Haemoglobin Levels as a Predictor of Functional Disability and Its Association with Sex Difference in Outcomes of Acute Ischemic Stroke Patients

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ABSTRACT

BACKGROUND

In patients of acute ischemic stroke, there is increased mortality associated with low admission haemoglobin. But limited studies exist on haemoglobin as prognostic predictor of functional outcome in elderly stroke patients. Also, the outcome of stroke is known to be consistently poorer in women than in men. We wanted to correlate this sex difference to haemoglobin variations.

METHODS

This is a prospective study of 80 patients, diagnosed with acute ischemic stroke conducted from October 2017 to September 2019. Admission haemoglobin levels were noted, and each patient was evaluated for stroke severity with MNIHSS and Charlson Index, a composite measure of comorbidities was computed. At the end of one week, functional outcome was assessed through Barthel index. Multiple Regression analysis was used to determine the relationship of admission haemoglobin to stroke outcomes after adjustment for neurological severity and medical comorbidities.

RESULTS

Out of 80 cases about 59% were elderly adults; 58.75% were male patients and 41.25% were female patients. 53.75% of these patients belonged to mild functional dependency according to Barthel index and the rest were in moderate to severe dependency. In the study, it was noted that higher the level of haemoglobin better the Barthel Index and hence better the functional outcome, when adjusted for comorbidities. Also, 42.4% of females had severe disability as opposed to 34% of males. However this relationship was not statistically significant.

CONCLUSIONS

Our study found a significant and positive correlation between admission haemoglobin and the functional outcome of acute ischemic stroke. Elderly patients with higher admission haemoglobin were found to have less severe disability following an acute ischemic stroke. Our study also established a cut off haemoglobin value of 12g/dL and above as being associated with overall favourable outcome in stroke patients. However, the difference in haemoglobin levels between male and female patients could not be correlated as a significant factor contributing to sex differences in stroke outcomes.

KEYWORDS

Elderly Stroke, Acute Ischemic Stroke, Anaemia, Haemoglobin and Stroke, Sex Difference in Stroke

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BACKGROUND

Ischemic stroke is defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.[1] Nearly 80% of all strokes are due to cerebral ischaemia.[2] Stroke is third most common cause of disability in the world and 28.5 million Disability Adjusted Life Years (DALYs) were lost due to stroke worldwide[3] the incidence rate of stroke in India is 119-145/100,000 based on the recent population- base studies.[4] While men are 7 times more likely to suffer from stroke, women tend to have worse outcomes of stroke even after adjusting baseline differences in age, pre- stroke function, and comorbidities.[5] This gender difference in stroke outcome has been linked to lower haemoglobin level among other parameters which is more prevalent in women.[6] Hence it is important to further study haemoglobin as a prognostic predictor of stroke outcomes while also investigating the effect it may have on sex difference.

Barthel Index, a 10 questionnaire scale is an effective tool for measuring Activities of Daily Living (ADL) following an ischemic stroke event. It is an ordinal scale that yields a 0-100 score. The scale is widely regarded as dependable scale for assessing stroke outcome, with high inter-rater reliability of 0.95.[7] in this study we use the Barthel index scoring as a measure of stroke outcome. We compare the effect of admission haemoglobin on Barthel index score while controlling for other co-morbid conditions that may independently affect the Barthel score. While some studies have previously established increased mortality associated with low admission haemoglobin, [8] only a handful of studies have attempted to draw a relationship with haemoglobin and functional outcome per se.

Our aim was to study haemoglobin levels in acute ischemic stroke patients as a prognostic predictor of functional outcome and also to investigate the haemoglobin levels in relation to sex differences in stroke outcomes.

METHODS

The study was a prospective cross-sectional study conducted in Kasturba medical college-associated hospitals in Mangalore, Karnataka, for a period of 2 years from October 2017 to September 2019. The study included 80 cases of acute ischemic stroke adults selected from inpatients. The diagnosis of acute ischemic stroke was confirmed from brain imaging (CT or MRI) and by definition the onset of stroke was 1 week or less. Admission haemoglobin levels were noted, and each patient was evaluated for stroke severity (MNIHSS) and Charlson Index, a composite measure of comorbidities was computed. Only those with a Charlson Comorbidity Index of <6 i.e. low-moderate level of severity of comorbidities, were included in the study. Further, the following cases were excluded from the study group- Pregnant women, hyper-acute ischemic stroke cases (onset <3 hours), those who have received intra-arterial or intra venous thrombolytics therapy or mechanical Embolectomy, recurrent stroke patients,[9] Patients with Polycythemia (Hb ≥16.5 g/dL for men ≥16.0 g/dL for women) and those patients who had post-ischemic-stroke seizures.[10]

At the end of 7 days Barthel Index was calculated and patient were divided into severe, moderate or mild dependency based on the score.[11] The data was then compiled into a master chart and for comparison, range, frequencies, percentages, means, standard deviations 't' values, 'p' values along with chi square for quantitative variables were calculated. A p value less than 0.05 was considered to denote a significant relationship.

RESULTS

Individuals were randomly chosen for study, comprised of adults of varied age groups, the distribution showing no significant difference with those >65 (highest stroke prevalence) and below 65. 59% of the total sample were male patients and 41% were female patients. (table 1). 54% patients falling into mild severity while 46% patients being moderately or severely disabled, when assessed at the end of one week of acute ischemic stroke. (table 2)

Age	Frequency	Percent
50 and below	8	10
51 - 60	25	31.25
61 - 70	27	33.75
71 - 80	1	1.25
Above 80	19	23.75
Total	80	100
Mean Age	>65 years	<65 years
	70.5	33
p Value	0.611 (NS)	

Table 1. Age Distribution in Study Group

Barthel Index	Frequency	Percent
Severe	30	37.5
Moderate	7	8.75
Mild	43	53.75
Total	80	100

Table 2. Frequency of Patients in Various Barthel Index Severity, at the End of 1 Week

	Pearson Correlation	P	
Barthel Index	.296	.008	Sig
Charlson Comorbidity Index	-.328	.003	Sig

Table 3. A Pearson Correlation Between Admission Hb v. Barthel Index and CCI

Model	Unstandardized Coefficients	Standardized Coefficients	Beta	t	p
	B	Std. Error			
(Constant)	1.151	.786		1.465	.147
Admission HB%	.113	.055	.223	2.057	.043
Charlson Comorbidity Index	-.179	.063	-.310	-2.861	.005
Model	R	R Square	Adjusted R Square	ANOVA P	
1	.437a	.191	.170	.000	

Table 4. Admission Hb compared to Barthel Index of Stroke Patients After Controlling Multiple Comorbidities with CCI

a. Predictors: (constant), Charlson Comorbidity Index, Admission HB%

The study shows positive correlation between Admission Hb and Barthel Index and a negative correlation between CCI and Admission Hb in patients with acute ischemic stroke. Higher the haemoglobin value, lower the CCI score with lesser comorbidities and mortality risk. Studying if relationship between Admission Hb% and Barthel Index is significant, after controlling for comorbidities with Charlson index. Predictors: (constant), Charlson Comorbidity Index, Admission HB%. Dependent Variable: Barthel Index. Studying if relationship between Admission Hb% and Barthel Index is significant, after Controlling for Hypertension. Predictors: (constant), HTN, Admission HB%. Dependent Variable: Barthel Index

Model	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	Beta		
(constant)	7.404	27.765		.267	.790
Admission HB%	4.639	2.054	.246	2.258	.027
HTN	-15.362	7.666	-.218	-2.004	.049
Model	R		R Square	Adjusted R Square	ANOVA P
1	.364a		.133	.110	.004
Table 5. Admission Hb Compared to Barthel Index of Stroke Patients After Controlling for Hypertension					
a. Predictors: (constant), HTN, Admission HB%					

		Admission HB%					
		Hb <12 g/dL		Hb ≥12 g/dL		Total	
		Count	Column N%		Column N%		Column N%
Age	<50	4	12.9%	4	8.2%	8	10.0%
	51-60	6	19.4%	19	38.8%	25	31.3%
	61-70	11	35.5%	16	32.7%	27	33.8%
	71-80	0	.0%	1	2.0%	1	1.3%
	Above 80	10	32.3%	9	18.4%	19	23.8%
	Total	31	100.0%	49	100.0%	80	100.0%
Sex	Female	13	41.9%	20	40.8%	33	41.3%
	Male	18	58.1%	29	59.2%	47	58.8%
	Total	31	100.0%	49	100.0%	80	100.0%
Table 6a. Haemoglobin and Stroke Outcome							

	Chi Square/Fishers Exact Test p	
Age	0.294	NS
Sex	0.921	NS
Barthel Index	0.005	HS
mRS	0.054	NS
Charlson Comorbidity Index	0.105	NS
HTN	0.259	NS
Table 6b. Sex Difference of Stroke Outcome		

The study shows that the positive relationship of admission haemoglobin with Barthel index after controlling for multiple comorbid conditions (which may independently affect BI). (table 4). Also, Hypertension, a disease not covered in CCI shows a negative relation with Barthel Index. (table 5). As evident from these tables, the relationship established is statistically significant in both cases.

Table 6. Comparison of clinical parameters after dichotomizing study data based on WHO criteria for Anaemia. The study shows Females had mean Hb of 12.39 while the men in the study had average Hb of 13.31. Table 8 illustrates the difference in Barthel Index between male and female patients. Overall the difference was not significant.

DISCUSSION

This study shows the effect of anemia on functional outcome in patients with acute ischemic stroke. There have been a handful of studies that have attempted this before but most have focused on mortality rather than functional outcome. Considering the latest trends of increased survival rate of stroke patients in India it is imperative to focus on rehabilitation measures and degree of disability.[4] Our study, consisted of a random selection of 80 patients of all adult age groups. About 34% of our patients were in elderly age group between ages of 61 to 70. Mortality is high in patients above 65 years of age.[12] Our study did not find the distribution with those above 65 years and those below it to be significant. Also in the study 58% of patients were male and 41.25% were female. In the study, 58.75% were male patients and 41.25% were female patients. Kimberly et al, a study that compared sex differences in acute ischemic stroke found female patients had significantly worse functional outcome than their male counterparts.

Barthel Index, a measure of ADL was used to measure functional outcome at the end of 7 days. Barthel index could be functionally divided into three categories.[10]

BI	Severity
0-50	Severe Dependency
51-70	Moderate Dependency
71-100	Mild Dependency
Table 7	

Our study had 53.75% of patients belonging to mild dependency and the rest were in moderate to severe dependency. A Charlson Index which is originally a measure of mortality based on six scores that correspond to various comorbidities like cardiovascular diseases, cerebrovascular diseases, Diabetes, Chronic kidney disease, chronic liver disease and malignancies. In our study Charlson index was used control all the confounding comorbid conditions.[11] Those with a score of more than 6 were excluded, but otherwise the sample size was well distributed with respect to CCI scores. Hypertension, a comorbid condition not exclusively a part of Charlson index was measured separately to rule out confounding. Hypertension has a complex relation with acute ischemic stroke. In our study 56% of the patients were hypertensive. A mNIHSS score to assess severity of acute ischemic stroke was also done on all patients in the study, with a median score of 7.89.

Relationship with Admission Haemoglobin

Our study shows negative correlation with admission haemoglobin and mNIHSS score. Patients who had lower haemoglobin tended to have a worse functional outcome. The Pearson correlation showed a statistically significant negative relationship. The relationship between Barthel Index and admission haemoglobin showed a positive correlation. Higher the level of haemoglobin better the Barthel Index and hence better the functional outcome. This relation was especially, highly significant for cases with mild disability (BI). Considering acute ischemic stroke is

independently affected by several disease conditions, when this relation was controlled for the comorbidities with Charlson index, the positive relation of admission Hb to Barthel Index remained significant. Similarly, when adjusted for hypertension, the relationship remained statistically significant.

Relationship of Functional Outcome with Sex Difference and Hb%

While there are numerous evidences that point to worse functional outcomes in females following acute ischemic stroke, our study attempted to draw a relationship between presence of lower haemoglobin in females and their poorer outcomes. In our study population the mean haemoglobin of females was 12.29 g/dL but those in male were 13.39 g/dL. 42.4% of females have severe disability according to Barthel index as opposed to 34% of males with severe BI. However, this relationship was not statistically significant and hence we choose not to comment on the possible relationship of sex difference with admission haemoglobin, in patients with acute ischemic stroke.

Anaemia and Functional Outcome

The patients' group was dichotomized based on WHO definition of anemia into those with haemoglobin <12g/dL and those with Hb≥12 g/dL. It was found that the Barthel index value of first group (of anemics) was lesser than those with Hb>12g/dL and this difference was significant.

CONCLUSIONS

Our study found a significant and positive correlation between admission haemoglobin and the functional outcome of acute ischemic stroke. Patients with higher admission haemoglobin were found to have less severe disability following an acute ischemic stroke. Admission haemoglobin also showed a negative correlation with mNIHSS score indicating that patients who had low haemoglobin presented with higher severity of acute ischemic stroke. Our study also established a cut off haemoglobin value of 12 g/dL and above as being associated with overall favourable outcome in ischemic stroke patients. Hence anaemic patients tended to have worse outcomes following a stroke. However, this study could not correlate the difference in haemoglobin levels between male and female patients as a significant factor contributing to sex differences in stroke outcomes. Our data shows higher admission Hb favouring functional outcomes. Hence correction of anaemia in acute ischemic stroke patients should be considered a priority and further studies in ischemic stroke patients could include treatment of anaemia as a timely interventional measure.

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