



The Role of Sodium and Glucose in the Prognosis of Patients with Aneurysmal Subarachnoid Hemorrhage: A Literature Review of New Evidence

O papel do sódio e da glicose no prognóstico de pacientes com hemorragia subaracnóidea aneurismática: Uma revisão de literatura das novas evidências

Zeferino Campos Dell'Orto¹ Isadora Valério da Silveira¹ Larissa da Silva Torres França¹
 Murillo Sampaio Ferreira Medeiros¹ Talita Cardoso Gomes¹ Bruno Alves Pinto¹
 Daniel Gonçalves de Oliveira¹ Gabryell Thiengo Lopes¹ Ivan Magalhães Viana¹

¹ Medicine Department, Universidade Federal de Juiz de Fora, Campus Governador Valadares, MG, Brazil

Arq Bras Neurocir 2024;43(1):e40–e47.

Address for correspondence Zeferino Campos Dell'Orto, Medical Student, Medicine Department, Universidade Federal de Juiz de Fora, Avenida Dr. Raimundo Monteiro Rezende, 330, sala 301, Centro, Governador Valadares, MG, Brazil
 (e-mail: zeferinocamposdellorto@hotmail.com).

Abstract

The present study aims to review the influence of glycemia and natremia on the propensity to develop complications, worse prognosis, and mortality risk in patients with aneurysmal subarachnoid hemorrhage (aSAH). This is an integrative literature review guided by the guiding question: “Do changes in blood glucose levels or plasma sodium concentration influence in-hospital morbidity and mortality in patients with aneurysmal subarachnoid hemorrhage?”. The search for articles was performed on the PubMed platform, limiting the selection to works published in English in the period from 2017 to 2022. The results found demonstrate that the role of sodium ions in changes in the prognosis of patients is complex, with hyponatremia being the main factor described to worse outcomes. In contrast, the part of hyponatremia is controversial and may not have prognostic value, and serum sodium concentration is increasingly an important item to be evaluated in patients with aSAH. As for glucose, the variability of this substrate, both hyperglycemia and hypoglycemia, may be correlated with in-hospital and long-term mortality in patients with aSAH. Thus, the present study concludes that changes in blood glucose values and plasma sodium concentration influence the in-hospital morbidity and mortality of patients with aSAH. However, it is emphasized that the analysis of the independent influence of each of the related predictors must be done with caution due to the heterogeneity of the results found.

Keywords

- neurosurgery
- hemorrhagic stroke
- intracranial aneurysm

received
 January 30, 2023
 accepted
 August 4, 2023
 article published online
 October 10, 2023

DOI <https://doi.org/10.1055/s-0043-1774749>.
 ISSN 0103-5355.

© 2023. Sociedade Brasileira de Neurocirurgia. All rights reserved.
 This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)
 Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

O presente estudo tem como objetivo a revisão da influência da glicemia e da natremia na propensão ao desenvolvimento de complicações, no pior prognóstico e no risco de mortalidade em pacientes com hemorragia subaracnóidea aneurismática (HSAa). Trata-se de uma revisão integrativa de literatura guiada pela questão norteadora: “Alterações nos valores da glicemia ou concentração de sódio plasmática influenciam na morbimortalidade intrahospitalar de pacientes com hemorragia subaracnóidea aneurismática?”. A busca de artigos foi realizada na plataforma PubMed, limitando a seleção para trabalhos publicados em língua inglesa no período de 2017 a 2022. Os resultados encontrados demonstram que o papel do íon sódio nas alterações no prognóstico dos pacientes é complexo, sendo a hipernatremia o principal fator descrito em relação a piores desfechos, enquanto o papel da hiponatremia é controverso e pode não ter valor prognóstico, e a concentração de sódio sérica apresenta-se cada vez mais como um item importante a ser avaliado no paciente com HSAa. Já quanto à glicose, a variabilidade desse substrato, tanto a hiperglicemia como também a hipoglicemia, pode estar correlacionada com a mortalidade hospitalar e a longo prazo em pacientes com HSAa. Assim, o presente estudo conclui que as alterações nos valores de glicemia e concentração de sódio plasmático têm influência na morbimortalidade intrahospitalar dos pacientes com HSAa. Entretanto, ressalta-se que a análise da influência independente de cada um dos preditores relacionados deve ser feita com cautela devido à heterogeneidade dos resultados encontrados.

Palavras-chave

- neurocirurgia
- acidente vascular cerebral hemorrágico
- aneurisma intracraniano

Introduction

Subarachnoid hemorrhage is a type of hemorrhagic stroke, whose incidence is associated, in ~ 80 to 85% of cases, with the rupture of an intracranial aneurysm, characterized by an aneurysmal subarachnoid hemorrhage (aSAH).^{1,2} Aneurysmal subarachnoid hemorrhage has a worldwide incidence of 9 per 100,000 individuals per year, represents 5% of strokes, has high mortality and disability rates, and its general prognosis depends on the volume of initial bleeding, the occurrence of rebleeding, and the degree of delayed cerebral ischemia.³

Among the most important risk factors for the development of brain aneurysms are high blood pressure, smoking, alcoholism, family history of the aneurysm in first-degree relatives, and female gender. In addition to these, autosomal dominant polycystic kidney disease is relevantly associated with the formation of aneurysms, and other conditions such as Marfan syndrome, Ehlers-Danlos syndrome type IV, neurofibromatosis, and fibromuscular dysplasia also have a weak association.³

As for the rupture, the location, size, and type of aneurysms are relevant to the increased risk. Aneurysms > 1 cm and located in the posterior circulation, especially at the top of the basilar artery, in the posterior cerebral artery, in the vertebrobasilar distribution, and the origin of the posterior communicating artery, were associated with a greater chance of rupture. Furthermore, saccular aneurysms account for 90% of aneurysm morphology and correspond to the most common cause of aSAH.³

In addition to the acute effects resulting from aSAH, and the mortality rate of ~ 35%,² patients with aSAH may

present secondary complications, which result in a worse prognosis and are associated with neurological sequelae such as cognitive alteration, and motor and/or behavioral deficit.⁴ The main complications include rebleeding, hydrocephalus, vasospasm, cerebral edema, and late cerebral ischemia.^{5,6} Among them, early rebleeding is the most frequent in the first 24 hours, being associated with mortality rates of 50 to 80%.⁷

Factors associated with worse clinical outcomes and incidence of complications after aneurysmal subarachnoid hemorrhage are older age, higher grades on the World Federation of Neurologic Surgeons (WFNS) scale at admission, larger aneurysms located in the posterior circulation, intraventricular hemorrhage, hematoma intracerebral injection and history of arterial hypertension, acute myocardial infarction, liver disease or previous subarachnoid hemorrhage.⁸ In addition, biomarkers and electrolytes correlated with an unfavorable evolution in aSAH, such as the glucose-potassium ratio, the glucose-phosphate index, sodium concentration, and plasma glucose, stand out.

Therefore, the present study aims to review the influence of glycemia and natremia on the propensity to develop complications, the worst prognosis, and the risk of mortality in patients with aneurysmal subarachnoid hemorrhage.

Material and Methods

This is an integrative literature review. The present study had as its guiding question: “Do changes in blood glucose values or in plasma sodium concentration influence in-hospital morbidity and mortality of patients with aneurysmal

subarachnoid hemorrhage?" based on the *PECOS* strategy: **Patient** – people with aneurysmal subarachnoid hemorrhage; **Exposure** – alterations in glycemia (hyper or hypoglycemia or glycemic variations) or plasma sodium concentrations (hyper or hyponatremia); **Control** – Normoglycemic and with normal sodium levels; **Outcome** – increased mortality; **Studies** – clinical trials, prospective and retrospective cohorts, case-control, and systematic reviews were included.

Inclusion Criteria

As for the inclusion criteria, complete articles were selected for the present work, published between 2017 and 2022, written in English, and belonging to the following types of study: clinical trial, prospective or retrospective cohort, case-control study, or systematic review. In addition, in their methodology, the studies should have performed at least one measurement of blood glucose (in the form of mean glucose per glycated hemoglobin or measurements of daily capillary glucose) or natremia of patients hospitalized for aSAH. Finally, the selected articles should present a statistical correlation between changes in glycemia or natremia with in-hospital mortality; or else demonstrate differences in clinical presentations or prognosis in patients with aSAH and glycemic and natremia alterations in comparison to aSAH patients with normoglycemic and normal sodium levels.

Exclusion Criteria

The established exclusion criteria were duplicate publications on platforms and search; publications inconsistent with the purpose of this research; publications with strong biases that compromise the reliability of the article and publications in languages other than English. In addition, case report studies, narrative reviews, and animal experimentation. Studies that used glycemic monitoring by cerebral microdialysis, whose focus of discussion was the drug treatments of glycemic alterations or natremia, and articles that report on ventriculoperitoneal shunt were also excluded.

Search and Identification of Articles

The search for articles was performed on the PubMed platform, limiting the results to articles published in the last 5 years (2017–2022) in English. To survey the articles, the following descriptors were used: *Glucose; Blood Glucose; Hyperglycemia; Hypoglycemia; Sodium; Hypernatremia; Hyponatremia; Potassium; Hyperkalemia; Hypokalemia* and their respective Entry Terms separated by the Boolean operator OR. Then we used the Boolean AND operator to include the *Aneurysmal Subarachnoid Hemorrhage* descriptor and its Entry Terms.

Results and Discussion

General Description of Results

Based on the described methodology, 106 results were found. After analyzing the titles and abstracts, 40 articles

were included for a full reading. Of these, the following were excluded: three because of the impossibility of accessing the complete material, another three because they did not present clear relationships with the objective of the research (glucose and sodium), in addition to three Keywordsget, is of factors for shunt or ventriculoperitoneal shunt. Furthermore, one study for not stratifying hypoglycemia, hypoxia, and hypotension as a cause for worse outcomes or mortality, and another for not using exposure and control groups to assess the risk of hyponatremia.

It was also decided to remove two items that contained their investigations associated with ischemic stroke and nonaneurysmal subarachnoid hemorrhage, which prevented their adequate participation in the present study. Ultimately, one element was removed as it focused on treatment impact. Thus, in the final analysis of the results, 26 articles were considered, 14 referring to sodium (► Fig. 1) and 12 to glucose (► Fig. 2).

Sodium Change

Primarily, it should be noted that dysnatremia events and fluctuations in serum sodium ion values are extremely prevalent in patients with aSAH. The main event is hyponatremia, present in ~ 30 to > 50%⁹ of the patients, followed by hypernatremia found between 31 and 33.6% of the cases and variations in sodium values in ~ 39.3% – considering the value of 12 mmol/L.¹⁰

Regarding prognosis, the role of such an ion is complex. Studies indicate that both hypernatremia and hyponatremia, or even variation in serum sodium concentration, are more common in patients with unfavorable evolution – including deaths, neurological sequelae, or a higher level of dependence – in-hospital or in later periods of up to 6 months.^{10–12}

However, the assessment of independent predictors for patient outcomes is more restrictive. The main factor described is hypernatremia, in which there are correlations of values > 145 mmol/L in the first 2 weeks with higher mortality during hospitalization or with a worse prognosis, in general, when considering the value of 146 mmol/L.¹¹ Specifically, Sokół et al.,¹³ established that values > 155 mmol/L were an independent predictor of mortality, with a specificity of 97.8% and a sensitivity of 47.6%. Furthermore, concentrations > 155 mmol/L were associated with unfavorable outcomes within 3 months.¹⁰ More broadly, a study showed that sodium in the blood, in addition to rebleeding, is an independent risk factor, leading to poor prognosis.¹⁴

The role of hyponatremia as a predictor is controversial. In most articles, it is demonstrated that it has no prognostic value in the short or long term, especially in terms of mortality.^{10,11,15,16} Kieninger et al.¹⁷ even demonstrated that the rate of poor outcome at discharge from the intensive care unit (ICU), 6 months after the bleeding event, was significantly lower in patients with moderate hyponatremia (125–129 mmol/L), allowing only a limited conclusion, as the diagnosis of hyponatremia regularly led to early and elaborate measures to achieve rapid normalization of the sodium level and maintain normonatremia in the later course of ICU treatment. A pathophysiological hypothesis proposed by

Título	Ano	Primeiro Autor	Periódico	Tipo de estudo
The impact of hormonal dynamics and serum sodium fluctuations on symptomatic vasospasm after subarachnoid hemorrhage	2022	Harada, T.	J Clin Neurosci	Prospective cohort
Sodium Variability and Probability of Vasospasm in Patients with Aneurysmal Subarachnoid Hemorrhage	2022	Chua, M.M.J	J Stroke Cerebrovasc Dis	Retrospective observational
Clinical Treatment and Prognostic Analysis of Patients with Aneurysmal Subarachnoid Hemorrhage	2021	Yang, X.	J Healthc Eng.	Comparative analysis
Dysnatremia and 6-Month Functional Outcomes in Critically Ill Patients With Aneurysmal Subarachnoid Hemorrhage: A Prospective Cohort Study	2021	Cohen, J.	Crit Care Explor.	Prospective cohort
Acute hyponatremia after aneurysmal subarachnoid hemorrhage: Frequency, treatment, and outcome	2021	Kieninger, M.	J Clin Neurosci.	Retrospective observational
Risk Factors for Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage: A Population-Based Study of 8346 Patients	2021	Rumalla, K.	World Neurosurg.	Retrospective observational
Long-Term Outcomes of Elderly Patients with Poor-Grade Aneurysmal Subarachnoid Hemorrhage	2020	Yoshikawa, S.	World Neurosurg.	Retrospective observational
Temporal Relationship between Hyponatremia and Development of Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage Patients: A Retrospective Observational Study	2020	Escamilla-Ocañas, C.E.	J Stroke Cerebrovasc Dis	Case-control
Prognostic models for neurological functional outcomes in aneurysmal subarachnoid hemorrhage patients with intracranial hematoma	2020	Wang, Z.	Clin Neurol Neurosurg	Retrospective cohort
Impact of Dysnatremia and Dyskalemia on Prognosis in Patients with Aneurysmal Subarachnoid Hemorrhage: A Retrospective Study	2019	Tam, C.W.	Indian J Crit Care Med.	Retrospective cohort
Hyponatremia After Spontaneous Aneurysmal Subarachnoid Hemorrhage-A Prospective Observational Study	2019	Ridwan, S.	World Neurosurg.	Prospective cohort
Predicting mortality in subarachnoid haemorrhage based on first-week routine blood tests	2018	Bartos, S.	Journal Clin Neurosci	Prospective cohort
Electronic Health Data Predict Outcomes After Aneurysmal Subarachnoid Hemorrhage	2018	Zafar, S.F.	Neurocrit Care	Retrospective cohort
Target Serum Sodium Levels During Intensive Care Unit Management of Aneurysmal Subarachnoid Hemorrhage	2017	Okazaki, T.	Shock	Retrospective observational

Fig. 1 Included articles referring to the prognostic value of sodium in aSAH.

Tam et al.¹⁰ would be the ability of brain neurons to adapt to the situation of hyponatremia, in a self-regulation mechanism, managing to reach a state of functional stability in less than 24 hours.

In contrast, Rumalla et al.¹⁸ and Escamilla-Ocañas et al.⁹ demonstrated that hyponatremia was significantly associated with cerebral vasospasm, a complication that very often precedes aSAH events.^{9,18} Escamilla-Ocañas et al.⁹ also reported that poor clinical results and longer hospital stays and ICU were significantly more evident in the hyponatremic

group, compared with the normonatremic group. Such data are, in part, supported by Ridwan et al. (2019),¹⁵ who found a correlation between the development of hyponatremia at any time during hospitalization and longer duration of hospital stay; however, with no impact on ICU stay.

Furthermore, some authors, when considering specific periods, such as the decrease in sodium between 14 and 21 days after hospitalization¹⁵ or values below the usual levels, such as 132 mmol/L,¹¹ found worse outcomes related to hyponatremia within 1 year or at hospital discharge,

Title	Year	First Author	Periodical	Type of Study
Association between hyperglycemia at admission and mortality in aneurysmal subarachnoid hemorrhage	2022	Jia, L.	J Clin Neurosci	Retrospective observational
Elevated Glucose-Potassium Ratio Predicts Preoperative Rebleeding in Patients With Aneurysmal Subarachnoid Hemorrhage	2022	Wang, J.	Front Neurol	Retrospective observational
Association Between Glycemic Gap and In-hospital Outcomes in Aneurysmal Subarachnoid Hemorrhage	2021	Sun, P.Y.	Front Neurol	Case-control
Association of Plasma Glucose to Potassium Ratio and Mortality After Aneurysmal Subarachnoid Hemorrhage	2021	Jung, H.M.	Neurol Frontal	Prospective cohort
Glycemic indices predict outcomes after aneurysmal subarachnoid hemorrhage: a retrospective single center comparative analysis	2021	McIntyre, M.K.	Sci Rep.	Retrospective cohort
Glucose Variability as Measured by Inter-measurement Percentage Change is Predictive of In-patient Mortality in Aneurysmal Subarachnoid Hemorrhage	2020	Sadan, O.	Neurocritical Care	Retrospective observational
Serum Glucose and Potassium Ratio as Risk Factors for Cerebral Vasospasm after Aneurysmal Subarachnoid Hemorrhage	2019	Matano, F.	Journal of Stroke and Cerebrovascular Diseases	Case-control
Association of Admission Serum Glucose-Phosphate Ratio with Severity and Prognosis of Aneurysmal Subarachnoid Hemorrhage	2019	Dingding, Z.	World Neurosurg.	Case-control
Serum glucose/potassium ratio as a clinical risk factor for aneurysmal subarachnoid hemorrhage	2017	Fujiki, Y.	Journal of Neurosurg	Retrospective cohort
Blood Glucose Variability: A Strong Independent Predictor of Neurological Outcomes in Aneurysmal Subarachnoid Hemorrhage	2018	Okazaki, T.	J Intensive Care Med	Retrospective observational
Elevated glycated hemoglobin level and hyperglycemia after aneurysmal subarachnoid hemorrhage	2017	Beseoglu, K.	Clin Neurol Neurosurg	Prospective cohort
Stress-Induced Hyperglycemia After Spontaneous Subarachnoid Hemorrhage and Its Role in Predicting Cerebrospinal Fluid Diversion	2017	Ray, B.	World Neurosurg	Retrospective observational

Fig. 2 Included articles referring to the prognostic value of glucose in aSAH.

respectively. Another impacting factor that can be considered is the treatment of such hydroelectrolytic conditions, which usually receive a more aggressive treatment of fluid replacement.¹⁰

Cohen et al.¹⁹ mention that there are several possible explanations for the discrepancy observed in the influence of hyponatremia on morbidity and mortality from aSAH, including the use of variable outcome measures, with only a few studies reporting the long-term neurological status; differences in the definition of hyponatremia (which can be categorized as present or absent or by varying threshold values and a varying number of samples) and reports from analyzes and models that do not take into account duration or severity (for example, temporal changes over an admission).

In turn, the variation in serum sodium concentration is increasingly an important item to be evaluated in patients with aSAH. Increased sodium variability was associated with

a longer hospital stay¹⁹ and, between the 1st and 3rd days, it was associated with higher in-hospital mortality.¹⁶ Also, Tam et al.¹⁰ detected that a variation > 12 mmol/L of sodium during hospitalization could be associated with a worse patient outcome, represented by states 1 to 3 of the Glasgow Outcome Scale in the 3 months following aSAH. Furthermore, within¹⁴ days of an aSAH episode and 6 months of hospital discharge, it has been associated with the development of symptomatic vasospasm²⁰ and poor neurological outcome,¹⁹ respectively, with progressive decreases in serum sodium being found to precede such complications.

It is speculated that this fluctuation is caused by a response to hormones, such as those related to stress, which begins to show inappropriate secretion after brain damage associated with aSAH.^{19,20}

Furthermore, Yoshikawa et al.,²¹ when analyzing patients with low-grade aSAH who were ≥ 70 years old and who

received treatment, demonstrated that the mean absolute daily difference in the normal plasma sodium level was significantly associated with the modified Rankin Scale scores in 3 and 12 months after aSAH.

Conversely, a study showed that there was no significant difference in serum sodium levels, over the first 14 days post-aSAH, in patients who later developed vasospasm, compared with those who did not, and that, in terms of outcomes neurological, functional, and mortality factors, changes in sodium levels over time were not associated with these outcomes.²²

Finally, some results support the use of tests referring to natriemia more comprehensively, since serum sodium values can be considered as an independent factor for mortality¹⁶ and its variations as predictors of a worse neurological condition at hospital discharge and within 6 months.^{10,11}

Glucose Change

At the time of aneurysm rupture, it may result in an increase in glucose within 72 hours after the onset of bleeding.⁷ As a result, in addition to hyponatremia events in individuals with aSAH, as already mentioned, we may have some changes in glucose.

In the study by Jia et al.,²³ it was described that 4,804 (70.9%) patients who suffered a spontaneous subarachnoid hemorrhage had hyperglycemia. Of these, a higher in-hospital mortality rate was identified for patients with more severe hyperglycemia in whom the odds of in-hospital mortality were higher, significantly higher in patients with moderate hyperglycemia (odds ratio [OR]: 2.61; 95% confidence interval [CI]: 1.52–3.06) and higher in patients with severe hyperglycemia (OR: 3.18; 95% CI 2.24–4.53; $p < 0.001$). The mortality of these patients may be related to changes in blood glucose.

Reinforcing this analysis, it was also identified in the study by Sun et al.²⁴ with 119 patients with aSAH who had a high admission glycemic interval (aGG) ≥ 30 mg/dL (66.4%), is associated with markers of disease severity and hospital outcomes, strengthening the concept that is an indicator of physiological response to stress to aSAH. Furthermore, aGG outperformed admission glucose in predicting in-hospital mortality and was equally accurate in the discerning poor composite outcome.

It is also notable that discussions in works regarding glucose variation and its relationship with the occurrence of vasospasm.^{25,26} The study by Matano et al.²⁵ including 333 patients, made a statistical correlation between ischemia due to cerebral vasospasm and glucose/potassium ratio ($p < 0.0001$), glucose ($p = 0.016$), and potassium ($p = 0.0017$). The glucose/serum potassium ratio was elevated in cerebral vasospasm (Spearman $r = 0.1207$; $p = 0.0279$).

Brief-form vasospasm is a common complication after aSAH and is a major contributor to the high morbidity and mortality rate of the disease. The pathophysiology of vasospasm is not well understood and probably involves an interaction between blood products, vasoactive substances, and inflammatory cascades.²⁷

In addition to the glucose/potassium ratio, the serum glucose-phosphate index is a potential marker of severity

and poor outcomes for patients with aSAH.²⁸ Higher blood glucose levels were identified in patients with rebleeding, in addition to patients in the group of rebleeding who had a significantly higher glucose/potassium ratio than patients without rebleeding.¹² Furthermore, Zhang et al.²⁹ reported that the glucose-phosphate ratio was significantly correlated with vasospasm ($r = 0.581$; $p < 0.001$) and DCI ($r = 0.523$; $p < 0.001$), resulting in an unfavorable prognosis.

As evidenced, high blood glucose levels on admission are associated with aSAH severity and worse evolution. A recent study addressed that cerebral vasospasm exacerbated by hyperglycemia may be a potential mechanism for the poor neurological outcomes observed.²⁹

The correlation of hyperglycemia with a poor prognosis has several scientific explanations; some experimental studies indicate that hyperglycemia induces apoptosis, while others claim that hyperglycemia increases the production of superoxide, damaging the blood-brain barrier, causing cerebral edema. Another explanation is that hyperglycemia impairs different components of innate immunity, leading to a systemic anti-inflammatory response.²⁰ Another explanation would be about cerebral vasospasm exacerbated by hyperglycemia being a potential mechanism for poor neurological outcomes.²⁹

On the other hand, the occurrence of hypoglycemia in patients with aSAH is associated with unfavorable neurological outcomes and risk of vasospasm.^{30,31} Therefore, glucose variability, both hyper and hypoglycemia, may be correlated with hospital mortality or with a poor prognosis in the long term in patients with aSAH.³²

Studies identified that previous hyperglycemia (diabetes mellitus [DM]) HAS does not seem to affect the neurological status from admission or the outcome at 6 months. However, hyperglycemia affects these elements, as it is probably a reflection of an acute brain injury.^{33,34} Therefore, this information suggests that the unfavorable prognosis is more related to post-aSAH hyperglycemia, but more studies should be performed for the discussion of the relationship between the prognosis of patients who have DM and who have suffered HAS.

Limitations

The present study has several limitations. Primarily, as this is secondary research, the reliability of the information depends on the quality of the primary data. To minimize this bias, the authors tried to stick to the methodology of each work, to include in the results only items with technical quality and scientific rigor. Second, due to the adopted style of integrative and nonsystematic review, certain studies may have escaped the scope of the evaluation. However, it is worth mentioning that the objective is to obtain and synthesize the most recent evidence on the subject and, for this, the recommendations for care in methodological preparation and selection criteria were followed.

In addition, the articles included distinctions in terms of location, sample number, laboratory evaluation method, time of collection, and the scale for analyzing the result – such as the Glasgow Outcome Score and the Modified Rankin

Scale, among others. However, the authors chose not to be very judicious about the complementary test used – provided that at least one measurement of serum sodium or blood glucose was performed – or the assessment scale to allow gathering the largest possible sample size and summarizing the current understanding of the impact of glycemia and natremia in mortality and neurological outcome of patients after aSAH. Thus, the present findings must be evaluated with caution, and systematic reviews and future meta-analyses will be necessary to determine with more precision the correct period to request laboratory evaluation and the values with greater influence on the prognosis.

Conclusion

The present study concludes that alterations in blood glucose values and plasma sodium concentration influence the in-hospital morbidity and mortality of patients with aSAH. However, it is emphasized that the analysis of the independent influence of each of the related predictors must be done with caution due to the heterogeneity of the results found. Sodium alterations, in general, are related to unfavorable consequences. Hyponatremia and fluctuation in serum levels of anxiety are more consistent as an independent risk factor, related to worse outcomes, while hyponatremia shows more controversial results, being more commonly described as having no prognostic value, although other studies describe clinical and negative results. longer ICU stay. As for variations in glucose levels, both hyperglycemia, and hypoglycemia, due to physiological changes, were also associated with poor prognosis and higher in-hospital mortality.

Conflict of Interests

The authors have no conflict of interests to declare.

Acknowledgments

None to declare.

References

- Macdonald RL, Schweizer TA. Spontaneous subarachnoid haemorrhage. *Lancet* 2017;389(10069):655–666
- Neifert SN, Chapman EK, Martini ML, et al. Aneurysmal Subarachnoid Hemorrhage: the Last Decade. *Transl Stroke Res* 2021;12(03):428–446
- D'Souza S. Aneurysmal Subarachnoid Hemorrhage. *J Neurosurg Anesthesiol* 2015;27(03):222–240
- Guaresi JR, Lung TC, Branco LTO, et al. Sequelas em pacientes com hemorragia subaracnóide por ruptura de aneurisma intracraniano. *Arq Catarin Med* 2011;40(02):
- Gerardo FC, Braga FM. Complicações precoces da hemorragia subaracnóide por ruptura de aneurisma. Parte I – Ressangramento e hidrocefalia aguda. *J Bras Neurocir* 2001;12(03):139–148
- Gerardo FC, Braga FM. Complicações precoces da hemorragia subaracnóide por ruptura de aneurisma. Parte II – Vasoespasmo sintomático. *J Bras Neurocir* 2002;13(01):16–31
- Wang J, Feng Q, Zhang Y, Qiu W, Gao H. Elevated Glucose-Potassium Ratio Predicts Preoperative Rebleeding in Patients With Aneurysmal Subarachnoid Hemorrhage. *Front Neurol* 2022;12:795376
- Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL. Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. *Stroke* 2007;38(08):2315–2321
- Escamilla-Ocañas CE, Venkatasubba Rao CP, Bershad E, Damani R. Temporal Relationship between Hyponatremia and Development of Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage Patients: A Retrospective Observational Study. *J Stroke Cerebrovasc Dis* 2020;29(06):104789
- Tam CW, Shum HP, Yan WW. Impact of dysnatremia and dyskalemia on prognosis in patients with aneurysmal subarachnoid hemorrhage: a retrospective study. *Indian J Crit Care Med* 2019;23(12):562–567
- Okazaki T, Hifumi T, Kawakita K, et al. Target serum sodium levels during intensive care unit management of aneurysmal subarachnoid hemorrhage. *Shock: Injury, Inflammation, and Sepsis. Shock* 2017;48(05):558–563
- Wang Z, Zhou J, Liang F, et al. Prognostic models for neurological functional outcomes in aneurysmal subarachnoid hemorrhage patients with intracranial hematoma. *Clin Neurol Neurosurg* 2020;191:105691
- Sokoł B, Wąsik N, Więckowska B, Mańko W, Juszkat R, Jankowski R. Predicting mortality in subarachnoid haemorrhage based on first-week routine blood tests. *J Clin Neurosci* 2018;58:100–107
- Yang X, Cheng Q, Li Y, Zheng Z, Liu J, Zhao Z. Clinical Treatment and Prognostic Analysis of Patients with Aneurysmal Subarachnoid Hemorrhage. *J Healthc Eng* 2021;2021:1250334
- Ridwan S, Zur B, Kurscheid J, et al. Hyponatremia After Spontaneous Aneurysmal Subarachnoid Hemorrhage-A Prospective Observational Study. *World Neurosurg* 2019;129:e538–e544
- Zafar SF, Postma EN, Biswal S, et al. Electronic health data predict outcomes after aneurysmal subarachnoid hemorrhage. *Neurocrit Care* 2018;28(02):184–193
- Kieninger M, Kerscher C, Bründl E, et al. Acute hyponatremia after aneurysmal subarachnoid hemorrhage: Frequency, treatment, and outcome. *J Clin Neurosci* 2021;88:237–242
- Rumalla K, Lin M, Ding L, et al. Risk Factors for Cerebral Vasospasm in Aneurysmal Subarachnoid Hemorrhage: A Population-Based Study of 8346 Patients. *World Neurosurg* 2021;145:e233–e241
- Cohen J, Delaney A, Anstey J, et al. Dysnatremia and 6-Month Functional Outcomes in Critically Ill Patients With Aneurysmal Subarachnoid Hemorrhage: A Prospective Cohort Study. *Crit Care Explor* 2021;3(06):e0445
- Harada T, Uozumi Y, Fukuoka H, et al; Kobe University SAH study collaborators. The impact of hormonal dynamics and serum sodium fluctuations on symptomatic vasospasm after subarachnoid hemorrhage. *J Clin Neurosci* 2022;103:131–140
- Yoshikawa S, Kamide T, Kikkawa Y, et al. Long-Term Outcomes of Elderly Patients with Poor-Grade Aneurysmal Subarachnoid Hemorrhage. *World Neurosurg* 2020;144:e743–e749
- Chua MMJ, Enríquez-Marulanda A, Gomez-Paz S, et al. Sodium Variability and Probability of Vasospasm in Patients with Aneurysmal Subarachnoid Hemorrhage. *J Stroke Cerebrovasc Dis* 2022;31(01):106186
- Jia L, Zhang Y, Wang P, et al. Association between hyperglycemia at admission and mortality in aneurysmal subarachnoid hemorrhage. *J Clin Neurosci* 2022;103:172–179
- Sun PY, Poblete RA, Nguyen PL, et al. Association Between Glycemic Gap and In-hospital Outcomes in Aneurysmal Subarachnoid Hemorrhage. *Front Neurol* 2021;12:714341
- Matano F, Fujiki Y, Mizunari T, et al. Serum glucose and potassium ratio as risk factors for cerebral vasospasm after aneurysmal subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis* 2019;28(07):1951–1957
- Fujiki Y, Matano F, Mizunari T, et al. Serum glucose/potassium ratio as a clinical risk factor for aneurysmal subarachnoid hemorrhage. *J Neurosurg* 2018;129(04):870–875
- Chen S, Feng H, Sherchan P, et al. Controversies and evolving new mechanisms in subarachnoid hemorrhage. *Prog Neurobiol* 2014;115:64–91

- 28 Jung HM, Paik JH, Kim SY, Hong DY. Association of plasma glucose to potassium ratio and mortality after aneurysmal subarachnoid hemorrhage. *Front Neurol* 2021;12:661689
- 29 Zhang D, Zhuang Z, Wei Y, et al. Association of Admission Serum Glucose-Phosphate Ratio with Severity and Prognosis of Aneurysmal Subarachnoid Hemorrhage. *World Neurosurg* 2019;127:e1145–e1151
- 30 McIntyre MK, Halabi M, Li B, et al. Glycemic indices predict outcomes after aneurysmal subarachnoid hemorrhage: a retrospective single center comparative analysis. *Sci Rep* 2021;11(01):158
- 31 Okazaki T, Hifumi T, Kawakita K, et al. Blood glucose variability: a strong independent predictor of neurological outcomes in aneurysmal subarachnoid hemorrhage. *J Intensive Care Med* 2018;33(03):189–195
- 32 Sadan O, Feng C, Vidakovic B, et al. Glucose variability as measured by inter-measurement percentage change is predictive of Inpatient mortality in aneurysmal subarachnoid hemorrhage. *Neurocrit Care* 2020;33(02):458–467
- 33 Beseoglu K, Steiger HJ. Elevated glycated hemoglobin level and hyperglycemia after aneurysmal subarachnoid hemorrhage. *Clin Neurol Neurosurg* 2017;163:128–132
- 34 Ray B, Ludwig A, Yearout LK, Thompson DM, Bohnstedt BN. Stress-induced hyperglycemia after spontaneous subarachnoid hemorrhage and its role in predicting cerebrospinal fluid diversion. *World Neurosurg* 2017;100:208–215