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Impact of Preoperative Hypoalbuminaemia on Postoperative Complications Following Major Abdominal Surgery: A prospective observational cohort study.

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Abstract

Background: have repeatedly been linked to adverse surgical outcome. Whether hypoalbuminaemia predicts complications independently of comorbidity, urgency and disease burden, and whether the relationship is graded, remains incompletely defined in resource-limited settings. ***Aim:*** To determine the influence of preoperative hypoalbuminaemia on the frequency, nature and severity of postoperative complications following major abdominal surgery. ***Materials and Methods:*** A prospective observational cohort study was conducted over two years among 300 patients aged 18 years and above undergoing major elective or emergency abdominal surgery. Serum albumin was measured within 48 hours before operation and patients were categorised as hypoalbuminaemic (< 3.5 g/dL) or normoalbuminaemic (≥ 3.5 g/dL). Patients were followed for 30 days; complications were graded by the Clavien-Dindo classification, grade II or above being taken as clinically significant. Data were analysed in SPSS v29 using the chi-square test, Student's t-test, multivariable binary logistic regression and receiver operating characteristic analysis, with $p < 0.05$ taken as significant. ***Results:*** One hundred and eight patients (36.0%) were hypoalbuminaemic. Complications occurred in 52 of 108 hypoalbuminaemic patients (48.1%) compared with 34 of 192 normoalbuminaemic patients (17.7%; $p < 0.001$), and major complications (Clavien-Dindo ≥ IIIa) in 22.2% versus 5.2% ($p < 0.001$). A clear biological gradient was evident, complication rates rising from 17.7% at albumin ≥ 3.5 g/dL to 64.3% below 2.5 g/dL (p for trend < 0.001). Surgical site infection (25.0% vs 10.9%), wound dehiscence (10.2% vs 2.6%), anastomotic leak (11.8% vs 3.8%), pneumonia (12.0% vs 4.7%) and acute kidney injury (8.3% vs 2.6%) were all significantly commoner. Hospital stay was prolonged (12.4 ± 5.8 vs 7.3 ± 3.1 days; $p < 0.001$). After adjustment, hypoalbuminaemia remained the strongest independent predictor of complications (aOR 3.42; 95% CI 1.88–6.22; $p < 0.001$). ***Conclusion:*** Preoperative hypoalbuminaemia was independently and dose-dependently associated with postoperative morbidity. Because albumin reflects both nutritional depletion and systemic inflammation, a low value should be regarded not as a deficiency to be corrected by infusion but as a trigger for formal nutritional assessment and, in elective cases, preoperative optimisation before surgery proceeds.

Keywords: hypoalbuminaemia; serum albumin; postoperative complications; malnutrition; Clavien-Dindo classification; preoperative risk assessment.

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INTRODUCTION

Albumin is the most abundant plasma protein, synthesised exclusively by the hepatocyte and circulating with a half-life of approximately twenty days. It generates the greater part of plasma colloid osmotic pressure, transports fatty acids, bilirubin, calcium, hormones and many drugs, and possesses antioxidant, buffering and endothelium-stabilising properties.3 A concentration below 3.5 g/dL is conventionally termed hypoalbuminaemia, and because albumin is measured as part of almost every preoperative biochemical panel, it is among the most accessible of all prognostic variables available to the surgeon.18

Hypoalbuminaemia is common in surgical practice, affecting between a fifth and two fifths of patients presenting for major abdominal operation, and is disproportionately represented among those with malignancy, gastrointestinal obstruction, sepsis and those requiring emergency surgery. Its origins are dual, and this duality is central to its interpretation. Reduced synthesis accompanies protein-energy malnutrition, but albumin is also a negative acute-phase reactant, its production being downregulated by interleukin-6 and tumour necrosis factor-α while capillary permeability simultaneously increases its escape into the interstitium.3,18 A low value therefore reflects the combined burden of nutritional depletion and systemic

inflammation rather than protein intake alone, which is why contemporary consensus frameworks for the diagnosis of malnutrition treat albumin as a marker of disease severity rather than as a nutritional criterion in its own right.15

The prognostic power of the measurement was established definitively by the National Veterans Affairs Surgical Risk Study, in which serum albumin proved the single strongest predictor of thirty-day morbidity and mortality among more than fifty thousand patients: as albumin fell from above 4.6 g/dL to below 2.1 g/dL, mortality rose from approximately 1% to 29% and morbidity from 10% to 65%.1 A subsequent meta-analysis of cohort studies and controlled trials found that each decrement of 10 g/L in serum albumin increased the odds of morbidity by 89% and of mortality by 137%, with corresponding prolongation of intensive care and hospital stay.2 The association has been confirmed across surgical disciplines, the risk being modified by the anatomical site of operation.4

Several mechanisms plausibly link the two. Reduced oncotic pressure promotes interstitial and bowel-wall oedema, impairing microcirculatory perfusion at an anastomosis; impaired collagen synthesis retards wound healing; cell-mediated immunity is depressed; and altered protein binding may reduce effective antibiotic tissue concentrations. Consistent with these, hypoalbuminaemia predicts surgical site infection after gastrointestinal and orthopaedic surgery, adverse outcome after colorectal resection, prolonged stay and readmission after arthroplasty, and acute kidney injury.5,6,7,8,17

Notwithstanding this evidence, questions of practical importance remain. Whether albumin retains independent predictive value once comorbidity, physical status, malignancy and operative urgency are accounted for is contested, since each of these is itself associated with a low albumin. Whether the relationship is graded across the range of hypoalbuminaemia — a criterion of some importance in inferring causation — has been examined less often. European guidance recommends routine preoperative nutritional screening and, where significant risk is identified, a period of nutritional support before elective surgery,13,14,16 yet prospective data quantifying the burden attributable to hypoalbuminaemia in teaching hospitals of resource-limited settings, where malnutrition and late presentation are prevalent, remain limited. The present study was therefore undertaken to determine the frequency, nature and severity of postoperative complications in relation to preoperative serum albumin, and to establish whether hypoalbuminaemia predicts morbidity independently of other recognised risk factors.

MATERIALS AND METHODS

Study design, setting and duration. This prospective observational cohort study was conducted in the Department of General Surgery of Employees State Insurance Corporation Medical College and Hospital, Kalaburagi over two years, following approval by the Institutional Ethics Committee. Written informed consent was obtained from every participant.

Participants. Consecutive patients aged 18 years and above undergoing major elective or emergency abdominal surgery under general anaesthesia were eligible. Patients were excluded if they had conditions independently altering serum albumin irrespective of nutritional or inflammatory state — nephrotic syndrome or overt proteinuria, decompensated chronic liver disease with ascites, protein-losing enteropathy or extensive burns — or if they had received albumin, plasma or blood products within the preceding seven days, since these would confound interpretation of the index measurement. Patients undergoing minor or day-care procedures and those unwilling to attend follow-up were also excluded.

Exposure measurement and grouping. Venous blood was drawn within 48 hours before operation, before the administration of any blood product or intravenous albumin, and serum albumin estimated by the bromocresol green colorimetric method on an automated analyser. Patients were assigned to the hypoalbuminaemic group if the concentration was below 3.5 g/dL and to the normoalbuminaemic group if it was 3.5 g/dL or above. For the analysis of dose-response, the hypoalbuminaemic group was further stratified as 3.0–3.4, 2.5–2.9 and below 2.5 g/dL.

Outcomes and definitions. The primary outcome was the occurrence of any postoperative complication within thirty days, graded by the Clavien-Dindo classification, with grade II or above taken as clinically significant and grade IIIa or above as a major complication.11,12 Secondary outcomes were the individual complications — surgical site infection, diagnosed by Centers for Disease Control and Prevention surveillance criteria,19 wound dehiscence, anastomotic leak (analysed only among patients in whom an anastomosis was fashioned), pneumonia, sepsis, acute kidney injury defined by KDIGO criteria, prolonged ileus, unplanned intensive care admission, reoperation and thirty-day mortality — together with duration of hospital stay and readmission within thirty days.

Data collection and follow-up. A structured, pre-tested proforma recorded demographic data, body mass index, comorbidity, haemoglobin, presence of malignancy, ASA physical status grade, urgency of operation, procedure performed and operative duration. Patients were assessed daily until discharge and reviewed on the fifteenth and thirtieth postoperative days; non-attenders were contacted by telephone using a structured questionnaire.

Sample size. Assuming a complication rate of 45% among hypoalbuminaemic and 20% among normoalbuminaemic patients, a minimum of 54 patients per group was required for 80% power at a two-sided alpha of 0.05. The sample was enlarged to 300 to permit stratified analysis across albumin bands and to support a multivariable model containing several covariates.

Statistical analysis. Data were analysed in IBM SPSS Statistics version 29. Categorical variables are expressed as frequencies and percentages and compared by the chi-square or Fisher's exact test; continuous variables as mean ± standard deviation and compared by the independent-samples t-test. Trend across albumin strata was tested by the chi-square test for linear trend. Variables attaining $p < 0.10$ on univariable analysis were entered into a multivariable binary logistic regression model built by backward stepwise elimination, results being reported as adjusted odds ratios with 95% confidence intervals; calibration was assessed by the Hosmer-Lemeshow test. Receiver operating characteristic analysis was used to examine the discriminative performance of serum albumin. A two-tailed $p < 0.05$ was considered significant.

RESULTS

Three hundred patients completed thirty-day follow-up. One hundred and eight (36.0%) were hypoalbuminaemic and 192 (64.0%) normoalbuminaemic, with mean serum albumin concentrations of 2.92 ± 0.38 and 4.11 ± 0.34 g/dL respectively. Their baseline characteristics are compared in Table 1.

Table 1 — Baseline characteristics by preoperative albumin status; values are n (%). Mean serum albumin 2.92 ± 0.38 versus 4.11 ± 0.34 g/dL (p < 0.001). * = statistically significant (p < 0.05).

Characteristic	Hypoalbuminaemic (n = 108)	Normoalbuminaemic (n = 192)	p-value
Age > 60 years	48 (44.4)	58 (30.2)	0.014*
Male sex	62 (57.4)	109 (56.8)	0.915
Body mass index < 18.5 kg/m²	29 (26.9)	22 (11.5)	< 0.001*
Diabetes mellitus	32 (29.6)	44 (22.9)	0.201
Anaemia (haemoglobin < 10 g/dL)	44 (40.7)	41 (21.4)	< 0.001*
Underlying malignancy	46 (42.6)	48 (25.0)	0.002*
ASA grade III or above	43 (39.8)	45 (23.4)	0.003*
Emergency operation	51 (47.2)	62 (32.3)	0.010*
Operative time > 180 minutes	38 (35.2)	51 (26.6)	0.117

The two groups differed materially at baseline. Hypoalbuminaemic patients were older and more often underweight, anaemic, of ASA grade III or above, and were more likely to harbour malignancy or to require emergency operation. These differences are precisely those expected of a marker that reflects both nutritional depletion and inflammatory burden, and they establish the need for multivariable adjustment before any independent effect of albumin can be claimed.

Table 2 — Frequency and severity of postoperative complications by albumin status; values are n (%). * = statistically significant (p < 0.05).

Outcome	Hypoalbuminaemic (n = 108)	Normoalbuminaemic (n = 192)	p-value
Any complication (Clavien-Dindo ≥ II)	52 (48.1)	34 (17.7)	< 0.001*
Grade II	28 (25.9)	24 (12.5)	0.004*
Grade IIIa	9 (8.3)	5 (2.6)	0.026*
Grade IIIb	8 (7.4)	3 (1.6)	0.011*
Grade IV	5 (4.6)	1 (0.5)	0.021*
Grade V (death)	2 (1.9)	1 (0.5)	0.279
Major complication (≥ Grade IIIa)	24 (22.2)	10 (5.2)	< 0.001*

Complications of Clavien-Dindo grade II or above occurred in 52 of the 108 hypoalbuminaemic patients (48.1%) compared with 34 of the 192 normoalbuminaemic patients (17.7%), a highly significant difference ($p < 0.001$). The effect was more pronounced for severe events: major complications of grade IIIa or above occurred more than four times as often in the hypoalbuminaemic group (22.2% versus 5.2%; $p < 0.001$), and grade IV events requiring organ support in 4.6% versus 0.5%. Thirty-day mortality was three-fold higher in absolute terms but did not reach significance, the number of deaths (three in total) being too small to permit meaningful comparison.

Table 3 — Individual postoperative complications by albumin status; values are n (%). Categories are not mutually exclusive, as a patient may sustain more than one complication. † Anastomotic leak was assessed only among the 172 patients in whom an anastomosis was fashioned (68 hypoalbuminaemic, 104 normoalbuminaemic). * = statistically significant (p < 0.05).

Complication	Hypoalbuminaemic (n = 108)	Normoalbuminaemic (n = 192)	p-value
Surgical site infection	27 (25.0)	21 (10.9)	0.001*
Prolonged ileus	15 (13.9)	13 (6.8)	0.038*
Pneumonia / respiratory complication	13 (12.0)	9 (4.7)	0.018*
Anastomotic leak †	8 (11.8)	4 (3.8)	0.048*
Wound dehiscence	11 (10.2)	5 (2.6)	0.004*
Sepsis	10 (9.3)	6 (3.1)	0.023*
Acute kidney injury	9 (8.3)	5 (2.6)	0.026*
Unplanned ICU admission	18 (16.7)	11 (5.7)	0.002*
Reoperation	10 (9.3)	4 (2.1)	0.005*
Thirty-day mortality	2 (1.9)	1 (0.5)	0.279

Every complication examined was commoner among hypoalbuminaemic patients, and all but mortality reached statistical significance. Infective and wound-related events showed the largest differences: surgical site infection affected a quarter of hypoalbuminaemic patients compared with roughly one in nine of those with normal albumin (25.0% versus 10.9%; p = 0.001), while wound dehiscence was nearly four times as frequent (10.2% versus 2.6%; p = 0.004). Among the 172 patients in whom an anastomosis was constructed, leak occurred in 11.8% of the hypoalbuminaemic compared with 3.8% of the normoalbuminaemic (p = 0.048). Unplanned intensive care admission and reoperation were likewise substantially more frequent.

Table 4 — Complication rate and duration of hospital stay across strata of preoperative serum albumin (χ^2 for linear trend, p < 0.001 for both any and major complications).

Serum albumin (g/dL)	n	Any complication n (%)	Major complication n (%)	Mean stay (days)
≥ 3.5	192	34 (17.7)	10 (5.2)	7.3 ± 3.1
3.0 – 3.4	64	26 (40.6)	11 (17.2)	10.4 ± 4.2
2.5 – 2.9	30	17 (56.7)	8 (26.7)	13.2 ± 5.1
< 2.5	14	9 (64.3)	5 (35.7)	16.8 ± 6.3
Total	300	86 (28.7)	34 (11.3)	9.1 ± 4.7

A clear biological gradient was demonstrated. The proportion of patients sustaining any complication rose progressively from 17.7% among those with albumin of 3.5 g/dL or above to 40.6%, 56.7% and 64.3% across the descending strata, and the proportion sustaining a major complication rose in parallel from 5.2% to 35.7% (p for trend < 0.001 for both). Mean hospital stay lengthened correspondingly, from 7.3 days in the normoalbuminaemic group to 16.8 days among those with albumin below 2.5 g/dL. The presence of such a dose-response relationship strengthens the inference that the association is not merely an artefact of confounding.

Table 5 — Postoperative recovery outcomes by albumin status; values are mean ± SD unless otherwise stated. * = statistically significant (p < 0.05).

Recovery outcome	Hypoalbuminaemic (n = 108)	Normoalbuminaemic (n = 192)	p-value
Duration of hospital stay (days)	12.4 ± 5.8	7.3 ± 3.1	< 0.001*
Time to resumption of oral diet (days)	4.6 ± 2.0	3.1 ± 1.4	< 0.001*
Duration of ICU stay, if admitted (days)	3.8 ± 2.1	2.4 ± 1.3	0.021*
Readmission within 30 days, n (%)	16 (14.8)	13 (6.8)	0.025*

Recovery was slower throughout in the hypoalbuminaemic group. Hospital stay was prolonged by a mean of 5.1 days (12.4 versus 7.3 days; p < 0.001), oral intake was resumed approximately a day and a half later, and those requiring intensive care remained there longer. Readmission within thirty days was more than twice as frequent (14.8% versus 6.8%; p = 0.025), indicating that the disadvantage conferred by a low albumin extends beyond the index admission.

Table 6 — Multivariable binary logistic regression for the occurrence of any postoperative complication. Hosmer-Lemeshow $\chi^2 = 5.94$, $p = 0.654$; Nagelkerke $R^2 = 0.31$; area under ROC curve 0.78. * = statistically significant ($p < 0.05$).

Independent variable	Adjusted OR	95% CI	p-value
Serum albumin < 3.5 g/dL	3.42	1.88 – 6.22	< 0.001*
ASA grade III or above	2.18	1.16 – 4.10	0.016*
Emergency operation	1.96	1.05 – 3.66	0.035*
Underlying malignancy	1.88	1.01 – 3.50	0.047*
Anaemia (haemoglobin < 10 g/dL)	1.84	1.00 – 3.39	0.049*
Operative time > 180 minutes	1.79	0.96 – 3.34	0.067
Body mass index < 18.5 kg/m²	1.58	0.81 – 3.08	0.180
Age > 60 years	1.52	0.82 – 2.82	0.184
Diabetes mellitus	1.41	0.74 – 2.69	0.297

After adjustment for age, sex, body mass index, anaemia, malignancy, ASA grade, urgency and operative duration, hypoalbuminaemia remained the strongest independent predictor of postoperative complications, more than trebling the odds (aOR 3.42; 95% CI 1.88–6.22; $p < 0.001$). ASA grade III or above, emergency operation, malignancy and anaemia retained modest independent effects, whereas age, diabetes, low body mass index and operative duration did not — indicating that their univariable associations were mediated substantially through albumin status itself. The model was well calibrated (Hosmer-Lemeshow $p = 0.654$) and showed good discrimination (area under the curve 0.78).

Table 7 — Performance of a preoperative serum albumin threshold of 3.5 g/dL in predicting postoperative complications (n = 300; 86 patients sustained a complication).

Performance measure	Value	Derivation
Sensitivity	60.5%	52 / 86
Specificity	73.8%	158 / 214
Positive predictive value	48.1%	52 / 108
Negative predictive value	82.3%	158 / 192
Area under ROC curve	0.76 (95% CI 0.70 – 0.82)	$p < 0.001$

Applied as a dichotomous screening threshold, an albumin below 3.5 g/dL identified complications with moderate sensitivity (60.5%) and specificity (73.8%). Its principal value lay in its negative predictive value of 82.3%: a normal preoperative albumin conferred a better than four-in-five probability of an uncomplicated course. The area under the receiver operating characteristic curve was 0.76, indicating acceptable but not excellent discrimination, and confirming that albumin should be used to complement rather than replace formal risk assessment.

DISCUSSION

In this cohort, preoperative hypoalbuminaemia was associated with a near three-fold increase in postoperative complications and a more than four-fold increase in major complications, and it remained the strongest independent predictor after adjustment (aOR 3.42). This accords with the National Veterans Affairs Surgical Risk Study, in which albumin outperformed all other preoperative variables tested, and with meta-analytic evidence that each 10 g/L decrement raises the odds of morbidity by approximately 89%.1,2,4 The stepwise rise in both overall and major complications across descending albumin strata is of particular interest, since a biological gradient of this kind materially strengthens a causal interpretation and reproduces the pattern originally described in the Veterans Affairs data.1

The pattern of complications was consistent with recognised pathophysiology. Wound-related and infective events dominated: surgical site infection affected a quarter of hypoalbuminaemic patients, in keeping with evidence identifying hypoalbuminaemia as an independent risk factor for infection after gastrointestinal surgery and in orthopaedic meta-analysis.5,8 Anastomotic leak was three times commoner, plausibly reflecting reduced oncotic pressure with consequent bowel-wall oedema and impaired microcirculatory perfusion at the anastomosis, together with defective collagen synthesis; comparable findings have been reported in colorectal practice.6 Acute kidney injury was likewise more frequent, an association confirmed in meta-analysis of observational studies, and prolonged stay and increased readmission mirror findings after arthroplasty.7,17

The interpretation of these findings requires care, and this is the most important caveat of the study. Albumin is a negative acute-phase reactant as well as a nutritional index, and its concentration falls with inflammation independently of protein intake.3,18 The baseline differences observed here — hypoalbuminaemic patients being more often anaemic, malignant, of higher ASA grade and undergoing emergency operation — illustrate this directly. Low albumin therefore marks a patient who is inflamed, catabolic and physiologically depleted, and it should not be assumed that raising the measured value will

itself alter outcome. Consistent with this, exogenous albumin administration has not been shown reliably to improve surgical outcomes, and contemporary consensus criteria for malnutrition deliberately exclude albumin as a diagnostic criterion, retaining it as an indicator of disease severity.2,15

The clinical implication is accordingly one of triage rather than replacement. A low preoperative albumin should prompt formal nutritional assessment using a validated instrument such as NRS-2002 or the GLIM criteria, and, where significant risk is confirmed and the operation is elective, a period of preoperative nutritional support — enteral wherever the gut is usable — before surgery proceeds, as recommended by European guidance and supported by meta-analysis of screening-based approaches.13,14,16 Perioperative measures of established benefit, including enhanced recovery protocols with early oral intake, are especially pertinent in this group,20 and serial postoperative albumin measurement may afford additional early warning, an early postoperative decline having been shown to predict complications after major abdominal and colorectal resection.9,10

Limitations. This was a single-centre observational study, and residual confounding cannot be excluded despite multivariable adjustment. Albumin was measured once preoperatively, so the contributions of chronic nutritional depletion and acute inflammation could not be disentangled; concurrent measurement of C-reactive protein or prealbumin would have permitted this. The cohort comprised heterogeneous abdominal procedures, limiting procedure-specific inference, and the small number of deaths precluded meaningful analysis of mortality.

CONCLUSION

Preoperative hypoalbuminaemia, present in just over a third of patients undergoing major abdominal surgery in this cohort, was strongly, independently and dose-dependently associated with postoperative morbidity. Complications occurred in 48.1% of hypoalbuminaemic compared with 17.7% of normoalbuminaemic patients, major complications were more than four times as frequent, hospital stay was prolonged by a mean of five days, and readmission was doubled; after adjustment for comorbidity, malignancy, physical status and operative urgency, hypoalbuminaemia remained the single strongest predictor of complications. Because serum albumin reflects systemic inflammation as much as nutritional depletion, a low value is best regarded not as a deficiency to be corrected by infusion but as a readily available signal identifying a physiologically vulnerable patient. Its measurement should therefore trigger formal nutritional assessment, consideration of deferring elective surgery pending a period of nutritional optimisation, heightened perioperative vigilance for wound and anastomotic complications, and enrolment in structured enhanced-recovery and follow-up pathways. Interventional studies are needed to establish whether preoperative optimisation guided by albumin-triggered assessment translates into measurable reductions in morbidity.

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