Original Article

Hypoalbuminemia as A Marker of Clinical and Angiographic Severity and In-Hospital Outcome in Acute Coronary Syndrome In BPKIHS, Dharan: A Cross Sectional Study

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Abstract

Background: Serum albumin, because of its anti-inflammatory, antioxidant, anticoagulant and anti-platelet aggregation action has been linked with onset, progression and severity and appears to influence clinical outcomes among Acute Coronary Syndrome (ACS) Patients.

Aims: This study aimed to describe the association of serum albumin levels 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 July 2024 and October 2024 were evaluated and analysed in relation to serum albumin levels. Statistical analysis was done using SPSS 23.

Results: A total of 100 patients with ACS admitted in the study period were included in the study. Serum albumin levels in ACS didn't show significant association with age, gender, Killip class or Type of ACS. Risk factors found to have significant association with hypoalbuminemia were hypertension (p 0.001) and dyslipidemia. (p 0.021). Hypoalbuminemia showed significant association with severity of Coronary artery disease in terms of vessels involved (p 0.004) and Gensini Score (p 0.01). Hypoalbuminemia was significantly associated with longer CCU stay (p 0.012) and Hospital stay (p<0.001). Hypoalbuminemia had significant association with Total adverse outcomes (p<0.001) and nonfatal outcome (p <0.001), but no significant association was found with mortality. (p 0.133).

Conclusion: Lower serum albumin were associated with higher severity of the ACS and in hospital adverse outcomes including higher non-fatal adverse outcomes and higher duration of CCU and hospital stay . Early stratification of disease based on biomarkers can guide early intervention to prevent bad outcomes.

Introduction

Coronary heart disease (CHD) is one of the major causes of mortality worldwide. The pathological process of CHD includes coronary atherosclerosis and spasm, and are mediated by lipid metabolism disorders, vascular endothelial cell injury, inflammation, and immune dysfunction.[1]

The term Acute Coronary Syndrome (ACS) encompasses a clinical spectrum of pathophysiology and presentations of symptomatic coronary disease, and encompasses ST elevation MI (STEMI), Non-ST elevation MI (NSTEMI) and Unstable Angina (UA). This is usually due to atherosclerotic plaque rupture, ulceration or erosion that results in intraluminal thrombus formation and compromises myocardial blood flow leading to myocardial necrosis and release of cardiac enzymes.[2]

Albumin, which accounts for approximately 50% of the plasma protein, is the most abundant circulating protein in the blood. It binds to and transports various substances in the plasma and maintains blood colloidal osmotic pressure. Albumin has anti-inflammatory, antioxidant, anticoagulant, and antiplatelet aggregation effects.[3] These effects can inhibit formation of coronary atherosclerosis, thereby having influence on occurrence and development of CHD.[3,4]

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Therefore, the relationship between albumin levels and CHD risk has attracted increasing attention.

Serum albumin concentration is a simple and inexpensive routine laboratory test and can provide relevant prognostic information in patients with cardiovascular diseases.

Low level of serum albumin is found to be associated with a higher risk of morbidity and mortality in coronary heart disease.[5-9] In ACS, the presence of hypoalbuminemia has been associated with increased severity of coronary lesions.[10,11] Furthermore, hypoalbuminemia on admission was found to be an independent predictor of no-reflow after primary percutaneous coronary intervention (PCI).[12]

The impact of a low serum albumin level during acute coronary syndrome has not yet been elucidated in Nepalese context. This study aimed to study the impact of albumin levels on presentation and clinical course of patients with acute coronary syndrome. Further, its association with angiographic findings were studied.

Materials and Methods

2.1. Study Design and Participants

This was an investigator-initiated, single centered hospital based, descriptive cross-sectional study. In this study, we recruited a total of 100 patients admitted for Acute Coronary Syndrome to B.P. Koirala Institute of Health Science, Dharna, Nepal, between April 2021 and September 2021, 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

2.2. Sample Size Calculation

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= 0.43

q = 1-p (proportion of target population not having a particular outcome = (1-0.43)

d = maximum error allowed=10%

Thus, the final sample size was calculated to be 94. 100 samples were taken for convenience.

2.3. Data collection

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

2.3. Ethics

The study was conducted after approval from the Institutional Review Committee of BPKIHS (Reference number IRC/279/080/81, Code no. IRC/2710/024, date of approval—5 July 2024). 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

2.4. Statistical Analysis

Reporting of baseline characteristics was done as Mean and Standard Deviation (Normal Distribution) and Medians and interquartile ranges (Skewed distribution) for continuous variables and as counts and percentages for Categorical variables. One way Anova test and Kruskal-Wallis test was used for continuous variables 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.).

RESULTS

3.1. Clinical characteristics

Over the period of 4 months from July 2024 to October 2024, 100 patients admitted to BPKIHS for Acute Coronary Syndrome fulfilling our inclusion and exclusion criteria were included in the study. Hypoalbuminemia was found in 30 patients.

3.1.1 Age and Gender

Out of 100 patients, 64 were male patients and 36 were female. Median age of presentation was 65 years (IQR 55-74).

Age and sex wise distribution of serum albumin is presented in Table 1. Serum albumin levels didn't show significant association with age in patients presenting with ACS.

Table 1: Age wise distribution of Serum Albumin Levels

Age Group	N	Serum Albumin (mg/dl) (Mean ±SD)	p Value
19-45	7	3.77±0.52	0.49
46-55	21	3.78±0.48	
56-65	24	3.83±0.48	
66-75	28	3.76±0.5	
76-85	19	3.6±0,45	
>85	1	3.0	
Total	100	3.75±0.48	

Table 2. Gender wise Distribution of Serum Albumin Levels

Values Mean±SD	Male (n=64)	Female (n=36)	p-value
Serum Albumin (mg/dl)	3.75±0.48	3.75±0.48	0.762

3.1.2 Disease Severity

Of the total patients, majority, 65 patients presented in Killip 2, 18 presented in Killip III class, 15 presented in Killip I while 2 presented in Killip 4. Association of levels of serum albumin with Killip Class is presented in Table 3. Serum Albumin was lower in patients presenting with higher Killip class, however it was not statistically significant.

Table 3. Serum Albumin levels and Killip Class at presentation

Value (mean ± SD)	Killip I (n = 15)	Killip II (n = 65)	Killip III (n = 18)	Killip IV (n = 2)	Total (n = 100)	p - value
Serum Albumin (mg/dl)	3.87 ± 0.55	3.77 ± 0.44	3.63 ± 0.55	3.35 ± 0.49	3.75 ± 0.48	0.3

3.1.3 Clinical Presentation

Most common presentations among admitted ACS patients was STEMI (71) followed by NSTEMI (21) and Unstable Angina (8).

No significant association was noted between Serum albumin levels and type of ACS as shown in Table 4.

Table 4. Serum Albumin Levels and ACS type

Value Mean ± SD	STEMI (n = 71)	NSTEMI (n = 21)	USA (n = 8)	Total (n = 100)	p value
Serum Albumin (mg/dl)	3.75 ± 0.5	3.7 ± 0.37	3.8 ± 0.57	3.75 ± 0.48	0.552

3.1.4 Risk Factors

The most common risk factor among admitted ACS patient was Smoking (77), followed by Systemic Hypertension (53), Diabetes Mellitus (33) and Dyslipidemia (29).

Hypertension and dyslipidemia were found have significant association with hypoalbuminemia.

Table 5. Risk Factors and Albumin Status

Risk Factor	All Patients (n = 100)	Hypoalbuminemia (n = 30)	Normoalbuminemia (n = 70)	P value
Diabetes Mellitus	33	11	22	0.261
Hypertension	53	16	37	0.001
Current Smoker	77	25	52	0.582
Dyslipidemia	29	9	20	0.021

3.1.5. Laboratory Parameters

Table 6: Laboratory parameters and serum albumin status

Value (Mean±SD)	Hypoalbuminemia	Normoalbuminemia	Total	p value
Hb (g/dL)	11.7 ± 1.8	13.1 ± 1.8	12.6 ± 1.9	0.001
WBC Count, $x10^3/mm^3$	11.1 ± 3.6	10.1 ± 3.7	10.4 ± 3.6	0.169
Neutrophil (%)	74.3 ± 12.5	72.1 ± 14.7	72.7 ± 14.1	0.463
Lymphocyte(%)	17.1 ± 9.6	21.1 ± 14.21	19.9 ± 13.1	0.191
Total Cholesterol (mg/dl)	161.1 ± 47.2	166.9 ± 50.4	165.23 ± 49.3	0.6
HDL (mg/dl)	38.4 ± 12.8	39 ± 12.9	38.8 ± 12.8	0.729
TG (mg/dl)	126 ± 48.1	140.1 ± 61.5	136.1 ± 57.9	0.44
LDL (mg/dl)	109 ± 43.3	115 ± 42.3	113.9 ± 42.4	0.44

3.1.6. Coronary artery disease status

Statistically significant association was noted between Severity and complexity of lesions and serum albumin level, as shown in Table 5 and 6.

Table 5: Serum Albumin Levels in CAD category

Value Mean ± SD	SVD (n=45)	DVD (n=24)	TVD (n=26)	p value
Serum albumin (mg/dl)	3.86±0.49	3.89±0.45	3.51±0.48	0.004

Table 6: Distribution of Gensini score in albumin level status

Value Median (IQR)	Hypoalbuminemia (n=30)	Normoalbuminemia (n=70)	p value
Gensini Score	78(46-90)	51.5 (32-78)	0.01

3.1.6. Duration of Hospital Stay

The median duration of CCU stay was 2 days (IQR 1-3 days).

The median duration of hospital stay was 3days (IQR 3-4 days).

Duration of hospital stay and CCU stay had significant association with hypoalbuminemia. (Table 5)

Table 6: Albumin Status and duration of hospital stay

Duration Median (IQR)	Hypoalbuminemia (n=30)	Normoalbuminemia (n=70)	P value
Hospital Stay	4(3-6)	3(2.75-4)	0.012
CCU stay	3(2-3.25)	2(1-2)	0.000

3.1.6 In Hospital adverse Outcome

Among 100 total admissions, 93 patients improved and were discharged, 5 patients expired and 2 were discharged on request/Left against medical advice. 21 patients had non fatal outcomes including heart failure, cardiogenic shock and arrhythmic complications.

The levels of serum albumin had statistically significant association with tota in hospital adverse outcomes. (Table 7)

Table 7: Albumin Status and Outcome

In hospital Adverse Outcome	Hypoalbuminemia (n=30)	NormoAlbuminemia (n=70)	p value
Death	3	2	0.133
Non-Fatal Adverse Outcome (New onset HF, Cardiogenic Shock)	13	7	<0.001
Total Adverse Outcome	16	9	<0.001

Discussion

Serum albumin, primarily synthesized in the liver, plays vital roles in various physiological functions, including maintaining oncotic pressure, transport of substances, and exhibits anti-inflammatory, antioxidant and anti-platelet activities.[3,13] Hypoalbuminemia has been associated with worse clinical outcomes and mortality in patients with Acute Coronary Syndrome.[5-9] Lower albumin in Acute coronary syndrome could be because of chronic inflammation and oxidative stress of the atherosclerosis process, or because of other associated conditions including liver disease, malnutrition, systemic inflammation or chronic infections.[14,15] Further, lower serum albumin levels may increase blood viscosity , disrupt endothelial functions and has been associated with higher risk of endothelial damage and thrombotic events linked to platelet activation and aggregation.[15,16]

In our study, Hypoalbuminemia was present in 30% of the patients. This is in line with various studies which have reported 30-50% prevalence of hypoalbuminemia in ACS. such as by Hartopo et al (43%), Polat et al (34%), Shah S et al (44%),[14,17,18]

The severity as depicted by CAG findings in terms of vessels involved and Gensini score, however showed significant association with the albumin levels suggesting severe and complex disease in Hypoalbuminemic patients. Kurtul et al had similar reports in terms of CAD severity assessed by Syntax score in which SA levels were significantly lower in patients with high SYNTAX score.[19] In a study by Cheng CW et al , in accordance with our study, Gensini score was found to be significantly higher in patient with hypoalbuminemia.[20] Parvez et al from their study also demonstrated significant association of serum albumin with the severity of coronary artery disease with low serum albumin carrying at least two-fold higher risk of having severe CAD, as measured by the Friesinger and Leaman score, in patients with ACS.[11] Further, hospital stay and CCU stay was found to be significantly higher in hypoalbuminemic patients compared to normoalbuminemic patients.

Our study demonstrated significant association between hypoalbuminemia and in hospital adverse outcomes in patients with acute coronary syndrome, though mortality didn't show significant association. Hartopo et al reported similar findings.[14] Gonzalez-Pacheco et al however reported higher rates of new onset heart failure and in hospital mortality rates in hypoalbuminemic patients.[7] Further , low serum albumin level was associated with worse long-term outcomes, independent of traditional risk factors.[6,9]

Albumin levels in our study didn't show signifincant association with types of ACS-STEMI, or NSTE-ACS. This finding was similar to findings by Hartopo et al.[14] However Shah S et al and Dhanju et al report significant association of STEMI with hypoalbuminemia.[18,21]

The findings of our study underscore the importance of serum albumin in acute coronary syndrome and demonstrates its prognostic implications. Clinicians should consider level of albumin in risk stratification to identify high risk patients, and to predict severity and outcomes in acute coronary syndrome, to guide therapeutic interventions.

Conclusion

Serum albumin levels were associated with higher severity and in hospital adverse outcomes including higher duration of hospital stay of the Acute Coronary Syndrome. Serum albumin levels could be valuable adjunct in assessing severity and prognosis in ACS. Further research should explore the potential therapeutic implications of targeting albumin levels in patients and to elucidate the mechanisms contributing to adverse outcomes in ACS.

Limitations of Study

Our study should be interpreted considering following limitations. Since this was a single centered study, the results cannot be generalized. Secondly, long term follow up of patients were not analysed in this study. Despite these limitations, to the best of our knowledge, this is the first study from Nepal regarding association of serum albumin with Acute Coronary Syndrome. There still is scarcity of data regarding implication of serum albumin with Acute Coronary Syndrome and further studies are needed.

Conflicts of Interest

The authors declare no conflict of interest.

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References

1. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005;352(16):1685-95.
2. Kotecha T, Rakhit RD. Acute coronary syndromes. Clin Med (Lond). 2016;16(Suppl 6):s43-s8.
3. Manolis AA, Manolis TA, Melita H, Mikhailidis DP, Manolis AS. Low serum albumin: A neglected predictor in patients with cardiovascular disease. Eur J Intern Med. 2022;102:24-39.
4. Hou XZ, Liu EQ, Liu SQ, Lv H, Cui HF, Han J. The negative association between serum albumin levels and coronary heart

disease risk in adults over 45 years old: a cross-sectional survey. Sci Rep. 2023;13(1):672.

5. Djoussé L, Rothman KJ, Cupples LA, Levy D, Ellison RC. Serum albumin and risk of myocardial infarction and all-cause mortality in the Framingham Offspring Study. Circulation. 2002;106(23):2919-24.

6. Wada H, Dohi T, Miyauchi K, Shitara J, Endo H, Doi S, et al. Impact of serum albumin levels on long-term outcomes in patients undergoing percutaneous coronary intervention. Heart Vessels. 2017;32(9):1085-92.

7. González-Pacheco H, Amezcua-Guerra LM, Sandoval J, Martínez-Sánchez C, Ortiz-León XA, Peña-Cabral MA, et al. Prognostic Implications of Serum Albumin Levels in Patients With Acute Coronary Syndromes. Am J Cardiol. 2017;119(7):951-8.

8. Zhu L, Chen M, Lin X. Serum albumin level for prediction of all-cause mortality in acute coronary syndrome patients: a meta-analysis. Biosci Rep. 2020;40(1).

9. Plakht Y, Gilutz H, Shiyovich A. Decreased admission serum albumin level is an independent predictor of long-term mortality in hospital survivors of acute myocardial infarction. Soroka Acute Myocardial Infarction II (SAMI-II) project. Int J Cardiol. 2016;219:20-4.

10. Kurtul A, Murat SN, Yarlioglues M, Duran M, Ocek AH, Koseoglu C, et al. Usefulness of Serum Albumin Concentration to Predict High Coronary SYNTAX Score and In-Hospital Mortality in Patients With Acute Coronary Syndrome. Angiology. 2016;67(1):34-40.

11. Parvez JM, Rahman MA, Islam AM, Aziz M, Mamun A, Arefin MM, et al. Association of Hypoalbuminaemia with the Angiographic Severity of Coronary Artery Disease in Patients with Acute Coronary Syndrome. University Heart Journal. 2022;18(1):44-9.

12. Kurtul A, Ocek AH, Murat SN, Yarlioglues M, Demircelik MB, Duran M, et al. Serum albumin levels on admission are associated with angiographic no-reflow after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Angiology. 2015;66(3):278-85.

13. Arques S. Human serum albumin in cardiovascular diseases. European journal of internal medicine. 2018;52:8-12.

14. Hartopo AB, Gharini PPR, Setianto BY. Low serum albumin levels and in-hospital adverse outcomes in acute coronary syndrome. International heart journal. 2010;51(4):221-6.

15. Joles JA, Willekes-Koolschijn N, Koomans HA. Hypoalbuminemia causes high blood viscosity by increasing red cell lysophosphatidylcholine. Kidney international. 1997;52(3):761-70.

16. Zhang W-J, Frei B. Albumin selectively inhibits TNFα-induced expression of vascular cell adhesion molecule-1 in human aortic endothelial cells. Cardiovascular research. 2002;55(4):820-9.

17. Polat N, Oylumlu M, Işik MA, Arslan B, Özbek M, Demir M, et al. Prognostic Significance of Serum Albumin in Patients With Acute Coronary Syndrome. Angiology. 2020;71(10):903-8.

18. Shah S. Significance of Serum Albumin in Patients with Acute Coronary Syndrome.

19. Chen YM, Zheng Y, Yu Y, Wang Y, Huang Q, Qian F, et al. Blood molecular markers associated with COVID-19 immunopathology and multi-organ damage. Embo j. 2020;39(24):e105896.

20. Cheng CW, Lee CW, Chien SC, Yeh HI, Chen CY. Serum Albumin was Associated with a Long Term Cardiovascular Mortality among Elderly Patients with Stable Coronary Artery Disease. Acta Cardiol Sin. 2024;40(1):87-96.

21. Dhanju AS, Chhina GS, Manekar P, Sandhu PS. A study of serum albumin levels in acute coronary syndrome and its correlation with clinical outcome. International Journal of Advances in Medicine. 2022;9(5):571.