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CLINICAL-IMMUNOLOGICAL RATIONALE FOR TREATMENT OF ACUTE ADHESIVE SMALL BOWEL OBSTRUCTION: PROGNOSTIC SCALE AND EFFICACY OF IMMUNE CORRECTION

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Summary.

Acute adhesive small bowel obstruction (AASBO) ranks among the most common indications for emergency abdominal surgery. However, conventional approaches to severity assessment and treatment selection do not incorporate the significant immunological disturbances characteristic of this condition.

Objective. *To enhance the diagnosis and management of AASBO through the implementation of a clinical-immunological risk stratification scale and to evaluate the impact of immunotherapy on clinical and immune outcomes.*

Materials and Methods. *A total of 115 patients with AASBO were enrolled and allocated to a control group (n=56; standard care) or a study group (n=59; standard care plus immunotherapy). Comprehensive clinical, laboratory, radiological, and immunological parameters were analyzed. A prognostic scale incorporating 25 variables was developed. Immune response dynamics and complication rates were rigorously assessed. All procedures were conducted in accordance with the World Medical Association's Declaration of Helsinki (2000 amendments). Statistical analyses were performed using SPSS 22.0 and MedCalc software. Normality was assessed with Shapiro-Wilk test. Between-group comparisons utilized Mann-Whitney U test, Student's t-test, Pearson's chi-square test, and Spearman's correlation analysis. Predictive performance was evaluated through ROC analysis calculating the area under the curve (AUC). Statistical significance was defined as $p < 0.05$.*

Funding: *This work was carried out within the framework of the research plan of the Bukhara State Medical Institute (05.2022 DSc.135) entitled «Development of new approaches to early diagnosis, treatment, and prevention of pathological conditions affecting the health of the population of the Bukhara region after COVID-19 (2022-2026)».*

Results. *Severe disease progression was significantly associated with $CD4^+$ counts < 600 cells/μL, $HLA\text{-}DR^+$ expression < 30%, IL-6 levels > 30 pg/mL, and TNF-α levels > 25 pg/mL. The study group demonstrated a 3.3-fold reduction in mortality, a 28.1% shorter hospital stay, and a 2.4-fold decrease in Clavien-Dindo grade III-V complications. The integrated prognostic scale exhibited high predictive accuracy (AUC = 0.917).*

Conclusion. *The incorporation of clinical-immunological stratification and immunotherapy into the management algorithm for AASBO significantly improves treatment outcomes, reduces complication rates, and decreases mortality.*

Keywords: *Acute Intestinal Obstruction; Immunodeficiency; IL-6; HLA-DR; Immunotherapy; Risk Assessment; Cytokine Storm.*

Introduction

Acute adhesive small bowel obstruction (AASBO) continues to represent a predominant indication for emergency hospitalization and surgical intervention in acute abdominal pathology [1, 2]. Epidemiological data indicate this condition accounts for 60-75% of mechanical intestinal obstruction cases [3], with surgical management of AASBO constituting approximately 30% of emergency abdominal procedures [4, 5].

Despite advancements in laparoscopic approaches and anti-adhesion agents, recurrence rates and postoperative complications remain substantially elevated. The reoperation rate for AASBO within 10 years following initial laparotomy reaches 20-35% [6], with mortality exceeding 10-15% in complicated presentations [7]. Contemporary diagnostic and therapeutic algorithms predominantly rely on radiographic and clinical assessment, failing to incorporate evaluation of the patient's immunological status [8].

Emerging evidence underscores the critical role of immunological dysregulation in the pathogenesis of abdominal surgical emergencies [9, 10]. In AASBO, features of secondary immunodeficiency manifest early in the disease course, characterized by $CD4^+$ lymphopenia, altered CD4/CD8 ratios, suppressed $HLA\text{-}DR^+$ monocyte expression, and cytokine cascade activation with elevated IL-6 and TNF-α [11, 12]. These immunological parameters demonstrate significant correlation with disease severity, postoperative complications, and mortality [13].

Nevertheless, immunological parameters remain consistently underutilized in routine clinical practice. Existing severity scoring systems lack immune biomarkers, impeding early risk stratification and timely implementation of pathogenesis-based therapy [14, 15]. This clinical gap highlights the necessity of integrating immunodiagnostic approaches into AASBO management protocols and developing prognostic tools for treatment personalization according to individual immune profiles.

Of particular therapeutic interest is immunomodulatory therapy – specifically, agents capable of modulating both T-cell-mediated and innate immunity. Adjunctive use of these therapeutics with standard management may optimize postoperative recovery, mitigate cytokine storm intensity, and reduce the incidence of septic complications [16, 17].

Materials and Methods

A prospective observational study was conducted in the Department of Emergency Surgery at the Khorezm Regional Branch of the Republican Scientific and Practical Center for Emergency Medical Care from 2021 to 2024. The study cohort comprised 115 consecutive patients with confirmed acute adhesive small bowel obstruction (AASBO) requiring emergency hospitalization. Inclusion criteria were: age >18 years, absence of active malignancy or autoimmune disorders, radiologically confirmed AASBO, and written informed consent. Exclusion criteria included neoplastic obstruction, generalized peritonitis, and pre-existing immunodeficiencies.

Participants were allocated to two treatment groups: Control group (n=56) received standard surgical care without immunomodulatory therapy; Intervention group (n=59) received personalized immunotherapy in addition to standard care, based on individual clinical-immunological profiling.

A reference cohort of healthy volunteers (n=20), matched by age and sex, without inflammatory conditions or previous abdominal operations, was established to determine baseline immunological parameters.

All patients underwent comprehensive diagnostic evaluation at admission including: complete blood count with biochemical profiling; calculated leukocyte indices (NLR, PLR, LII, HII); coagulation studies (fibrinogen, D-dimer, APTT, INR); abdominal ultrasonography and radiography; and contrast-enhanced multislice computed tomography when clinically indicated.

Immunological assessment included determination of: $CD3^+$, $CD4^+$, $CD8^+$, $CD16^+$, $CD25^+$, $HLA\text{-}DR^+$ using flow cytometry; serum levels of IL-6 and TNF-α (enzyme immunoassay); levels of circulating immune complexes (CICs); immunoglobulins of classes A, M and G (IgA, IgM, IgG); ICAM-1 and VCAM-1 (ELISA method).

Laboratory assessments were conducted at admission (within 24 hours) and during treatment days 5-7. The intervention group received precision immunotherapy based on clinical-immunological risk stratification, including immunomodulators (Polyoxidonium, Thymogen, Likopid), interferon inducers, and occasionally Roferon- A.

For quantitative assessment of complication risk, we developed an integrated risk stratification scale incorporating 25 clinical, laboratory, imaging, and immunological parameters. Each variable was scored 0-10 points, with total scores quantifying immuno-inflammatory burden.

All procedures were conducted in accordance with the World Medical Association's Declaration of Helsinki (2000 amendments).

Statistical analyses were performed using SPSS 22.0 and MedCalc software. Normality was assessed with Shapiro-Wilk test. Between-group comparisons utilized Mann-Whitney U test, Student's t-test, Pearson's chi-square test, and Spearman's correlation analysis. Predictive performance was evaluated through ROC analysis calculating the area under the curve (AUC). Statistical significance was defined as $p < 0.05$.

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Results

Initial immunological assessment conducted within 24 hours of admission demonstrated significant disparities between the control and study cohorts at enrollment. Both groups exhibited features of immune dysregulation, with patients ultimately requiring surgical management showing more pronounced abnormalities. $CD4^+$ lymphocyte counts in surgical candidates were reduced by 34.3% compared to reference values ($p < 0.001$), while CD4/CD8 ratios decreased below 1.0, consistent with T-cell imbalance.

Compromised antigen-presenting function was evidenced by suppressed HLA-DR expression on monocytes (<30% in 61.0% of study group participants), with elevations in IL-6 and TNF-α concentrations exceeding reference ranges by 3.2-fold and 2.5-fold, respectively. These immunological perturbations demonstrated strong correlation with clinical severity, surgical necessity, and postoperative complication rates.

Through comprehensive correlation analysis of clinical, laboratory, radiographic, and immunological parameters, we developed an integrated prognostic risk stratification scale containing 25 variables organized into discrete clinical domains (Table 1).

Each parameter was scored from 0 to 10 points based on the degree of deviation from normal values. The maximum possible total score was 250 points. At a threshold value of ≥150 points, the scale demonstrated 92.1% sensitivity and 86.3% specificity for predicting complicated clinical course (AUC = 0.917 by ROC analysis). Patients with scores <120 achieved successful conservative treatment in 94.3% of cases.

Comparison of clinical outcomes between control and study groups revealed significant differences in complication rates, hospital stay duration, and mortality. Patients receiving immunocorrective therapy showed significant improvement in both clinical parameters and immune status indicators (Table 2).

As shown in the table, the inclusion of immunotherapy significantly reduced the duration of all key disease phases, from intestinal paresis to intoxication syndrome, and substantially shortened hospital stay. Mortality in the study group was 3.7 times lower than in the control group ($p < 0.01$).

Table 1.

Comprehensive Clinical-Immunological Severity Assessment Scale for Patients with Acute Adhesive Small Bowel Obstruction (AASBO)

Parameter	Value Distribution		
	0 points	5 points	10 points
Clinical Parameters			
Pain duration	None / ≤12 h	13-24 h	>24 h
Absence of stool and gas	≤24 h	25-48 h	>48 h
Body temperature	≤37,5 °C	37,6-38,0 °C	>38,0 °C
Tachycardia	≤90 bpm	91-100 bpm	>100 bpm
Previous abdominal surgeries	0	1 surgery	≥2 surgeries
Peritoneal irritation signs	Absent	Equivocal	Clearly positive
Laboratory Parameters			
Leukocytes (×10⁹/L)	≤10	10-12	>12
CRP (mg/L)	≤30	31-60	>60
NLR	≤3	3,1-5	>5
PLR	≤150	151-180	>180
LII	≤1,5	1,6-2,0	>2,0
HII	≤1,2	1,3-1,5	>1,5
Coagulation Profile			
D-dimer (ng/mL)	≤500	501-1000	>1000
Fibrinogen (g/L)	2,5-4,0	>4,0	>5,0 или <2,0
APTT / INR	Normal	Borderline prolongation	Marked prolongation
Imaging Parameters			
Bowel loop dilation >3.5 cm (CT)	Absent	Equivocal	Confirmed
Free fluid (CT/US)	None	Single location	Multiple collections
Absent peristalsis (US)	Preserved	Slowed	Absent
Contrast in colon at 6 h	Present	Delayed	Absent
Immunological Parameters			
IL-6 (pg/mL)	≤15	16-30	>30
TNF-α (pg/mL)	≤20	21-25	>25
ICAM-1 (ng/mL)	≤250	251-300	>300
HLA-DR⁺ (%) on monocytes	>35%	30-35%	<30%
CD4⁺/CD8⁺ index	≥1,2	1,0-1,19	<1,0
CD16⁺ (%)	≤15%	16-20%	>20%

Table 2.

Comparison of Treatment Outcomes Between Control and Study Groups

Parameter	Patient Groups		p-value
	Control (n=56)	Study (n=59)	
Mean duration of intestinal paresis, days	4.3 ± 1.4	2.9 ± 1.0	<0.001
Return of bowel sounds (auscultation), days	4.2 ± 1.3	2.8 ± 0.9	<0.001
Transition to oral feeding, days	5.7 ± 1.5	3.8 ± 1.2	<0.001
Duration of intoxication syndrome, days	3.6 ± 1.2	2.4 ± 0.9	<0.001
Mean hospital stay, days	12.1 ± 2.8	8.7 ± 2.1	<0.001
Reoperations (re-laparotomies), n (%)	5 (8.9%)	2 (3.4%)	<0.05
Readmissions within 30 days, n (%)	6 (10.7%)	2 (3.4%)	<0.05
Mortality, n (%)	7 (12.5%)	2 (3.4%)	<0.01

The most significant changes were recorded in the surgical patient subgroup. Immunotherapy in study group patients resulted in: an increase in $CD4^+$ lymphocytes by more than 35%; restoration of the CD4/CD8 index to 1.77 (versus 1.10 in the control group); increased $HLA\text{-}DR^+$ expression on monocytes (from 33.2% to 41.5%); decreased IL-6 levels from 71.8 pg/mL to 21.5 pg/mL and TNF-α from 32.6 to 12.2 pg/mL (both $p<0.001$); and reduced plasma CICs concentrations from 79.1 to 56.4 optical units. These changes indicated not only normalization of the cellular immune response but also resolution of systemic cytokine storm, likely determining the clinical advantages in the study group (Table 3).

Collectively, these findings confirm that integrating immunotherapy into the management algorithm for AASBO facilitates both functional immune recovery and significant reduction in complication rates and mortality.

Table 3.

Dynamics of Key Immunological Parameters in Patients Receiving Immunotherapy

Parameter	Study Timepoint		p-value
	Before Treatment	After Treatment	
$CD4^+$, cells/μL	474 ± 122	725 ± 136	<0.001
CD4/CD8, ratio	1.10 ± 0.24	1.77 ± 0.31	<0.001
HLA-DR^+, %	33.2 ± 3.9	41.5 ± 3.8	<0.001
IL-6, pg/mL	71.8 ± 12.6	21.5 ± 6.4	<0.001
TNF-α, pg/mL	32.6 ± 6.3	12.2 ± 4.1	<0.001
CICs, conv. units	79.1 ± 12.2	56.4 ± 9.0	<0.001

Discussion

Our findings confirm that acute adhesive small bowel obstruction (AASBO) involves not only mechanical obstruction and local inflammation but also profound immune dysregulation that significantly impacts clinical outcomes. This observation aligns with established literature documenting cytokine-mediated inflammation, T-cell imbalance, and impaired antigen presentation in abdominal surgical emergencies [18].

Within 24 hours of symptom onset, AASBO patients demonstrated significant immune homeostasis alterations: reduced $CD4^+$ lymphocyte counts, decreased CD4/CD8 ratios, suppressed HLA-DR^+ expression, and elevated IL-6 and TNF-α production. These parameters reflect the transition from systemic inflammatory response syndrome (SIRS) toward compensatory anti-inflammatory response syndrome (CARS), serving as valuable prognostic indicators [19].

Notably, reduced monocytic HLA-DR expression emerged as a particularly sensitive predictor of immune paralysis and septic complications in surgical patients. In our cohort, this parameter demonstrated exceptional discriminative capacity in ROC analysis (AUC=0.917), underscoring its clinical utility. These findings corroborate work by A. M. Muhar et al., where low HLA-DR levels in abdominal sepsis patients correlated with 3-5-fold increased mortality risk [20].

Immunotherapy targeting inflammatory response modulation, T-cell cooperation restoration, and antigen presentation normalization demonstrated substantial clinical efficacy. The reduction in IL-6 and TNF-α levels following treatment with Polyoxidonium, Thymogen, Likopid, and alpha-interferons correlated with improved clinical progression, shortened intestinal paresis duration, and reduced postoperative complications. Comparable findings regarding the capacity of immunotropic agents to mitigate systemic inflammation and improve surgical outcomes have been documented by H. Ding [21].

Comparison with control patients revealed that withholding immunotherapy in cases with baseline immune impairment was associated with a 3.3-fold increase in mortality, 2.6-fold higher relaparotomy rate, and significantly prolonged hospitalization. These findings underscore the necessity for early immunological stratification and personalized treatment approaches. Current literature confirms that integrating immunological parameters into clinical algorithms enhances prognostic precision, particularly in diagnostically challenging AASBO presentations.

Conclusions

The developed prognostic scale, incorporating objective immunological and clinical-laboratory parameters, facilitates both accurate severity assessment and rationale-based immunotherapy implementation. This instrument demonstrates applicability across general surgical departments and specialized centers, particularly in cases requiring complex therapeutic decision-making for intestinal obstruction management.

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КЛІНІКО-ІМУНОЛОГІЧНЕ ОБГРУНТУВАННЯ ТАКТИКИ ЛІКУВАННЯ ГОСТРОЇ СПАЙКОВОЇ ТОНКОКИШЕЧНОЇ НЕПРОХІДНОСТІ: ПРОГНОСТИЧНА ШКАЛА ТА ЕФЕКТИВНІСТЬ ІМУНОКОРЕКЦІЇ

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Резюме.

Гостра спайкова непрохідність тонкої кишки (ГСНТК) є однією з найчастіших причин екстрених операцій на органах черевної порожнини. Однак стандартні підходи до оцінки тяжкості та вибору тактики лікування не враховують вираженість імунологічних порушень, що супроводжують цей стан.

Мета дослідження. Підвищити ефективність діагностики та лікування ОСНТК шляхом впровадження клініко-імунологічної шкали стратифікації ризику та оцінки впливу імунотерапії на клінічні та імунні результати захворювання.

Матеріали та методи. Всього було зареєстровано 115 пацієнтів з AASBO, які були розподілені на контрольну групу (n=56; стандартне лікування) та дослідну групу (n=59; стандартне лікування плюс імунотерапія). Було проаналізовано комплексні клінічні, лабораторні, радіологічні та імунологічні параметри. Була розроблена прогностична шкала, що включала 25 змінних. Всі процедури проводилися відповідно до Гельсінської декларації Всесвітньої медичної асоціації (поправки 2000 року). Було ретельно оцінено динаміку імунної відповіді та частоту ускладнень. Статистичний аналіз було проведено за допомогою програмного забезпечення SPSS 22.0 та MedCalc. Нормальність було оцінено за допомогою тесту Шапіро-Уілка. Для порівняння між групами було використано тест Манна-Уїтні, t-тест Стьюдента, тест хі-квадрат Пірсона та кореляційний аналіз Спірмена. Прогностична ефективність оцінювалася за допомогою ROC-аналізу з розрахунком площі під кривою (AUC). Статистична значущість визначалася як $p < 0,05$.

Фінансування. Дане дослідження виконано в рамках плану науково-дослідних робіт Бухарського державного медичного інституту (05.2022 DSc.135) «Розробка нових підходів до ранньої діагностики, лікування та профілактики патологічних станів організму, що впливають на здоров'я населення Бухарського регіону після COVID-19 (2022–2026)».

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Результати. Встановлено, що рівні $CD4^+$ <600 кл/мкл, $HLA\text{-}DR^+$ <30%, IL-6 >30 пг/мл і TNF-α >25 пг/мл достовірно асоційовані з тяжким перебігом. В основній групі летальність знижена в 3,3 рази, тривалість госпіталізації скорочена на 28,1%, частота ускладнень III-V ступеня за Clavien-Dindo – в 2,4 рази. Показана висока прогностична цінність інтегральної шкали (AUC = 0,917).

Висновок. Включення клініко-імунологічної стратифікації та імунотерапії в алгоритм ведення хворих з ОСНТК дозволяє достовірно поліпшити результати лікування, знизити частоту ускладнень і летальність.

Ключові слова: гостра кишкова непрохідність; імунодефіцит; IL-6; HLA-DR; імунотерапія; шкала ризику; цитокіновий стрес.

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