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EDITED BY
Nazarii Kobyliak,
Bogomolets National Medical University, Ukraine

REVIEWED BY
Yongfang Xie,
School of Bioinformatics, Chongqing University of Posts and Telecommunications, China
Suchitra M.R.,
SASTRA University, India

*CORRESPONDENCE
Hexiao Shen
shenhxmyt@163.com
Guang Fu
fuguang71@163.com
Yi Dai
31646802@qq.com

†These authors have contributed equally to this work

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Fecal microbiota transplantation in patients recovering from severe pneumonia: an exploratory single-arm pilot study

Fang Zhou[1†], Can Yu[1†], Yongling Lv[2†], Jun Zhang[1], Liping Yu[1], Tingting Shu[1], Lei Duan[3], Xianfeng Zhou[4], Guolong Li[2], Chao Zheng[1], Juan Wu[5], Yuan Xu[1], Yuanyuan Li[1], Hexiao Shen[2*], Guang Fu[3*] and Yi Dai[1*]

[1]Wuhan Hospital of Traditional Chinese Medicine, Wuhan, China, [2]School of Life Science, Hubei University, Wuhan, Hubei, China, [3]Wuhan Puren Hospital, Wuhan, China, [4]School of Materials and Chemical Engineering, Hubei University of Technology, Wuhan, China, [5]Hubei University of Chinese Medicine, Hube, Wuhani, China

Objective: To explore the potential association of fecal microbiota transplantation (FMT) with gastrointestinal symptoms and intestinal dysbiosis in patients recovering from severe pneumonia.

Methods: A total of 15 adult patients with confirmed severe pneumonia were enrolled. One patient died and two were excluded from clinical analysis because timely blood routine data were unavailable; therefore, 12 patients were included in the clinical evaluation. FMT was administered once daily for six consecutive days via a colonoscopically placed catheter at the cecum. Clinical evaluations and blood samples were conducted at baseline and one week post-treatment. Fecal samples from six patients were collected at baseline and six months post-FMT and analyzed using metagenomic sequencing.

Results: After FMT treated for one week, five out of 12 patients reported symptom improvement, and nine out of 10 who had experienced fever before showed resolution within two weeks following treatment. Analysis of the gut microbiota (Beta diversity) revealed that the gut microbiota composition of recipients converged toward that of their donors post-FMT, which suggests that the improvement in symptoms might be related to FMT treatment. Specifically, at the phylum level, the relative abundance of Proteobacteria and Actinobacteria decreased, whereas Firmicutes and Bacteroidetes increased after FMT compared to baseline. At the genus level, a significant enrichment of common commensal bacteria (e.g. *Phocaeicola*, *Parabacteroides*, *Lachnospira*, and *Phascolarctobacterium*) was observed after FMT, while pathogenic genera such as *Vibrio*, *Streptococcus*, and *Enterobacter* were significantly reduced. Further analysis of the functions of the microbial community revealed a significant shift in microbial functional profiles toward the donor state after FMT, marked by the upregulation of core metabolic and cellular processes and the downregulation of pathways linked to infections, which collectively indicate a functional restoration of the gut microbiome.

Conclusions: This study suggests that FMT may be closely related to the improvement of symptoms in patients with severe pneumonia and the restoration of intestinal microbial homeostasis. These findings suggest that FMT may be associated with therapeutic benefit and could represent a feasible rehabilitative strategy for individuals recovering from severe pneumonia.

KEYWORDS

FMT, gut microbiota, homeostasis, metagenomes, severe pneumonia

1 Introduction

Numerous symbiotic bacteria reside on the mucosal surfaces of human organs, including the skin, gastrointestinal tract, and respiratory system. The vast majority of these microorganisms is as high as trillions, and the vast majority of them are located in the gastrointestinal tract (Gill et al., 2006). In recent years, extensive research has demonstrated the beneficial roles of commensal microbiota, including their capacity to modulate host immunity, resist infections, enhance nutrient metabolism, and maintain intestinal homeostasis (Gilbert et al., 2018; Negi et al., 2019a, 2019b). Notably, the "gut-lung axis" represents a critical bidirectional communication pathway between the gut microbiota and the lungs, which has been shown to influence pulmonary health (Keely et al., 2012). Indeed, multiple studies have established an association between alterations in gut microbial composition and susceptibility to respiratory infections (Groves et al., 2020). The intestinal microbiota regulates the systemic immune response through metabolites (such as short-chain fatty acids) and the migration of immune cells, influencing the lung's ability to defend against pathogens (Wen et al., 2021). Consequently, intestinal microbiota dysbiosis can exacerbate the severity of respiratory tract infections, possibly by disrupting immune homeostasis and leading to excessive inflammatory responses (Sencio et al., 2021).

Pneumonia remains one of the leading causes of mortality worldwide, posing a substantial global health burden. According to the Global Burden of Disease Study 2023, lower respiratory infections (defined as physician-diagnosed pneumonia or bronchiolitis) caused an estimated 2.50 million deaths (95% uncertainty interval 2.24-2.81 million) and 98.7 million disability-adjusted life-years (DALYs) in 2023, representing the world's leading infectious cause of death (GBD 2023 LRI Collaborators, 2025). Children younger than 5 years and adults aged 70 years and older carry the highest burden, with preschoolers accounting for 610,000 deaths and older adults representing nearly half of all pneumonia fatalities (approximately 1.2 million deaths) (FIRS, 2025).Streptococcus pneumoniae continues to account for the largest share of LRI deaths globally (634,000 deaths, 25.3%), followed by Staphylococcus aureus (271,000 deaths, 10.9%) and Klebsiella pneumoniae (228,000 deaths, 9.1%) (GBD 2023 LRI Collaborators, 2025). In the United States, pneumonia mortality remains significant, with a crude death rate of 12.2 per 100,000 population reported in 2024 (CDC, 2026).

Severe community-acquired pneumonia (CAP), or severe pneumonia, is a severe clinical subtype with poor prognosis. According to the 2016 Chinese Thoracic Society guidelines, severe community-acquired pneumonia (CAP) is diagnosed by fulfilling any one major criterion or at least three minor criteria. The major criteria include requirement for tracheal intubation with mechanical ventilation, and septic shock necessitating vasoactive agents despite aggressive fluid resuscitation. Minor criteria comprise respiratory rate ≥30 bpm, oxygenation index ≤250 mm Hg, multilobar pulmonary infiltrates, altered mental status, blood urea nitrogen ≥7.14 mmol/L, and systolic blood pressure <90 mm Hg requiring active fluid resuscitation. The recovery phase is defined based on clinical, physiological and inflammatory improvements as outlined in the same guideline (Cao et al., 2018). Intestinal dysbiosis and impaired gut barrier function have been consistently observed in patients with severe pneumonia (Perdijk et al., 2024). Disruption of the gut microbiota may adversely affect the recruitment and function of immune cells in the lungs, potentially increasing vulnerability to severe pneumonia infection and contributing to worse clinical outcomes (Anand and Mande, 2018; Legoux et al., 2020). Reduced abundance and diversity of gut microbiota are linked to various pathological conditions. For instance, elderly individuals typically exhibit lower microbial diversity, with a marked decline in beneficial genera such as *Bifidobacterium* (Claesson et al., 2012). It is therefore plausible that a cross-talk mechanism exists between the lung and gut microbiota in the context of severe pneumonia, potentially influencing disease progression—particularly in elderly or immunocompromised individuals who are at higher risk of severe outcomes. Furthermore, emerging evidence highlights a significant interaction between gut microbiota and angiotensin-

Abbreviations: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALP, Alkaline Phosphatase; CG, Cholyglycine; GDH, Glutamate Dehydrogenase; TP, Total Protein; ALB, Albumin; GLO, Globulin; NG, Not Given; TBIL, Total Bilirubin; DBIL, Direct Bilirubin; IBIL, Indirect Bilirubin; GGT, Gamma-Glutamyl Transferase; TBA, Total Bile Acid; GLU, Glucose; CO2CP, Carbon Dioxide Combining Power; BUN, Blood Urea Nitrogen; CREA, Creatinine; UA, Uric Acid; CysC, Cystatin C; K, Potassium; Na, Sodium; Cl, Chloride; Ca, Calcium; MBC, Mononuclear Blood Cell; LYM%, Lymphocyte Percentage; MON%, Monocyte Percentage; NEU%, Neutrophil Percentage; EOS%, Eosinophil Percentage; BAS%, Basophil Percentage; RBC, Red Blood Cell; HCT, Hematocrit; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Hemoglobin; MCHC, Mean Corpuscular Hemoglobin Concentration; RDW, Red Cell Distribution Width; HGB, Hemoglobin; PLT, Platelet; MPV, Mean Platelet Volume; PDW, Platelet Distribution Width; PCT, Plateletcrit; P-LCR, Platelet-Large Cell Ratio; RDW-SD, Red Cell Distribution Width-Standard Deviation; NEU#, Neutrophil Absolute Count; LYM#, Lymphocyte Absolute Count; MON#, Monocyte Absolute Count; EOS#, Eosinophil Absolute Count; BAS#, Basophil Absolute Count.

converting enzyme 2 (ACE2), a key regulator of dietary amino acid homeostasis, innate immunity, and microbial ecology, which also plays a role in viral entry and replication (Hashimoto et al., 2012). These findings suggest that targeting the gut microbiota may represent a novel therapeutic strategy or a viable adjunctive treatment for severe pneumonia.

Fecal microbiota transplantation (FMT) is an effective intervention for restoring gut microbial balance and replenishing beneficial microbes (Hensley-McBain et al., 2016; Ooijevaar et al., 2019). Studies have indicated that FMT can enhance immune function and may serve as a potential therapy for individuals with infectious diseases (Ekmekciu et al., 2017; Wardill et al., 2019; Kim et al., 2020). Studies have shown that bacteria that produce butyric acid can protect against bacterial pneumonia (Kullberg et al., 2025). Multiple meta-analyses have shown that probiotic intervention (including Bifidobacterium, Enterococcus, Lactobacillus, and Streptococcus, etc.) can significantly reduce the incidence of ventilator-associated pneumonia (VAP), shorten the length of ICU stay (by an average of 1.65 days), and reduce the duration of mechanical ventilation, as well as lower the mortality rate (Anvarifard et al., 2024). Oral probiotics can regulate respiratory immune responses through signaling pathways. Bifidobacteria can promote the balance of Th1/Th2 cells and upregulate the secretion of IFN-γ, IL-4 and IL-12 in the spleen (Ye et al., 2025). Additionally, FMT can regulate the host's immune response, for instance, by influencing T cell differentiation, promoting the production of anti-inflammatory cytokines (such as IL-10) and inhibiting the release of pro-inflammatory cytokines (such as IL-6, TNF-α), thereby alleviating excessive inflammatory responses in the lungs and promoting lung tissue repair (Horn and Sonnenberg, 2024; Dong et al., 2024). Collectively, these findings support the potential of FMT as a therapeutic and rehabilitative approach for managing severe pneumonia.

Given the high prevalence of gastrointestinal manifestations and immune dysregulation in post-severe pneumonia patients, we hypothesize that FMT may be associated with beneficial effects on intestinal microbial homeostasis and with alleviation of gastrointestinal symptoms, and may mitigate persistent severe pneumonia-related gut dysfunction. In this pilot study, we recruited 15 patients recovering from severe pneumonia to evaluate the safety, efficacy, and microbiological impact of FMT, aiming to evaluate the potential of FMT in improving conditions associated with intestinal microbiome disruption.

2 Materials and methods

2.1 Study population

A total of 15 adult patients with confirmed severe pneumonia were recruited from Wuhan Puren Hospital in December 2022. All participants voluntarily enrolled in this clinical trial and provided written informed consent. Inclusion criteria were as follows: 1) age between 26 and 91 years, with no restrictions based on gender; 2) laboratory confirmation of intestinal dysfunction-related conditions characterized by symptoms such as nausea, vomiting, diarrhea, abdominal distension, or mucus discharge; and 3) a positive diagnosis for severe pneumonia. Exclusion criteria included: 1) pregnancy or plans for pregnancy during the study period; 2) uncertainty regarding the procedure or a history of significant medical risks; 3) presence of advanced-stage disease or imminent risk of mortality; 4) participation in any other clinical trial within three months prior to enrollment; 5) concurrent infections such as pneumonia, peritonitis, or pleural tumors requiring treatment with restricted-use antimicrobial agents; 6) recent receipt of any form of microbiota-based therapy; 7) severe cardiac, pulmonary, hepatic, or renal insufficiency; 8) positive serological tests for tuberculosis, syphilis, or HIV; 9) severe anemia (hemoglobin < 6 g/dL), generalized lymphadenopathy, or marked leukopenia; and 10) any condition arising during the study that might compromise participant compliance, completion of the trial, or present clinical contraindications to the intervention. Throughout the study, the research team provided comprehensive guidance to ensure proper administration of the transplant procedure and appropriate supportive care. All participants were instructed to refrain from using antibiotics or anti-inflammatory medications for at least two weeks before and during the intervention period. A detailed timeline documenting each patient's diagnosis, hospital discharge, and study enrollment was compiled. This study was approved by the Medical Ethics Review Board of Wuhan Puren Hospital (Ethics Number: LHLL202200101).

2.2 Study purpose and outcomes

In this study, blood routine tests, blood biochemical parameters, and intestinal microbial metagenomic data were collected from all patients before and after FMT. The clinical and laboratory changes after FMT were assessed by evaluating changes in blood routine and biochemical indices one week post-transplantation. Additionally, microbial diversity and metagenomic profiles before and after FMT were compared to further investigate the impact of FMT on gut microbiota restoration and bacterial engraftment.

2.3 Intervention procedures

The fecal microbiota from qualified donors was isolated and encapsulated using automated processing technology (Maintainbio tech. Ltd. (Wuhan)., Wuhan, China). Prior to transplantation, patients were sedated, and the fecal microbiota samples were thawed and allowed to reach room temperature one hour in advance. During the procedure, colonoscopy was performed to ensure catheter placement at the cecum. Fecal microbiota was administered via a colon catheter (Maintainbiotech. Ltd. (Wuhan)). Patients were positioned in the left lateral decubitus position and instructed to maintain normal breathing throughout the procedure. The catheter was flushed with 20 mL of saline for 2–3 minutes before each infusion. Subsequently, 50 mL of fecal microbiota suspension was slowly infused through the catheter over approximately 3 minutes. After infusion, the catheter was flushed again with 5 mL of saline, and patients were required to remain recumbent for at least 2 hours post-procedure. To ensure patient privacy and psychological comfort, the preparation and administration were conducted in a private setting. Temperature control during

sample handling is critical, as excessive cold may trigger immediate bowel movement, potentially compromising engraftment. Patients were advised to avoid antibiotics and alcohol consumption for at least six months following fecal microbiota transplantation. FMT was administered once daily for six consecutive days (treatment days 1 to 6); the 50 mL infusion described above was repeated on each treatment day.

2.4 Metagenomic sequencing of fecal microbiota

Six patients provided fecal samples at baseline (before FMT) and six months after FMT, and four donors also provided fecal samples. Among them, one donor transplanted feces to two patients. Fecal samples were collected from both donors and severe pneumonia patients before and after FMT using dedicated fecal sampling tubes. Each sample was labeled with relevant identification information and immediately stored in an ultra-low temperature freezer at -80 °C to preserve microbial integrity. Genomic DNA was extracted from the stool samples using the HiPure Stool DNA Mini Kit (Magen, Guangzhou, China). DNA library preparation was performed according to the manufacturer's protocol for the FS Pro DNA Lib Prep Kit V2 (ABclonal, Wuhan, China), including steps of fragmentation, end repair, dA tailing, and adapter ligation. The constructed DNA libraries were stored at -20 °C until shipment for sequencing. Sequencing was conducted on the BGI DNBSEQ-T7 platform (BGI, Shenzhen, China) using a standard BGI pipeline with PE150 read chemistry. Raw reads were processed to remove PCR duplicates using FastUniq (v1.1). Adaptor sequences and low-quality reads were filtered out using Trimmomatic (v0.39), and host-derived contaminant sequences were subsequently removed to generate clean reads. *De novo* assembly of clean reads into contigs was performed using MEGAHIT. Open reading frames (ORFs) within the contigs were predicted *de novo* using MetaGeneMark. Taxonomic classification of the assembled contigs was conducted using Kraken2.

2.5 Statistical analysis

Alpha diversity indices, including Chao1 and Shannon, were calculated using the R package 'vegan' (version 2.5-6) to assess microbial richness and diversity within samples. A distance matrix between samples was constructed based on the binary Jaccard dissimilarity metric. Beta diversity was evaluated through Principal Coordinate Analysis (PCoA) and Non-metric Multidimensional Scaling (NMDS), both derived from the computed distance matrix. A heatmap of species abundance profiles was generated to visualize key taxa exhibiting differential abundance across sample groups. Additionally, LEfSe (Linear Discriminant Analysis Effect Size) analysis was performed to identify taxonomic biomarkers by combining Kruskal-Wallis rank sum tests with linear discriminant analysis (LDA). Statistical comparisons for detecting significantly divergent taxa were conducted in R (version 3.4.1) using paired Wilcoxon signed-rank tests for pre-post comparisons and unpaired rank-sum tests, depending on data distribution and variance assumptions. All figures were generated using R scripts (version 4.3.1) within RStudio (version 2023.06.1).

3 Results

3.1 Baseline characteristics of patient

A total of 15 patients with confirmed severe pneumonia received FMT. One patient died during the study period, and two patients were excluded from the analysis due to the lack of timely blood routine data. Therefore, 12 patients were included in the clinical and symptom evaluation (Table 1). All enrolled participants met the diagnostic criteria for severe pneumonia issued by the Chinese Thoracic Society in 2016 at the early disease stage. After conventional anti-infection and supportive treatment, the clinical conditions of most patients gradually improved. At the time of

TABLE 1 Baseline characteristics of 12 patients with severe pneumonia.

Number	Gender	Age	Date of diagnosis	Date of FMT	Date of relief	Severity of severe pneumonia
1	Female	55	2022/12/6	2022/12/10	2022/12/15	Non-severe
2	Male	47	2022/12/6	2022/12/9	2022/12/22	Non-severe
3	Female	26	2022/12/5	2022/12/9	2022/12/14	Non-severe
4	Female	64	2022/12/7	2022/12/11	2022/12/16	Non-severe
5	Female	43	2022/12/11	2022/12/11	2022/12/14	Non-severe
6	Male	82	2022/12/18	2022/12/30	2023/1/5	Non-severe
7	Female	71	2022/12/23	2022/12/29	2023/2/7	severe
8	Female	91	2022/12/28	2022/12/31	2023/1/20	severe
9	Female	81	2022/12/25	2022/12/31	2023/1/3	Non-severe
10	Male	66	2022/12/19	2022/12/31	2022/1/5	severe
11	Female	49	2022/12/1	2022/12/7	2022/12/8	Non-severe
12	Female	64	2022/12/27	2023/1/1	2023/1/6	Non-severe

study enrollment, nine patients had relieved symptoms and presented only mild clinical manifestations, and no deterioration or re-progression to severe pneumonia occurred during hospitalization. Three patients still maintained severe clinical status at enrollment. The age of the 12 included patients ranged from 26 to 91 years, and 9 (75%) were female. Fecal microbiota samples before and after FMT from six patients were used for gut microbiota analysis, while the other six patients were lost to follow-up and excluded from microbial analysis.

3.2 Gastrointestinal symptoms and blood routine examination before and after FMT

In general, 5 out of 12 patients experienced gastrointestinal symptoms to varying degrees before and after diagnosis. These symptoms included constipation, diarrhea, abdominal distension, gastric acid reflux, and proctitis. Gastrointestinal manifestations were present at hospital admission and persisted following discharge. After approximately one week of continuous FMT treatment, five patients reported subjective improvement in their gastrointestinal symptoms. Concurrently, systemic and respiratory symptoms were common at baseline. Among the 12 patients, 10 presented with fever at baseline, with 9 achieving resolution within two weeks post-FMT. One patient experienced intermittent fever lasting approximately one month before complete defervescence. Notably, other respiratory symptoms, such as cough, sore throat, chest tightness, and shortness of breath also showed clear improvement after FMT, suggesting a potential broader symptomatic benefit (Table 2). Most laboratory findings indicated that routine blood parameters in post-severe pneumonia patients, including complete blood count indices, remained within normal reference ranges both before and after FMT, with no statistically significant changes observed, which may be attributed to the relatively short interval between sample collections, potentially insufficient to capture meaningful physiological changes (Table 3).

3.3 Serum biochemical indices of severe pneumonia patients before and after FMT

Significant changes were observed in serum levels of TBIL, DBIL, IBIL, GGT, GLU, CO2CP, ALP, and P-LCR in severe pneumonia patients following FMT compared to baseline ($P < 0.05$). Notably, there was a significant reduction in the concentrations of TBIL, DBIL, IBIL, and P-LCR after FMT (Table 3). Additionally, the magnitude of improvement in GGT, GLU, CO2CP, and ALP levels was greater post-FMT relative to pre-FMT values, with statistically significant differences ($P < 0.05$) (Figure 1).

3.4 Richness and diversity of gut microbiota after FMT

The fecal microorganisms of the donors and the patients before and after FMT were analyzed. The results show that at the phylum level, Firmicutes, Proteobacteria, Bacteroidetes, and Actinobacteria were the predominant bacterial taxa across all groups. Following FMT, the relative abundance of Proteobacteria and Actinobacteria decreased, while that of Firmicutes and Bacteroidetes increased compared to pre-FMT levels (Figure 2A). The Chao index and Shannon index were used to assess species richness and diversity, respectively. The results showed that fecal microbial richness and diversity slightly decreased after FMT compared to baseline levels; however, no statistically significant difference was observed between the two time points. In contrast, both the Chao and Shannon indices in donors were higher than those in recipients; however, these differences did not reach statistical significance when compared to pre- and post-FMT samples (Figures 2B, C). Furthermore, beta diversity analysis based on the binary Jaccard dissimilarity metric suggested a significant shift in fecal microbial composition between the pre- and post-FMT samples. Notably, the microbial profile after FMT showed greater similarity to that of the donor than before FMT (Figures 2D, E).

TABLE 2 Symptoms in 12 patients with severe pneumonia before and after fecal microbiota transplantation (FMT).

Symptom categories	Specific ymptoms	Pre-FMT n(%)	Symptoms relieved Post-FMT n(%)
GI symptoms	Constipation	1 (8.3%)	1 (100%)
	abdominal distension	3 (25.0%)	2 (66.7%)
	Diarrhea	5 (41.7%)	5 (100%)
	Gastrectasia/Acid reflux	3 (25.0%)	3 (100%)
	GI symptoms (in total)	5 (41.7%)	5 (100%)
Respiratory symptoms	sore-throat	2 (16.7%)	2 (100%)
	cough	8 (66.7%)	7 (87.5%)
	oppression in chest	1 (8.3%)	1 (100%)
	expectoration	2 (16.7%)	2 (100%)
Generalized symptoms	muscular soreness	1 (8.3%)	1 (100%)
	fever	10 (83.3%)	9 (90.0%)

10.3389/fcimb.2026.1917445

TABLE 3 Clinical data included in this study.

Variable	6 month post-FMT	Baseline	P value	Variable	6 month post-FMT	Baseline	P value
ALT	26.68 ± 16.78	23.78 ± 12.75	0.280	MBC	8.51 ± 3.52	7.4 ± 3.71	0.227
AST	20.85 ± 6.90	26.79 ± 12.41	0.067	LYM%	18.41 ± 9.59	22.20 ± 12.05	0.145
ALP	71.21 ± 12.43	61.64 ± 15.20	0.044	MON%	7.73 ± 3.52	6.91 ± 2.65	0.211
CG	2.01 ± 0.84	1.96 ± 1.33	0.446	NEU%	72.59 ± 10.50	69.66 ± 13.74	0.242
GDH	4.7 ± 2.99	4.56 ± 3.69	0.457	EOS%	0.97 ± 1.22	0.84 ± 1.02	0.376
TP	67.27 ± 7.63	67.45 ± 6.34	0.459	BAS%	0.28 ± 0.25	0.39 ± 0.29	0.177
ALB	36.94 ± 6.12	36.10 ± 6.26	0.221	RBC	4.00 ± 0.63	3.95 ± 0.54	0.374
GLO	30.34 ± 5.00	31.35 ± 5.05	0.255	HCT	36.73 ± 5.80	35.71 ± 5.49	0.237
NG	1.25 ± 0.29	1.19 ± 0.34	0.226	MCV	91.17 ± 5.40	90.39 ± 5.74	0.149
TBIL	6.73 ± 2.89	9.98 ± 4.01	0.021	MCH	30.66 ± 2.36	30.43 ± 1.63	0.307
DBIL	2.33 ± 0.90	3.50 ± 1.59	0.020	MCHC	336.09 ± 12.72	339.09 ± 11.16	0.312
IBIL	4.41 ± 2.70	6.48 ± 3.17	0.047	RDW	13.07 ± 1.70	12.35 ± 0.67	0.057
GGT	26.62 ± 12.11	21.48 ± 11.40	0.033	HGB	123.45 ± 22.50	120.55 ± 17.96	0.239
TBA	5.09 ± 4.57	4.63 ± 5.25	0.403	PLT	273.82 ± 89.86	249.73 ± 75.02	0.192
GLU	9.93 ± 4.68	7.62 ± 3.70	0.019	MPV	12.12 ± 2.13	13.37 ± 2.19	0.076
CO2CP	25.74 ± 2.20	23.95 ± 1.82	0.045	PDW	10.03 ± 1.30	10.48 ± 1.11	0.060
BUN	6.10 ± 3.39	5.28 ± 1.50	0.165	PCT	0.27 ± 0.09	0.26 ± 0.08	0.320
CREA	83.45 ± 70.01	63.96 ± 14.15	0.164	P-LCR	22.37 ± 7.70	25.89 ± 7.40	0.022
UA	287.45 ± 127.26	275.22 ± 120.81	0.305	RDW-SD	41.95 ± 3.51	40.66 ± 1.71	0.094
CysC	1.22 ± 0.57	1.02 ± 0.21	0.122	NEU#	6.45 ± 3.27	5.54 ± 3.79	0.260
K	3.95 ± 0.43	3.76 ± 0.56	0.106	LYM#	1.38 ± 0.46	1.31 ± 0.42	0.362
Na	138.75 ± 4.07	138.32 ± 4.27	0.380	MON#	0.63 ± 0.40	0.47 ± 0.22	0.104
Cl	101.76 ± 4.73	102.77 ± 4.66	0.216	EOS#	0.09 ± 0.14	0.04 ± 0.04	0.139
Ca	2.17 ± 0.19	2.13 ± 0.19	0.181	BAS#	0.02 ± 0.02	0.03 ± 0.03	0.392

ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALP, Alkaline Phosphatase; CG, Cholyglycine; GDH, Glutamate Dehydrogenase; TP, Total Protein; ALB, Albumin; GLO, Globulin; NG, Not Given; TBIL, Total Bilirubin; DBIL, Direct Bilirubin; IBIL, Indirect Bilirubin; GGT, Gamma-Glutamyl Transferase; TBA, Total Bile Acid; GLU, Glucose; CO2CP, Carbon Dioxide Combining Power; BUN, Blood Urea Nitrogen; CREA, Creatinine; UA, Uric Acid; CysC, Cystatin C; K, Potassium; Na, Sodium; Cl, Chloride; Ca, Calcium.

3.5 Fecal microbiota composition altered after FMT in severe pneumonia patients

At the genus level, notable differences in the relative abundance of fecal microbiota were observed between post-FMT and pre-FMT samples. A total of 29 genera exhibited significant differences ($P < 0.05$) after FMT compared to the pre-intervention state (Figure 3A). Among these, the abundance of *Phocaeicola*, *Parabacteroides*, *Lachnospira*, *Phascolarctobacterium*, *Megamonas*, *Rhizous*, and *Providencia* increased significantly, while genera such as *Rhizopus*, *Bordetella*, *Staphylococcus*, *Acidovorax*, and *Anaerococcus* decreased. Notably, an increase in *Bacteroides* and *Prevotella*, though not pronounced across the entire cohort, was more evident in patients 1 and 3, who reported substantial clinical improvement of marked gastrointestinal symptoms post-FMT (Supplementary Figures S1A, B).

At the species level, Species that significantly increased after FMT included *Phocaeicola_vulgatus*, *Bacteroides_thetaiotaomicron*, *Oscillospiraceae_bacterium*, *Parabacteroides_distasonis*, *Phascolarctobacterium_faecium*, *Ruminococcaceae_bacterium*, *Alistipes_putredinis*, and *Methanobrevibacter_smithii* compared to pre-FMT levels. In contrast, species that significantly decreased after FMT primarily included *Vibrio_cholerae*, *Streptococcus_cristatus*, *Streptococcus_anginosus*, *Rhizopus_arrhizus*, *Enterobacter_kobei*, and *Bordetella_pertussis*, *Rothia_mucilaginosa* (Figure 3B). The top differentially abundant species are displayed in Figure 3C. Comparative analysis revealed 1211 bacterial species differed significantly between recipients before FMT and donors, and 721 species between post- FMT recipients and donors with 421 species were shared in both comparisons (Figure 3D). Using random forest analysis, we further identified the most discriminative species for classification, which were predominantly *Firmicutes_bacterium, Vescimonas_fastidiosa, Alistipes_putredinis, Mycobacteroides_abscessus, Rhodococcus_fascians* (Figure 3E).

3.6 Functional profiling of the fecal microbiota following FMT

Functional analysis based on KEGG orthology (KO) suggested a shift in the fecal microbial gene profiles of recipient after FMT toward those of donors. While functional composition differed significantly between pre- and post-FMT recipient samples, post-FMT samples showed increased functional similarity to donor

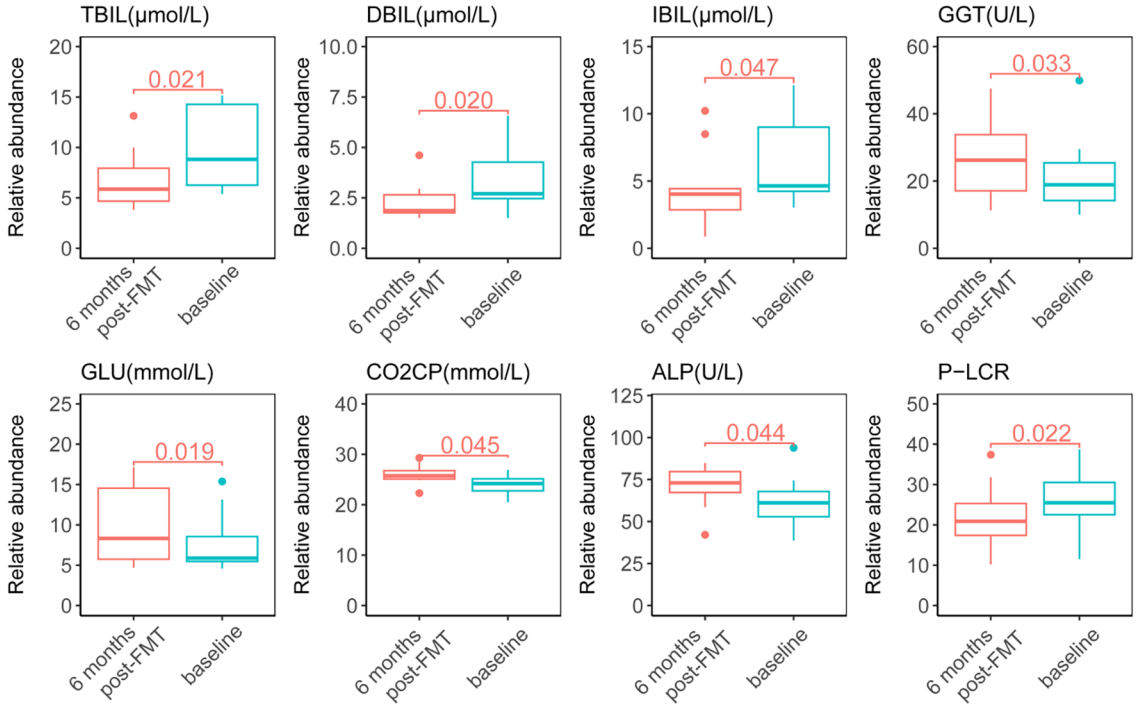


FIGURE 1
Changes in clinical parameters of patients before and after fecal microbiota transplantation (FMT). Paired comparisons between time points were performed using the Wilcoxon signed-rank test. TBIL, Total Bilirubin; DBIL, Direct Bilirubin; IBIL, Indirect Bilirubin; GGT, Gamma-Glutamyl Transferase; GLU, Glucose; CO2CP, Carbon Dioxide Combining Power; ALP, Alkaline Phosphatase; P-LCR, Platelet-Large Cell Ratio; Sample size, n = 12 patients at both pre-FMT and post-FMT stages. A p-value < 0.05 was considered statistically significant.

samples. KEGG analysis showed that metabolism, genetic information processing, and cellular processes were the most abundant functional categories across all groups (Supplementary Figure S2). Furthermore, carbohydrate metabolism exhibited the highest relative abundance (> 6%) in both the post-FMT and donor groups, followed by amino acid metabolism and energy metabolism. Notably, the relative abundance of these three metabolic pathways increased after FMT compared to pre-FMT levels (Supplementary Figure S2). Further comparative analysis of KEGG pathway abundances between recipients' pre- and post-FMT samples revealed differences in several functional categories, including replication and repair, signaling molecules and interaction, translation, and pathways related to infectious diseases (bacterial infections), xenobiotics biodegradation and metabolism, and immune system diseases (Figure 4A). In contrast, pathways associated with infectious diseases (e.g., bacterial infections), xenobiotics biodegradation and metabolism, and certain metabolic functions were downregulated. (Figure 4A). KEGG pathway enrichment analysis indicated a higher degree of functional similarity between recipients after FMT and donors. A total of 35 enriched pathways were identified between recipients before FMT and donors, whereas 25 enriched pathways were detected between recipients after FMT and donors. Of these, 9 pathways were common to both comparisons (Figure 4B). The top four enriched pathways shared between these two groups included Pathways in cancer, Neuroactive ligand–receptor interaction, Degradation of aromatic compounds, and Cytokine–cytokine receptor interaction (Figures 4C, D).

4 Discussion

The most common symptoms of patients with severe pneumonia include fever and respiratory tract involvement; however, a considerable number of patients also present with gastrointestinal (GI) symptoms such as diarrhea, nausea, vomiting and abdominal pain (Sun et al., 2025). The underlying mechanisms of GI symptoms may involve disruption of the intestinal mucosal barrier and the induction of pro-inflammatory mediators. At the same time, it can lead to intestinal flora imbalance due to factors such as antibiotic use, stress response and malnutrition, manifested as decreased microbial diversity, increased potential pathogenic bacteria and reduced beneficial bacteria (Sun et al., 2025; Tian et al., 2024). The imbalance of intestinal flora can damage the intestinal barrier function, promote the translocation of bacteria and toxins into the bloodstream, and exacerbate the systemic inflammatory response (Sun et al., 2025). The gut microbiota can activate both innate and adaptive immune responses, leading to the release of proinflammatory cytokines into systemic circulation, which contributes to widespread inflammation. Furthermore, severe pneumonia patients experiencing diarrhea have

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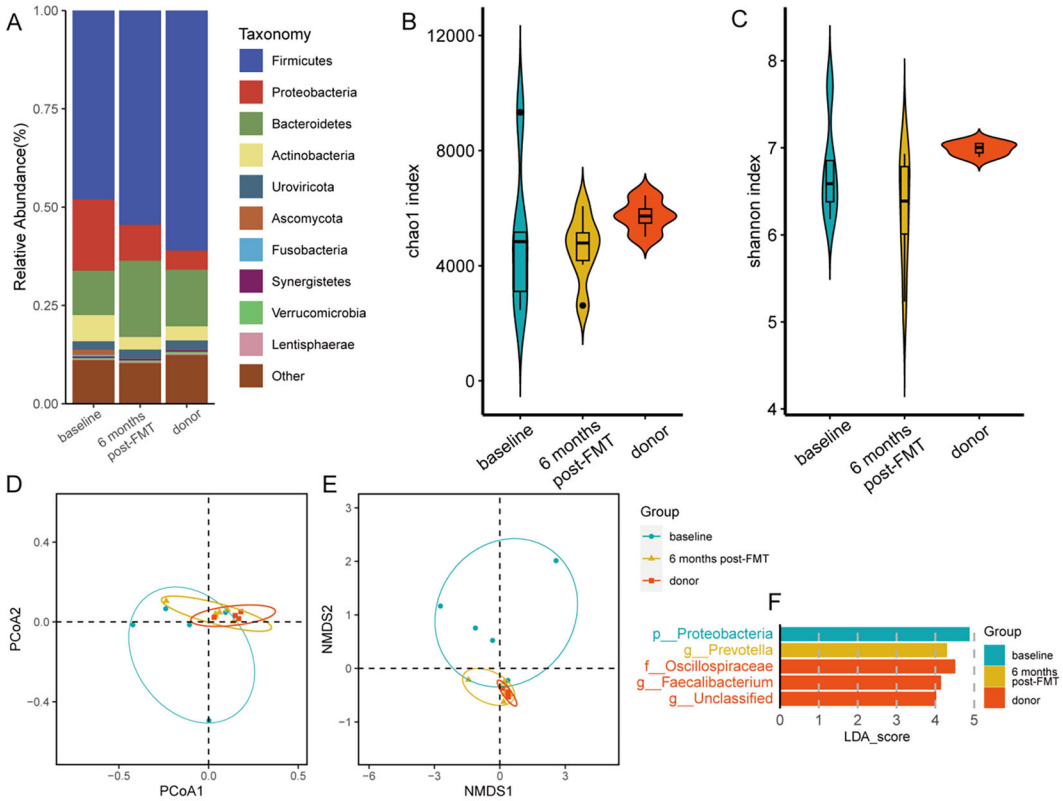


FIGURE 2
Alterations in gut microbiota composition before and after fecal microbiota transplantation (FMT) in patients with severe pneumonia. **(A)** Relative abundances of the dominant bacterial phyla across the three groups: pre-FMT, post-FMT, and donor. **(B, C)** Comparisons of alpha diversity indices, including microbial richness (Chao1 index) and Shannon diversity index. **(D, E)** Beta diversity differences among pre-FMT, post-FMT, and donor samples, visualized using principal coordinates analysis (PCoA) and non-metric multidimensional scaling (NMDS). **(F)** Linear discriminant analysis effect size (LEfSe) was applied to identify taxonomic biomarkers exhibiting significant differences among the three groups.

been shown to exhibit elevated serum levels of interleukin-6 (IL-6) and procalcitonin (PCT), biomarkers associated with inflammatory bowel conditions (Jullien et al., 2020). This pattern was also observed in our study. Pulmonary injury is a primary factor contributing to intestinal microbial dysbiosis. Evidence suggests that alterations in gut microbiota composition are correlated with disease severity and the magnitude of the host inflammatory response in severe pneumonia. Therefore, interventions such as probiotics or FMT may represent potential therapeutic strategies for managing the disease. Indeed, in early February 2020, the fifth edition of the guidelines issued by China's National Health Commission recommended the use of probiotics to maintain intestinal microbial balance and prevent secondary bacterial infections in patients with severe pneumonia. Notably, the relative abundances of *Lactobacillus*, *Bifidobacterium*, and *Faecalibacterium* have been identified as particularly significant indicators of gut health (Ferreira-Halder et al., 2017; Feng et al., 2019).

In this study, whether FMT represents an effective strategy to alleviate persistent post-severe pneumonia symptoms by modulating the intestinal microbiome was further investigated. The results showed that there were significant changes in gut microbial composition and clinical improvement following FMT, particularly among patients with severe gastrointestinal manifestations. This study focused on severe pneumonia patients experiencing intestinal dysfunction, revealing notable shifts in fecal microbiota composition before and after FMT. At the phylum level, the relative abundances of *Firmicutes*, *Proteobacteria*, *Bacteroidetes*, and *Actinobacteria* prior to FMT were 48.0%, 18.2%, 11.2%, and 6.6%, respectively. Following FMT, these values shifted to 54.5%, 9.2%, 19.4%, and 3.2%. The increased abundance of *Firmicutes* and *Bacteroidetes* approached levels typically observed in healthy populations—approximately 60% and 20%, respectively (Dethlefsen et al., 2007; Stewart et al., 2018). In contrast, *Actinobacteria* and *Proteobacteria* are generally present at lower relative abundances in healthy individuals (Mobeen et al., 2018). Notably, the elevated proportion of Proteobacteria pre-FMT, as identified through LEfSe analysis based on species abundance, suggests its potential role as a microbial biomarker for dysbiosis in the pre-intervention state. Post-FMT levels of Actinobacteria (3.2%) and Proteobacteria (9.2%) showed a trend toward normalization, approaching the average values observed in donor samples and the general population.

At the genus level, the relative abundances of *Phocaeicola*, *Parabacteroides*, *Lachnospira*, *Phascolarctobacterium*, *Megamonas* and *Providencia* were significantly increased after FMT compared to baseline. Further species-level analysis revealed marked increases

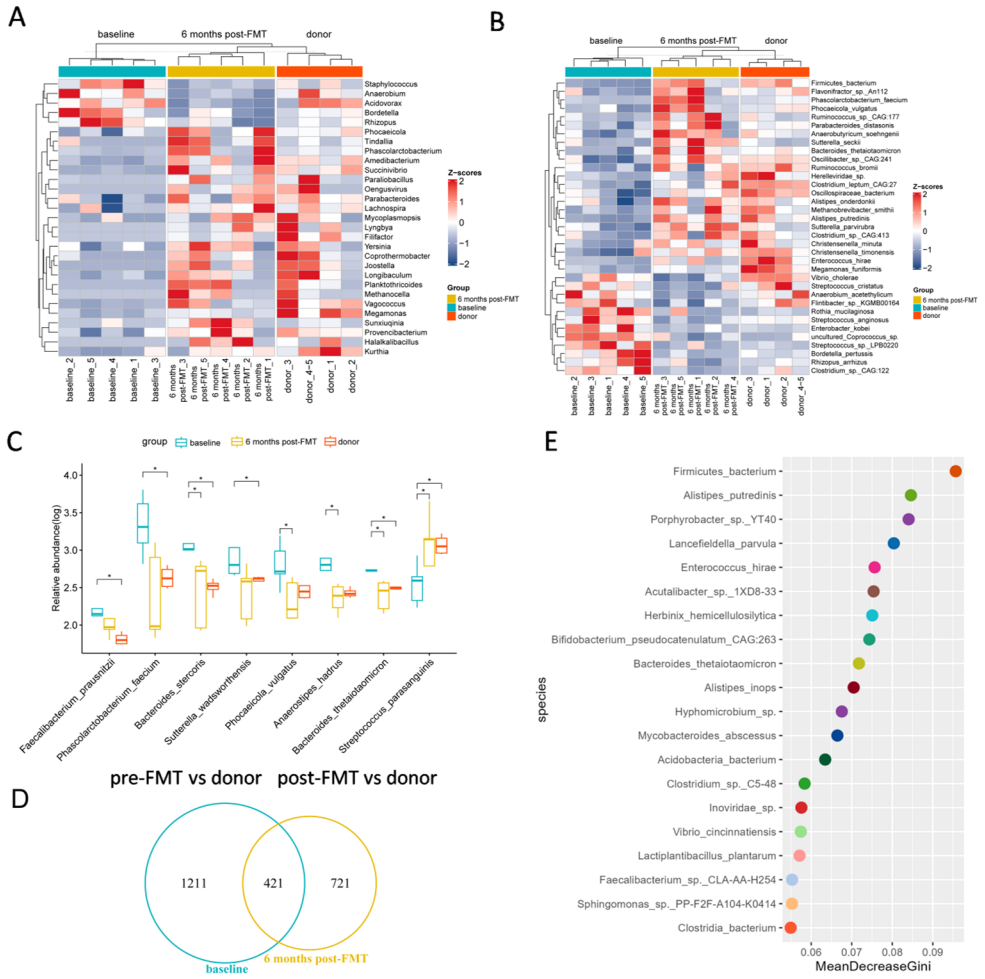


FIGURE 3
Microbial species with significant changes before and after fecal microbiota transplantation (FMT) in patients with severe pneumonia. **(A)** Heatmap showing significantly altered relative abundances of individual genera. **(B)** Heatmap displaying significantly changed relative abundances of individual species. **(C)** Boxplot illustrating the relative abundance changes of the top eight differentially abundant species. **(D)** Venn diagram comparing significantly differentially abundant species between the pre-FMT vs. donor and post-FMT vs. donor groups. **(E)** Random forest analysis based on the relative abundance of individual species to identify key discriminative taxa.

in *Phascolarctobacterium_faecium*, *Bacteroides_thetaiotaomicron*, *Parabacteroides_distasonis*, *Ruminococcus_sp.*, *Oscillibacter_sp.*, *Clostridium_sp.*, and others. Previous studies have indicated that *Phascolarctobacterium_faecium* may contribute to detoxification within the intestinal microbiota and exerts beneficial effects on gastrointestinal health (Wu et al., 2017; Ogata et al., 2019). Moreover, *Bacteroides_thetaiotaomicron* produces succinate, which supports the growth of *Phascolarctobacterium* via the succinate-propionate pathway. The coexistence with succinate-producing bacteria is essential for *Phascolarctobacterium*, which often shows positive associations with *Oscillibacter_sp.* and *Clostridium_sp.* (Ogata et al., 2019; Bhandarkar et al., 2021). *Parabacteroides distasonis* is considered part of the human core microbiota and has been shown to negatively correlate with obesity, non-alcoholic fatty liver disease, and type 2 diabetes. It can modulate multiple signaling pathways through the production of succinate and secondary bile acids, suggesting a role in systemic metabolic regulation. These properties indicate its potential as a next-generation probiotic for metabolic disorders (Wang et al., 2019). *Oscillospira* (often represented by operational taxonomic units related to *Ruminococcaceae*) is commonly found in the intestines of humans and animals and has been associated with various conditions, including obesity, cachexia, gallstone formation, and chronic constipation, exhibiting complex correlations with disease progression. Importantly, *Oscillospira* species are capable of producing short-chain fatty acids such as butyrate, which are key indicators in the identification of candidate "next-generation probiotics" (Feng et al., 2020). Therefore, these findings suggest that FMT was associated with improvement in gastrointestinal symptoms in post-severe pneumonia patients. And these results support further investigation of FMT in randomized controlled trials for restoring intestinal homeostasis and alleviating gut-related sequelae in individuals recovering from severe pneumonia.

However, there were also several limitations in this study. First, the majority of participants were middle-aged or elderly individuals (median age 65 years, range 26–91 years), with a notable female predominance (75%). Given the well-documented age-related decline

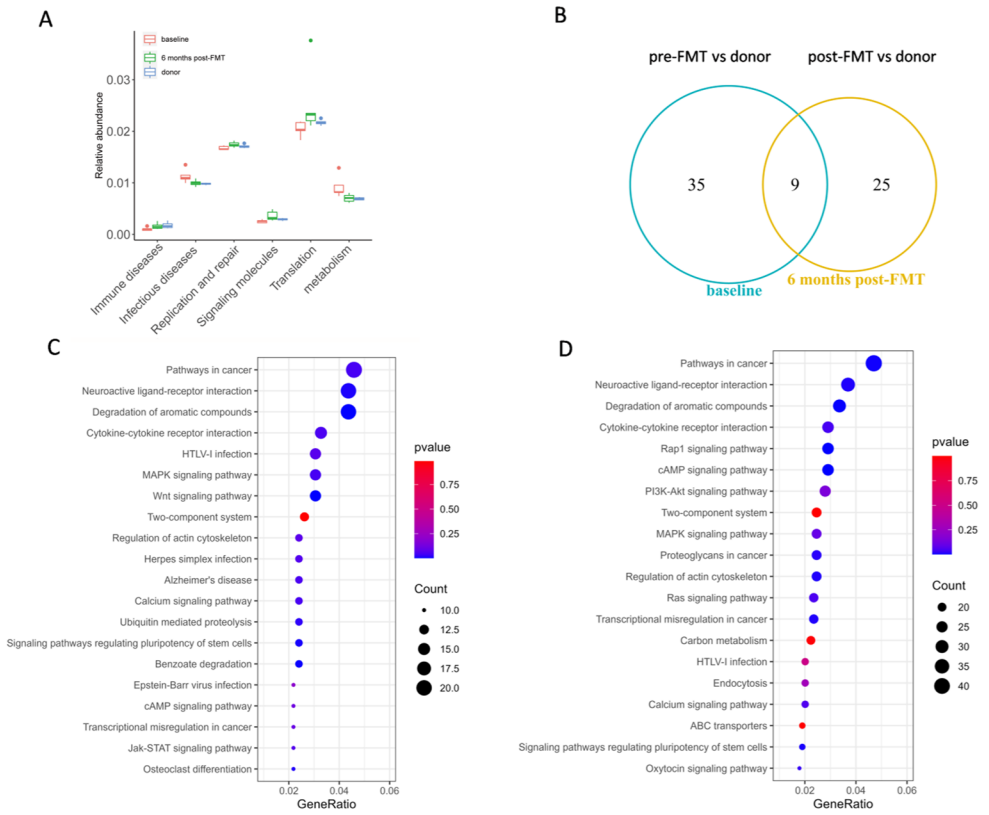


FIGURE 4
Functional composition analysis of the metagenomes. **(A)** The analysis of differences in KEGG pathway annotation of samples before and after fecal microbiota transplantation in patients with severe pneumonia. **(B)** Venn diagram comparing significantly different KEGG pathways between the pre-FMT vs. donor and post-FMT vs. donor groups. **(C, D)** Top 20 enriched KEGG pathways identified in the enrichment analysis for the pre-FMT vs. donor **(C)** and post-FMT vs. donor **(D)** comparisons.

in gut microbial diversity and the potential influence of sex on microbiota composition and immune responses, the generalizability of our findings to younger populations or male-predominant cohorts remains uncertain. Therefore, the conclusions of this study should be interpreted cautiously and are primarily applicable to the demographic represented in this cohort. Second, the sample size is relatively small, which limits the statistical power to detect subtle differences or elucidate underlying mechanisms associated with FMT treatment. Third, this was a single-arm clinical trial without a parallel control group receiving sham or placebo interventions, thereby limiting the ability to draw causal inferences regarding treatment effects. This study adopts a single-arm non-controlled design without setting up a parallel natural recovery control group. Intestinal function and gut microbiota of severe pneumonia patients in the convalescent stage may gradually improve along with the spontaneous physical rehabilitation of the disease. Owing to the absence of a control cohort for natural recovery observation, it is difficult to completely distinguish and quantify the respective contributions of spontaneous self-recovery and FMT intervention to the improvements in gastrointestinal symptoms, serum biochemical indices and gut microbial structure remodeling. Further well-designed randomized controlled trials with a natural recovery control group are required to eliminate the confounding interference of spontaneous rehabilitation and independently verify the actual efficacy of FMT in regulating intestinal flora and improving intestinal symptoms. Therefore, in the future, it will be necessary to conduct large-scale randomized controlled trials to more accurately determine the role of fecal microbiota transplantation in severe pneumonia and the recovery process. Last but not the least, due to limited donor availability, we utilized multi-donor FMT administered at various time points to enhance microbial diversity in recipients. While this approach may increase microbial richness, it introduces variability that could affect treatment consistency. Future studies should consider donor-recipient matching based on microbial compatibility to minimize potential confounding factors and improve the precision of FMT outcomes.

Conclusion

In this study, FMT was found to be associated with the modest improvements in blood biochemical parameters. Concurrently, recovery of the intestinal microbiota and alleviation of gastrointestinal symptoms were observed, suggesting that FMT may serve as a potential therapeutic and rehabilitative intervention for patients recovering from severe pneumonia.

Data availability statement

The datasets presented in this study can be found in NCBI online repositories, the accession of project: PRJNA995907.

Ethics statement

The studies involving humans were approved by Ethics Committee of Wuhan Traditional Chinese Medicine Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

FZ: Investigation, Project administration, Writing – original draft. CY: Investigation, Methodology, Writing – original draft. YLL: Investigation, Methodology, Writing – original draft. JZ: Data curation, Investigation, Writing – original draft. LY: Data curation, Investigation, Writing – original draft. TS: Data curation, Investigation, Writing – original draft. LD: Formal analysis, Visualization, Writing – original draft. XZ: Formal analysis, Software, Visualization, Writing – original draft. GL: Formal analysis, Software, Visualization, Writing – original draft. CZ: Writing – original draft, Validation, Visualization. JW: Writing – original draft, Validation, Visualization. YX: Writing – review & editing, Validation, Visualization. YYL: Writing – review & editing, Validation, Visualization. HS: Funding acquisition, Resources, Supervision, Validation, Writing – review & editing. GF: Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing. YD: Funding acquisition, Project administration, Resources, Supervision, Writing – review & editing.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcimb.2026.1917445/full#supplementary-material

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