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## Predictive impact of haemoglobin level in ruptured cerebral aneurysms

Anaemia is a multicausal clinical condition affecting nearly one in two patients with aneurysmal subarachnoid haemorrhage (aSAH). Cerebral oxygen delivery depends on blood flow and Hb concentration. In acute brain injury, including aSAH, compensatory mechanisms are impaired, making anaemic patients more susceptible to cerebral hypoxia. Although the impact of elevated Hb levels in aSAH remains insufficiently studied, both low and high Hb levels are believed to influence cerebral perfusion, particularly under conditions of cerebral vasospasm.

**Objective** — to determine the impact of baseline Hb level on the prediction of the clinical course and outcome in patients with ruptured cerebral aneurysms.

**Materials and methods.** A retrospective single-centre cross-sectional study was conducted. It involved the analysis of 492 medical records of patients in the acute phase of cerebral aneurysms (CA) rupture. Patients were divided into three groups according to Hb levels. The analysis included demographic and clinical data, Hb levels, anatomical and morphological features of CA, treatment method, complications, and outcomes.

**Results and discussion.** Patients with elevated Hb levels were significantly older ( $p = 0.013$ ). Female sex was significantly associated with both low and high Hb levels, with women being nearly twice as likely to belong to the low Hb group ( $p = 0.013$ ) and 5.6 times more likely to belong to the high Hb group ( $p < 0.001$ ). Patients with high Hb levels had significantly reduced odds of developing pneumonia ( $p = 0.026$ ). Elevated Hb levels were associated with a 2.4-fold increase in the likelihood of being discharged with the Hospital Assessment Scale 2 ( $p = 0.039$ ).

**Conclusions.** These findings suggest that both decreased and elevated Hb levels are differentially associated with age, sex, incidence of pneumonia, and treatment outcomes in patients with ruptured CA.

**Keywords:** cerebral aneurysm, subarachnoid haemorrhage, haemoglobin, outcome.

Anaemia is a multicausal clinical condition that affects nearly one in two patients with aneurysmal subarachnoid haemorrhage (aSAH) [3, 11]. The amount of oxygen delivered to the brain depends on cerebral blood flow and the arterial blood oxygen level, which in turn is determined by the haemoglobin (Hb) concentration. In healthy individuals with normovolaemic anaemia, a range of compensatory mechanisms is activated to maintain adequate oxygen delivery to the brain by increasing cerebral blood flow. However, once Hb levels fall below a critical threshold (approximately 5.0—6.0 g/dL), these compensatory mechanisms reach their limit and can no longer sustain sufficient oxygen supply to cerebral tissue. In cases of acute brain injury, including aSAH, the threshold at which anaemia becomes critical is

higher. Moreover, patients with aSAH frequently experience haemodynamic instability or acute cardiac dysfunction, both of which can impair cerebral perfusion. These factors suggest that patients with aSAH and concomitant anaemia are more vulnerable to the development of cerebral tissue hypoxia [4, 9].

Several studies have reported associations between anaemia and presence of cerebral vasospasm (CV), delayed cerebral ischaemia, unfavourable outcomes, including mortality [2—4, 12].

At the same time, Li et al. suggest that not only low, but also excessively high Hb concentrations may have adverse effects in patients with aSAH. During the acute phase of cerebral aneurysm (CA) rupture, Hb released from lysed erythrocytes may affect brain tissue. Previous studies have shown that Hb may

contribute to the occurrence of CV by reducing nitric oxide production, inhibiting potassium channel activity, and stimulating the release of endothelin-1 [6].

**Objective** — to determine the impact of baseline Hb level on the prediction of the clinical course and outcome in patients with ruptured cerebral aneurysms.

### Materials and methods

A retrospective single-centre cross-sectional study was conducted. It involved the analysis of 492 medical records of patients in the acute phase of cerebral aneurysms (CA) rupture.

Inclusion criteria were: (1) subarachnoid haemorrhage (SAH) due to ruptured CA, confirmed by CT and CT angiography; (2) availability of a complete blood count performed within the first three days after admission; (3) microsurgical or conservative treatment; (4) age 18 years and more.

Exclusion criteria included: (1) traumatic SAH or other triggers of intracranial bleeding (e.g., arteriovenous malformations, coagulopathies, etc.); (2) history of anaemia, thalassaemia, and other haematological disorders; (3) patients who underwent a blood transfusion within three months prior to admission.

Patients were divided into three groups based on Hb levels:

- group I — female patients with Hb < 12.0 g/dL and male patients with Hb < 13.0 g/dL;
- group II — female patients with Hb 12.0—15.5 g/dL and male patients with Hb 13.0—17.0 g/dL;
- group III — female patients with Hb > 15.5 g/dL and male patients with Hb > 17.0 g/dL.

Hb level was determined within 3 days of admission. The analysis included: demographic data (age, sex), length of hospital stay, treatment method (microsurgical or conservative), time interval between CA rupture and surgery, and treatment outcomes at discharge based on the Hospital Assessment Scale (HAS) [10]. The severity of the patient's condition at admission was assessed using the modified World Federation of Neurosurgical Societies (mWFNS) scale. Grades I—III were considered as a good clinical condition, while Grades IV—V were classified as a poor clinical condition. The size of the ruptured aneurysm was determined via CT angiography, taking into account the maximum dome diameter. In cases of multiple aneurysms, the size of the ruptured one was used. The distribution of haemorrhage was assessed via CT. It is known that the Fisher scale does not take into account the parenchymal component, although its volume may significantly increase the total amount of bleeding. Therefore, we distinguished the following types of haemorrhage: isolated aSAH, aSAH with intraventricular haemorrhage, aSAH with intracerebral haemorrhage, or a combination of all three. Intracranial complications included CV, hydrocephalus, and epidural or subdural haematoma. Additional complications included infections (pneumonia, urinary

tract infection, meningitis) and conditions requiring tracheostomy.

Statistical analysis was performed using the Jamovi software, version 2.3.28.0. Descriptive data were presented as absolute numbers and frequencies. Continuous variables were expressed as mean  $\pm$  standard deviation (SD) for normally distributed data, or as median and interquartile range (IQR) for non-normally distributed data. The Shapiro—Wilk test was used to assess the normality of distribution. For comparison between two independent groups, Student's t-test was used for normally distributed variables. The Kruskal—Wallis test was applied to compare three independent groups when distributions were non-normal.  $\chi^2$  test was used to assess associations between categorical variables. A  $p < 0.05$  was considered statistically significant. Statistically significant results were further analysed using binomial and multinomial logistic regression.

The study adhered to the ethical standards outlined in the Ethical Code of the World Medical Association (Declaration of Helsinki). Ethical approval was granted by the Ethics Committee of Odesa National Medical University (Protocol No. 06036, 11 June 2025).

### Results and discussion

A total of 66 out of 492 patients were transferred for further endovascular treatment. As a result, 426 medical records of patients in the acute phase of CA ruptured were analysed. Hb levels were available for 399 of these patients, who were subsequently included in the final analysis.

Baseline characteristics for the three groups are presented in Table 1. Patients in the third group tended to be older, whereas those in the first and second groups were on average younger. Women predominated in the first and especially in the third group, while men were slightly more frequent in the second group. Across all groups, the most frequent type of haemorrhage among patients was isolated aSAH, occurring in about two out of five cases. Additional intraventricular haemorrhage was seen in roughly one quarter of cases, with somewhat higher frequency in the third group. Intracerebral haemorrhage was most typical for the first group, whereas it was relatively rare in the third. At admission, over half of the patients in each group presented with mWFNS grades I—III. Regarding management, microsurgical treatment predominated, especially in the second and third groups. CV occurred in about half of the patients, whereas hydrocephalus and epidural or subdural hematomas were less common. Among infections, pneumonia was most frequent in the first group, less so in the second, and rare in the third. Urinary tract infections and meningitis were uncommon in all groups. Tracheostomy was required in roughly one quarter of patients in the first group, fewer in the second, and rarely in the third. At discharge, patients in the first and second groups more frequently achieved

Table 1  
Baseline characteristics for the groups

Characteristics	Patient groups			p-value
	I	II	III	
Number of patients	72	295	32	
Age, Mean $\pm$ SD	50.3 $\pm$ 14.9	52.0 $\pm$ 11.7	57.9 $\pm$ 11.2	0.013 <sup>a</sup>
Sex				
▪ Female	47 (65.3 %)	144 (48.8 %)	27 (84.4 %)	< 0.001
▪ Male	25 (34.7 %)	151 (51.2 %)	5 (15.6 %)	
Type of haemorrhage				
▪ Isolated aSAH	27 (37.5 %)	119 (40.3 %)	15 (46.9 %)	0.323 <sup>b</sup>
▪ aSAH and intraventricular haemorrhage	19 (26.4 %)	78 (26.4 %)	12 (37.5 %)	
▪ aSAH and intracerebral haemorrhage	17 (23.6 %)	51 (17.4 %)	2 (6.3 %)	
▪ aSAH with both ventricular and intracerebral haemorrhage	9 (12.5 %)	47 (15.9 %)	3 (9.3 %)	
mWFNS at admission				
▪ I—III	41 (56.9 %)	186 (63.1 %)	20 (62.5 %)	0.631 <sup>b</sup>
▪ IV—V	31 (43.1 %)	109 (36.9 %)	12 (37.5 %)	
Treatment method				
▪ Microsurgical	50 (69.4 %)	232 (78.6 %)	28 (87.5 %)	0.087 <sup>b</sup>
▪ Conservative	22 (30.6 %)	63 (21.4 %)	4 (12.5 %)	
Size of ruptured CA, Median (IQR)	7.0 (4.5)	7.0 (4.5)	6.0 (3.0)	0.799 <sup>c</sup>
Time interval between CA rupture and surgery, Median (IQR)	4.0 (9.0)	4.0 (8.5)	4.0 (13.3)	0.969 <sup>c</sup>
CV				
▪ Yes	32 (44.4 %)	151 (51.2 %)	15 (46.9 %)	0.561 <sup>b</sup>
▪ No	40 (55.6 %)	144 (48.8 %)	17 (53.1 %)	
Hydrocephalus				
▪ Yes	7 (9.7 %)	49 (16.6 %)	7 (21.9 %)	0.219 <sup>b</sup>
▪ No	65 (90.3 %)	246 (83.4 %)	25 (78.1 %)	
Epidural or subdural hematoma				
▪ Yes	9 (12.5 %)	23 (7.8 %)	2 (6.3 %)	0.392 <sup>b</sup>
▪ No	63 (87.5 %)	272 (92.2 %)	30 (93.7 %)	
Pneumonia				
▪ Yes	25 (34.7 %)	76 (25.8 %)	2 (6.3 %)	0.009 <sup>b</sup>
▪ No	47 (65.3 %)	219 (74.2 %)	30 (93.7 %)	
Urinary tract infections				
▪ Yes	4 (5.6 %)	12 (4.1 %)	4 (12.5 %)	0.113 <sup>b</sup>
▪ No	68 (94.4 %)	283 (95.9 %)	28 (87.5 %)	
Meningitis				
▪ Yes	6 (8.3 %)	13 (4.4 %)	3 (9.4 %)	0.258 <sup>b</sup>
▪ No	66 (91.7 %)	282 (95.6 %)	29 (90.6 %)	
Conditions requiring tracheostomy				
▪ Yes	17 (23.6 %)	50 (16.9 %)	3 (9.4 %)	
▪ No	55 (76.4 %)	245 (83.1 %)	29 (90.6 %)	
Treatment outcome based on HAS				
▪ HAS 0	28 (38.9 %)	130 (44.1 %)	12 (37.5 %)	0.003 <sup>b</sup>
▪ HAS 1	2 (2.8 %)	29 (9.8 %)	4 (12.5 %)	
▪ HAS 2	18 (25.0 %)	69 (23.4 %)	15 (46.9 %)	
▪ HAS 3	24 (33.3 %)	67 (22.7 %)	1 (3.1 %)	

Notes. <sup>a</sup>Student's *t*-test; <sup>b</sup> $\chi^2$  test; <sup>c</sup>Kruskal—Wallis test.

Table 2  
Results of logistic regression for the groups

Characteristics	Patient group					
	I		II		III	
	OR (95 % CI)	p	OR (95 % CI)	p	OR (95 % CI)	p
Age	0.99 (0.97—1.01)	0.304	—	—	1.04 (1.01—1.07)	0.011
Sexa (reference: male)	1.97 (1.15—3.37)	0.013	—	—	5.66 (2.12—15.1)	< 0.001
Pneumonia (reference: no) <sup>b</sup>	1.53 (0.88—2.66)	0.129	—	—	0.192 (0.04—0.82)	0.026
Treatment outcome (reference: HAS 0) <sup>a</sup>						
• HAS 1	0.32 (0.07—1.42)	0.134	—	—	1.49 (0.45—4.97)	0.512
• HAS 2	1.21 (0.63—2.34)	0.569	—	—	2.36 (1.04—5.31)	0.039
• HAS 3	1.66 (0.89—3.09)	0.108	—	—	0.162 (0.02—1.27)	0.083

Notes. <sup>a</sup> Multinomial logistic regression; <sup>b</sup> binomial logistic regression.

HAS 0, whereas those in the third group most often had HAS 2.

Statistically significant variables from Table 1 were included in further analyses, including multinomial and binomial logistic regression (Table 2).

Statistical analysis showed that older age was associated with a higher likelihood of elevated Hb, though the model's predictive power was modest. Female patients were nearly 2 and 5.6 times more likely to belong to the low and high Hb level groups, respectively. Additionally, patients with elevated Hb levels were approximately 2.4 times more likely to be discharged with HAS score 2. At the same time, patients with high Hb levels had significantly lower odds of developing pneumonia. The findings of our study are only partially consistent with the existing literature. Li R et al. reported that even an admission Hb level > 14.9 g/dL was associated with an unfavourable functional outcome specifically at 90 days post-discharge (defined as a modified Rankin Scale score  $\geq$  3), whereas in our study, poor outcomes at discharge were associated with higher Hb levels. Additionally, the authors demonstrated that elevated Hb levels were linked to a higher risk of delayed cerebral ischaemia and deep vein thrombosis. However, no statistically significant association was found between high Hb levels and the risk of pneumonia in their study. Interestingly, older age and female sex were more frequently observed among patients with Hb  $\leq$  14.9 g/dL [6]. Aslo, it was found that patients with Hb levels above 19.0 g/dL and 21.0 g/dL had a higher incidence of pseudo-SAH. Moreover, the number of male patients in the group with Hb levels > 19.0 g/dL was significantly higher [5]. In contrast, we observed paradoxical results regarding sex and Hb levels: female patients had a higher likelihood of

belonging to both the low and high Hb groups. At the same time, other studies confirm that anaemia is more commonly observed in women [1, 7].

In our analysis, no statistically significant association was found between different admission Hb levels and the development of CV. As noted above, two main hypotheses have been proposed in the literature regarding the mechanism by which Hb levels may influence CV. In a systematic review by M. Said, et al., anaemia at admission was not associated with the occurrence of cerebral infarction. However, the same review reported that a drop in Hb levels to 9.0—10.0 g/dL during the acute phase of CA rupture significantly increased the risk of CV (by 2.2 times) and cerebral infarction (by nearly 2.1 times) [8]. Another study by M. Said, et al. also confirmed an association between anaemia within 14 days after aneurysm rupture and a higher incidence of cerebral CV. Nevertheless, the question of causality remains unresolved: is anaemia a consequence of conservative treatment for CV, or is it a contributing factor to reduced cerebral perfusion, manifesting as CV? [7].

### Conclusions

Admission Hb level is an important factor influencing the course and treatment outcomes in patients with CA rupture. Female sex was significantly associated with both low and high Hb levels. Elevated Hb levels were associated with older age, a reduced likelihood of developing pneumonia, and an increased risk of being discharged with HAS score 2. No association was found between Hb level and the risk of CV. These findings contribute to the existing evidence on the complex role of Hb in the prognosis of CA rupture and highlight the need for further prospective studies to better understand the underlying pathophysiological mechanisms behind the observed associations.

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*Participation of authors: project administration, conceptualization, writing (review & editing) — Yu. S.; resources, investigation, writing (preparation of original draft) — A. R.; resources, investigation, formal analysis — K. Ya.; formal analysis, methodology — D. H.*

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## Предиктивний вплив рівня гемоглобіну при розриві мозкових аневризм

Анемія — це поліетіологічний клінічний стан, що розвивається майже в кожного другого пацієнта з аневризматичним субарахноїдальним крововиливом (аСАК). Кількість кисню, яка надходить до головного мозку, залежить від мозкового кровотоку та рівня гемоглобіну (Hb). При гострому ураженні головного мозку, зокрема при аСАК, компенсаторні механізми порушуються, що робить пацієнтів з анемією вразливішими до розвитку гіпоксії тканин головного мозку. Хоча вплив підвищеного рівня Hb при аСАК недостатньо вивчений, існує думка, що як низький, так і високий рівень Hb може чинити вплив на мозкову перфузію, зокрема в умовах вазоспазму.

**Мета роботи** — визначити вплив ініціального рівня Hb на прогноз клінічного перебігу та результат лікування в пацієнтів із розривом мозкових аневризм.

**Матеріали та методи.** Проведено ретроспективне одноцентрове кроссекційне дослідження. Проаналізовано 492 історії хвороби пацієнтів у гострий період розриву мозкових аневризм (МА). Пацієнтів було розподілено на три групи залежно від рівня Hb. Аналізували такі дані пацієнтів: демографічні та клінічні характеристики, вміст Hb, анатомо-морфологічні характеристики МА, метод лікування, ускладнення, результат лікування.

**Результати та обговорення.** Виявлено, що пацієнти з підвищеним рівнем Hb були в середньому старшого віку ( $p = 0,013$ ). Жіноча стать була вірогідно пов'язана як із низьким, так і з високим рівнем Hb: жінки майже вдвічі частіше належали до групи з низьким рівнем Hb ( $p = 0,013$ ) і в 5,6 рази частіше до групи з високим рівнем Hb ( $p < 0,001$ ). У пацієнтів із високим рівнем Hb була вірогідно нижчою ймовірність розвитку пневмонії ( $p = 0,026$ ). Підвищений рівень Hb асоціювався зі зростанням ймовірності виписки з оцінкою 2 за Hospital Assessment Scale ( $p = 0,039$ ).

**Висновки.** Отримані результати свідчать, що як знижений, так і підвищений рівень Hb мали різну асоціацію з віком, статтю, частотою розвитку пневмонії та результатами лікування в пацієнтів із розривом МА.

**Ключові слова:** мозкова аневризма, субарахноїдальний крововилив, гемоглобін, результат лікування.

### ДЛЯ ЦИТУВАННЯ

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