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Preoperative Immunonutrition and Postoperative Infectious Complications Following Major Gastrointestinal Surgery

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ABSTRACT

Background: Infection is a common cause of morbidity following major gastrointestinal surgery. The potential benefits of immunonutrition in local surgical populations are unclear, although immunonutrition may boost immune competence and tissue recovery before surgery.

Objective: To assess the relationship between immunonutrition before surgery and postoperative infectious complications after major gastrointestinal surgery.

Methods: The study was a prospective comparative cohort study performed at the Department of Surgery, Khyber Medical University Institute of Medical Sciences, DHQ Teaching Hospital, KDA Kohat, from February 2025 to January 2026. Seventy adult patients scheduled for elective major gastrointestinal surgery were randomly assigned to either the immunonutrition group or the standard-care group, with each group including 35 individuals. The immunonutrition group received an oral formula of arginine, omega-3 fatty acids, and nucleotides for 7 days before surgery. The main outcome was the incidence of any infectious complication within 30 days. Independent associations were analyzed using multivariable logistic regression.

Results: Infectious complications occurred in 5 (14.3%) patients receiving immunonutrition and 14 (40.0%) controls (p=0.016). There was no difference between the two groups in terms of surgical-site infection rate (5.7% vs. 25.7%, p=0.045). Overall postoperative complications were also reduced (25.7% versus 51.4%; p=0.049), and mean hospital stay was shorter (8.3±2.9 versus 10.7±4.1 days; p=0.006). Preoperative immunonutrition was still an independent risk factor for reducing risk of infection (adjusted odds ratio 0.23, 95% confidence interval 0.06–0.84; p=0.026).

Conclusion: Preoperative immunonutrition was associated with fewer postoperative infections, reduced overall morbidity, and shorter hospitalization after major gastrointestinal surgery. These results suggest that nutritional optimization during the perioperative period is important in patients who undergo the right kind of surgery.

Keywords: Immunonutrition; gastrointestinal surgery; postoperative infection; surgical-site infection; nutritional support

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INTRODUCTION

Major gastrointestinal surgery is associated with substantial physiological stress, systemic inflammation, metabolic disturbance, and temporary impairment of immune function [1]. These responses can impair host defence, impair the integrity of the intestinal barrier, and may make the host more vulnerable to postoperative infections [2]. Although the technique of operation, antimicrobial prophylaxis, perioperative monitoring, and enhanced recovery protocol have been improved, infectious complications are still a significant source of morbidity following complex gastrointestinal operations [3,4].

Surgical-site infection, pneumonia, intra-abdominal abscess, urinary tract infection, bloodstream infection, and sepsis are frequent postoperative infectious complications [5]. They can cause delays in wound healing, longer hospitalizations, the need for intensive care or reoperation, and higher health care costs and mortality. This is especially true of patients with gastrointestinal malignancy, recent weight loss, decreased oral intake, hypoalbuminaemia, or nutritional deficits. Major gastrointestinal disorders can also affect nutrition via obstruction, malabsorption, chronic inflammation, and catabolism due to the presence of a tumour [6].

Traditional nutritional support is mainly focused on the intake of energy, protein, vitamins, and minerals. Immunonutrition takes this one step further, using certain nutrients that can modulate inflammatory and immune processes [7]. Arginine, omega-3 fatty acids, and nucleotides are common components of immunonutritional formulations. Arginine helps lymphocyte's function, the synthesis of collagen, the production of nitric oxide, and to heal wounds. Omega-3 fatty acids may help to suppress the overproduction of pro-inflammatory mediators, and nucleotides help to stimulate the proliferation and function of immune cells and the intestinal epithelial tissue [8].

Pre-operative immunonutrition might be especially valuable as this enables feeding and immunological preparation before the onset of operative stress [9]. Several clinical trials have indicated that supplemental immune-enrichment before surgery may help lower the incidence of postoperative infections and length of hospital stay. But the benefit has not been uniform for all patients and procedures. Treatment effectiveness may differ based on nutrition status, surgical complexity, underlying disease, formula type, amount of time on supplement, and compliance [10].

Data on the regular application of immunonutrition as a pre-surgical nutritional support is still scarce in many resource-limited settings in which surgery is a regular occurrence and malnutrition and postoperative infection are common. Therefore, incorporating immunonutrition into the standard pathway of perioperative management requires local evaluation. The present study aimed to assess the relationship between immunonutrition preoperatively and postoperative infectious complications in patients undergoing major gastrointestinal surgery. Secondary outcomes were individual infectious complications, overall postoperative morbidity, intensive care admission, and length of hospital stay [11].

MATERIALS AND METHODS

The study was a prospective comparative cohort study conducted in the Department of Surgery at Khyber Medical University Institute of Medical Sciences, DHQ Teaching Hospital, KDA Kohat, from February 2025 to January 2026. The Institutional Research and Ethics Committee of Khyber Medical University Institute of Medical Sciences accepted the research before its initiation (Ref. No. KMU-IMS/IREC/2025/017). Informed permission in writing was acquired from all subjects. The confidentiality and anonymity of patients were maintained throughout this investigation, and all methods adhered to the ethical standards established in the Declaration of Helsinki.

The study was conducted on 70 adult patients who were admitted for elective major gastrointestinal surgery using non-probability consecutive sampling method. Preoperative nutritional management was used to split the patients into two groups of 35 patients each. The immunonutrition group was given an oral immune-enriched nutritional formula before surgery, while the control group received standard pre-operative dietary care. Major gastrointestinal surgery was considered surgery that was elective or involved resection and reconstruction, or anastomosis of oesophagus, stomach, small intestine, colon, rectum, pancreas, or hepatobiliary tract.

Eligible patients were 18-75 years of age, of either sex, who were undergoing elective major gastrointestinal surgery and were able to accept oral nutritional intake. Excluded were patients who had an emergency surgical procedure, minor gastrointestinal surgery, surgery with no gastrointestinal resection, and surgery without an intra-abdominal infection. Those patients who had severe hepatic or renal failure, active systemic infection, pregnancy, immunosuppressive therapy, known allergy to the nutritional formula, or who were otherwise unable to complete the supplementation period were also excluded.

The immunonutrition group had an oral formula supplement containing arginine, omega-3 fatty acids, and nucleotides for seven days before surgery. The supplement was given in portions, each day, along with the patients' normal diet. All intake was recorded daily; those taking at least 80% of the prescribed supplementation were deemed adherent. Patients in the control group were instructed on the normal diet and had the normal pre-operative nutritional counselling. Each patient was treated following the departmental routine per-operative care, which included glycaemic monitoring, antimicrobial prophylaxis, maintenance of normothermia, post-operative feeding as per departmental protocol, pain management, and early mobilization.

The baseline data encompassed age, sex, body mass index, smoking status, diabetes mellitus, hypertension, primary gastrointestinal diagnosis, recent weight loss, hemoglobin concentration, serum albumin level, American Society of Anesthesiologists physical status classification, and nutritional risk status. Operative data consisted of the type of operation, operative approach, length of surgery, blood loss, blood transfusion during surgery, gastrointestinal anastomosis performed, and intensive care after surgery.

The main outcome studied was the occurrence of any postoperative infectious complication within 30 days of surgery. Infectious complications were defined as superficial, deep, or organ-space surgical-site infection, pneumonia, urinary tract infection, intra-abdominal abscess or infected collection, bloodstream infection, and sepsis. Diagnosis was made by clinical examination alone or combined with laboratory, microbiological, or radiological results as necessary. Surgery-related complications, anastomotic leakage, overall postoperative morbidity, unplanned intensive care unit admission, reoperation, 30-day readmission, postoperative hospital length of stay, and 30-day mortality were secondary outcomes.

Patients were evaluated daily after admission and on the 30th postoperative day via outpatient visits or by phone. The study investigators recorded the data on a specially designed data-collection form. Post-surgery complications were checked and verified by the surgical team.

The data was analyzed using IBM SPSS Statistics Version 26.0. Continuous data were expressed as mean and standard deviation, whereas categorical variables were presented as frequencies and percentages. An independent-samples t-test was used for continuous data, while the chi-square test or Fisher's exact test was applied for categorical variables. A multivariable binary logistic regression was conducted to ascertain the independent relationship between preoperative immunonutrition and postoperative infectious problems, after controlling for any confounding demographic, nutritional, and surgical factors. Adjusted odds ratios (AOR) accompanied with 95% confidence intervals (CI) were presented. P-values deemed statistically significant were established at < 0.05.

RESULTS

A total of 78 patients scheduled for major gastrointestinal surgery were evaluated for eligibility. Eight patients were excluded: three needed emergency surgery, two had an active systemic illness, two could not handle oral supplements, and one declined to participate. Ultimately, 70 participants (35 patients in each group) were recruited for the study. All individuals adhered to the 30-day postoperative protocol.

The study population included 41 male and 29 female patients. In the immunonutrition group, 21 patients (60.0%) were male, and 14 patients (40.0%) were female, whereas the control group included 20 male patients (57.1%) and 15 female patients (42.9%). The mean age was 56.8±11.4 years in the immunonutrition group and 58.1±12.0 years in the control group. No notable differences were observed between the groups regarding age, sex distribution, body mass index, diabetes mellitus, smoking history, nutritional risk, serum albumin, hemoglobin, malignant gastrointestinal disease, American Society of Anesthesiologists physical status classification, surgical approach, duration of surgery, estimated blood loss, or perioperative blood transfusion. Table 1 delineates the baseline and operative features.

The most common procedure performed was colorectal resection, which was performed in 15 patients (42.9%) and 14 patients (40.0%) in the immunonutrition and control groups, respectively. Gastric surgery was performed in 8 (22.9%) and 9 (25.7%) patients, respectively. Seven patients (20.0%) in each group underwent hepatopancreatobiliary surgery. In both groups, 5 (14.3%) of the patients had major oesophageal or small-bowel surgery.

5 (14.3%) patients in the preoperative immunonutrition group and 14 (40.0%) in the standard nutritional care group had postoperative infectious complications. This was statistically significant (p=0.016). There was an absolute risk reduction of 25.7 percentage points, and the unadjusted odds ratio for infectious complications in the postoperative period was 0.25 (95% CI: 0.08-0.80) for those who received immunonutrition.

Surgical-site infection was observed in 2 (5.7%) patients in the immunonutrition group and 9 (25.7%) patients in the control group, representing a statistically significant difference (p=0.045). One (2.9%) immunonutrition patient and 5 (14.3%) controls developed pneumonia. Two (5.7%) and 6 (17.1%) patients had developed intra-abdominal infection, respectively. The immunonutrition group had a lower frequency of urinary tract infection and bloodstream infection or sepsis, but these differences were not statistically significant. Table 2 shows the postoperative infectious and clinical outcomes.

A postoperative complication was seen in 9 (25.7%) immunonutrition patients and 18 (51.4%) normal nutrition patients, and was significantly different between the two groups (p=0.049). Anastomotic leakage occurred in 2 (5.7%) patients in the immunonutrition group and 5 (14.3%) patients in the control group. Three (8.6%) and 8 (22.9%) patients, respectively, experienced complications of Clavien–Dindo grade III or greater.

Four (11.4%) patients in the immunonutrition group and 10 (28.6%) controls had to be admitted to the intensive care unit, but this was not statistically significant. One (2.9%) patient in the immunonutrition group and four (11.4%) patients in the control group required a reoperation. Two (5.7%) of the control patients died, but none of the immunonutrition patients died within 30 days.

Patients receiving immunonutrition had significantly reduced mean postoperative hospital stay when compared to the control group. Table 2 shows the mean duration of hospitalization, which was 8.3±2.9 days in the immunonutrition group and 10.7±4.1 days in the control group (p=0.006).

A parsimonious multivariable binary logistic-regression model was developed because of the limited number of postoperative infectious events, n = 19. Preoperative immunonutrition, Nutritional Risk Screening 2002 score, and operative approach were included in the model. When adjusted for age, BMI, sex, diabetes, hypertension, smoking, BMI at diagnosis, and surgery type, preoperative immunonutrition was still independently associated with decreased odds of postoperative infectious complications (adjusted odds ratio 0.23, 95% confidence interval 0.06–0.84, p=0.026).

A Nutritional Risk Screening 2002 score of three or higher was independently associated with increased odds of postoperative infectious complications, with an adjusted odds ratio of 4.32 (95% confidence interval 1.33–14.07; p=0.015). Higher odds of infection were seen with open surgery, but it wasn't statistically significant. Table 3 shows the multivariable analysis.

The Hosmer–Lemeshow goodness-of-fit test was satisfactory (p=0.721) for the regression model. These results indicated that when nutritional risks and operative approaches were controlled for, immunonutrition before surgery was an independent predictor of reduced postoperative infection rates.

Table 1: Baseline and operative characteristics of the study participants

Characteristic	Immunonutrition group, n=35	Control group, n=35	p-value
Age, years	56.8±11.4	58.1±12.0	0.644
Male sex	21 (60.0)	20 (57.1)	0.808
Female sex	14 (40.0)	15 (42.9)	0.808
Body mass index, kg/m²	23.6±3.7	23.1±3.9	0.584
Diabetes mellitus	8 (22.9)	10 (28.6)	0.584
Current or former smoker	9 (25.7)	10 (28.6)	0.788
Nutritional Risk Screening 2002 score ≥3	11 (31.4)	13 (37.1)	0.615
Serum albumin, g/dL	3.51±0.48	3.39±0.52	0.319
Haemoglobin, g/dL	11.8±1.6	11.5±1.7	0.450
Malignant gastrointestinal disease	27 (77.1)	28 (80.0)	0.771
American Society of Anesthesiologists class III–IV	14 (40.0)	16 (45.7)	0.629
Open surgical approach	15 (42.9)	18 (51.4)	0.473
Operative duration, minutes	187±52	196±58	0.497
Estimated blood loss, mL	330±180	365±195	0.438
Perioperative blood transfusion	5 (14.3)	7 (20.0)	0.526

Table 2: Postoperative outcomes according to preoperative nutritional management

Outcome	Immunonutrition group, n=35	Control group, n=35	p-value
Any infectious complication	5 (14.3)	14 (40.0)	0.016
Surgical-site infection	2 (5.7)	9 (25.7)	0.045
Pneumonia	1 (2.9)	5 (14.3)	0.198
Intra-abdominal infection	2 (5.7)	6 (17.1)	0.259
Urinary tract infection	1 (2.9)	3 (8.6)	0.614
Bloodstream infection or sepsis	0 (0.0)	2 (5.7)	0.493
Any postoperative complication	9 (25.7)	18 (51.4)	0.049
Anastomotic leakage	2 (5.7)	5 (14.3)	0.428
Clavien–Dindo grade III or higher complication	3 (8.6)	8 (22.9)	0.188
Unplanned intensive care unit admission	4 (11.4)	10 (28.6)	0.133
Reoperation	1 (2.9)	4 (11.4)	0.356
Thirty-day readmission	2 (5.7)	6 (17.1)	0.259
Thirty-day mortality	0 (0.0)	2 (5.7)	0.493
Postoperative hospital stay, days	8.3±2.9	10.7±4.1	0.006

Table 3: Multivariable logistic-regression analysis of factors associated with postoperative infectious complications

Variable	Adjusted odds ratio	95% confidence interval	p-value
Preoperative immunonutrition	0.23	0.06–0.84	0.026
Nutritional Risk Screening 2002 score ≥3	4.32	1.33–14.07	0.015
Open surgical approach	1.37	0.42–4.43	0.599

DISCUSSION

The present study found that preoperative immunonutrition was associated with a lower frequency of postoperative infectious complications among patients undergoing major gastrointestinal surgery [1]. Infectious complications occurred in 14.3% of patients receiving immunonutrition compared with 40.0% of those receiving standard preoperative nutritional care. The association was statistically significant even after adjustment for nutritional risk at baseline and surgical approach, indicating that this decrease was not completely attributable to differences in these variables [2,3].

Major gastrointestinal surgery is associated with a strong inflammatory and catabolic response, which can temporarily impair immune defence, barrier function of the gut, and wound healing [4]. These physiologic changes are especially significant in patients with gastrointestinal malignancy, decreased ingestion, weight loss, and a nutritional deficit. In the pre-surgical period, immune-enriched nutritional formulas could play a role in enhancing the patient's metabolic and immunological status before exposure to surgical stresses [5].

This reduction in infectious complications in the immunonutrition group might be due to the synergic activity of the components of the formula: arginine, omega-3 fatty acids, and nucleotides [6]. Arginine is used for the activity of lymphocytes, the formation of collagen, the production of nitric oxide, and tissue repair [7]. Omega-3 fatty acids have been shown to modify overreacting inflammatory responses and to modify the production of inflammatory mediators. Nucleotides help promote the growth and activity of cells of the immune system and of fast-growing epithelial cells in the gut. These nutrients, together, could promote wound healing, the integrity of the gastrointestinal barrier, and resistance to postoperative infections [8].

The incidence of surgical-site infection was significantly lower in the group that received Immunonutrition [9]. Surgical-site infection developed in only 5.7% of the patients in the immunonutrition group as opposed to 25.7% in the control group. There are several factors that contribute to surgical-site infections, such as nutrition, tissue perfusion, immune function, operative contamination, glycaemic control, length of operation, and wound care practices. The decrease in the current study indicates that, besides the classic infection prevention strategies like antimicrobial prophylaxis, aseptic surgical technique, normothermia, and control of glucose in the perioperative period, nutritional optimization before surgery may be a complementary tool [10,11].

Numerically, fewer patients receiving immunonutrition developed pneumonia, intra-abdominal infection, urinary tract infection, bloodstream infection, and sepsis. Differences in these individual complications, however, were not statistically significant [12]. This could be due to the relatively small number of people in the study and the small number of events for each infection. The study was better equipped to reveal a difference in the overall infectious outcome, rather than specific postoperative infections [13].

The overall postoperative complication rate was also lower in the patients who received immunonutrition. 25.7% of the immunonutrition group had any postoperative complication, while 51.4% of the control group did [14]. Immunonutrition mainly aims to act on metabolic, inflammatory, and immune pathways, but nutritional prehabilitation in preparation for surgery may also benefit overall physiological reserve and ensure better postoperative recovery. However, there were no significant differences in anastomotic leakage, re-operation, intensive care unit admission, or mortality between the groups. These severe outcomes were not very common, and the study was not designed to show statistically significant differences in such outcomes [15].

The mean postoperative hospital stay was statistically significantly shorter in the group of patients in which immunonutrition was used. The patients in the immunonutrition group stayed an average of 8.3 days in the hospital, while those in the control group stayed for an average of 10.7 days. This may relate to the reduced incidence of infectious and other postoperative complications that were observed, and the shorter hospital stay. Additional antibiotic therapy, wound care, radiological studies, drainage, intensive monitoring, and/or reoperation are often necessary in postoperative infections, which can prolong both recovery and discharge [16,17].

Nutritional risk was an independent risk factor for postoperative infectious complications. The adjusted odds ratio of infection for patients with a Nutritional Risk Screening 2002 (NRS 2002) score of three or greater was >4 [18]. This discovery highlights the need for standard pre-op nutritional-risk assessment before large bowel surgery. Malnutrition can affect the cellular immunity, decrease protein synthesis, decrease the strength of the respiratory muscles, slow down the formation of collagen, and decrease the tolerance for the stresses of surgery. So, it is important that nutritional screening is included in standard assessment before surgery – even if a patient does not look underweight [19].

In the adjusted analysis, open surgery was related to an increased risk for postoperative infection, but this was not statistically significant [20]. Opens tend to be larger than minimally invasive surgery and involve more exposure of tissue, more pain following surgery and possibly slower mobility. Nevertheless, decisions about the operative approach may also be dependent on the severity of the disease and the complexity of the surgery. This small sample size may have hampered the ability to establish an independent association between open surgery and infection [21].

There are several limitations to the study. First, it was performed in a single institution with a relatively small number of patients (70), which makes generalizing the findings difficult [22]. Second, there was no randomisation of allocation to immunonutrition and standard nutritional care. The choice to prescribe immunonutrition was made as part of standard patient care, and there may have been unmeasured differences between the groups that influenced the results. Third, the study contained various categories of major gastrointestinal surgery with different baseline risks for postoperative infection. Fourth, immune and inflammatory biomarkers were not assessed, which would have allowed for an assessment of the biological response to supplementation. Fifthly, the regression model used was limited by the small number of infectious events. Lastly, only 30 days of outcomes were assessed, and the study didn't look at treatment-related costs, quality of life, long-term recovery, or survival [23].

The study had several strengths in spite of these limitations. Data was collected using a prospective design, males and females were included, postoperative infections were determined by clinical criteria, and all patients were followed up for 30 days. Several clinically relevant outcomes were also examined, and a parsimonious multivariable model was used, based on the small number of infectious events [24,25].

The results indicate that immunonutrition before surgery can be a part of a larger strategy of nutrition and enhanced recovery. But immunonutrition should not take the place of proven infection prevention strategies.g Three larger multicentre RCTs are needed to support the causal relationship of immunonutrition, elucidate the population most likely to benefit, the most effective formulation and duration of use, and cost-effectiveness in local health care systems [20-25].

CONCLUSION

There was a significant association between preoperative immunonutrition and reduced postoperative infectious complications in patients who underwent major gastrointestinal surgery. Patients who received immune-enriched nutritional supplementation had reduced surgical-site infections, reduced overall complications, and reduced post-op hospital stay. Nutritional risk was an independent risk factor for postoperative infection. These results indicate that immunonutrition before surgery could be a useful part of a multimodal approach for the care of patients undergoing surgery. However, the study was observational with a small sample from a single centre, and further large randomized studies are required to determine causality and inform routine clinical use.

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Authors' Contributions: M.A.A. conceived and designed the study and supervised its conduct. H. contributed to patient assessment, perioperative data collection, and data compilation. S.I.A. contributed to patient recruitment, surgical evaluation, interpretation of findings, and manuscript revision. All authors reviewed and approved the final manuscript.

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Data Availability: The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

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