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Enteral nutrition, gut microbiota alterations, and SIBO-related outcomes in critically ill patients: a systematic review

Nutrisi enteral, perubahan mikrobiota usus, dan luaran terkait pertumbuhan berlebih bakteri usus halus (SIBO) pada pasien kritis: tinjauan sistematis

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Evangelista Pangkahila[1*], I Wayan Gede Sutadarma[2], I Wayan Weta[3]

Abstract

Background: Critically ill patients frequently develop gut dysbiosis, characterized by reduced microbial diversity and increased colonization by opportunistic pathogens. These alterations may contribute to gastrointestinal dysfunction and are associated with small intestinal bacterial overgrowth (SIBO)-related outcomes. Enteral nutrition is a key nutritional strategy for critically ill patients and may influence gut microbiota composition; however, its role in modulating the microbiota and its implications for SIBO-related outcomes remain unclear.
Objectives: This systematic review aimed to synthesize evidence on the relationship between enteral nutrition and gut microbiota modulation in critically ill adults and explore its potential implications for SIBO-related gastrointestinal outcomes.
Methods: A systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines and registered in the PROSPERO database (CRD420261384432). Literature searches were performed in PubMed and Google Scholar for studies published between 2020 and 2026. Observational studies and randomized controlled trials involving critically ill patients receiving enteral nutrition, with outcomes related to the gut microbiota, gastrointestinal function, or SIBO were included. Data were extracted and synthesized narratively and thematically.
Results: Seven studies were included in the meta-analysis. Evidence from studies directly assessing microbiota has demonstrated reduced microbial diversity and increased abundance of opportunistic pathogens during critical illness. Studies evaluating fiber- or prebiotic-containing enteral formulas suggested potential increases in short-chain fatty acid (SCFA)-producing bacteria, although the findings remained inconsistent and were influenced by antibiotic exposure and clinical severity. Only one of the included studies directly evaluated SIBO.
Conclusion: Enteral nutrition may influence the gut microbiota composition in critically ill patients; however, direct evidence regarding SIBO remains limited. Further prospective studies using standardized microbiota and SIBO assessment methods are needed before the clinical implications for nutritional practice can be more clearly established.

Keywords:
Critically ill patients, dysbiosis, enteral nutrition, gut microbiota, small intestinal bacterial overgrowth

Abstrak

Latar Belakang: Pasien kritis sering mengalami disbiosis usus yang ditandai dengan penurunan keragaman mikrobiota dan peningkatan kolonisasi bakteri oportunistik. Perubahan ini dapat berkontribusi terhadap disfungsi gastrointestinal dan berpotensi berkaitan dengan luaran yang berhubungan dengan Small Intestinal Bacterial Overgrowth (SIBO). Nutrisi enteral merupakan strategi terapi nutrisi utama pada pasien kritis dan dapat memengaruhi komposisi

[1] Department of Clinical Nutrition, Faculty of Medicine, Udayana University/Prof. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia. E-mail: angelpangkahila@gmail.com
[2] Department of Clinical Nutrition, Ngoerah Hospital/Faculty of Medicine, Udayana University, Denpasar, Indonesia. E-mail: gede_sutadarma@unud.ac.id
[3] Department of Clinical Nutrition, Ngoerah Hospital/Faculty of Medicine, Udayana University, Denpasar, Indonesia. E-mail: wy_weta@unud.ac.id

Penulis Koresponding
Evangelista Pangkahila: Department of Clinical Nutrition, Faculty of Medicine, Udayana University/Prof. I.G.N.G Ngoerah General Hospital, Denpasar, Bali, Indonesia. E-mail: angelpangkahila@gmail.com

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mikrobiota usus, namun perannya dalam modulasi mikrobiota serta implikasinya terhadap luaran terkait SIBO masih belum sepenuhnya dipahami.
Tujuan: Tinjauan sistematis ini bertujuan mensintesis bukti mengenai hubungan antara nutrisi enteral dan modulasi mikrobiota usus pada pasien dewasa dalam kondisi kritis serta mengeksplorasi kemungkinan implikasinya terhadap luaran gastrointestinal yang berhubungan dengan SIBO
Metode: Tinjauan sistematis ini dilakukan sesuai pedoman Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) dan telah terdaftar pada basis data PROSPERO (CRD420261384432). Penelusuran literatur dilakukan melalui PubMed dan Google Scholar untuk artikel yang dipublikasikan pada tahun 2020–2026. Studi observasional dan randomized controlled trials yang melibatkan pasien kritis dengan pemberian nutrisi enteral serta memiliki luaran terkait mikrobiota usus, fungsi gastrointestinal, atau SIBO diikutsertakan. Data diekstraksi dan disintesis secara naratif.
Hasil: Tujuh studi memenuhi kriteria inklusi. Bukti dari studi yang secara langsung mengevaluasi mikrobiota menunjukkan adanya penurunan keragaman mikrobiota dan peningkatan dominasi bakteri oportunistik selama kondisi kritis. Studi yang mengevaluasi formula nutrisi enteral yang mengandung serat atau prebiotik menunjukkan potensi peningkatan bakteri penghasil short-chain fatty acids (SCFA), meskipun hasil yang diperoleh masih tidak konsisten dan dipengaruhi oleh paparan antibiotik serta tingkat keparahan kondisi klinis. Hanya satu studi yang secara langsung mengevaluasi SIBO.
Kesimpulan: IMD memberikan manfaat besar bagi kesehatan dan perkembangan bayi, serta mendukung keberhasilan menyusui.

Kata Kunci:
Dysbiosis, mikrobiota usus, nutrisi enteral, pasien kritis, *small intestinal bacterial overgrowth*

Introduction

Critically ill patients admitted to the Intensive Care Unit (ICU) experience complex physiological alterations involving systemic inflammatory responses, impaired splanchnic perfusion, metabolic stress, and neuroendocrine dysregulation. These disturbances may impair gastrointestinal function by altering intestinal motility, reducing absorptive capacity, increasing intestinal permeability, and disrupting mucosal integrity. Gastrointestinal dysfunction has increasingly been recognized as an important contributor to malnutrition and inadequate nutrient delivery in critically ill patients. Enteral nutrition (EN) is the preferred nutritional support strategy for critically ill patients because it helps maintain gastrointestinal physiology and intestinal barrier function. However, adequate enteral feeding is frequently limited by enteral feeding intolerance, which refers to the inability to achieve the prescribed nutritional targets because of gastrointestinal symptoms or impaired gastrointestinal function. Clinically, enteral feeding intolerance may present as gastric residual accumulation, vomiting, abdominal distension, diarrhea, or reduced feeding progression, and has been associated with insufficient nutritional intake, prolonged intensive care unit stay, and poorer clinical outcomes (Blaser et al., 2021; McClave et al., 2016; Reintam Blaser et al., 2020; Singer et al., 2019). Early enteral nutrition is also associated with stimulation of gastrointestinal activity and maintenance of intestinal homeostasis (Blaser et al., 2021; Singer et al., 2019). Despite these benefits, achieving optimal enteral nutrition delivery remains challenging because enteral feeding intolerance occurs in approximately 30–50% of critically ill patients and is commonly manifested by increased gastric residual volume, diarrhea, vomiting, abdominal distension, and the inability to achieve nutritional targets (Reintam Blaser et al., 2020; Park et al., 2025).

The gastrointestinal tract serves as a digestive organ and a complex ecosystem inhabited by diverse microbial communities that contribute to host metabolism and immune regulation. The gut microbiota plays a fundamental role in maintaining gastrointestinal homeostasis through nutrient metabolism, short-chain fatty acid (SCFA) production, protection against pathogenic colonization, and modulation of inflammatory responses. However, critically ill patients are particularly susceptible to gut microbiota disruption due to multiple factors, including broad-spectrum antibiotic exposure, proton pump inhibitor use, gastrointestinal dysmotility, impaired intestinal perfusion, and critical illness–related stress responses (Haak & Wiersinga, 2021; Wozniak et al., 2022; Wozniak et al., 2024). These factors frequently result in gut

dysbiosis, characterized by reduced microbial diversity and increased dominance of opportunistic pathogens. Such alterations may impair intestinal barrier function, increase intestinal permeability, and trigger inflammatory pathways that exacerbate gastrointestinal dysfunction and negatively affect the tolerance to enteral nutrition (Reintam Blaser et al., 2020; Haak & Wiersinga, 2021; Wozniak et al., 2022).

One clinically relevant consequence of gut microbiota imbalance is *Small Intestinal Bacterial Overgrowth* (SIBO), which is defined as an abnormal increase in bacterial populations within the small intestine (Pimentel et al., 2020; Quigley, 2020). SIBO may interfere with digestion and nutrient absorption through mechanisms such as bile acid deconjugation, nutrient competition, and excessive bacterial fermentation. In critically ill patients, altered intestinal motility, medication exposure, prolonged immobilization, and changes in the intestinal environment may increase susceptibility to SIBO. Previous evidence suggests that gut dysbiosis and SIBO are associated with prolonged ICU stays, increased infection risk, and poorer clinical outcomes (Wozniak et al., 2024; Karakosta et al., 2024). However, evidence regarding the influence of enteral nutrition on gut microbiota composition remains inconsistent. Fiber- and prebiotic-enriched enteral formulations have shown potential benefits in promoting beneficial bacterial populations and enhancing SCFA production; however, these effects appear to vary depending on antibiotic exposure, nutritional composition, and clinical conditions of the patient (Freedberg et al., 2020; Serbanescu et al., 2025).

Several studies have investigated microbiota alterations and gastrointestinal outcomes in critically ill patients receiving enteral nutrition. Current evidence consistently demonstrates that critically ill patients experience gut dysbiosis, characterized by diarrhea, enteral feeding intolerance, and increased mortality (Wozniak et al., 2024; Ni et al., 2022; Xiao et al., 2023; Park et al., 2025). However, studies directly examining the relationship between enteral nutrition, gut microbiota modulation, and SIBO are limited. Most studies conducted in critically ill populations primarily evaluate alterations in gut microbiota composition without directly measuring SIBO or assessing its clinical significance. Existing literature also tends to report microbiota changes and gastrointestinal outcomes separately, rather than integrating both aspects into a comprehensive understanding of microbiota–SIBO interactions. Consequently, the specific role of enteral nutrition in driving microbial alterations and its potential implications for SIBO-related outcomes in critically ill patients remain unclear.

To our knowledge, previous studies and reviews have largely focused on enteral nutrition strategies, alterations in the gut microbiota, and gastrointestinal outcomes in critically ill patients as separate areas of investigation. Evidence directly integrating enteral nutrition, microbiota modulation, and SIBO-related outcomes remains limited, particularly because most studies do not directly assess SIBO. Therefore, rather than establishing a causal relationship, this systematic review aimed to synthesize and summarize the available evidence to explore potential interactions among enteral nutrition, changes in the gut microbiota, and gastrointestinal outcomes in critically ill patients and to identify current gaps for future research. Understanding these relationships may help improve future nutritional decision-making in critically ill populations, particularly regarding enteral formula composition, timing of enteral nutrition initiation, and management of feeding-related gastrointestinal complications. However, current evidence remains insufficient to support specific microbiota-targeted nutritional recommendations, highlighting the need for further prospective studies.

Methods

Study Design and Registration

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The completed PRISMA 2020 checklist is provided in Supplementary Material 1 to improve transparency and reporting completeness. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420261384432.

The review was conducted in accordance with the registered protocol, and no major deviations from the study objectives, eligibility criteria, or primary outcomes were observed. This review was designed to synthesize evidence regarding enteral nutrition and gut microbiota modulation and to explore its possible implications

for Small Intestinal Bacterial Overgrowth (SIBO)-related outcomes among critically ill patients.

Kerangka PICO dalam tinjauan ini mencakup populasi berupa pasien dewasa dalam kondisi kritis yang dirawat di unit perawatan intensif (ICU). Intervensi atau paparan yang dikaji meliputi pemberian nutrisi enteral serta intervensi atau pemeriksaan yang berkaitan dengan mikrobiota usus. Kelompok pembanding dapat berupa perbedaan metode pemberian nutrisi enteral, kelompok kontrol, atau tidak adanya intervensi, sesuai dengan desain masing-masing penelitian. Luaran yang dinilai mencakup perubahan mikrobiota usus, gangguan gastrointestinal, intoleransi pemberian makan, serta temuan yang berkaitan dengan pertumbuhan berlebih bakteri di usus halus atau *small intestinal bacterial overgrowth* (SIBO).

Data Sources and Search Strategy

A structured literature search was conducted using the PubMed and Google Scholar databases to identify relevant studies published between January 2020 and May 2026. Search terms were developed using combinations of Medical Subject Headings (MeSH) and free-text terms with the Boolean operators. The search strategy included combinations of the following keywords: ("gut microbiota" OR "microbiome" OR "gut dysbiosis" OR "intestinal flora") AND ("enteral nutrition" OR "enteral feeding" OR "early enteral nutrition") AND ("small intestinal bacterial overgrowth" OR "SIBO") AND ("critically ill" OR "intensive care unit" OR "ICU"). For Google Scholar, the screening was limited to the first 200 results ranked by relevance to reduce duplication and improve the feasibility of the study selection. The literature search was completed in May 2026.

The full database-specific search strategies are provided in Supplementary Material 2. Additional manual searches of the reference lists of eligible studies were conducted to identify potentially relevant articles.

Eligibility Criteria

Studies were included if they met the following criteria: (1) involved adult critically ill patients aged ≥18 years admitted to the Intensive Care Unit (ICU); (2) included medical, surgical, trauma, septic shock, mechanically ventilated, or mixed ICU populations; (3) patients received enteral nutrition as the primary route of nutritional support for at least 24 h or according to study-defined enteral feeding protocols; (4) reported outcomes related to gut microbiota composition, gastrointestinal function, feeding intolerance, or findings associated with small intestinal bacterial overgrowth (SIBO); (5) used accepted microbiota assessment methods, including sequencing-based approaches (e.g., 16S rRNA sequencing), microbial profiling, stool microbiome analysis, or validated microbiological assessments; (6) studies assessing SIBO used recognized diagnostic approaches, including hydrogen and/or methane breath testing or study-defined diagnostic criteria; (7) observational studies or randomized controlled trials; and (8) published in English between January 2020 and May 2026.

The publication period was restricted to 2020–2026 to focus on contemporary evidence reflecting recent developments in critical care nutrition practices, microbiota assessment technologies, and the growing interest in microbiota-related gastrointestinal outcomes. Studies were excluded if they were review articles, editorials, conference abstracts without full text, case reports, animal studies, studies involving pediatric populations (<18 years), studies not involving critically ill populations, or studies that did not report outcomes relevant to the objectives of this review.

Study Selection and Data Extraction

Study selection was conducted independently by two reviewers through title and abstract screening, followed by full-text assessment according to the predefined eligibility criteria. Disagreements were resolved through discussion and consensus-building.

Data extraction was performed using a standardized extraction form, including author, publication year, country, study design, sample size, patient population, enteral nutrition intervention, microbiota assessment methods, outcomes, and principal findings.

Risk of Bias Assessment

Two reviewers independently assessed the methodological quality of the included studies. The Cochrane Risk of Bias version 2 (RoB 2) tool was used for randomized controlled trials, and the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool was used for observational studies. Risk of bias assessments were categorized as low,

moderate, serious, or critical, according to established criteria.

Data Synthesis and Analysis

Due to heterogeneity in study design, patient populations, enteral nutrition strategies, microbiota assessment methods, and reported outcomes, a quantitative meta-analysis was not performed. The findings were synthesized narratively by grouping studies according to enteral nutrition characteristics, microbiota-related outcomes, gastrointestinal and SIBO-related outcomes, and clinical implications.

A formal certainty-of-evidence assessment using the GRADE approach was not performed because of variability in study methodologies and outcome reporting. Therefore, the findings should be interpreted as exploratory evidence rather than definitive clinical recommendations.

Ethical Considerations

Ethical approval was not required for this study because it involved the analysis of previously published studies and did not include direct interaction with human participants or access to identifiable patient data. Nevertheless, all included studies were selected from published research conducted in accordance with ethical standards and institutional approvals.

Results

Study Selection

Based on a literature search conducted in PubMed and Google Scholar, 215 records were identified. After duplicate records were removed, 170 articles underwent title and abstract screening, of which 130 were excluded because they were irrelevant to the review objectives. Subsequently, 40 full-text articles were assessed for eligibility, and 33 articles were excluded after full-text evaluation. Finally, seven studies fulfilled the inclusion criteria and were included in the qualitative synthesis of the results. The study selection process is shown in Figure 1.

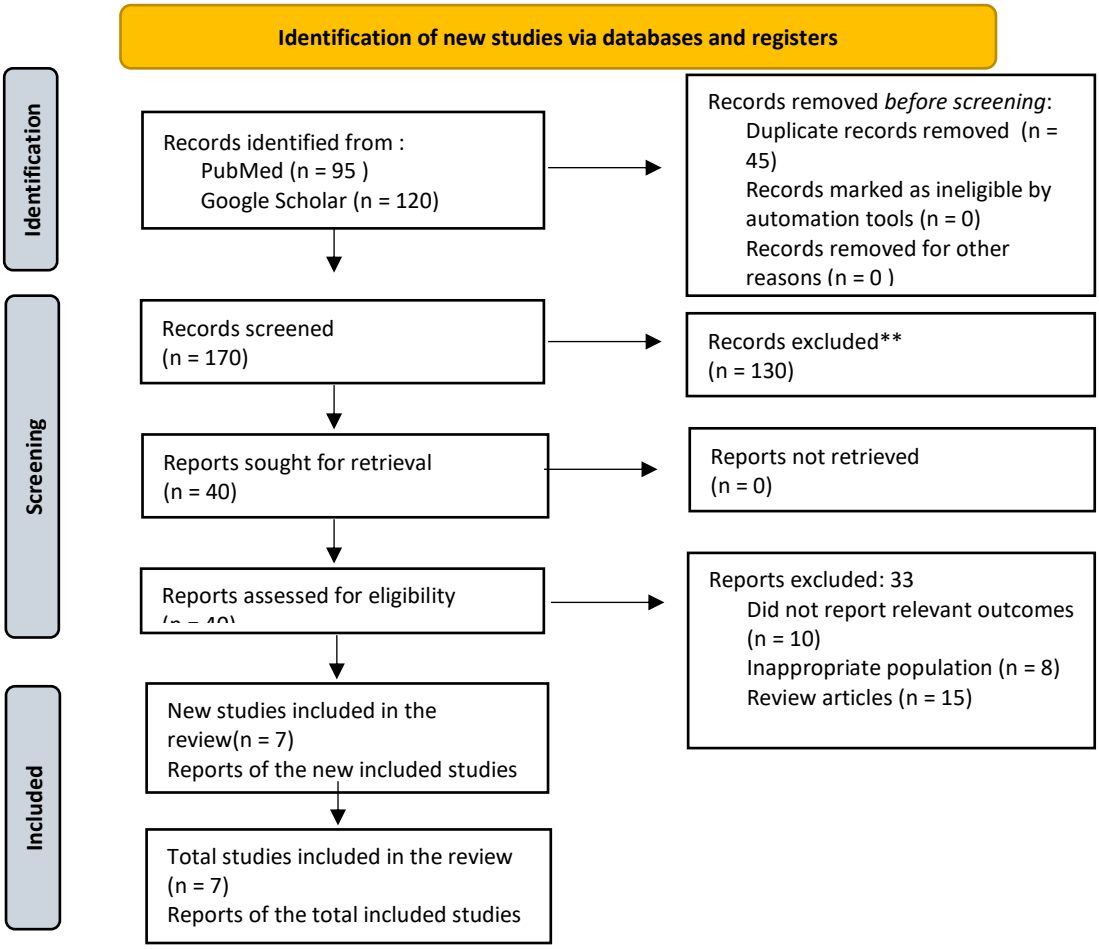

Figure 1. PRISMA flow diagram of the study selection process

Characteristics of Included Studies

The seven included studies comprised prospective cohort studies, observational studies, and randomized controlled trials involving critically ill patients admitted to the Intensive Care Unit.

Most studies have evaluated the relationship between enteral nutrition, gut microbiota alterations, and gastrointestinal outcomes. Microbiota assessment was predominantly performed using 16S rRNA sequencing, while some studies used hydrogen breath testing to evaluate Small Intestinal Bacterial Overgrowth and clinical outcomes such as diarrhea, feeding intolerance, infection, short-chain fatty acid production, and mortality. The characteristics of the included studies are summarized **in** Table 1**.**

Table 1. Characteristics of studies included in the systematic review

Author (Year)	Method	Enteral Nutrition Intervention	Nutritional Composition	Outcomes & Main Findings
Wozniak et al. (2024)	Poland: prospective cohort study involving 96 critically ill patients admitted to the ICU. Assessment: 16S rRNA gene sequencing was performed.	Routine nutritional management during ICU stay.	Not reported specifically.	Outcomes: The outcomes were gut microbiota diversity and mortality. Main findings: Reduced gut microbiota diversity was associated with a higher risk of mortality in critically ill patients.
Freedberg et al. (2020)	United States: randomized controlled trial involving 20 ICU patients receiving broad-spectrum antibiotics. Assessment: Gut microbiota profiling and short-chain fatty acid analysis were performed.	Fiber-containing enteral nutrition was compared with standard enteral nutrition for 14 days.	Enteral formula containing dietary fibers.	Outcomes: Microbiota composition and short-chain fatty acid (SCFA) production. Main findings: Fiber supplementation increased the abundance of short-chain fatty acid-producing bacteria and helped maintain the gut microbial diversity.
Ni et al. (2022)	China: observational study involving 67 ICU patients receiving enteral nutrition. Assessment: 16S rRNA gene sequencing was performed.	Standard enteral nutrition was administered during the ICU admission.	Not reported specifically.	Outcomes: Gut microbiota alterations and enteral nutrition-associated diarrhea were observed. Main findings: Patients with diarrhea exhibited lower microbial diversity and higher abundance of potentially pathogenic bacteria than healthy controls.
Karakosta et al. (2024)	Greece: prospective observational study involving 104 critically ill ICU patients. Assessment: Hydrogen breath test.	No specific enteral nutrition intervention was provided, and SIBO-related findings were assessed at a single time point.	Not applicable.	Outcomes: SIBO prevalence, infection, and ICU length of stay were assessed. Main findings: SIBO was identified in 36.5% of patients and was associated with a higher incidence of infection and longer ICU stay.
Serbanescu et al. (2025)	United States: randomized controlled trial involving 17 mechanically ventilated	Enteral nutrition was supplemented with short-	Enteral formula enriched with short-	Outcomes: Changes in the gut microbiota composition and dynamics. Main findings: Prebiotic supplementation

	trauma patients admitted to the ICU. Assessment: 16S rRNA gene sequencing was performed.	chain fructooligosaccharides for 14 days.	chain fructooligosaccharides.	influenced microbiota composition, although the effects varied with antibiotic exposure and the patients' clinical condition.
Xiao and Xu (2023)	China: prospective observational study involving 200 ICU patients receiving enteral nutrition. Assessment: Clinical assessment and multivariate analysis.	Enteral nutrition was administered throughout the ICU stay.	Not reported specifically.	Outcomes: Enteral feeding intolerance and clinical outcomes were assessed. Main findings: Feeding intolerance was frequent and was associated with greater disease severity and poorer clinical outcomes.
Park et al. (2025)	South Korea: retrospective cohort study involving 94 ICU patients with septic shock. Assessment: Clinical gastrointestinal assessment was performed.	Assessment of enteral nutrition tolerance during the ICU admission period.	Not reported specifically.	Outcomes: Feeding intolerance and mortality. Main findings: Feeding intolerance occurred in 81.9% of patients and was associated with increased 90-day mortality.

Gut Microbiota Alterations and Clinical Outcomes

Studies that directly assessed gut microbiota composition have demonstrated alterations in microbial diversity and an increased abundance of opportunistic pathogenic bacteria during critical illness. In particular, studies evaluating patients with enteral nutrition-associated diarrhea have reported lower microbial diversity and a greater predominance of microorganisms, such as Enterococcus and Klebsiella. In contrast, several included studies focused primarily on gastrointestinal outcomes, feeding intolerance, or clinical complications and did not directly evaluate the microbiota composition. Therefore, the interpretation of microbiota-related findings should be limited to studies that performed direct microbiological assessments.

Reduced microbial diversity is also associated with an increased mortality risk (Wozniak et al., 2024; Ni et al., 2022). Several studies have reported that enteral nutrition formulations enriched with fiber or prebiotics increase the abundance of short-chain fatty acid (SCFA)-producing bacteria, which contribute to intestinal barrier integrity and immune regulation (Freedberg et al., 2020; Serbanescu et al., 2025). However, these effects vary according to antibiotic exposure and clinical conditions. Some studies have suggested that prebiotic supplementation under conditions of severe dysbiosis may promote the growth of pathogenic bacteria, indicating that microbiota responses are highly dependent on patient-specific factors (Serbanescu et al., 2025). Gut microbiota disturbances are also associated with enteral feeding intolerance. More than half of critically ill patients experience feeding intolerance, which is associated with higher disease severity and poorer clinical outcomes (Xiao & Xu, 2023; Park et al., 2025).

Small Intestinal Bacterial Overgrowth Findings

One observational study directly evaluated Small Intestinal Bacterial Overgrowth (SIBO) in critically ill patients using hydrogen breath testing and reported a prevalence of 36.5%. In that study, SIBO was associated with increased infection rates and prolonged ICU stays, although no consistent association with mortality was observed.

However, the interpretation of these findings should be cautious because the evidence was derived from a single study, and SIBO diagnosis using hydrogen breath testing may be influenced by altered intestinal motility, antibiotic exposure, and physiological disturbances commonly present in critically ill populations. Therefore, these findings should not be generalized to all critically ill patients and require confirmation through further studies that use standardized diagnostic approaches.

Risk of Bias Assessment

Risk of bias assessment demonstrated variability across the included studies. Several observational studies showed moderate to serious overall risk of bias, particularly in domains related to confounding, participant selection, outcome measurement and incomplete reporting. In contrast, randomized controlled trials generally demonstrated more favorable methodological profiles and a lower apparent risk of bias across the assessed domains. Therefore, the interpretation of the findings should consider the potential limitations arising from methodological heterogeneity and study-level bias. Detailed assessments are shown in Figures 2 and 3.

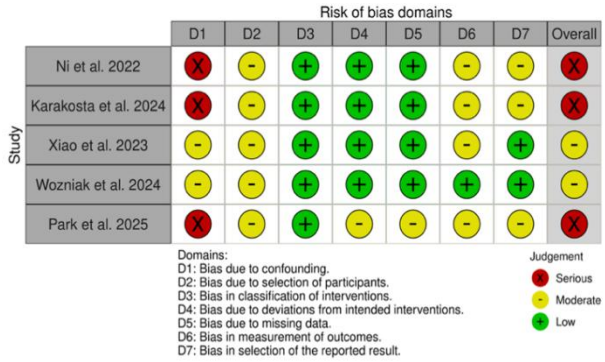

Figure 2. Risk of bias assessment in observational studies.

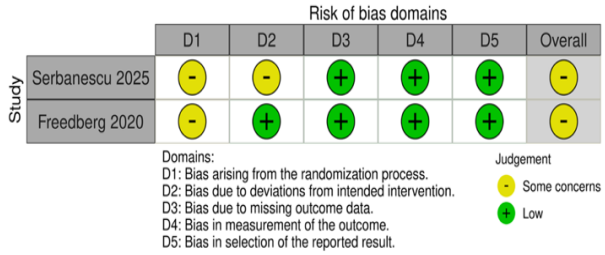

Figure 3. Risk of bias assessment in randomized controlled trials.

Discussion

This systematic review aimed to synthesize the current evidence regarding the relationship between enteral nutrition and gut microbiota modulation and to explore its possible implications for small intestinal bacterial overgrowth (SIBO)-related outcomes among critically ill patients. Studies directly evaluating the gut microbiota have shown that critical illness is associated with reduced microbial diversity and increased abundance of opportunistically pathogenic bacteria (Wozniak et al., 2024; Ni et al., 2022). Studies assessing enteral nutrition strategies suggest that fiber or prebiotic-enriched formulations may influence microbial composition by affecting short-chain fatty acid (SCFA)-producing bacteria, although the findings remain heterogeneous (Freedberg et al., 2020; Serbanescu et al., 2025). Studies focusing on gastrointestinal outcomes have reported that enteral feeding intolerance is associated with poorer nutritional adequacy and adverse clinical outcomes (Xiao et al., 2023; Park et al., 2025). Direct evidence regarding SIBO remains limited because only one of the included studies specifically evaluated this outcome; therefore, conclusions regarding SIBO should be interpreted cautiously (Karakosta et al., 2024). These findings suggest that enteral nutrition may influence intestinal microbial dynamics during critical illness, although the clinical significance of these interactions remains unclear (Blaser et al., 2021; Singer et al., 2019; Freedberg et al., 2020).

The present findings are consistent with previous evidence showing that critical illness profoundly affects the intestinal physiology and microbial composition. Critical illness is associated with systemic inflammation, intestinal hypoperfusion, oxidative stress, and disruption of epithelial barrier integrity, all of which contribute to alterations in microbial ecology (Haak & Wiersinga, 2021; Wozniak et al., 2022; Wozniak et al., 2024). The intestinal microbiota normally exists in a balanced environment in which commensal microorganisms support nutrient metabolism, regulate immune responses, produce beneficial metabolites, and maintain barrier functions (Haak & Wiersinga, 2021). In critically ill patients, multiple factors, including broad-spectrum antibiotics, proton pump inhibitors, vasopressor therapy, mechanical ventilation, prolonged fasting, and gastrointestinal dysmotility may disrupt the microbial balance and promote gut dysbiosis (Haak & Wiersinga, 2021; Wozniak et al., 2022; Wozniak et al., 2024). These alterations contribute to the loss of commensal microorganisms and increased colonization by pathogenic bacteria (Wozniak et al., 2024; Ni et al., 2022).

The reduction in microbial diversity observed in critically ill patients may have important physiological implications. Reduced microbial diversity has been associated with the

loss of microbial resilience and reduced production of beneficial metabolites, such as short-chain fatty acids. Short-chain fatty acids, including acetate, propionate, and butyrate, contribute to the maintenance of epithelial integrity, regulation of immune responses, and suppression of intestinal inflammation **(**Freedberg et al., 2020; Serbanescu et al., 2025). Reduced production of these metabolites may compromise intestinal barrier function and increase intestinal permeability, facilitating bacterial translocation and systemic inflammatory activation (Haak & Wiersinga, 2021; Woźniak et al., 2022). These mechanisms may explain the observed association between dysbiosis and adverse clinical outcomes, including enteral feeding intolerance, infection, and increased mortality (Wozniak et al., 2024; Ni et al., 2022; Park et al., 2025). Our findings also demonstrated that enteral nutrition may influence the gut microbiota composition; however, the observed effects varied across studies. Several studies have reported that fiber-containing or prebiotic-enriched enteral formulas promote the growth of short-chain fatty acid–producing bacteria and improve microbial balance. These findings are supported by evidence demonstrating that fermentable substrates may stimulate beneficial microorganisms and support intestinal barrier integrity. Short-chain fatty acids generated through microbial fermentation may strengthen epithelial tight junctions and modulate inflammatory responses (Freedberg et al., 2020; Serbanescu et al., 2025). Consequently, enteral nutrition may contribute not only to energy provision but also to the preservation of gastrointestinal physiology; however, its potential effects on the gut microbiota may vary with the formula composition, fiber and prebiotic content, illness severity, antibiotic exposure, and baseline microbial characteristics.

However, the beneficial effects of enteral nutrition on microbiota composition have not been consistently observed across studies. Serbanescu et al. demonstrated that under severe dysbiosis, particularly among critically ill patients receiving broad-spectrum antibiotics, prebiotic supplementation may promote the expansion of pathogenic microorganisms, such as *Enterobacteriaceae*. These findings indicate that microbiota responses to nutritional interventions are highly dependent on baseline microbial conditions and clinical characteristics (Serbanescu et al., 2025). Therefore, microbiota-targeted nutritional interventions should be individualized and interpreted in the context of patient-specific conditions. An important aspect identified in this review is the relationship between microbiota disturbance and gastrointestinal dysfunction. Enteral feeding intolerance remains one of the most common complications among critically ill patients and frequently interferes with the achievement of nutritional goals in these patients. The relationship between the gut microbiota and gastrointestinal function is bidirectional. Microbiota disturbances may impair intestinal motility, increase bacterial fermentation, and alter intestinal permeability, whereas prolonged fasting and inadequate nutritional delivery may further aggravate dysbiosis (Reintam Blaser et al., 2020; Xiao et al., 2023; Park et al., 2025). This interaction may create a cycle in which gastrointestinal dysfunction and microbiota disturbance reinforce each other (Xiao et al., 2023; Park et al., 2025).

The findings of this review further suggest that small intestinal bacterial overgrowth may coexist with gut microbiota disturbance in critically ill patients; however, direct evidence supporting this relationship is limited (Karakosta et al., 2024; Wozniak et al., 2024). Small intestinal bacterial overgrowth is characterized by excessive bacterial colonization within the small intestine and may impair digestion and nutrient absorption through mechanisms involving bile acid deconjugation, competition for nutritional substrates, and excessive fermentation (Pimentel et al., 2020; Quigley, 2020; Quigley & Murray, 2021).

Karakosta et al. reported that the prevalence of small intestinal bacterial overgrowth in critically ill patients was approximately 36.5%. The study also demonstrated an association between small intestinal bacterial overgrowth and increased infections, as well as prolonged ICU stay. Reduced gastrointestinal motility due to sedation, opioid administration, and critical illness may facilitate intestinal stasis and bacterial accumulation. Furthermore, broad-spectrum antibiotics and acid-suppressive therapy may further disrupt the microbiota balance and reduce protective mechanisms against bacterial colonization (Karakosta et al., 2024). Reduced short-chain fatty acid production may impair intestinal motility and mucosal integrity, thereby facilitating bacterial overgrowth in the small intestine. A comparison with the previous literature indicates that although

evidence regarding microbiota alterations in critically ill patients is relatively consistent, direct evidence specifically evaluating small intestinal bacterial overgrowth remains limited (Wozniak et al., 2024; Karakosta et al., 2024; Ni et al., 2022; Xiao et al., 2023; Park et al., 2025). Most studies have evaluated microbiota diversity, nutritional interventions, or gastrointestinal outcomes independently, rather than integrating these components into a comprehensive pathophysiological framework (Wozniak et al., 2024; Freedberg et al., 2020; Ni et al., 2022). Therefore, this review provides additional insights by integrating enteral nutrition, gut microbiota modulation, and the risk of small intestinal bacterial overgrowth into a unified conceptual model.

From a clinical perspective, these findings suggest that enteral nutrition strategies should not focus exclusively on caloric delivery but should also consider microbiota-related effects. Early enteral nutrition administered within 24–48 h may help preserve intestinal barrier integrity and support gastrointestinal function (Blaser et al., 2021; Singer et al., 2019). The formula composition should also be carefully considered, as nutritional substrates may influence bacterial fermentation and microbial balance (Reintam Blaser et al., 2020). This review had several strengths. To our knowledge, this is one of the first systematic reviews to integrate enteral nutrition, gut microbiota modulation, and the risk of small intestinal bacterial overgrowth into a unified pathophysiological framework. Furthermore, this review included both microbiological and clinically relevant outcomes such as feeding intolerance, infection, and mortality (Wozniak et al., 2024; Karakosta et al., 2024; Ni et al., 2022; Xiao et al., 2023; Park et al., 2025).

However, this study has several limitations. The number of included studies was relatively small, and substantial heterogenei ty existed in terms of study design, interventions, microbiota assessment methods, and reported outcomes. Most of the included studies were observational, which limited causal inference. Furthermore, direct evidence of small intestinal bacterial overgrowth remains limited, as only one study specifically evaluated this condition (Karakosta et al., 2024). Therefore, future prospective studies involving direct assessment of small intestinal bacterial overgrowth are required to further clarify the relationship between enteral nutrition, microbiota modulation, and clinical outcomes in critically ill populations.

Conclusion

This systematic review suggests that critically ill patients frequently experience gut dysbiosis, which is associated with gastrointestinal complications and adverse outcomes. Enteral nutrition, particularly fiber- or prebiotic-enriched formulas, may influence the gut microbiota composition and abundance of short-chain fatty acid (SCFA)-producing bacteria, although the findings remain inconsistent and appear to be affected by antibiotic exposure and clinical severity. Direct evidence of Small Intestinal Bacterial Overgrowth (SIBO) in critically ill patients remains limited. Further prospective studies using standardized microbiota and SIBO assessment methods are needed before specific enteral nutrition strategies can be recommended for SIBO-related risk reduction in patients with obesity.

Several limitations should be acknowledged, including the limited number of heterogeneous studies and the scarcity of direct evidence evaluating the small intestinal bacterial overgrowth. Future prospective studies with direct assessment of small intestinal bacterial overgrowth are needed to strengthen the current evidence.

Declaration of Conflict of Interest

The authors declare that they have no financial, personal, or professional relationships with any individuals, institutions, or organizations that could have inappropriately influenced the design, conduct, interpretation, or reporting of this systematic review.

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