Iran Red Crescent Med J. 2023 September; 25(9): e2499 doi: 10.32592/ircmj.2023.25.9.2499

Published online 2023 September 20 **Original Article**

Preoperative Hypoalbuminemia and Development of Surgical Site Infection and Anastomotic Leakage in Emergency Colorectal Surgery

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Received 2022 November 13; **Revised** 2023 November 22; **Accepted** 2023 July 22.

Abstract

Background: Although hypoalbuminemia is a well-known predictor of postoperative complications, including surgical site infection (SSI) and anastomotic leakage (AL) in gastrointestinal surgery patients, which requires necessary interventions before surgery, there is limited opportunity for preoperative optimization and intervention in emergency colorectal surgeries.
Objectives: Therefore, this study aimed to assess the relationship between preoperative serum albumin levels and the development of SSI and AL in emergency colorectal surgery patients.
Methods: In this cohort study, patients who underwent emergency colorectal surgery during 17 months, were assessed. Albumin level was measured before surgery, and patients were followed for 1 month after surgery to identify the development of SSI and AL.
Results: In total, 173 patients were enrolled in the study, but data analysis was performed on 170 patients. They were divided into hypoalbuminemia group (n=98, 57.6%) and non-hypoalbuminemia group (n=72, 42.4%). The mean ages of patients in each group were 57.17±16.19 and 51.61±16.14 years old, respectively (P=0.028). The AL was observed in 4 (2.4%) patients; 3 patients in the hypoalbuminemia group and one patient in the non-hypoalbuminemia group (P=0.205, relative risk=2.33, 95% CI: 0.42-12.82). The SSI was observed in 13 patients (7.6%) during the 1-month follow-up; 8 patients (5.1%) had superficial SSI and 5 (3.2%) had deep ones. Albumin level was significantly lower in patients with AL (2.9±0.48), compared to those without AL (3.6±0.7 g/dL). Moreover, albumin level was higher in patients with SSI (3.11±0.62), compared to patients without SSI (3.6±0.7 g/dL). The incidence of complications, either AL or SSI, was significantly higher in hypoalbuminemia patients, compared to non-hypoalbuminemia patients (P=0.017, Odds Ratio=4.24, 95% CI: 1.29-13.9). Adjusted OR for age was 3.82 (95% CI: 1.15-12.75, P=0.029); therefore, a 13.5% reduction in OR indicated that age is a confounding factor.
Conclusion: Preoperative hypoalbuminemia was significantly associated with post-development of complications in emergency colorectal surgery and older age and lower preoperative albumin levels may serve as valuable indicators for the identification of patients at higher risk of complications.

Keywords: Anastomotic leakage, Biomarker, Colorectal surgery, Emergency surgery, Hypoalbuminemia, Surgical site infection

1. Background

Emergency colorectal surgery is often performed in patients with acute conditions, such as perforation, obstruction, uncontrollable bleeding, or ischemia, and is associated with a higher risk of morbidity and mortality, compared to elective surgery (1,2). These patients are prone to hypoalbuminemia, which is an agent for the fluid balance of the body, transporting hormones and vitamins while preventing edema.

The prevalence of hypoalbuminemia in patients who need emergency colorectal surgery varies depending on the population being studied and the definition of hypoalbuminemia, location, and stage of the disease, tumor size, age, and pre-existing medical conditions of the subjects of the study (3,4). In a study carried out by Ionescu et al., the prevalence of hypoalbuminemia in patients with colorectal cancer was 28.9%. In line with the aforementioned study, Lai et al. and Lohsiriwat et al. reported that the occurrence of hypoalbuminemia in patients with colorectal cancer ranged from 18.6% to 23%. However, Ñamendys-Silva et al. reported a high incidence of 82% in critically ill cancer patients (5), (4), (6), (3). These high incidence rates support the need for preoperative nutritional screening and interventions, provided the condition of the patient permits such measures.

Several studies have investigated the relationship between hypoalbuminemia and outcomes after emergency colorectal surgery (2). Indeed, patients with hypoalbuminemia have a higher risk of developing surgical site infection (SSI), anastomotic leakage (AL), and other postoperative complications (7). This is because albumin plays a crucial role in wound healing and immune function (8). In this regard, preoperative hypoalbuminemia was associated with an increased risk of postoperative complications, including wound infections and anastomotic leaks, prolonged hospital stay, and higher mortality rates after emergency colorectal surgery (3,5).

The SSI encompasses wound infections, regional extension, and infections in organs or spaces following surgery and they can occur within a specific timeframe after surgery and result in prolonged

hospital stays and increased costs (9). Risk factors for SSI include body mass index, gender, operating time, wound classification, blood transfusion, comorbidities, suture material, stoma formation, and emergency operations (10).

Likewise, AL is a serious complication in gastrointestinal surgeries, particularly in procedures involving the esophagus, colon, and pancreas (11). Factors contributing to AL include surgical technique, operative time, and non-surgical factors, such as gender, hypotension, hypoalbuminemia, anemia, and postoperative fluid management (12).

2. Objectives

Therefore, it is essential to manage hypo-albuminemia before emergency colorectal surgery. This can involve nutritional support, such as the provision of protein-rich meals or administration of intravenous albumin.

In some cases, it may be necessary to delay surgery until the albumin levels of the patients improve in order to reduce the risk of complications (13,14). However, due to the emergent nature of these emergency colorectal surgeries, there is limited opportunity for preoperative optimization and intervention. Therefore, it was crucial to evaluate these patients to predict and anticipate the appropriate management strategies in our country, Iran. Therefore, this study aimed to investigate the potential association between preoperative hypoalbuminemia and the development of SSI or AL during a 1-month follow-up of the patients who underwent emergency colorectal surgery.

3. Methods

3.1. Study design and participants

A prospective cohort study was conducted on patients who underwent emergency colorectal surgery in Taleghani Hospital, Tehran, Iran for 17 months from February 2019 to August 2020.

3.2. Data collection

Medical records were used to collect the demographic data of patients, including age, gender, and preoperative albumin level; in addition, a history of diabetes and arterial hypertension was also retrieved from the medical records. Serum albumin levels of less than 3.5 g/dL were defined as hypoalbuminemia. Albumin level was measured by blood sample before surgery.

3.3. Outcomes

Patients were followed up for 1 month to identify postoperative development of AL as the primary outcome or SSI as the secondary outcome. Definitions provided by the Centers for Disease Control and Prevention were used to classify SSI as superficial incisional and deep incisional (15). The AL was defined as "a communication between the intra and extra-luminal compartments" (16), including any discharges from the drain, the surgical wound, and rectum fistula that was confirmed either clinically or by computerized tomography scan and radiological contrast series (17).

3.4. Ethical Considerations

The study and its objectives were explained to all patients who were included in the study. The consent form was obtained from all patients, and the study was approved by the local Ethics Committee with the reference number of Ir.sbmu.msp.rec.1395538.

3.5. Statistical analysis

Statistical analyses were performed in SPSS software (SPSS for Windows, version 25, SPSS Inc., Chicago, IL, USA). The patients were divided into groups based on their hypoalbuminemia status. Normality distribution was assessed using Kolmogorov–Smirnov test and histogram. Categorical variables were reported as percentages and quantitative variables were presented as mean values. The groups were statistically compared using ki² (for categorical variables) and the student t-test for quantitative variables. Risk Ratio and 95% CI were reported for the primary and secondary outcomes.

Moreover, albumin level was compared in outcome-positive patients i.e., those with SSI and AL, and the psychometrica website was used to calculate the standardized mean difference. Logistic regression analysis was performed to assess the adjusted Odds Ratio (OR), a *P* value of less than 0.05 was considered statistically significant. In addition, a post-hoc power calculation was performed to assess the power of 170 participants using g-power, and a power of 82% was calculated with respect to 0.05 of α error.

4. Results

In total, 173 patients underwent emergency colorectal surgery in this study. The albumin level of three patients was not clarified and they were excluded from the study. Hence, data analysis was performed on 170 patients. Regarding gender, 91 patients (53%) were male and 79 were female (47%). The mean serum albumin level of [atients before surgery was 3.58±0.71g/dL. The albumin levels of male and female patients were 3.58±0.73 and 3.57±0.67 g/dL, respectively (*P*=0.940).

Overall, 98 patients (57.6%) had preoperative hypoalbuminemia and 72 patients (42.4%) had preoperative normal albumin levels (non-hypoalbuminemia group).

The mean ages of patients in hypo and non-hypo albumin groups were 57.17 ±16.19 and 51.61 ± 16.14 years old, respectively (*P*=0.028). Concerning gender

and comorbidities, there was no significant difference between the two study groups according to Table 1.

Table 1. Baseline characteristics among hypoalbuminemia and non-hypoalbuminemia groups

	Hypoalbuminemia (n=72)	Non-hypoalbuminemia (n=98)	P value
Male (%)	37 (51.4)	54 (55.1)	*0.373
Age (years)	57.17±16.19	51.61±16.14	**0.028
DM	11 (18.0%)	16 (16.8%)	*0.832
HTN	12 (19.7%)	14 (14.7%)	*0.510

DM: Diabetes Mellitus, HTN: Hypertension
* Chi-squared test
**Independent Sample t-test

4.1. Anastomotic leakage

The AL was observed in 4 out of 170 (2.4 %) patients; 3 of them were in the hypoalbuminemia group (4.1%) and 1 of them was in the non-hypoalbuminemia group (1.02%) (*P*=0.205, relative risk: 2.33, 95% CI: 0.42-12.82 in hypoalbuminemia vs. non-hypoalbuminemia).

The mean ages of the patients with and without leakage were 53.7±16.24 and 62.5±21.23 years old, respectively (*P*=0.290). Regarding their gender, three of them were male.

Albumin level, as a continuous variable, was compared in the patients with and without leakage and was significantly lower in patients with AL (2.9±0.48 vs. 3.6±0.7 g/dL). The standardized mean difference was -1.004 with a 95% CI of -0.007 to -2.002 (Figure 1A).

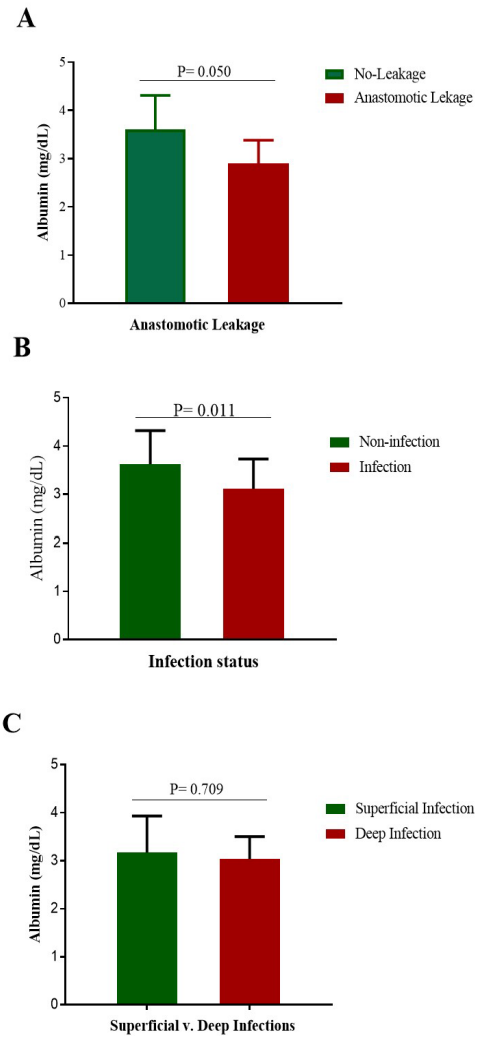

Figure 1. Albumin level in different outcomes, A) Albumin level was significantly lower in patients with anastomotic leakage (2.9±0.48 vs. 3.6±0.7 g/dL), B) Albumin level was significantly lower in patients with infection (3.11±0.62 vs. 3.6±0.7 g/dL) and C) There was no significant difference regarding infectious severity, albumin level was 3.17±0.76 vs. 3.03±0.47 g/dL in patients with superficial vs. deep infection, respectively

4.2. Surgery Site Infection

In total, SSI was observed in 13 out of 170 (7.6%) participants during 1-month follow-up, 9 of whom belonged to the hypoalbuminemia group (12.5%) and 4 of whom were in the non-hypoalbuminemia group (4.1%) (*P*=0.041, relative risk: 1.72, 95% CI: 1.14 to 2.6, in hypoalbuminemia vs. non-hypoalbuminemia).

The mean age of the patients with SSI was 57.77±14.4 years old and in the no infection group was 53.65±16.5 years old (*P*=0.384). Regarding the gender of the patients with SSI, 8 patients (8.8%) were male and 5 patients (6.3%) were female. Albumin level as a continuous variable was compared in SSI patients and was significantly lower in patients with infection, compared to those without infection (3.11±0.62 vs. 3.6±0.7 g/dL, 13 patients). The standardized mean difference was -0.75 with a 95% CI of -0.18 to -1.3 (Figure 1B).

Regarding the severity of infection, in total, 8 patients (5.1%) had superficial SSI, 5 patients (3.2%) had deep SSI, and there was not any organ/space SSI. Regardless of SSI classification, the median preoperative albumin level was 3.3 g/dL (from 2.1 g/dL to 4.3 g/dL) in patients with any type of SSI group versus 3.7 g/dL (from 2.2 g/dL to 7.9 g/dL) in patients without any type of SSI group. Patients with any type of SSI had significantly lower preoperative albumin levels (p=0.011), compared to those without any type of SSI; however, there was no significant difference with respect to albumin level between superficial SSI and deep SSI groups (*P*=0.709) (Figure1C).

4.3. Multivariable analysis

To control the effect of age, a composite variable composed of AL or SSI was compared in two study groups. The incidence of all complications was significantly higher in hypoalbuminemia patients as it was observed in 4 out of 98 patients in the non-hypoalbuminemia (4.1%) and 11 out of 72 patients in the hypoalbuminemia group (15.3%) (*P*=0.017, OR=4.24 and 95% CI: 1.29-13.9).

Multivariable analysis revealed that adjusting OR for age was 3.82 (95% CI: 1.15-12.75, *P*=0.029). Therefore, a 13.5% reduction in OR indicated that age is a confounding factor for the assessment of the relationship between hypoalbuminemia and surgical complications.

5. Discussion

In this study, emergency colorectal surgeries were performed on patients with various conditions, including colon cancer, colon adenocarcinoma, sigmoid colon, jejunal adenocarcinoma, rectal adenocarcinoma, appendicitis, and rectovaginal fistula. The present study revealed that 57.6% of the patients had preoperative hypoalbuminemia and a significant correlation was observed between hypoalbuminemia and SSI. Indeed, it was observed that albumin level was significantly low in both SSI and AL patients.

Multivariable analysis, adjusting for age, indicated that the occurrence of post-operation complications was 3.82 folds higher in patients with hypoalbuminemia, compared to normal albumin levels. Additionally, no significant difference was found between patients with superficial and deep infections in terms of albumin levels.

Older age and lower preoperative albumin levels may serve as valuable indicators for identifying patients at higher risk of complications. Further research is needed to explore the underlying mechanisms and potential interventions to mitigate the impact of hypoalbuminemia on surgical outcomes.

In this study, the prevalence of infection at the surgical site was less than 13%, with the majority of cases having superficial SSI without organ or space involvement. These findings are consistent with those of a study conducted by Sanjay et al., which reported the prevalence of SSI in patients undergoing emergency abdominal surgery to be 26.08%, which is 32% higher than that in the present study. In elective surgeries, the infection site prevalence was 19.5%. Interestingly, 40% of patients with hypoalbuminemia had an infection at the surgical site, which was higher, compared to other comorbidities, such as diabetes and anemia (18).

In a study involving children who underwent emergency abdominal surgery, it was observed that the difference in albumin levels before and after surgery can serve as a stress factor. If this difference exceeds 0.5 g/dl, there is a significantly higher incidence rate of postoperative complications, such as SSI and AL (19). However, in another study, no significant relationship was found between albumin levels and the incidence of surgical site infection, despite a reported 20% occurrence rate of SSI in cases with hypoalbuminemia (20).

To address the issue of AL, it is noteworthy that the results of a multicenter study utilizing machine learning on a large sample size of 11,375 patients undergoing colocolic and colorectal anastomosis surgery demonstrated that hypoalbuminemia and malnutrition are important risk factors for AL (21). This highlights the importance of correcting malnutrition and hypoalbuminemia before surgery to reduce the occurrence of such complications. Additionally, a study performed by Paliogiannis et al. indicated a relationship between the C-reactive protein to albumin ratio (CAR) as a biomarker and the incidence of AL. The CAR ratio was found to be higher in patients with AL, compared to those without AL (22).

Based on the findings of the present study, appropriate antibiotic therapy is recommended to prevent surgical site infections in patients with

hypoalbuminemia. Specifically, a study performed by Patil et al. reported 21 cases of SSI in 100 patients undergoing emergency abdominal surgery. The most common organisms isolated were *Escherichia coli* (52.38%) and *Klebsiella pneumonia* (19.05%), with other cases involving Streptococcus pyogenes, Acinetobacter, Citrobacter freundii, Enterococcus, and Klebsiella oxytoca (23). Therefore, implementation of a targeted antibiotic therapy strategy to cover potential infections is crucial in these cases.

The present study contributes valuable insights to the association between preoperative hypoalbuminemia and the development of surgical site infections in emergency colorectal surgery patients. It underscores the significance of identifying and addressing malnutrition as a critical factor influencing surgical outcomes. Future studies should focus on the elucidation of the underlying mechanisms, validating our findings in larger prospective cohorts, and implementing multidisciplinary approaches to optimize preoperative care and reduce complications in this patient population.

Overall, emergency colorectal surgery is a critical procedure that requires prompt and effective management to minimize the risk of postoperative complications and improve patient outcomes. The prevalence of emergency colorectal surgery in Iran, as in other countries, underscores the importance of implementing effective strategies for the management of hypoalbuminemia and the reduction of consecutive complications.

6. Conclusion

This study showed that preoperative hypoalbuminemia was significantly associated with the development of postoperative complications in patients undergoing emergency colorectal surgery with older age and lower preoperative albumin levels. These may serve as valuable indicators for identifying patients at higher risk of complications.

Acknowledgments

The authors wish to thank Mr. Mohammad Hasanzadehkiabi for his cooperation in data collection.

Footnotes

Conflicts of Interest: The authors have no conflicts of interest to declare.
Funding: None.
Ethical Statements: The study and its objectives were explained to all patients who were included in the study. The consent form was obtained from all patients, and the study was approved by the local Ethics Committee with the reference number of Ir.sbmu.msp.rec.1395538.

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