Beyond Anemia, Iron deficiency in Acute Coronary Syndrome: Clinical and Angiographic profile and In hospital Outcomes in a Tertiary Hospital in Eastern Nepal

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ABSTRACT

BACKGROUND

Iron, being important enzymatic cofactor for mitochondrial function, essential in cellular oxygen metabolism and mitochondrial function, it deficiency may lead to myocardial ischemia–reperfusion injury and may exacerbate myocardial damage in Acute Coronary Syndrome (ACS) and has been linked with onset, progression and severity and appears to influence clinical outcomes .

AIMS

This study aimed to describe the association of iron deficiency with clinical characteristics, severity and outcomes among ACS patients in a tertiary tropical hospital in Nepal.

METHODS

This was a descriptive cross-sectional study where clinical and angiographic profile of patients presenting with ACS, admitted in BPKIHS between January 2024 and December 2024 were evaluated and analysed in relation to Iron deficiency and anemia. Statistical analysis was done using SPSS 23.

RESULTS

A total of 183 patients with ACS admitted in the study period were included in the study. Prevalance of iron deficiency and anemia was found to be 43.17% and 45.35% respectively. Iron deficiency in ACS didn't show significant association with age, gender,traditional like Diabetes, Hypertension, dyslipidemia and family history or Type of ACS. Iron deficieny showed significant association with anemia (p <0.001), Killip Class (p 0.0946) and severity of Coronary artery disease in terms of Gensini Score (p 0.01). However iron deficiency was not found to have significantly association with with vessel score (0.06), CCU stay (p 0.126) or Hospital stay (p<0.219). Iron deficiency had significant association with Total adverse outcomes (p<0.001) and nonfatal outcome (p <0.001), irrespective of anemia, but no significant association was found with mortality. (p 0.441).

CONCLUSIONS

Iron deficiency were associated with higher severity of the ACS and in hospital adverse outcomes including higher non fatal adverse outcomes. Early stratification of disease based on biomarkers can guide early intervention to prevent bad outcomes

KEY WORDS

Iron deficiency, Anemia, Acute Coronary Syndrome, Outcome

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INTRODUCTION

Iron is a fundamental micronutrient essential for metabolic and physiologic processes, and plays essential role for oxygen transport and storage , mitochondrial function, skeletal and cardiac muscle metabolism, and besides have role in synthesis and degradation of proteins, lipids and ribonucleic acids as well as immune and neural function. 1-4

Iron deficiency(ID) is common in patients with cardiovascular disease. Up to 60% of patients with coronary artery disease, and an even higher proportion of those with heart failure (HF) or pulmonary hypertension have Iron deficiency.5

Insufficient dietary iron, reduced iron absorption due to increases in hepcidin secondary to the low-grade inflammation associated with atherosclerosis and congestion or reduced gastric acidity, and increased blood loss due to anti-thrombotic therapy or gastro-intestinal or renal disease may all cause ID. 5 Iron depletion may exacerbate ischemic injury and may be associated with worse clinical outcomes, prolonged hospital stay and morbidity and mortality.

Besides , iron deficiency may lead to Anemia , which has been reported to have adverse prognostic value.6 Despite this, iron status is not routinely assessed in ACS patients and its potential influence on prognosis remains under appreciated.

This study hence may help better understand the epidemiology and clinical implication of iron deficiency and anemia in Acute Coronary Syndrome.

However, a recent meta-analysis that included seven cohort studies (generally of small dimension and with high heterogeneity) of patients with ACS who were stratified by ID status showed an overall ID prevalence of 43%. [7]

METHODS

This was an investigator-initiated, single centered hospital based, descriptive cross-sectional study. In this study, we recruited a total of 183 patients admitted for Acute Coronary Syndrome to B.P. Koirala Institute of Health Science, Dharna, Nepal, between January 2024 and December 2024, fulfilling the following inclusion and exclusion criteria were included into the study.

Inclusion Criteria

- Cases of acute coronary syndrome: ST elevation MI and non-ST elevation ACS, which included NSTEMI and Unstable angina
- Age more than 18 yrs.
- Patient giving consent for study

Exclusion Criteria:

- Patients with chronic heart failure
- Chronic Kidney disease
- Hepatic cirrhosis
- Known malignancy
- Acute stroke and sepsis
- Chronic inflammatory diseases

Sample size for prevalence study was calculated by the formula:

Sample size (n) = Z^2 pq/d^2

where, n = desired sample size , Z = standard normal deviate; set at 1.96 corresponding to 95% confidence interval, p = proportion of population having a particular outcome, q = 1-p (proportion of target population not having a particular outcome , d = maximum error allowed=5%

183 samples were taken into study.

All participants underwent thorough detailed medical history, clinical evaluation and relevant investigations. Variables including age, gender, hypertension, diabetes, smoking status, alcohol consumption, dyslipidemia, serum iron profile, Killip Class, Angiographic findings including number of vessels involved and Gensini Score, Length of Hospital stay and Outcome were extracted into Data Collection Sheet.

The study was conducted after approval from the Institutional Review Committee of BPKIHS. The study was conducted according to the principles expressed in the Declaration of Helsinki, and the results are reported according to the strengthening the reporting of observational studies in epidemiology (STROBE) guideline

Reporting of baseline characteristics was done as Medians and interquartile ranges (IQRs) for continuous variables and as counts and percentages for Categorical variables. Kruskal-Wallis test was used for continuous variable and Chi squared tests for comparison across groups. p-values were tabulated with a level of significance set at <0.05. All data were analysed using IBM Statistical Packages for Social Sciences (SPSS), version 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

Iron deficiency (ID) is defined as ferritin <100 µg/l (absolute ID) or ferritin 100–299 µg/l and transferrin saturation (TSAT) <20% (functional ID). [8,9]

Anemia is defined as Hb <13 mg/dl in men and less than 12g/dl in non pregnant women.[10]

RESULTS

Total of 183 patients of ACS were admitted in BPKIHS during the study period. 79 patients (43.17%) were found to have iron deficiency and 83 (45.35%) patients had anemia. Iron deficiency showed no significant association was noted with age , sex and traditional risk factors including diabetes and hypertension.

Killip Class showed significant association with iron deficient patient presenting in higher Killip class. Iron deficient patients were found to have more severe lesion in terms of Gensini score , however no significant association was noted with the vessel score. No significant association was seen in terms of CCU or hospital stay. Mortality didn't show significant association with iron deficiency but total in hospital adverse outcome showed significant association.

Iron deficiency was significantly associated with anemia with iron deficient patients noted to have lower level of hemoglobin.

Comparisons of characteristics between patients with iron deficiency and without iron deficiency is shown in table 1.

Table 1: Characteristics between patients with iron deficiency and without iron deficiency

Characteristics	ID	No ID N=79	Total N=104	p value
Age (median , IQR)	65(57-74)	63.5(55-72)	65(56-73)	0.656
gender M:F	45:34	68:36	183	0.246
Risk Factors (n)				
DM	25	34	59	0.881
HTN	38	47	85	0.696
Dyslipidemia	27	49	76	0.079
Smoking	57	82	139	0.294
Family History	17	18	35	0.473
Killip Class (n)				
Class I	12	21	33	0.046
Class II	51	76	127	
Class III	15	7	22	
Class IV	1	0	1	
HR(median , IQR)	84(76-88)	84(76-90)	84(76-88)	0.541
SBP(median , IQR)	110(90-130)	120(100-130)	110(90-130)	0.148
DBP(median , IQR)	70(60-80)	80(62-90)	70(60-90)	0.060
Type of ACS (n)				
NSTEACS	24	36	60	0.545
STEACS	55	68	123	
Vessel Score (n)				
SVD	33	51	84	0.620
DVD	28	32	60	
TVD	18	21	39	
Gensini Score(median , IQR)	56(40-90)	48(32-64)	50(36-72)	0.010
LVEF(median , IQR)	40 (35-45)	40(35-45)	40(35-45)	0.026
CCU stay(median , IQR)	3(1-3)	2(2-3)	2(2-3)	0.126
Hospital Stay(median , IQR)	4(3-6)	4(3-5)	4(3-5)	0.219
Hematological and Lab Parameters (median , IQR)				
Hb	11.7 (10.7-13)	13.2(12-14.3)	12.5 (11.2-13.9)	<0.001
Presence of Anemia	53	32	85	<0.001
Total Count	10755(7850-13092)	9780(8055-11740)	10000(8015-12980)	0.556

N to L ratio	4.6(2.6-7.1)	4.17(2.37-7.0)	4.35(2.4-7.0)	0.302
Bilirubin Total	0.7(0.5-1.0)	0.7(0.4-1.06)	0.7(0.4-1.0)	0.825
Bilirubin Direct	0.1(0.1-0.2)	0.1(0.1-0.2)	0.1(0.1-0.2)	0.837
ALT	32(20-50)	34(22.5-45)	34(22-45)	0.922
AST	55(29.75-101.25)	50(35-89)	52.5(32-95)	0.862
Total Protein	7.15(6.5-7.5)	7.0(6.7-7.4)	7.1(6.6-7.5)	0.942
Albumin	4.0(3.47-4.3)	4.0(3.7-4.2)	4.0(3.6-4.3)	0.990
Total Cholesterol	149(116-184)	174(132-209)	164(129-195)	0.044
LDL	92(74-123)	112.5(83.5-149.5)	105(81-132)	0.061
HDL	37(30-43.5)	37(32-45.75)	37(31-45)	0.509
TG	114(85-168)	149(99.25-188.75)	132(89-177)	0.035
Iron Profile (median , IQR)				
Iron	29.5(21-43.5)	54.5(37.5-66.5)	42.5(24.7-56)	<0.001
TIBC	268.5(224-332.25)	212(179-245)	234(195-287)	<0.001
Transferrin Saturation	11.41(6.97-17.32)	25.48(17-36.25)	17.16(9-26.18)	<0.001
Ferritin	76(46-144)	310(210-391)	184(76-310)	<0.001
In hospital Adverse Outcome				
Death	3	2	5	0.441
Non-Fatal Adverse				
Outcome				
(New onset HF,				
Cardiogenic				
Shock)	26	7	33	<0.001
Total	29	9	38	<0.001

Gensini score was compared between various groups and anemia and ID. It varies significantly with higher Gensini sore in patient with Iron Deficiency and anemia, compared to those without, as shown in table 2.

Table 2. Distribution of Gensini score across anemia and iron deficiency groups

Groups	Number (%)	Gensini score (Median, IQR)	p value
ID with anemia	53 (28.96)	58 (41-92)	0.014
ID without anemia	26 (14.,21)	49(31-89)	
No ID, anemia	32(17.49)	52 (40-69)	
No ID, No anemia	72(39.34)	45.5 (32-63)	
Total	183(100)	50(36-72)	

DISCUSSION

Iron deficiency is a major heart failure co-morbidity present in about 50% of patients with heart failure , and numerous important clinical trials have underscored the necessity for iron supplementation and its impact on patient's quality of life.11-14. However data on iron deficieny and its impact on ACS is still lacking.

Iron is an important enzymatic cofactor for mitochondrial function, essential in cellular oxygen metabolism and hance mitochondrial dysfunction may lead to myocardial ischemia–reperfusion injury and may exacerbate myocardial damage in ACS.15 Some studies have suggested the role of intravenous iron administration in improving infarct healing and left ventricular remodelling in ACS. 16

Our study showed that iron deficiency is present in significant proportion of patient presenting with acute coronary syndrome (43.17% of patients), similar to other studies like Esteves et al (48%)17, Silva et al (36%)18 , Merono et al (61%)19 and a metaanalysis by Reinhold J et al. 7 Some study have however reported lower prevalence of iron deficiency as by Zeller et al(29%) .9 Similar anemia was present in 45.35% of ACS patients, comparable to previous studies which have reported prevalence to be between 40-60%.6, 20

Iron deficiency was significantly associated with anemia , similar to other studies.9, 21 Patients with iron deficiency and anemia tend to have higher Gensini score suggesting higher angiographic severity. Though iron deficiency was not found to have significant association with vessel score, it showed significant association in terms of Gensini score, with higher scores in iron deficient ACS patients . Iron deficient had significantly more severe presentation in terms of Killip class. Similar finding of independent association of iron deficiency with severity of CAD was reported in previous studies. 9, 22

ID has been reported as a predictor of a composite of mortality and severity in a cohort of patients admitted with ACS.9, 17, 18, 23 However in a study by Masini et al , iron deficiency didn't predict in hospital outcomes , but higher post discharge events.24 Our study though couldn't establish significant association of iron deficiency and anemia with mortality, in hospital adverse outcomes were significantly higher in patients with iron deficiency.

The findings of our study further reinforces the importance of measuring iron profile and anemia status in acute coronary syndrome and demonstrates its prognostic implications. Clinicians should consider anemia and iron deficiency in risk stratification to identify high risk patients, and to predict severity and outcomes in acute coronary syndrome and to guide therapeutic interventions.

CONCLUSION

Iron deficiency and anemia are common among patients presenting with Acute Coronary Syndrome and are associated with greater severity in terms of clinical presentation and angiographic severity and in hospital adverse outcomes. Routine assessment of iron profile and anemia status could be valuable adjunct in assessing severity and prognosis in ACS. Further studies are needed to explore the potential therapeutic implications of correction of iron deficiency and anemia in patients and to elucidate the mechanisms contributing to adverse outcomes in ACS.

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