-limited settings.

5. LIMITATIONS

Although the study reflected that tSH is associated with more negative outcomes than aSH, it has certain limitations. The major limitation of this study is the small sample size (n = 68) compared to the prevalence of SH in the population. Secondly, the study did not control for the odds of age, gender, medication history, and risk factors in evaluating the progression of traumatic and aneurysmal SH. The correlation analysis could not depict whether the various factors considered for predisposition to SH, either alone or in combination with others, influence SH severity, hence, it is a limitation.

6. CONCLUSIONS

The study showed that mortality risk is greater with tSH compared to non-traumatic aSH, while age is statistically correlated with severity, but gender is more related to pattern of SH. Also, the severity of SH influences the occurrence of increased deaths due to SH. Trauma is a major risk factor for predisposition to SH. While assessing for the severity of SH the WFNS correlates better with the outcomes in comparison to the Modified Fischer grading, but the latter is recommended when the assessment of SH severity is more specific.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Conflict of interest

The authors report no conflict of interest, and no external or industry funding was involved.

9. Authors' contribution

AS, KB, HA: Proposal writing, Proposal editing, Data collection, Data cleaning, Data analysis, Manuscript writing, Manuscript editing, and Manuscript submission.

IA: Proposal writing, Proposal editing, Data collection, Data cleaning, Data analysis, Manuscript writing, and Manuscript editing.

DB: Proposal writing, Proposal editing, Data collection, Data cleaning, and Manuscript writing.

SB, WB: Proposal writing, Data collection, and Manuscript writing.

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