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Association between Hemoglobin Levels and Severity of Coronary Artery Disease among Patients Presenting with ST-Segment Elevation Myocardial Infarction

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ABSTRACT

Objective: This study aimed to elucidate the association between hemoglobin levels (anemia) and the severity of coronary artery disease (CAD) among patients experiencing ST-segment elevation myocardial infarction (STEMI).

Methods: This prospective cohort study included patients aged 20 to 80 years presenting with STEMI to Liaquat National Hospital and Medicare General and Cardiac Hospitals between September 2023 and February 2024. Anemia was categorized as per the criteria defined by the World Health Organization based on the hemoglobin levels. The severity of CAD was assessed based on the number of vessels affected and the Syntax Score system derived from coronary angiography.

Results: Of the 228 patients included in the study, 122 were anemic based on hemoglobin levels. The Syntax Score was significantly higher in the anemic group compared to the non-anemic group (27.97±7.15 vs. 24.62±7.04, p<0.01). One-way ANOVA showed significant differences in mean Syntax Scores across anemia severity levels, with the severely anemic group having the highest scores (F (3, 224) = 4.310, p = 0.006). Logistic regression indicated that lower hemoglobin levels were significantly associated with higher CAD severity (β = -0.556, t = -2.284, p = 0.023), and male gender also correlated with higher Syntax Scores (β = 2.294, t = 2.165, p = 0.031). The ROC curve analysis revealed an area under the curve (AUC) of 0.537, indicating that hemoglobin alone is not a strong predictor of multivessel disease in this population.

Conclusion: Lower hemoglobin levels are significantly associated with increased severity of CAD in patients with STEMI, emphasizing the need for careful anemia management in CAD patients.

Keywords: Acute Coronary Syndrome, ST-Elevation, Myocardial Infarction, Anemia, Hemoglobin.

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [3,4]Critical analysis and manuscript review; [5,6]Data analysis; Manuscript Editing.

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Introduction

Myocardial ischemia in coronary artery disease (CAD) primarily stems from coronary artery stenosis, resulting in insufficient blood and oxygen supply to the myocardium, thus creating an imbalance between demand and supply.[1] Atherosclerotic plaque formation restricts coronary blood flow, exacerbating the ischemic condition.[1]Cardiovascular disease (CVD) risk exhibits a nuanced relationship with hemoglobin concentration,[2-5] both elevated and decreased. Anemia emerges as an independent risk factor for cardiovascular complications, with even minor declines in hemoglobin concentration posing heightened risks for cardiovascular events

and mortality.[6] It is well-known that due to persistent volume overload chronic anemia leads to cardiac remodeling, including left ventricular hypertrophy, while acute anemia triggers reversible hemodynamic shifts.[7] Compensatory mechanisms, such as tachycardia and increased cardiac output, attempt to counteract the oxygen deficit.[7] Chronic inflammation and oxidative stress further exacerbate Anemia, activating neurohormonal pathways and fostering a pro-atherogenic environment.[8]

Epidemiological research highlights the complex association between cardiovascular diseases and hemorheological parameters, emphasizing the pivotal role of blood rheology in tissue perfusion and disease pathogenesis.[9,10] Studies assessing the impact of hemoglobin reduction on cardiovascular outcomes have yielded conflicting findings, with some advocating for blood transfusions in select populations. In contrast, others report no significant mortality differences between anemic and non-anemic cohorts.[11]

Understanding the intricate relationship between Anemia and CAD holds promise for refining risk assessment strategies and optimizing anemia management to mitigate CAD incidence. In this context, we aimed to elucidate the association between hemoglobin levels (anemia) and the severity of CAD among patients experiencing STEMI, thereby contributing to enhanced risk stratification and therapeutic interventions in CAD management.

Methodology

This prospective cross-sectional study was conducted at the Department of Cardiology, Liaquat National Hospital, and Medicare General and Cardiac Hospitals from September 2023 to February 2024. The ethical approval was obtained from the Institutional bioethical committee, University of Karachi [Reference No. IBC KU-411/2024; Dated 18-04-2024], ensuring adherence to ethical guidelines and standards. The study adhered to the principles outlined in the Declaration of Helsinki and all patients provided informed consent before participation.

A sample size of 214 patients was determined using an Open Epi Sample size calculator, with a prevalence of Anemia set at 16.7%[12] and a margin of error of 5%. The study included patients of both sexes, aged 20 to 80 years, presenting to the emergency department with characteristic symptoms of STEMI, confirmed by ST-segment elevation >1 mm in at least two contiguous leads accompanied by chest pain lasting more than 20 minutes. Exclusion criteria comprised patients with kidney or liver failure, history of anticoagulation therapy, missing data on prevalent CAD or hemoglobin levels, history of cardiac surgery or valvular disease, previous acute myocardial infarction, pre-existing bundle branch block, non-sinus rhythm on electrocardiograms, poor quality echocardiographic images, and those testing positive for COVID-19.

The primary endpoint of the study was to evaluate the relationship between hemoglobin levels (anemia) and the severity of CAD as measured by the Syntax Score. And the secondary endpoint was to assess the ability of hemoglobin levels to predict the presence of multi-vessel disease in patients with STEMI, using ROC curve analysis.

Hemoglobin levels were used to determine anemia status. As per the World Health Organization criteria, mild anemia was characterized by hemoglobin levels of 11-12.9 g/dl for males and 11-11.9 g/dl for females. Moderate anemia was indicated by hemoglobin levels of 10-10.9 g/dl for both males and females, while severe anemia was identified by hemoglobin levels below 10 g/dl for both genders.[13] The severity of CAD was assessed based on the number of affected vessels and the Syntax Score derived from coronary angiography. The number of vessels affected were labeled as

single, two-vessel, and multi-vessel according to the luminal diameter narrowing i.e., ≥ 50% luminal narrowing for the left main coronary artery and 70% for the major coronary arteries, also only those vessels were considered which had a diameter of ≥ 1.5 mm. The Syntax scores were calculated using dedicated software including the coronary arteries with a diameter of 1.5 mm having lesions causing ≥ 50% of stenosis.[14]

In addition to the CAD severity and anemia status, baseline data including age, BMI, gender, marital status, co-morbidities, and tobacco use etc. were collected using a pre-designed proforma. Furthermore, the data regarding laboratory parameters, TIMI Risk Score assessed using TIMI risk assessment tool, Troponin, Creatinine, Glomerular Filtration Rate, and lipid profile were also documented.

The collected data were analyzed using SPSS version 26 software. The categorical variables were assessed using the chi-square test, facilitating comparisons between the patients with and without anemia. For continuous variables, comparisons were conducted via Student's t-tests, Mann-Whitney U-test, or one-way ANOVA (as appropriate). Logistic regression analysis was used to evaluate the association between hemoglobin levels and CAD severity (Syntax Score). The analysis was controlled for age, gender, hypertension, and diabetes mellitus. The role of hemoglobin levels to predict multi-vessel disease in patients with STEMI was assessed using Receiver Operating Characteristic (ROC) curve analysis. To quantify predictive performance, the analysis involved various cut-off values of hemoglobin, calculating sensitivity and false positive rates at each threshold. The coordinates of the ROC curve at various hemoglobin thresholds were used to determine the sensitivity and specificity.

A significance level of $p < 0.05$ was applied to determine statistical significance.

Results

Table I presents the baseline characteristics of the 228 participants, divided into non-anemic (n=106) and anemic (n=122) groups based on hemoglobin levels. Angiographic findings revealed statistically no significant association between the presence of multivessel disease and Anemia (p=0.095).

A significant difference was observed in the Syntax Scores across the anemia severity levels, with an F-value of 4.310 and a p-value of 0.006 (Table II).

Table III illustrates the laboratory findings of the participants, categorized into non-anemic and anemic groups based on hemoglobin levels. Syntax Score, a measure of CAD severity, was significantly higher in the anemic group ($p < 0.01$).

The regression analysis revealed that for every one-unit decrease in hemoglobin levels, there was a corresponding decrease of 0.556 units in the Syntax Score ($\beta = -0.556$, $t = -2.284$, $p = 0.023$, 95% CI [-1.036, -0.076]), indicating a significant association between lower hemoglobin levels and higher CAD severity (Table 4). Furthermore, being male ($\beta = 2.294$, $t = 2.165$, $p = 0.031$, 95% CI [0.206, 4.383]) was significantly associated with higher Syntax Scores, while the presence of diabetes mellitus ($\beta = 1.873$, $t = 1.769$, $p = 0.078$, 95% CI [-0.214, 3.960]) showed a marginally significant positive association. However, hypertension did not demonstrate a significant relationship with Syntax Score ($\beta = -0.501$, $t = -0.436$, $p = 0.663$, 95% CI [-2.766, 1.764]).

The ROC curve yielded an area under the curve (AUC) of 0.537, displaying the predictive role of hemoglobin levels for multivessel disease (Figure 1).

PCI-Percutaneous Coronary Intervention

Values are given as n (%). *p<0.05 is considered statistically significant. LB-Lower Bound; UB-Upper Bound. - Sig. represents the significance level of each variable.

Table I: Baseline Characteristics of Participants					
Variables		**Total (n=228)**	**Anemia**		**p-value**
			No (n=106)	**Yes (n=122)**	
Age (Years); Mean ± SD		63.49±9.97	62.75±9.59	64.14±10.29	0.293
BMI (Kg/m^2); Mean ± SD		28.10±3.94	28.31±4.11	27.91±3.80	0.446
Gender	Female	84(36.8)	43(40.6)	41(33.6)	0.277
	Male	144(63.2)	63(59.4)	81(66.4)	
Marital Status	Married	223(97.8)	105(99.1)	118(96.7)	0.230
	Single	5(2.2)	1(0.9)	4(3.3)	
Cardiogenic Shock	No	221(96.9)	102(96.2)	119(97.5)	0.566
	Yes	7(3.1)	4(3.8)	3(2.5)	
Prior Heart Failure	No	227(99.6)	106(100.0)	121(99.2)	0.350
	Yes	1(0.4)	-	1(0.8)	
Dyslipidemia	No	196(86.0)	95(89.6)	101(82.8)	0.138
	Yes	32(14.0)	11(10.4)	21(17.2)	
Hypertension	No	55(24.1)	26(24.5)	29(23.8)	0.894
	Yes	173(75.9)	80(75.5)	93(76.2)	
Family History of Premature CAD	No	218(95.6)	104(98.1)	114(93.4)	0.086
	Yes	10(4.4)	2(1.9)	8(6.6)	
Prior MI	No	209(91.7)	99(93.4)	110(90.2)	0.378
	Yes	19(8.3)	7(6.6)	12(9.8)	
Currently on Dialysis	No	20489.5 ()	104(98.1)	100(82.0)	<0.01*
	Yes	24(10.5)	2(1.9)	22(18.0)	
Atrial Fibrillation or Flutter	No	221(96.9)	104(98.1)	117(95.9)	0.334
	Yes	7(3.1)	2(1.9)	5(4.1)	
Chronic Lung Disease	No	218(95.6)	101(95.3)	117(95.9)	0.820
	Yes	10(4.4)	5(4.7)	5(4.1)	
Chronic Liver Disease	No	225(98.7)	105(99.1)	120(98.4)	
	Yes	3(1.3)	1(0.9)	2(1.6)	0.646
Diabetes Mellitus	No	77(33.8)	41(38.7)	3629.5 ()	0.144
	Yes	151(66.2)	65(61.3)	86(70.5)	
Prior PCI	No	201(88.2)	96(90.6)	105(86.1)	0.294
	Yes	27(11.8)	10(9.4)	17(13.9)	
Prior CABG	No	217(95.2)	101(95.3)	116(95.1)	0.944
	Yes	11(4.8)	5(4.7)	6(4.9)	
Prior Known CAD	No	184(80.7)	87(82.1)	97(79.5)	0.624
	Yes	44(19.3)	19(17.9)	25(20.5)	
Tobacco Use	Never	173(75.9)	83(78.3)	90(73.8)	0.874
	Former	31(13.6)	13(12.3)	18(14.8)	
	Current-Every Day	22(9.6)	9(8.5)	13(10.7)	
	Current-Some days	2(0.9)	1(0.9)	1(0.8)	
Cardiomyopathy or LV Systolic Dysfunction	No	201(88.2)	93(87.7)	108(88.5)	0.854
	Yes	27(11.8)	13(12.3)	14(11.5)	
Heart Failure	No	218(95.6)	104(98.1)	114(93.4)	0.086
	Yes	10(4.4)	2(1.9)	8(6.6)	
PCI	No	102(44.7)	49(46.2)	53(43.4)	0.673
	Yes	126(55.3)	57(53.8)	69(56.6)	
Diagnostic Cath	No	12(5.3)	9(8.5)	3(2.5)	0.042*
	Yes	216(94.7)	97(91.5)	119(97.5)	
PCI with Stent	No	112(49.1)	53(50.0)	59(48.4)	0.805
	Yes	116(50.9)	53(50.0)	63(51.6)	
No of Treated Vessels	No Vessel Involved	112(49.1)	53(50.0)	59(48.4)	0.798
	Single Vessel	103(45.2)	46(43.4)	57(46.7)	
	Two Vessel	13(5.7)	7(6.6)	6(4.9)	
Multivessel disease	Yes	211(92.5)	95(89.6)	116(95.1)	0.095
	No	17(7.5)	11(10.4)	6(4.9)	

Table II: Association between anemia severity and SYNTAX score						
Anemia Severity	Mean	SD	SE	95% CI		p-value
				LB	UB	
Normal	24.62	7.04	0.68	23.27	25.98	0.006*
Mild	28.28	6.53	0.80	26.69	29.88	
Moderate	27.93	8.34	1.58	24.69	31.16	
Severe	27.22	7.53	1.45	24.25	30.20	

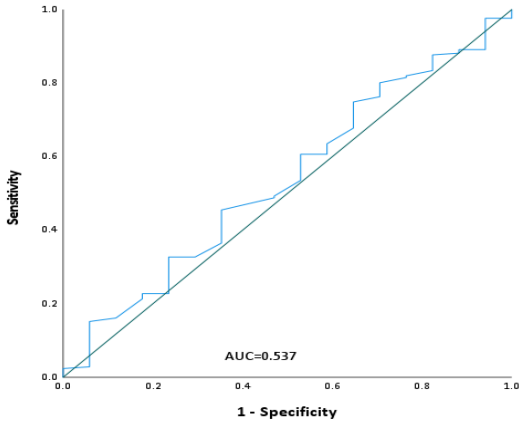

Figure 1. ROC curve Predicting multiple vessel disease on basis of hemoglobin

Table III: Laboratory findings.				
Variables	Total (n=228)	Anemia		p-value
		No (n=106)	Yes (n=122)	
TIMI Risk Score	2.72±1.08	2.53±1.02	2.86±1.10	0.065
TIMI Risk Score Percentage	12.45±5.99	11.44±5.52	13.17±6.23	0.076
Troponin (ng/mL)	6.52±8.17	7.11±8.17	6.01±8.17	0.314
Creatinine (mg/dL)	1.47±1.36	1.02±0.37	1.87±1.75	<0.01*
Glomerular Filtration Rate	76.23±38.58	83.41±28.85	68.93±45.57	0.048*
Hemoglobin (g/dL)	12.64±2.10	14.23±1.14	11.26±1.72	<0.01*
Total Lipids (mg/dL)	713.62±139.68	712.94±138.61	714.21±141.18	0.946
Cholesterol (mg/dL)	187.45±77.50	185.25±72.89	189.36±81.55	0.691
Triglycerides (mg/dL)	179.60±54.85	178.01±57.98	180.98±52.17	0.684
High-Density Lipoprotein (mg/dL)	38.00±8.62	37.68±7.95	38.29±9.19	0.597
Low-Density Lipoprotein (mg/dL)	167.67±39.08	165.43±42.68	169.61±35.73	0.422
Very Low-Density Lipoprotein (mg/dL)	29.99±12.74	28.70±12.43	31.11±12.95	0.154
Syntax Score	26.41±7.28	24.62±7.04	27.97±7.15	<0.01*

Table IV: Regression Analysis assessing association between hemoglobin levels and CAD severity (Syntax Score).							
	Unstandardized Coefficients		Standardized Coefficients	t- statistic	Sig.	95.0% CI	
	B	SE	Beta			LB	UB
(Constant)	28.657	4.826		5.939	.000	19.147	38.167
Hemoglobin Levels	-.556	.243	-.160	-2.284	.023	-1.036	-.076
Age	.039	.048	.053	.805	.422	-.057	.135
Hypertension	-.501	1.149	-.030	-.436	.663	-2.766	1.764
Diabetes Mellitus	1.873	1.059	.122	1.769	.078	-.214	3.960
Gender (Male)	2.294	1.060	.152	2.165	.031	.206	4.383

Discussion

Our current study discovered a significant association between Syntax Scores and anemia severity based on hemoglobin levels ($F(3, 224) = 4.310$, $p = 0.006$). Similarly, a Chinese study also reported a positive association between HbA1c levels and the SYNTAX score after accounting for a comprehensive array of established cardiovascular risk factors and medication histories.[15] However, a few studies report no significant association between HbA1c and CAD severity among either diabetic or non-diabetic patients.[16,17]

The regression analysis revealed that for every one-unit decrease in hemoglobin levels, there was a corresponding decrease of 0.556 units in the Syntax Score, indicating a significant association between lower hemoglobin levels and higher CAD severity. This finding indicates the potential utility of HbA1c as an independent predictor of CAD and its severity, aligning with prior research across diverse patient populations.[18-21] Similar to our findings, Yan et al. demonstrated in their study that HbA1c was associated with a significant increase of 1.49 units in Syntax score ($p<0.0001$).[15] After adjusting for gender, age, BMI, smoking, Cr, TG, HDL-C, LDL-C, TC, SBP, DBP (model 1), the Syntax score increased by 1.17 increase in HbA1c ($p=0.0031$).[15]

Additionally, we found no statistically significant association between the presence of multivessel disease and Anemia. Conversely, Lorente et al. observed a higher incidence of multivessel disease and left main coronary stenosis among patients with Anemia, although without significant differences in terms of coronary revascularization.[22]

This study's generalizability may be restricted because it was conducted at a single tertiary care institution, potentially limiting the applicability of the findings to diverse populations or healthcare settings. Although efforts were made to minimize the impact of confounding variables through statistical adjustment, residual confounding may persist due to unmeasured or inadequately measured factors, potentially affecting the observed associations. Furthermore, the study's cross-sectional design precludes the establishment of temporal relationships or causality between Anemia and CAD severity.

To build on the current findings, future research should focus on longitudinal studies to explore the temporal sequencing between anemia and CAD, enabling the identification of causal relationships and the dynamic interactions between these conditions over time. Moreover, understanding the underlying biological mechanisms linking anemia to CAD severity is crucial. Investigating these pathways could lead to the development of targeted therapeutic interventions for anemic patients with CAD, potentially improving their prognosis. Effective management of anemia in this population might reduce the burden of ischemic heart disease and improve overall cardiovascular health outcomes.

Conclusion

In conclusion, our study revealed a significant association between lower hemoglobin levels and increased severity of CAD among patients presenting with STEMI. Specifically, patients with Anemia demonstrated higher Syntax Scores, indicating more severe CAD. Logistic regression analysis confirmed that each unit decrease in hemoglobin corresponded with a substantial increase in CAD severity. This study supports the inclusion of hemoglobin concentration as a vital parameter in risk stratification models for CAD.

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