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ORIGINAL ARTICLE

Effects of Synbiotic Supplementation on Biochemical, Coagulation, and Hematological Parameters in Intensive Care Unit Patients with Multiple Trauma and Traumatic Brain Injury

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ABSTRACT

Background: Synbiotic supplementation may support gastrointestinal and systemic homeostasis among intensive care unit (ICU) patients. This study evaluated the effects of short-term synbiotic supplementation on biochemical, renal, hepatic, coagulation, electrolyte, and hematological parameters in ICU-admitted patients with traumatic brain injury (TBI).

Methods: This double-blind, placebo-controlled randomized clinical trial enrolled 62 ICU patients with TBI (Glasgow Coma Scale 4-14) at Al-Zahra Medical Sciences Hospital, Isfahan, from December 2024 to June 2025. Participants were randomized 1:1 to receive synbiotics (3.6×10^9 CFU/day probiotics plus inulin, 20 g/day) or placebo (maltodextrin) via gavage for 1 week. Blood samples were collected at baseline and post-intervention to assess biochemical, electrolyte, coagulation, and hematological parameters.

Results: No significant between-group differences were observed in parameters, including fasting blood sugar, blood urea nitrogen, liver enzymes, coagulation indices, electrolytes, and blood cell counts. However, synbiotic supplementation led to significant within-group reductions in serum creatinine (p=0.001), sodium (p=0.002), and chloride (p<0.001), as well as neutrophil percentage (p=0.038), and a significant increase in platelet count (p=0.002).

Conclusion: Short-term synbiotic supplementation was associated with significant within-group improvements in laboratory parameters. However, between-group differences were not statistically significant, suggesting that larger and longer studies are needed to establish clinical relevance.

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Introduction

Traumatic brain injury (TBI) is a major global public health problem and remains one of the leading causes of morbidity, mortality, and long-term disability worldwide (1-4). It affects individuals across different age groups and is frequently associated with prolonged hospitalization, functional impairment, and high healthcare burden (2, 5-7). Patients with moderate to severe TBI often require admission to the intensive care unit (ICU), where close monitoring, nutritional support, and management of systemic complications are essential parts of care (8-10). The clinical course of TBI is complex and can be influenced by several systemic factors during ICU admission, including metabolic disturbances, renal and hepatic function, coagulation status, electrolyte imbalance, and hematological changes (11-13).

These laboratory parameters are routinely monitored in critically ill patients because they may reflect disease severity, treatment response, nutritional status, organ function, and overall clinical stability (14-16). Alterations in blood glucose, kidney function tests, liver enzymes, coagulation indices, electrolytes, and blood cell parameters are common in ICU patients and may affect prognosis and recovery (14, 15). Nutritional support plays an important role in the management of critically ill patients, particularly those with TBI who often require enteral feeding due to impaired consciousness and reduced oral intake. Early enteral nutrition is commonly used to maintain gastrointestinal function, support metabolic demands, and reduce complications related to critical illness. In this context, nutritional supplements that may help maintain gut function and systemic homeostasis have gained increasing attention (17-19).

Synbiotics are nutritional supplements that combine probiotics and prebiotics. Probiotics are live microorganisms that may provide health benefits when administered in adequate amounts, while prebiotics are substrates that support the growth or activity of beneficial microorganisms. The combination of these two components may help improve gastrointestinal tolerance, support microbial balance, and influence clinical and laboratory outcomes in critically ill patients (20-23). Previous studies in ICU and trauma populations have suggested that probiotic or synbiotic supplementation may have beneficial effects on selected clinical outcomes; however, findings remain inconsistent, and evidence in patients with TBI is still limited. Despite growing interest in synbiotic supplementation in critical care, limited data are available regarding its effects on routine laboratory parameters in ICU patients with traumatic brain injury. Evaluating these parameters may help clarify whether short-term synbiotic supplementation has measurable effects on biochemical, renal, hepatic, coagulation, electrolyte, mineral, and hematological status in this population. Therefore, this double-blind, placebo-controlled randomized clinical trial aimed to evaluate the effects of short-term synbiotic supplementation on selected biochemical, renal, hepatic, coagulation, electrolyte, mineral, and hematological parameters in ICU-admitted patients with traumatic brain injury.

Materials and Methods

This study was a double-blind, placebo-controlled, randomized clinical trial designed to evaluate the efficacy of synbiotic supplementation in patients with multiple traumas, including TBI, who were admitted to the ICU. Participants were recruited from the ICU at Al-Zahra Hospital in Isfahan between late December 2024 and June 2025. The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (ethics code: IR.SUMS.SCHEANUT.REC.1403.035) and adhered to the principles outlined in the Declaration of Helsinki. Given the patients' impaired consciousness, written informed consent was obtained from their legal guardians. The trial was registered with the Iranian Registry of Clinical Trials (identifier: IRCT20241109063642N1) too. The findings presented herein represent partial results of the investigation, with additional outcomes to be reported in subsequent publications.

Patients aged 20-80 years with various injuries, including TBI, were eligible for inclusion. All participants met the criteria of confirmed diagnosis of TBI; intact gastrointestinal function permitting enteral feeding; Glasgow Coma Scale (GCS) score ranging from 4 to 14; Injury Severity Score (ISS) indicative of mild to severe injury; initiation of enteral nutrition within 48 hours of admission; anticipated ICU stay exceeding 48 hours; survival for at least 12 hours following ICU admission; body mass index (BMI) greater than 18.5 kg/m^2; and absence of pregnancy or lactation. Exclusion criteria encompassed the need for procedures necessitating fasting periods longer than 8 hours, development of infectious complications such as sepsis or disseminated intravascular coagulation (DIC), and laboratory evidence of acute renal or hepatic failure.

For this double-blind trial, the synbiotic and placebo sachets were packaged in identical containers by the manufacturer, distinguished solely by coded labels. The sachets were indistinguishable in appearance, color, and odor. Blinding was maintained for researchers, participants, laboratory

personnel, outcome assessors, and data analysts until the completion of all final analyses. Eligible participants were randomized in a 1:1 ratio to either the synbiotic or placebo group. Randomization was conducted by an independent statistician using a random number table, with allocation codes stored in sealed envelopes until the study's conclusion.

Participants assigned to the intervention group received two synbiotic sachets daily, each containing 10 g of a formulation with 1.8×10^9 colony-forming units (CFU) of probiotics (comprising *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Streptococcus thermophilus*, and *Bifidobacterium longum*) plus inulin. Thus, the daily dose totaled 20 g, equivalent to 3.6×10^9 CFU of probiotics, administered via gavage over a 1-week period. The control group received two placebo sachets daily, each containing 10 g of maltodextrin (totaling 20 g per day), also administered via gavage for 1 week. The placebo sachets were identical in appearance to the synbiotic sachets. Both the synbiotic and placebo products (Biogen) were provided by Tak Gene Zist Company, Iran. All participants received standard ICU care as clinically indicated, including daily evaluations, with adjunctive therapies supplemented by essential standard treatments for their underlying conditions. Adverse events and potential complications related to the intervention were monitored throughout the study period. No adverse events related to synbiotic or placebo administration were observed or reported during the intervention.

Patients' data, including age, sex, marital status, educational level, current medications, and comorbidities, were extracted from medical records. Because patients were admitted to the ICU and direct standing measurements were not feasible, height was estimated using ulna length. Body weight was estimated using mid-upper arm circumference and standard weight-estimation tables, and the estimated values were compared with available clinical records. The level of consciousness was evaluated using GCS scores documented in the medical records. Disease severity was assessed using the Sequential Organ Failure Assessment score (SOFA) and the Acute Physiology and Chronic Health Evaluation score (APACHE II) based on clinical and laboratory data recorded at ICU admission.

Following confirmation of TBI by a critical care specialist, eligible participants were enrolled. Fasting venous blood samples were collected from each patient at baseline and at the end of the intervention. The laboratory parameters assessed in the present analysis included fasting blood sugar (FBS), blood urea nitrogen (BUN), serum creatinine (Cr), liver enzymes of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), coagulation indices, electrolytes, minerals, and hematological indices. FBS, BUN, Cr, ALT, AST, ALP, phosphorus (P), magnesium (Mg), chloride (Cl^-), and calcium (Ca) were measured using standard enzymatic or colorimetric methods with an automated clinical chemistry analyzer according to the manufacturer's instructions and routine hospital laboratory protocols.

Sodium (Na) and potassium (K) were measured using ion-selective electrode methods. Prothrombin time (PT) and partial thromboplastin time (PTT) were assessed using standard clot-based coagulation methods. Hematological parameters, including white blood cell count (WBC), lymphocyte percentage (Lym%), neutrophil percentage (Neut%), red blood cell count (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count (PLT), were measured using an automated hematology analyzer. All laboratory measurements were performed in the hospital laboratory under standard quality-control procedures.

Data were analyzed using SPSS software (version 26, IBM Corp., Armonk, NY, USA), with statistical significance defined as $p<0.05$. All analyses were performed according to the intention-to-treat (ITT) principle. Missing outcome data resulting from death or early discharge were handled using multiple imputation methods prior to statistical analyses. Within-group comparisons were performed using paired t-tests for normally distributed variables and Wilcoxon signed-rank tests for non-normally distributed variables. Between-group comparisons were conducted using independent t-tests for normally distributed variables and Mann-Whitney U tests for non-normally distributed variables. Categorical variables were analyzed using chi-square tests. Quantitative data are presented as mean±standard deviation (SD), and qualitative data are expressed as frequencies (percentages).

Results

A total of 62 eligible patients were enrolled and analyzed, comprising 47 men and 15 women. The mean age of participants was 41.87±19.24 years. Baseline demographic and clinical characteristics of the intervention and control groups were presented in Table 1. The two groups were comparable in terms of sex, weight, SOFA score, and APACHE score. However, age differed significantly between the groups ($p=0.04$), with patients in the intervention group being younger than those in the control group.

Table 1: Baseline demographic and clinical characteristics.

Characteristic	Intervention	Control	*P* value
Age (years), mean±SD	37.00±17.58	46.74±9.87	0.045
Sex: Male, n (%)	26 (83.9%)	21 (67.7%)	0.138
Sex: Female, n (%)	5 (16.1%)	10 (32.3%)	-
Weight (kg), mean±SD	77.60±18.80	75.11±14.80	0.579
SOFA score, mean±SD	7.09±2.65	6.74±2.42	0.584
APACHE score, mean±SD	14.83±7.29	15.35±6.39	0.768

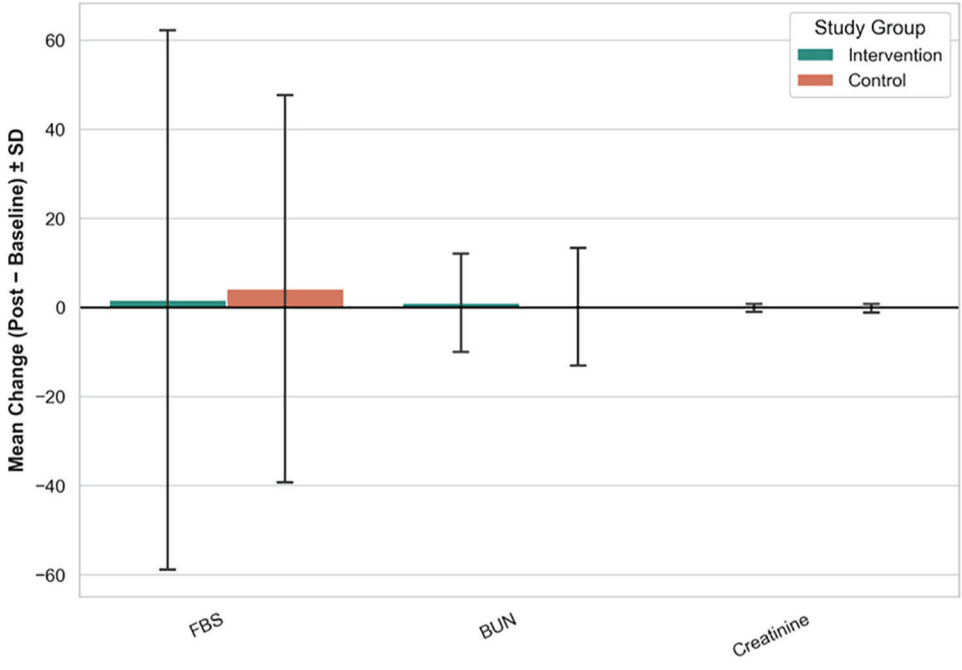

Figure 1: Mean change (post-intervention minus baseline) in metabolic and renal indices in the intervention and control groups. Bars represent mean change and error bars indicate standard deviation (SD). Fasting blood sugar (FBS), Blood urea nitrogen (BUN).

Therefore, age was considered a potential baseline imbalance and should be taken into account when interpreting the study findings.

Metabolic (FBS) and renal parameters (Cr, BUN) were presented in Figure 1. In the intervention group, no statistically significant changes were observed in FBS or BUN. Serum Cr showed a significant within-group reduction (mean change: −0.23±0.96 mg/dL, p=0.001). In the control group, Cr did not significantly change (mean change: −0.14±0.89 mg/dL, p=0.128). No statistically significant between-group differences were found for any metabolic or renal parameter (all p values >0.05).

ALT increased in the intervention group, with a mean change of 9.45±119.67 U/L; however, this change was not statistically significant (p=0.272). In the control group, ALT increased by a mean of 3.04±170.30 U/L (p=0.524). Between-group comparison demonstrated no statistically significant difference in ALT changes (p=0.647). Similarly, AST showed a mean increase of 5.88±69.65 U/L in the intervention group (p=0.510), whereas it decreased by 14.29±170.05 U/L in the control group (p=0.813). No significant between-group difference was identified for AST changes (p=0.693). ALP increased significantly within both the intervention (66.91±117.50 U/L, p=0.006) and control groups (104.97±418.44 U/L, p=0.004), with a greater rise observed in the control group. Nevertheless, the between-group comparison did not show a statistically significant difference in ALP changes (p=0.356) (Table 2).

In the intervention group, PT demonstrated a small mean reduction (−0.56±3.91), which was not statistically significant (p=0.666). In contrast, the control group exhibited a larger reduction (−0.01±1.82) that reached statistical significance (p<0.001). Despite these within-group findings, the between-group comparison revealed no statistically significant difference in PT changes (p=0.693). PTT showed no meaningful change in the intervention group (-0.08±4.66), and this within-group change was not statistically significant (p=0.767). No significant between-group difference was found for PTT changes (p=0.909) (Figure 2).

Table 2: Effect of synbiotic supplementation on liver enzymes.

Outcome	Group	Baseline mean±SD	Post mean±SD	Change mean±SD	P within	P between (Δ)
ALT (U/L)	Intervention	75.03±96.03	84.48±59.51	9.45±119.67	0.272	0.647
	Control	105.60±156.63	108.64±143.48	3.04±170.30	0.524	
AST (U/L)	Intervention	69.83±56.21	75.72±45.37	5.88±69.65	0.510	0.693
	Control	101.03±145.80	86.74±91.11	−14.29±170.05	0.813	
ALP (U/L)	Intervention	168.74±68.42	235.65±96.06	66.91±117.50	0.006	0.356
	Control	169.03±120.18	274.00±454.29	104.97±418.44	0.004	

Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP).

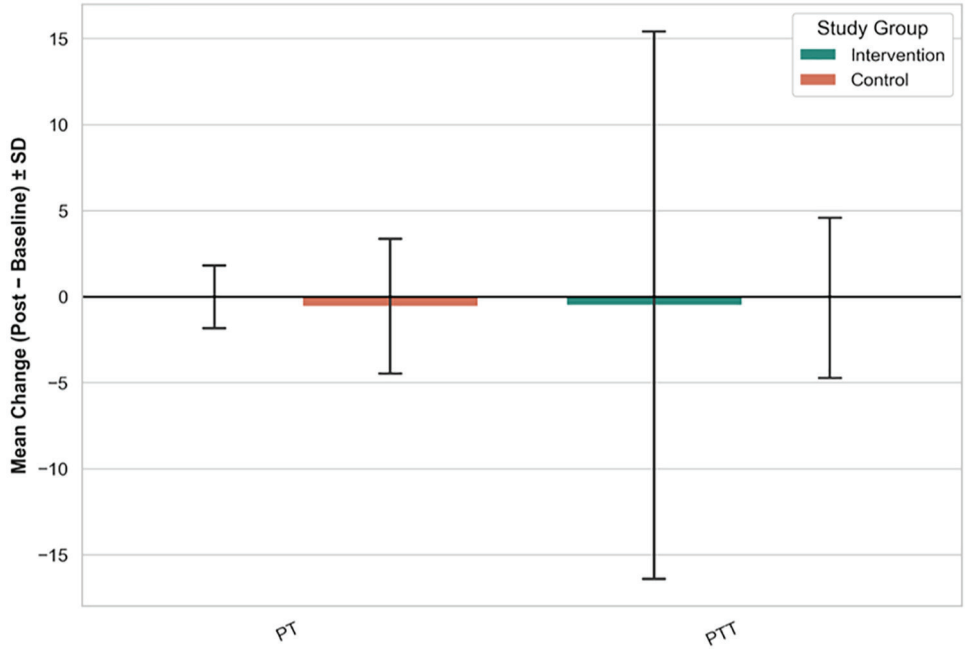

Figure 2: Mean change (post-intervention minus baseline) in coagulation indices in the intervention and control groups. Bars represent mean change and error bars indicate standard deviation (SD). Outcomes include prothrombin time [(PT); seconds] and partial thromboplastin time [(PTT); seconds].

Table 3: Baseline, post-intervention, and change values of serum electrolytes and minerals in the synbiotic intervention and placebo control groups among ICU patients with traumatic brain injury.

Outcome	Group	Baseline mean±SD	Post mean±SD	Change mean±SD	P within	P between (Δ)
Sodium (Na, mmol/L)	Intervention	139.50±25.51	135.51±24.90	−3.98±6.31	0.002	0.927
	Control	144.48±5.60	141.38±6.20	−3.10±6.96	0.006	
Potassium (K, mmol/L)	Intervention	4.24±0.72	4.14±0.57	−0.10±0.75	0.538	0.317
	Control	4.14±0.53	4.33±0.64	0.19±0.72	0.222	
Phosphorus (P, mg/dL)	Intervention	3.01±1.32	3.18±1.32	0.17±1.85	0.524	0.540
	Control	2.82±0.94	2.80±1.01	−0.02±1.15	0.984	
Magnesium (Mg, mg/dL)	Intervention	1.92±0.32	1.89±0.67	−0.03±0.64	0.696	0.949
	Control	1.93±0.25	1.90±0.39	−0.03±0.36	0.336	
Chloride (Cl, mmol/L)	Intervention	110.05±20.39	102.12±19.38	−7.94±9.80	<0.001	0.535
	Control	113.36±9.44	108.07±10.52	−5.29±14.58	0.018	
Calcium (Ca, mg/dL)	Intervention	8.32±0.85	7.84±0.97	−0.48±1.23	0.591	0.893
	Control	8.23±0.93	7.71±0.82	−0.52±1.01	0.058	

Electrolyte and mineral parameters were presented in Table 3. Sodium decreased significantly in both the intervention group (mean change: −3.98±6.31 mmol/L, p=0.002) and the control group (mean change: −3.10±6.96 mmol/L, p=0.006). Chloride also decreased significantly within both groups, with a mean change of −7.94±9.80 mmol/L (p<0.001) in the intervention group and −5.29±14.58 mmol/L (p=0.018) in the control group. Calcium showed no significant reduction in the intervention group (mean change: −0.48±1.23 mg/dL, p=0.591) and in the control group (mean change: −0.52±1.01 mg/dL, p=0.058).

Table 4: Baseline, post-intervention, and change values of hematological parameters in the synbiotic and placebo groups among ICU patients with traumatic brain injury.

Outcome	Group	Baseline mean±SD	Post mean±SD	Change mean±SD	P within	P between (Δ)
WBC (10^3/µL)	Intervention	19887.38±31630.74	28721.53±57190.59	8834.16±50460.23	0.102	0.398
	Control	29446.26±48142.28	28587.90±47140.02	−858.36±45162.67	0.863	
Lymphocyte (%)	Intervention	12.55±7.41	15.08±7.97	2.52±9.34	0.061	0.125
	Control	39.04±144.20	45.35±179.97	6.21±37.22	0.692	
Neutrophil (%)	Intervention	79.33±8.44	75.77±9.74	−3.56±10.63	0.037	0.143
	Control	79.85±7.37	77.52±12.81	−2.33±13.65	0.946	
RBC (10^6/µL)	Intervention	3.84±0.69	3.74±0.60	−0.10±0.80	0.643	0.647
	Control	3.75±0.77	3.65±0.71	−0.09±0.62	0.318	
Hemoglobin (g/dL)	Intervention	11.03±2.17	10.84±1.76	−0.20±2.38	0.746	0.486
	Control	10.85±2.28	10.37±1.59	−0.48±2.06	0.112	
Hematocrit (%)	Intervention	32.85±5.94	31.93±4.38	−0.92±6.20	0.636	0.882
	Control	32.31±6.60	31.89±4.55	−0.45±5.89	0.433	
MCV (fL)	Intervention	85.62±3.65	85.55±2.83	−0.08±2.29	0.742	0.513
	Control	87.47±5.68	87.50±5.37	0.03±3.23	0.581	
MCH (pg)	Intervention	28.82±1.92	28.78±1.37	−0.04±1.60	0.992	0.360
	Control	28.90±2.01	28.63±1.81	−0.26±1.31	0.315	
MCHC (g/dL)	Intervention	33.07±2.24	33.36±1.29	0.29±2.51	0.649	0.531
	Control	33.13±1.57	32.95±1.39	−0.18±1.48	0.706	
Platelets (/µL)	Intervention	153741.93±74843.82	237098.03±142121.76	83356.10±128567.01	0.001	0.499
	Control	173742.93±95330.99	220387.09±106739.14	46644.16±143163.20	0.061	

White blood cell (WBC), Red blood cell (RBC), Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC).

Changes in potassium, phosphorus, and magnesium were not statistically significant within either group. No statistically significant between-group differences were found for any electrolyte or mineral parameter (All p values >0.05).

Hematological parameters were presented in Table 4. In the intervention group, neutrophil percentage decreased significantly (mean change: −3.56±10.63%, p=0.037) and platelet count increased significantly (mean change: 83356.10±128567.01/µL, p=0.001). No statistically significant changes were observed for the other hematological parameters. In the control group, no significant changes were seen except a non-significant increase in platelet count (p=0.061). No statistically significant between-group differences were found for any hematological parameter (All p values >0.05).

Discussion

This randomized controlled trial investigated the effects of short-term synbiotic supplementation in ICU patients with TBI, focusing on a subset of metabolic, renal, hepatic, coagulation, electrolyte, and hematological parameters. In the synbiotic (intervention) group, statistically significant within-group improvements were observed, including reductions in serum sodium, chloride, and neutrophil percentage, as well as a substantial increase in platelet count. Most between-group comparisons with the placebo arm did not reach statistical significance; however, the difference in platelet count change approached significance. These findings indicate that synbiotic supplementation may exert subtle modulatory effects on systemic homeostasis, electrolyte balance, and hematological parameters in critically ill TBI patients, likely mediated by gut microbiota modulation and the gut-brain axis. Although the clinical relevance of these changes appears limited in this short-term, partial analysis, the results support further investigation of synbiotics as an adjunctive therapy in neurocritical care.

Synbiotic supplementation was associated with favorable within-group changes in renal and electrolyte indices in the intervention arm. The observed reductions in sodium and chloride levels may reflect improved fluid homeostasis or attenuated systemic inflammation, consistent with the known role of gut microbiota in regulating ion transport and immune responses. Changes in fasting blood sugar, blood urea nitrogen, and creatinine were generally modest and comparable between groups. Liver enzymes of ALT and ALP increased in both arms without significant between-group differences, most likely due to trauma-related hepatic stress rather than any direct effect of the synbiotic.

Coagulation indices of PT and PTT did not show any significant effect following the intervention. In contrast, electrolyte and mineral parameters illustrated clear within-group reductions in sodium, chloride in the synbiotic group. Such changes were common in patients with TBI due to fluid resuscitation, diuretic use, and systemic inflammation. The observed pattern in this study suggests that synbiotics may contribute to maintaining electrolyte homeostasis; however, the between-group differences remained non-significant.

The possible mechanism may be related to the primary effect of prebiotics on mineral absorption, which is associated with their role as "colonic food" (24). Since prebiotics are not digested and reach the colon, they are fermented by gut bacteria, resulting in the production of SCFAs (24). Consequently, the reduction in intestinal pH may enhance mineral absorption (e.g., calcium) by increasing mineral availability and facilitating their uptake (24). Moreover, SCFAs can promote intestinal epithelial cell growth, increase absorptive surface area, and improve colonic blood flow, thereby contributing to enhanced mineral absorption (24). Since fluid administration and other clinical factors in ICU patients can influence electrolyte levels, the findings should be interpreted with caution. Further studies with larger sample sizes and longer supplementation periods may be needed to identify clinically meaningful differences.

Hematological parameters provided the most promising signals. In the synbiotic group, neutrophil percentage decreased significantly, while platelet count increased markedly. These changes may attenuate TBI-associated neutrophilia and thrombocytopenia, both of which exacerbate secondary brain injury through oxidative stress and microvascular dysfunction. The selective immunomodulatory profile (no significant alterations in WBC, lymphocytes, RBC indices, or other red-cell parameters) is consistent with strain-specific anti-inflammatory effects of the multi-species probiotic formulation. Collectively, these hematological shifts serve as indirect markers of reduced systemic inflammation, reinforcing the mechanistic link between gut microbiota restoration and neuroprotection in TBI (24).

Our results are in line with a growing body of evidence supporting microbiota-targeted therapies in neurotrauma. Randomized trials have reported improvements in inflammatory markers, shortened ICU stay, and better clinical recovery with probiotics or synbiotics in TBI and multiple-trauma cohorts by Noshadi *et al.* and Abbaszadeh *et al.* (25, 26). The significant platelet increase and neutrophil reduction observed in our synbiotic group mirror the immunomodulatory benefits described in these studies of seven-strain probiotics in severe TBI. Recent narrative reviews further highlight the mechanistic role of gut microbiota restoration in attenuating neuroinflammation and oxidative stress through the gut-brain axis described by Pagkou *et al.* and Vosoughian *et al.* (27, 28).

Beyond inflammatory and clinical outcomes, the potential effects of probiotics and synbiotics on biochemical parameters, including electrolyte and mineral status were investigated. Consistent with our findings, Mirzaeian *et al.* did not observe any significant changes in serum sodium, potassium, or phosphorus levels following synbiotic supplementation in hemodialysis patients (29). Beneficial effects of probiotics or prebiotics on mineral absorption, such as increased copper absorption following fructooligosaccharide consumption in postmenopausal women were also demonstrated (30). An increased serum sodium level after probiotic supplementation in patients with cirrhosis was also depicted (31).

These discrepancies may be related to differences in the type and composition of supplements, study populations, intervention duration, and underlying clinical conditions. In the present study, synbiotic supplementation had no significant effect on liver or kidney function markers. Similar findings were reported by Firouzi *et al.*, who found no improvements in liver enzymes (ALT, AST, and ALP) after 12 weeks of probiotic supplementation in patients with type 2 diabetes and normal liver function (32). Likewise, Mirzaeian *et al.* observed no significant changes in BUN or Cr following two months of synbiotic supplementation in patients undergoing hemodialysis (29).

In contrast, Eslamparast *et al.* reported significant improvements in liver function tests after 28 weeks of synbiotic supplementation in patients with non-alcoholic fatty liver disease (NAFLD) (33). A meta-analysis by Liu *et al.* revealed that synbiotic supplementation significantly reduced BUN level in patients with chronic kidney disease, particularly in studies with intervention durations of at least three months (34). The differences across studies are likely related to variations in patient populations, underlying diseases, intervention duration, and the type and formulation of the synbiotic used. By focusing on ICU TBI patients and providing partial data on secondary physiological outcomes, the present trial adds to this expanding literature and highlights the potential complementary role of synbiotics alongside standard neurocritical care.

Key limitations include the modest sample size

(n=62) and the short 1-week intervention period. TBI heterogeneity (GCS of 4-14) and universal reliance on enteral nutrition may also have influenced results. Despite these constraints, the observed within-group improvements in key hematological and electrolyte parameters suggest that synbiotics could serve as a safe, low-cost adjunctive strategy to support systemic stability in ICU TBI management. Future studies should incorporate longer supplementation (≥14 days), larger multicenter designs, comprehensive biomarker panels, and gut microbiota sequencing to establish causality and identify responders. Mechanistic investigations linking microbial metabolite changes to neurological outcomes will be particularly valuable.

Conclusion

Short-term synbiotic supplementation in ICU patients with TBI was associated with significant within-group improvements in platelet count and neutrophil percentage in the intervention arm, and a marginally significant between-group difference in platelet count. These subtle modulatory effects support the therapeutic potential of synbiotics via the gut-brain axis, although robust between-group superiority was not observed in this partial analysis. Full evaluation of the primary inflammatory and oxidative stress markers is essential to determine whether synbiotics can meaningfully mitigate secondary brain injury and improve clinical outcomes in this vulnerable population.

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Author's Contribution

ME contributed to the study conception, implementation, data collection, and manuscript drafting. MB contributed to the study design, supervised study implementation, and critically revised the manuscript. AA contributed to the study design. BA contributed to patient management and study implementation in the ICU. MZ performed statistical analyses. ZR contributed to study implementation. SS contributed to manuscript editing. MHE conceived and supervised the study and critically revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare that they have no competing interests

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