

Original Research Article

Association of Hemoglobin Decrement with Poor Outcome of Aneurysmal Subarachnoid Hemorrhage

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Abstract:

Objective: To determine the frequency of favorable outcome and correlation of hemoglobin decrement with poor outcome after 3 months in patients with aneurysmal subarachnoid hemorrhage.

Study Design Longitudinal study.

Place and Duration of Study: Neurology Department, Fauji Foundation Hospital, Rawalpindi, from 18th June 2025 to 17th September 2025.

Methodology: Total 124 patients aged 30-70 years, regardless of gender, who have had an aneurysmal subarachnoid hemorrhage lasting less than 48 hours were included. Individuals with established heart conditions, chronic liver failure, head injury patients and any brain lesion that occupies space were excluded. The outcome (At three months, the Modified Rankin Score (mRS) was used to evaluate patient outcomes. At three months following commencement, an mRS score of 0-3 was regarded as a favorable outcome, whereas a score of 4-6 was regarded as a poor outcome) after three months was recorded. The lowest value entered into the electronic medical record system was referred to as minimum hemoglobin. The hemoglobin concentration at admission less the minimum hemoglobin concentration was used to calculate hemoglobin decrement; if the result was negative, it was written as 0.

Results: Of the 124 patients with aSAH who were enrolled in this study, 82 (66.13%) had a satisfactory outcome at three months, while 42 (33.87%) had a poor prognosis. Mean serum hemoglobin levels were 9.32 ± 1.23 g/dl and mean Modified Rankin Score was 3.03 ± 1.15 . Correlation of hemoglobin decrement with poor outcome of aneurysmal subarachnoid hemorrhage was found to be -0.680 which is statistically significant.

Conclusion: In conclusion, patients with aSAH who have hemoglobin depletion while in the hospital may have a worse prognosis.

Keywords: subarachnoid hemorrhage, hemoglobin decrement, outcome.

INTRODUCTION

More than 30% of patients die from aneurysmal subarachnoid hemorrhage (aSAH), a severe cerebrovascular catastrophe that leaves about 25% of survivors with neurological impairments [1]. Anemia is a frequent side effect following SAH; research indicates that approximately 50% of patients may experience anemia while in the hospital [2]. Patients with post-SAH anemia also have a higher risk of poor outcome and delayed cerebral ischemia (DCI) [3]. According to earlier research, vasospasm and a poor neurological prognosis at discharge are predicted by lower mean hemoglobin levels during the acute phase of aSAH [4]. But research on whether blood transfusions can treat anemia following a SAH is currently at a standstill [5].

Blood transfusions did not significantly lower the incidence of cerebral infarction, according to a tiny RCT on the viability of treating anemia following a SAH [6]. More hemoglobin decrement throughout hospitalization was linked to DCI and a poor outcome in patients with SAH, regardless of hemoglobin levels, according to a recent study by Asghar et al [7].

The prognosis of aSAH is further impacted by pneumonia, a common extracranial consequence that is also common in anemic patients [8]. Of the 480 patients with aSAH who were enrolled in the trial, 414 (71.1%) had a satisfactory outcome at three months, while 66 (28.9%) had a poor prognosis. Using the ROC curve, the cut-off value for determining the extent of hemoglobin drop was 12.5 g/l. Significant correlations

were seen between hemoglobin decrease over the cutoff value and poor prognosis, cerebral infarction (9.0% vs 26.0%), and pneumonia (8.0% vs 29.0%; $p < 0.001$) [9]. Since there isn't a local study on the subject, the study's justification is to ascertain whether hemoglobin depletion during hospitalization is associated with the prognosis of aneurysmal subarachnoid hemorrhage in our community. Due to a lack of medical facilities and financial restraints, most patients in Pakistan report relatively late compared to other developed nations because a substantial portion of the population lives in rural regions and has a low socioeconomic standing. It is unclear how the clinical relevance of hemoglobin decline from admission to discharge affects aSAH patients' outcomes. We postulated that, regardless of admission Hb levels, a declining Hb trend is linked to worse outcomes. Thus, we aimed to investigate the relationship between Hb decline and outcomes in aSAH patients.

METHODOLOGY

This longitudinal study was carried out from 18th June to 17th September 2025 by the Department of Neurology, Fauji Foundation Hospital, Rawalpindi. Following institutional ethical review committee approval, non-probability sequential selection was used to choose 124 patients who met the inclusion criteria. Every patient will be asked for their informed permission. Sample size was calculated using WHO sample size calculator by taking favorable outcome after 3 months in patients with aneurysmal subarachnoid hemorrhage as 71.1%, margin of error 8% and 95% confidence level [9]. The calculated sample size came out as 124. All individuals between the ages of 30 and 70, irrespective of gender, who have experienced an aneurysmal subarachnoid hemorrhage (any of the following occurs: Within 24 hours, focal symptoms (one-sided weakness, speech difficulties, and cranial nerve palsy) manifest; the GCS is less than 8/15; the non-contrast CT scan of the brain reveals a loss of gray-white matter interface, hypo-density of the insular cortex and basal ganglia; a high attenuating (bright) clot; low attenuating (dark) cerebrospinal fluid (CSF); and normal brain tissue. These symptoms last for less than 48 hours. Individuals with established heart conditions, chronic liver failure, head injury patients and any brain lesion that occupies space were excluded.

We took note of demographic information such as age (in years), gender (male or female), length of SAH, stroke severity, diabetes mellitus (yes or no), hypertension (yes or no), dyslipidemia (yes or no), BMI, and hemoglobin levels at presentation. Every patient was treated in accordance with ward policy. The outcome (At three months, the Modified Rankin Score (mRS) was used to evaluate patient outcomes. At three months following commencement, an mRS score of 0–3 was regarded as a favorable outcome, whereas a score of 4–6 was regarded as a poor outcome) after three months was recorded. The lowest amount of hemoglobin that could be entered into the electronic

medical record system was called the minimum. We calculated the hemoglobin decrease by subtracting the minimum hemoglobin concentration from the hemoglobin concentration at admission. If the answer was negative, it was recorded as 0. All data was gathered using a specially created proforma (attached). SPSS version 25 was used to enter and analyze all of the obtained data. The means and standard deviations or median (IQR) was used to display quantitative information such as age (in years), height, weight, BMI, length of the SAH, NIHSS score, mRS score, hemoglobin upon presentation and hemoglobin decrement. Qualitative information was displayed as frequency and percentages, including gender, stroke severity, diabetes mellitus (yes or no), hypertension (yes or no), dyslipidemia (yes or no), and outcome (favorable/poor). Spearman correlation was measured between hemoglobin decrement and a poor prognosis for aneurysmal subarachnoid hemorrhage. P-value of less than 0.05 was considered significant. Data stratification by age, gender, stroke severity, duration of SAH, diabetes mellitus (yes or no), hypertension (yes or no), and dyslipidemia (yes or no) was used to control effect modifiers. The chi square/fisher exact test was used after stratification to see their effect on outcome. Pearson correlation was also measured between hemoglobin decrement and a poor prognosis for aneurysmal subarachnoid hemorrhage after stratification. A P value of less than 0.05 was considered significant

RESULTS

Participants in the study had a mean age of 57.12 ± 11.24 years, with ages ranging from 30 to 70 years. Of the 124 patients, 74 (59.68%) were men and 50 (40.32%) were women, resulting in a male to female ratio of 1.5:1. The average length of illness in our sample was 18.60 ± 3.58 hours. The distribution of patients with additional confounding variables is shown below. Duration >24 hours (58.06%), hypertension (64.52%), and dyslipidemia (54.03%) were more frequent among participants. Moderate stroke severity was the most common category (44.35%), followed by severe (34.68%) and mild stroke (20.97%) (Table 1).

Table 1. Distribution of patients with other confounding variables (n=124)

Confounding variables		Frequency	%age
Age (years)	30-50	72	58.06
	51-70	52	41.94
Gender	Male	74	59.68
	Female	50	40.32
Duration (hours)	≤ 24	52	41.94

	>24	72	58.06
Diabetes mellitus	Yes	65	52.42
	No	59	47.58
Hypertension	Yes	80	64.52
	No	44	35.48
Dyslipidemia	Yes	67	54.03
	No	57	45.97
Severity of stroke	Mild	26	20.97
	Moderate	55	44.35
	Severe	43	34.68

Of the 124 patients with aSAH who were enrolled in this study, 82 (66.13%) had a satisfactory outcome at three months, while 42 (33.87%) had a poor prognosis (Figure 1).

Figure 1. Frequency of favorable outcome after 3 months in patients with aneurysmal subarachnoid hemorrhage (n=124)



Mean serum hemoglobin levels were 9.32 ± 1.23 g/dl and mean Modified Rankin Score was 3.03 ± 1.15 . Correlation of hemoglobin decrement with poor outcome of aneurysmal subarachnoid hemorrhage was found to be -0.680 which is statistically significant (Table 2).

Table 2. Correlation of hemoglobin decrement with poor outcome of aneurysmal subarachnoid hemorrhage

	Mean \pm SD	Spearman's rho	P-value
Serum hemoglobin levels	9.32 ± 1.23	-0.680	0.0001
mRS score	3.03 ± 1.15		

Age and duration showed significant associations with the outcome ($p < 0.05$). Patients aged 30–50 years and those with duration > 24 hours had higher positive

outcomes. No significant association was observed for gender, diabetes, hypertension, dyslipidemia, or stroke severity. (Table 3).

Table 3. Stratification of favorable outcome with respect to confounders

		Yes (n=82)	No (n=42)	P-value
Age (years)	30-50	56 (77.78%)	16 (22.22%)	0.0013
	51-70	26 (50.0%)	26 (50.0%)	
Gender	Male	52 (70.27%)	22 (29.73%)	0.236
	Female	30 (60.0%)	20 (40.0%)	
Duration (hours)	≤ 24	28 (53.85%)	24 (46.15%)	0.014
	> 24	54 (75.0%)	18 (25.0%)	
Diabetes mellitus	Yes	45 (69.23%)	20 (30.77%)	0.444
	No	37 (62.71%)	22 (37.29%)	
Hypertension	Yes	52 (65.0%)	28 (35.0%)	0.720
	No	30 (68.18%)	14 (31.82%)	
Dyslipidemia	Yes	47 (70.15%)	20 (29.85%)	0.305
	No	35 (45.45%)	22 (54.55%)	
Severity of stroke	Mild	18 (69.23%)	08 (30.77%)	0.836
	Moderate	37 (67.27%)	18 (32.73%)	
	Severe	27 (62.79%)	16 (37.21%)	

Ferritin levels showed a significant negative correlation with mRS score across all demographic and clinical subgroups (Spearman's rho ranging from -0.554 to -0.809 ; $p = 0.0001$). Higher ferritin levels were consistently associated with lower mRS scores,

indicating better functional outcomes. This significant inverse relationship remained consistent irrespective of age, gender, duration, comorbidities, and stroke severity (Table 4).

Table 4. Stratification of correlation with respect to confounders

Age (years)	Ferritin levels	mRS score	Spearman's rho	P-value
	Mean ± SD	Mean ± SD		
30-55	9.54 ± 1.23	2.72 ± 0.94	-0.809	0.0001
56-80	9.02 ± 1.19	3.46 ± 1.29	-0.554	0.0001
Gender				
Male	9.51 ± 1.22	2.95 ± 1.21	-0.661	0.0001
Female	9.04 ± 1.20	3.16 ± 1.06	-0.623	0.0001
Duration(h r)				
≤24	9.11 ± 1.28	3.42 ± 1.23	-0.666	0.0001
>24	9.48 ± 1.19	2.75 ± 1.02	-0.674	0.0001
Diabetes mellitus				
Yes	9.47 ± 1.28	2.95 ± 1.16	-0.653	0.0001
No	9.16 ± 1.16	3.12 ± 1.15	-0.707	0.0001
Hypertension				
Yes	9.43 ± 1.26	3.0 ± 1.13	-0.672	0.0001
No	9.13 ± 1.16	3.09 ± 1.22	-0.698	0.0001
Dyslipidemia				
Yes	9.54 ± 1.22	2.89 ± 1.14	-0.652	0.0001
No	9.07 ± 1.21	3.19 ± 1.16	-0.684	0.0001

Severity of stroke				
Mild	9.41 ± 1.22	2.92 ± 1.09	-0.736	0.0001
Moderate	9.22 ± 1.17	3.09 ± 1.11	-0.607	0.0001
Severe	9.40 ± 1.33	3.02 ± 1.26	-0.702	0.0001

DISCUSSION

According to our research, individuals with aneurysmal subarachnoid hemorrhage (aSAH) who experience hemoglobin depletion while in the hospital have a much worse prognosis three months later. We discovered through causal mediation analysis that hemoglobin deficiency impacts the prognosis of patients with aSAH, potentially through a higher risk of cerebral infarction.

Research indicates that over 50% of patients may develop anemia during hospitalization, corroborating the prevalent notion that anemia frequently occurs subsequent to SAH.¹⁰ Patients with post-SAH anemia exhibit an elevated risk of delayed cerebral ischemia and a poorer outcome [11-14]. Moreover, studies have indicated that a low mean hemoglobin level during the acute phase of aSAH is indicative of an unfavorable prognosis post-discharge and may lead to vasospasm [15]. In the current study, we also found that the group with a poor prognosis had a lower minimum hemoglobin concentration and a more pronounced degree of hemoglobin decrement. The results from previous studies mostly align with our conclusions.

But research on whether blood transfusions can treat anemia following a SAH is currently at a standstill [16]. The safety and effectiveness of transfusing low hemoglobin levels within three days of the onset of aSAH were investigated in a previous modest randomized controlled trial (RCT), which found no significant differences between the treatment and control groups in terms of new-onset cerebral infarcts or delayed cerebral ischemia (DCI) [17]. The two groups' mortality rates did not differ significantly, according to a follow-up analysis using propensity score matching [18].

Adding hemoglobin decrement did not make a statistically meaningful difference between low hemoglobin and a negative prognosis. We suspect that the decrease in hemoglobin, rather than the anemia caused by the drop in hemoglobin, may be what affects the prognosis of SAH patients. This is why transfusion therapy doesn't seem to help their prognosis. The most common issues that affect the prognosis of people with aSAH are DCI and the cerebral infarction that comes with it [19]. Many studies have shown a strong link between anemia and DCI after aSAH. According to our research, hemoglobin deficiency over the cutoff point of

12.5 g/l was substantially linked to cerebral infarction, and poor prognosis.

Pneumonia is very likely to strike patients with aSAH. Research indicates that between 13 and 37 percent of individuals with aSAH had postoperative lung infections [20]. According to China Stroke Statistics 2019, pneumonia was the most common comorbidity among stroke patients in China (29.7% for SAH) [21]. According to published research, pneumonia following a SAH is substantially linked to a bad prognosis [22]. Furthermore, anemia—specifically, hemoglobin levels below 10 mg/dl—may make hospitalized patients with community-acquired pneumonia much more likely to die [23]. Few research, nevertheless, have examined the relationship between anemia and the prognosis of aSAH with pneumonia. According to a study, hemoglobin deficiency beyond the cutoff value of 12.5 g/l may raise the risk of pneumonia considerably, and the prognosis of SAH is impacted by pneumonia by about 38.5%.⁹

Disseminated intravascular coagulation (DIC) and vasospasm brought on by an accumulation of nitric oxide synthases in red blood cells are two related complications of decreased cerebral oxygen delivery in SAH that worsen the reduced oxygen delivery and result in additional ischaemia and infarction. Additionally, brain damage can cause diffusion hypoxia even in the absence of macrovascular ischaemia, requiring additional neuroprotection through optimal oxygen supply [24]. Additional research supports this idea as well, showing that a transfusion increased hemoglobin and arterial oxygen content by 15% [25]. Anaemia was also linked to increased cerebral tissue hypoxia and discomfort, as shown by Kurtz et al. utilizing microdialysis sampling and neurological monitoring [26]. The SaHaRa randomized controlled trial strengthened the case that a liberal transfusion threshold might not be harmful in aSAH by showing that in patients with aSAH and anemia, a liberal RBCT strategy did not reduce the risk of an unfavorable neurological outcome at 12 months when compared to a restrictive strategy [27].

Limitations

Our study has certain limitations. First, because the study was conducted at a single location, selection bias was inevitable. This bias was made worse by the omission of cases that had onset times longer than 48 hours. Second, this is a cross-sectional study, and it did not include several confounding factors that could influence the outcome, such as the antiplatelet medicines, transfusion of blood, and hemoglobin drop causes. Third, certain individuals with asymptomatic cerebral infarction may be missed by CT because MRI and CT have varying sensitivity in detecting acute cerebral infarction.

CONCLUSION

In conclusion, patients with aSAH who have hemoglobin depletion while in the hospital may have a worse prognosis; this link may arise because hemoglobin depletion raises the risk of complications.

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