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Hypoalbuminemia Severity and Major Adverse Cardiovascular Events (MACE): Evidence From a Hospital-Based Prospective Observational Study From Eastern Uttar Pradesh, India

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Abstract

Background

The absolute burden of major adverse cardiovascular events (MACE) among patients with hypoalbuminemia, and its variation across severity grades of hypoalbuminemia, is not well characterized in Indian hospital settings.

Methods

This prospective hospital-based observational study enrolled 268 adults with serum albumin ⩽3.50 g/dL presenting at a tertiary care center in eastern Uttar Pradesh and followed them for three months. Hypoalbuminemia was classified as mild (3.01-3.50 g/dL), moderate (2.50-3.00 g/dL), or severe (<2.50 g/dL). MACE was defined as myocardial infarction, heart failure, atrial fibrillation, or acute ischemic stroke. Prevalence was estimated with 95% confidence intervals (CIs); associations were assessed using Pearson's chi-square test or exact tests, and trend was assessed using the Cochran-Armitage test.

Results

MACE was identified in 39/268 participants (14.6%; 95% CI 10.8-19.3). Stroke was the most frequent component (19/268, 7.1%), followed by heart failure (10/268, 3.7%). MACE prevalence differed across hypoalbuminemia grades (Pearson χ^2=7.85, df=2, p=0.020) and decreased across increasing severity: 23/104 (22.1%) with mild, 9/88 (10.2%) with moderate, and 7/76 (9.2%) with severe hypoalbuminemia (Cochran-Armitage z=−2.54, p=0.011). Stroke prevalence also differed by grade (Pearson χ^2=8.11, df=2, p=0.017; trend z=−2.05, p=0.040) and was higher among women than men (14/125, 11.2% vs. 5/143, 3.5%; Pearson χ^2=6.01, df=1, p=0.014). Age group was not significantly associated with MACE.

Conclusion

Among adults with hypoalbuminemia in this single-center study, approximately one in seven had MACE, the most common being stroke. The lower observed prevalence of MACE in the more severe hypoalbuminemia groups should not be interpreted as a protective effect; it may reflect differences in acute illness, competing conditions, and selection into the hospital-based sample. Larger prospective studies are needed to clarify these associations.

Categories: Cardiology, Public Health, Internal Medicine
Keywords: atrial fibrillation, hypoalbuminemia, india, major adverse cardiovascular events, stroke

Introduction

Cardiovascular diseases (CVD) remain the leading cause of death globally, accounting for an estimated 19.8 million deaths in the year 2022 [1], and India carries a large and rising share of this burden, with marked heterogeneity across its states [2]. Major adverse cardiovascular events (MACE), a composite of clinically important outcomes such as myocardial infarction (MI), stroke, heart failure (HF) and cardiovascular death, are widely used to summarize this burden, although the components included vary considerably between studies [3].

Serum albumin is the most abundant circulating protein and is measured routinely in almost every hospitalized patient. Beyond maintaining colloid oncotic pressure, albumin transports drugs, hormones, and fatty acids, scavenges reactive oxygen species through its free cysteine-34 thiol, inhibits platelet aggregation, and helps preserve endothelial integrity [4,5]. Its concentration falls with systemic

inflammation, capillary leak, hepatic or renal dysfunction, and malnutrition, and during acute illness it behaves more as a negative acute-phase reactant than as a pure nutritional index [4,6]. In clinical practice, hypoalbuminemia is conventionally defined as serum albumin below 3.5 g/dL [4] and is often graded as mild, moderate, or severe to guide the search for underlying disease. It is common among hospitalized patients and is a consistent marker of in-hospital and long-term mortality [7].

A growing body of evidence links low albumin to cardiovascular outcomes. In more than 100,000 adults in the Copenhagen General Population Study, lower plasma albumin predicted incident ischemic heart disease, MI, and, most strongly, ischemic stroke, and an updated meta-analysis confirmed an approximately two-fold higher CVD risk per 10 g/L lower albumin [8]. Epidemiological and Mendelian randomization data have also associated lower albumin with incident atrial fibrillation (AF) [9]. In patients with coronary artery disease undergoing percutaneous coronary intervention (PCI), lower albumin independently predicted MACE and long-term mortality [10,11]; in HF it accompanies congestion, diuretic resistance and death [12]; after acute MI it predicts long-term survival [13]; and after ischemic stroke it predicts early cardiovascular complications [14]. These data have prompted calls to regard low albumin as a neglected yet readily available cardiovascular risk marker [15].

Nevertheless, important gaps remain. Most studies have been conducted in disease-specific cohorts from high-income countries, have treated albumin as a continuous variable or a single dichotomous cut-off, and have reported relative risks rather than the absolute burden of events among patients who already have hypoalbuminemia. Whether the prevalence of MACE, and of its individual components, rises across conventional clinical grades of hypoalbuminemia has seldom been examined in general medical settings, and Indian data are scarce. This question is particularly relevant in India, where a rapidly growing burden of cardiometabolic disease [2] coexists with undernutrition, chronic infection and late presentation, so that the determinants of low albumin on a medical ward may differ from those in Western cohorts.

Against this background, we therefore aimed to estimate the hospital-based prevalence of MACE and its individual components among adults with hypoalbuminemia attending a tertiary care center in eastern Uttar Pradesh and compare their prevalence across mild, moderate, and severe categories of hypoalbuminemia.

Materials And Methods

Study design, setting and ethics

This hospital-based prospective observational study was conducted in the Department of General Medicine, All India Institute of Medical Sciences (AIIMS), Gorakhpur, Uttarer Pradesh, India, over 12 months after approval by the Institutional Human Ethics Committee (IHEC/AIIMS-GKP/BMR/297/2024, dated August 20, 2024). Written informed consent was obtained from each participant or a legally acceptable representative, and the study conformed to the Declaration of Helsinki. Reporting follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement [16].

Participants

Adults (≥18 years) attending the Medicine outpatient department or admitted to the medical wards or intensive care unit with serum albumin ≤3.50 g/dL were enrolled through convenience sampling. Patients with known chronic liver disease, kidney disease, diabetes mellitus or hyperthyroidism (conditions that independently alter albumin concentration and cardiovascular risk), pregnant women, and patients with recent surgery were excluded.

Exposure and clinical evaluation

Serum albumin was estimated in the institutional clinical biochemistry laboratory at enrolment and graded a priori as mild (3.01-3.50 g/dL), moderate (2.50-3.00 g/dL) or severe (<2.50 g/dL) hypoalbuminemia [17]. Demographic details, cardiovascular history (hypertension, ischemic heart disease, valvular heart disease, dyslipidemia, previous stroke), and tobacco and alcohol use were recorded on a structured case record form. All participants underwent clinical examination, complete blood count, renal and liver function tests, serum electrolytes, urinalysis, glycated hemoglobin, fasting lipid profile, thyroid function tests, serology for HIV, hepatitis B and hepatitis C, chest radiography, abdominal ultrasonography, 12-lead electrocardiography (ECG), transthoracic echocardiography and cardiac troponin estimation; neuroimaging (computed tomography and/or magnetic resonance imaging of the brain) was used to confirm or exclude acute ischemic stroke. Participants were reviewed at one and three months.

Outcomes

The primary outcome was MACE, defined as at least one of the four specified components present at the index evaluation or occurring during the follow-up. Myocardial infarction (MI) was diagnosed according to the Fourth Universal Definition, requiring ischemic symptoms and/or new ischemic ECG changes together with a rise in cardiac troponin I on two samples taken at least six hours apart [18]. Heart failure (HF) was defined by the universal definition as symptoms and/or signs caused by a structural or functional cardiac

abnormality, corroborated by elevated natriuretic peptides or objective evidence of congestion, and classified by left ventricular ejection fraction; the H2FPEF score supported the diagnosis of HF with preserved ejection fraction [19,20]. Atrial fibrillation (AF) was diagnosed on ECG by the absence of discrete P waves with irregularly irregular RR intervals [21]. Stroke was defined as an acute focal neurological deficit with an acute infarct on neuroimaging [22]. A patient with more than one event was counted once for overall MACE and once under each relevant component.

Sample size

The minimum required sample size was calculated using the single population proportion formula:

$$n = \frac{Z^2 \times p \times q}{d^2},$$

where n = minimum required sample size; Z = standard normal deviate at 95% confidence level (1.96); p = expected prevalence of MACE among patients with hypoalbuminemia (4.7%, or 0.047) [23]; q = (1-p) (0.953); and d = absolute precision (3%, or 0.03).

Substituting the values: $n = \frac{1.96^2 \times 0.047 \times 0.953}{0.03^2} = \frac{0.1721}{0.0009} = 191.2.$

Thus, the minimum required sample size was 192 participants; this was inflated to 250 to allow for a 10%-15% non-response rate.

Statistical analysis

Data were entered in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) and analyzed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables are presented as counts and percentages; prevalence estimates are presented with Wilson score 95% confidence intervals (CIs). Associations were assessed using Pearson's chi-square test or Fisher's exact test (Fisher-Freeman-Halton extension for larger contingency tables) when expected cell counts were small. Linear trend across the three hypoalbuminemia grades was assessed using the Cochran-Armitage trend test. Post hoc pairwise comparisons used Fisher's exact test with Bonferroni correction. Unadjusted odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated using the Woolf method. Statistical analyses were performed using Python (version 3; Python Software Foundation, Beaverton, OR, USA) and SciPy (SciPy project). Because the number of outcome events was small, multivariable regression was not attempted. All tests were two-sided, with $p<0.05$ considered statistically significant.

Results

Participant characteristics

A total of 268 adults were enrolled and included in the analysis, exceeding the target sample size of 250, as we included all eligible participants who came during the study period, as shown in the participant flow diagram (Figure *1*).

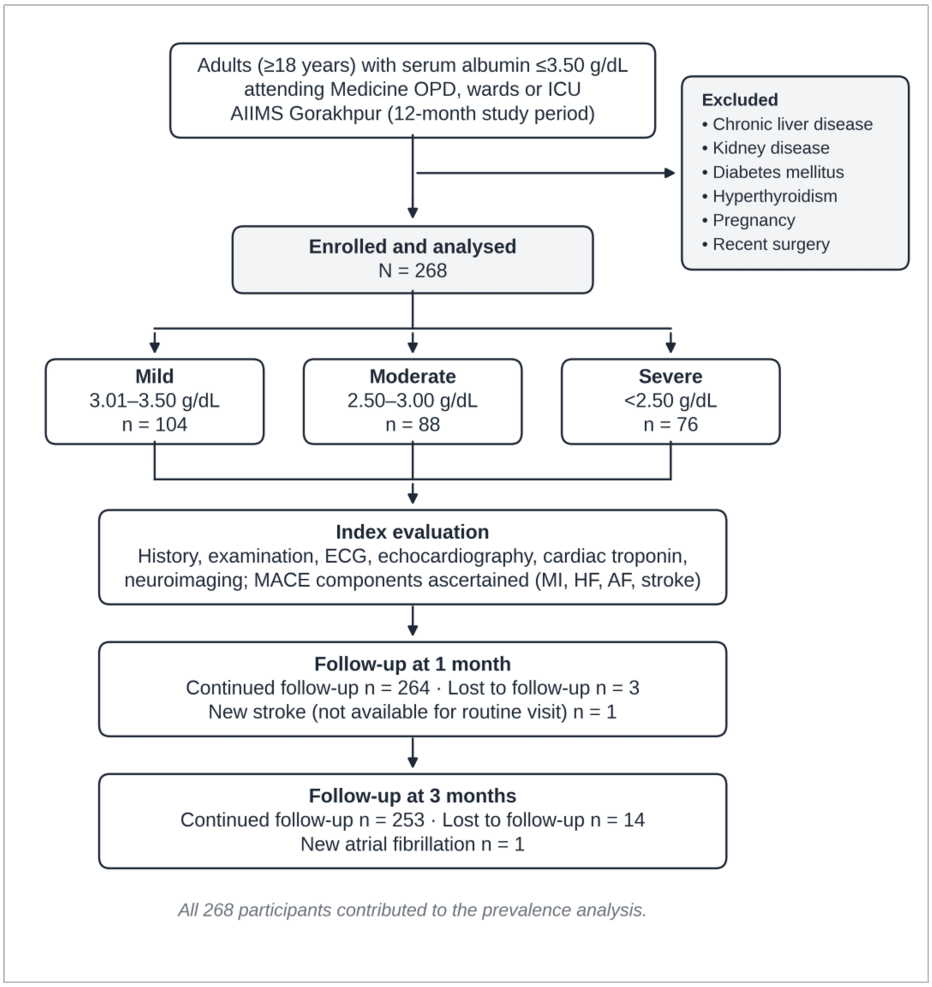

FIGURE 1: Participant flow diagram

AIIMS, All India Institute of Medical Sciences; OPD, outpatient department; ICU, intensive care unit; ECG, electrocardiography; MACE, major adverse cardiovascular events; MI, myocardial infarction; HF, heart failure; AF, atrial fibrillation; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology

There were 143 men (53.4%) and 125 women (46.6%). Participants aged 41-80 years accounted for 182/268 (67.9%) of the sample; 11/268 (4.1%) were older than 80 years. Mild hypoalbuminemia was the most frequent grade (104/268, 38.8%), and 76/268 (28.4%) had severe hypoalbuminemia (Table *1*). Follow-up was documented for 264/268 participants (98.5%) at one month and 253/268 (94.4%) at three months. Only those participants who completed at least one month of follow-up were included for the ascertainment of incident MACE.

Characteristic	n	%
Sex		
Male	143	53.4
Female	125	46.6
Age group (years)		
18–40	75	28.0
41–60	91	34.0
61–80	91	34.0
>80	11	4.1
Grade of hypoalbuminemia (serum albumin)		
Mild (3.01–3.50 g/dL)	104	38.8
Moderate (2.50–3.00 g/dL)	88	32.8
Severe (<2.50 g/dL)	76	28.4

TABLE 1: Demographic charcteristics and grade of hypoalbuminemia among the study participants (N = 268)

Values are n (%).

Prevalence of MACE

At least one MACE was identified in 14.6% (95% CI 10.8-19.3) of participants, comprising 42 events because three patients had two events each (Table *2*). Stroke was the most common cause, affecting 7.1% of the study cohort and almost half of those with MACE, followed by HF; MI and AF were each seen in fewer than 3% of participants.

Outcome	n	Prevalence, % (95% CI)	Share of patients with MACE (n = 39), %
Any MACE	39	14.6 (10.8–19.3)	—
No MACE	229	85.4 (80.7–89.2)	—
Components of MACE			
Stroke	19	7.1 (4.6–10.8)	48.7
Heart failure	10	3.7 (2.0–6.7)	25.6
Myocardial infarction	7	2.6 (1.3–5.3)	17.9
Atrial fibrillation	6	2.2 (1.0–4.8)	15.4

TABLE 2: Prevalence of major adverse cardiovascular events (MACE) and their components among the study participants (N = 268)

Values are n (%) unless otherwise indicated.

MACE Across Hypoalbuminemia Severity Grades

The prevalence of MACE differed significantly across hypoalbuminemia grades (p = 0.020) but, contrary to expectation, declined as hypoalbuminemia became more severe, from 22.1% in mild to 10.2% in moderate and 9.2% in severe hypoalbuminemia (p for trend = 0.011; Table *3*).

Outcome	Mild (n = 104) n (%)	Moderate (n = 88) n (%)	Severe (n = 76) n (%)	p-value	p for trend
Any MACE	23 (22.1)	9 (10.2)	7 (9.2)	0.020[a]	0.011
Stroke	13 (12.5)	2 (2.3)	4 (5.3)	0.017[a]	0.040
Heart failure	6 (5.8)	3 (3.4)	1 (1.3)	0.307[b]	0.117
Myocardial infarction	3 (2.9)	3 (3.4)	1 (1.3)	0.799[b]	0.550
Atrial fibrillation	3 (2.9)	2 (2.3)	1 (1.3)	0.880[b]	0.486

TABLE 3: Severity of MACE and its components across grades of hypoalbuminemia (N=268)

Values are n (%).

[a]Pearson chi-square test; [b]Fisher–Freeman–Halton exact test; p for trend by the Cochran–Armitage test. Percentages are of patients within each grade.

Bonferroni-adjusted pairwise p-values (Fisher's exact test). Any MACE: mild vs. moderate 0.098, mild vs. severe 0.077, moderate vs. severe 1.000. Stroke: mild vs. moderate 0.038, mild vs. severe 0.375, moderate vs. severe 1.000.

Mild, 3.01–3.50 g/dL; moderate, 2.50–3.00 g/dL; severe, <2.50 g/dL

MACE, major adverse cardiovascular events

Compared with moderate and severe grades combined, mild hypoalbuminemia carried 2.6-fold higher odds of MACE (OR 2.63, 95% CI 1.31-5.25; p = 0.007), whereas moderate and severe grades did not differ (OR 1.12, 95% CI 0.40-3.17; Figure *2A*). After Bonferroni correction, no individual pairwise difference in overall MACE remained significant. Among components, only stroke varied significantly with severity (p = 0.017; p for trend = 0.040), being most frequent in mild hypoalbuminemia; the mild-moderate contrast persisted after correction (adjusted p = 0.038; OR 6.14, 95% CI 1.35-28.02). MI, HF, and AF showed no association with severity grades (Figure *2*).

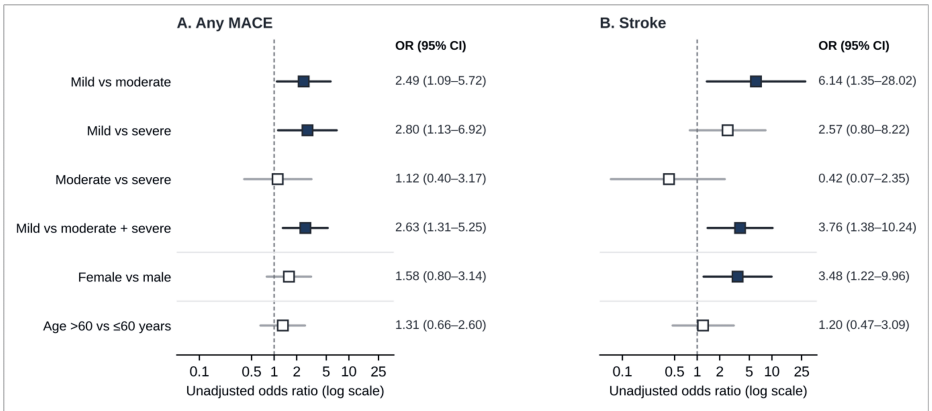

FIGURE 2: Unadjusted ORs with 95% CIs (Woolf method) for (A) any MACE and (B) stroke, by hypoalbuminemia grade, sex, and age group

Each comparison is expressed as the first group relative to the second (reference) group; the x-axis is logarithmic. Filled squares indicate CIs that exclude 1. Estimates are unadjusted and are not corrected for multiple comparisons.

OR, odds ratio; CI, confidence interval; MACE, major adverse cardiovascular event

MACE by Sex and Age

Stroke was about three times as frequent in women as in men (p = 0.014; Table *4*), corresponding to an unadjusted OR of 3.48 (95% CI 1.22-9.96; Figure *2B*), whereas overall MACE, MI, HF, and AF did not differ

significantly by sex.

Outcome	Female (n = 125) n (%)	Male (n = 143) n (%)	p-value
Any MACE	22 (17.6)	17 (11.9)	0.186[a]
Stroke	14 (11.2)	5 (3.5)	0.014[a]
Heart failure	5 (4.0)	5 (3.5)	1.000[b]
Myocardial infarction	1 (0.8)	6 (4.2)	0.126[b]
Atrial fibrillation	2 (1.6)	4 (2.8)	0.688[b]

TABLE 4: Distribution of MACE and its components by sex (N=268)

Values are n (%).

[a]Pearson's chi-square test; [b]Fisher's exact test.

MACE, major adverse cardiovascular events

Neither overall MACE nor any individual component was associated with age group (Table *5*), although the proportion with MACE was numerically highest in the very small subgroup aged over 80 years.

Outcome	18–40 y (n = 75) n (%)	41–60 y (n = 91) n (%)	61–80 y (n = 91) n (%)	>80 y (n = 11) n (%)	p-value	p for trend
Any MACE	11 (14.7)	11 (12.1)	14 (15.4)	3 (27.3)	0.529	0.491
Stroke	6 (8.0)	5 (5.5)	7 (7.7)	1 (9.1)	0.799	0.934
Heart failure	2 (2.7)	3 (3.3)	4 (4.4)	1 (9.1)	0.603	0.341
Myocardial infarction	3 (4.0)	2 (2.2)	2 (2.2)	0 (0.0)	0.848	0.382
Atrial fibrillation	1 (1.3)	1 (1.1)	3 (3.3)	1 (9.1)	0.275	0.137

TABLE 5: . Distribution of MACE and its components by age-group (N=268)

Values are n (%).

Fisher–Freeman–Halton exact tests were used for comparisons across age groups; Cochran–Armitage tests were used for tests of trend.

MACE, major adverse cardiovascular events

Discussion

In this hospital-based study of adults with hypoalbuminemia from eastern Uttar Pradesh, roughly one in seven patients had a major adverse cardiovascular event, and stroke accounted for nearly half of these. MACE prevalence differed across grades of hypoalbuminemia, but the gradient ran opposite to the dose-response relation reported in population and disease-specific cohorts: events clustered in mild hypoalbuminemia, whereas moderate and severe grades had similar and lower prevalence. Stroke was the only component associated with severity grade and was also more frequent in women. These findings describe a substantial absolute cardiovascular burden in hypoalbuminemic medical patients, and they also show how case-mix and the timing of albumin measurement shape associations observed in hospital settings.

The overall prevalence of 14.6% is not directly comparable with incidence estimates from cohorts that followed event-free participants for years. In the Copenhagen General Population Study, lower albumin predicted ischemic heart disease, MI, and stroke over a median of 8.5 years, with the steepest gradient for

ischemic stroke (hazard ratio 1.46 per 10 g/L decrease) [8]. Among 204 patients with stable coronary disease undergoing PCI, albumin below 4.0 g/dL carried a 3.5-fold higher hazard of MACE [10], and similar associations have been reported after PCI in larger cohorts [11], after acute MI [13] and in HF, where hypoalbuminemia accompanies congestion, hepatic dysfunction and malnutrition [12]. Our cross-sectional estimate therefore complements, rather than replicates, these longitudinal data: it quantifies how often clinically overt MACE is present, or occurs within three months, in patients who already have low albumin. The small contribution of MI and AF, and the absence of cardiovascular death as a component, probably reflect the medical-ward case-mix, the exclusion of patients with diabetes and kidney disease, and the short follow-up. Differences in MACE definitions across studies, highlighted by a systematic review of observational analyses [3], further limit direct comparison. The modest contribution of HF deserves comment, because hypoalbuminemia is frequent in HF and arises from hemodilution, hepatic congestion, gut edema with protein loss, and cardiac cachexia [12]; many such patients would also have had kidney disease or diabetes and were therefore excluded. The pooled estimate from 14 earlier cohorts, which placed the risk ratio for CVD at close to two per 10 g/L lower albumin [8], was derived largely from community-dwelling populations and cannot be translated directly to acutely ill inpatients.

Stroke dominated the event profile and was the only component related to albumin grade. This concords with population data in which the association of low albumin with CVD is strongest for ischemic stroke [8], and with registry data in which more than one-quarter of patients with acute ischemic stroke had albumin below 35 g/L at admission and low albumin was associated with up to two-fold higher long-term mortality [24]. Low albumin after ischemic stroke also predicts early cardiovascular complications [14]. Biologically, reduced albumin diminishes plasma antioxidant capacity, impairs the endothelial glycocalyx, and increases platelet reactivity and blood viscosity, mechanisms that favor cerebral thrombosis [5,25,26]. However, the direction of the association cannot be established in a cross-sectional design. Acute stroke itself triggers an acute-phase response, and dysphagia, reduced intake, and aspiration infection can lower albumin within days, so that many strokes may have caused, rather than followed, mild hypoalbuminemia [6,27]. The higher stroke prevalence in women should be interpreted similarly: sex differences in stroke are well described and are shaped by age, AF burden, hypertension, and hormonal factors [28], none of which could be adjusted for here.

The inverse gradient between albumin grade and MACE contrasts with the graded risk described in most studies [8,15] and deserves careful interpretation. First, the timing of measurement matters. Albumin was measured at presentation, when patients with an acute vascular event are captured early in the acute-phase response, typically with a modest fall in albumin; prospective data from medical inpatients show that admission albumin reflects inflammation more than nutritional status [6]. Second, profound hypoalbuminemia in general medical practice is usually driven by sepsis, malignancy, protein-losing states and advanced malnutrition [4,29]. Patients in whom these conditions predominate are admitted for non-cardiovascular reasons, and some may die or deteriorate from competing causes before a cardiovascular event is recognized; competing risks of this kind bias crude event proportions downward in the sickest stratum [30]. Third, restricting enrolment to hospital patients with low albumin, while excluding those with chronic liver disease, kidney disease and diabetes, conditions the sample on factors related both to albumin and to cardiovascular risk, and such selection can generate spurious or even reversed associations (collider bias) [31]. Fourth, events in the moderate and severe grades were few, and no pairwise contrast for overall MACE survived correction for multiple testing, so the gradient itself is statistically fragile. Our data should therefore not be read as evidence that mild hypoalbuminemia is more harmful than severe hypoalbuminemia, but rather that, on a medical ward, a mild fall in albumin frequently accompanies an acute vascular event. In the Indian setting, where infection and undernutrition remain common reasons for medical admission, the deepest grades of hypoalbuminemia are even more likely to reflect non-cardiovascular disease. Future studies should therefore model albumin as a continuous exposure against a normoalbuminemic reference, distinguish prevalent from incident events, record the timing of albumin measurement relative to symptom onset, and use competing-risk methods [30].

Clinically, these findings support a pragmatic message. Serum albumin is inexpensive, universally available, and already measured in most medical admissions. In hypoalbuminemic patients, including those with only mild reductions, clinicians should actively look for cerebrovascular and cardiac events through targeted neurological examination, ECG, troponin estimation, and echocardiography where indicated. Conversely, severe hypoalbuminemia should prompt evaluation for sepsis, malignancy, and malnutrition, which may coexist with and mask cardiovascular disease. Whether correcting hypoalbuminemia through nutritional support or treatment of the underlying disease improves cardiovascular outcomes remains untested [12,15]. Because albumin is already on the admission panel, a structured cardiovascular and neurological screen triggered by hypoalbuminemia would add little cost and could be evaluated prospectively as a simple quality-improvement intervention.

This study has several strengths: a pre-specified clinical grading of hypoalbuminemia, standardized definitions of each MACE component based on current universal definitions and guidelines, uniform investigation of every participant, and high retention at three months. Several limitations should also be acknowledged. The study was conducted at a single tertiary center using convenience sampling, which limits generalizability and may introduce selection and referral bias. A small sample and a very short follow-up, combining events present at enrolment with those occurring during follow-up, preclude causal or temporal

inference. There was no normoalbuminemic comparison group, so the excess risk attributable to hypoalbuminemia could not be quantified. Albumin was measured once, and inflammatory markers, natriuretic peptides, renal function, nutritional indices, and comorbidities were not entered into a multivariable model because events were few; all odds ratios are therefore unadjusted. Cardiovascular death and coronary revascularization were not included as MACE components, and events were diagnosed by treating clinicians without independent blinded adjudication. Finally, due to the small sample size, subgroup analyses by age and sex had limited power. Larger multicenter prospective studies that include normoalbuminemic controls, serial albumin measurements, and adjustment for inflammation and comorbidity are needed.

Conclusions

Among adults with hypoalbuminemia seen at a tertiary care center in Northern India, about one in seven had a major adverse cardiovascular event, most often stroke. MACE prevalence varied significantly across the severity grades of hypoalbuminemia and was highest in the mild group and lowest in the severe group, a pattern more plausibly explained by acute-phase changes, competing illness, and selection than by any protective effect of lower albumin. Stroke was the only component associated with albumin grade and was more common in women. Serum albumin may serve as an inexpensive prompt for systematic cardiovascular and cerebrovascular assessment in medical patients, but its prognostic value needs confirmation in prospective controlled studies.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Mohammad Abu Bashar, Vidyacharan ., Brijesh K. Chaudhry, Kanishka Kumar, Ajay Mishra

Critical review of the manuscript for important intellectual content: Mohammad Abu Bashar, Vidyacharan ., Brijesh K. Chaudhry, Kanishka Kumar, Ajay Mishra, Priyanka Budhwani

Supervision: Mohammad Abu Bashar, Brijesh K. Chaudhry, Kanishka Kumar, Ajay Mishra

Acquisition, analysis, or interpretation of data: Vidyacharan ., Priyanka Budhwani

Drafting of the manuscript: Vidyacharan .

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Human Ethics Committee, All India Institute of Medical Sciences (AIIMS), Gorakhpur issued approval IHEC/AIIMS-GKP/BMR/297/2024, dated August 20, 2024. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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