ScienceDirect

Obesity Medicine

Volume 57, September 2025, 100643

Gut microbiome alterations in type 2 diabetes following COVID-19: A comprehensive review

Nilanjana Bose [a], Deepa Bisht [b], M. Vinod Kumar [c], Kazi Anika Nawar [a], Benjo Chalissery [d], D. Neha [e], Nikita Dung Dung [e], Shivani Rawat [b], Deepika Ahuja [f] ✉, Ranjay Kumar Choudhary [f g] ✉, Alak Kumar Syamal [a]

Show more

https://doi.org/10.1016/j.obmed.2025.100643 ↗

Highlights

- COVID-19 worsens metabolic dysfunction in type 2 diabetes via gut microbiome alterations.
- Post-infection dysbiosis increases insulin resistance and impairs glucose control.
- Inflammation impacts gut-lung and gut-brain axes in diabetics.
- Gut microbiome is a key target in post-COVID diabetes care.
- Probiotics and diet need more research for control.

Abstract

The COVID-19 pandemic has raised growing concern over its long-term effects, particularly in individuals with pre-existing metabolic conditions such as type 2 diabetes. Beyond its well-known impact on the respiratory and immune systems, emerging research highlights the virus's influence on gut microbiota, a key player in metabolic regulation. This review explores how COVID-19-induced inflammation, immune dysregulation, and direct gastrointestinal effects contribute to disruptions in gut microbial composition and function. Such imbalances may worsen insulin

resistance, impair glucose metabolism, and aggravate glycemic control in diabetic patients. We discuss current evidence linking gut dysbiosis to metabolic deterioration in post-COVID type 2 diabetes, emphasizing the role of the gut-lung axis and cytokine storm in this interaction. Recognizing the gut microbiome as a modifiable factor opens new possibilities for targeted interventions, such as probiotics, dietary modulation, and microbiota-based therapies. Understanding these mechanisms is essential not only for managing diabetes in the post-COVID context but also for developing integrative strategies that address the gut microbiome's role in metabolic health. This review underscores the need for further research to elucidate causal relationships and optimize gut-targeted therapeutic approaches in diabetes care following COVID-19 infection.

Introduction

The COVID-19 pandemic, produced by the novel coronavirus SARS-CoV-2, has had a huge influence on the health, economies, and societies of the world since its inception in late 2019 (Hao et al., 2022). These residual symptoms, often termed “Long COVID” or “post-acute sequelae of SARS-CoV-2 infection” (PASC), have become a large public health issue (Griffin, 2024). The precise mechanisms behind Long COVID are not entirely known but possible explanations are ongoing inflammation, viral reservoirs, autoimmunity, and vascular and organ injury in the process of acute infection (Davis et al., 2023). Research indicates that a high proportion of COVID-19 survivors between 10% and more than 30% depending on the population in question and the definition applied develop long-term symptoms (Sudre et al., 2021). These long-term effects have critical implications for healthcare systems, workforce productivity, and broader societal function. Continuous research is indispensable in building on effective treatments, rehabilitation measures, and palliative care for affected individuals (Filip et al., 2022); Kogevinas et al. (2025). Consequently, Long COVID is not just a health problem but also a socio-economic one that requires a concerted global response.

The idea behind performing an extensive review of the interaction among COVID-19, long-term health consequences, and the gut microbiota is the increasing appreciation that the pandemic has not just resulted in acute disease but also released a chain of chronic illnesses that require prolonged medical care and scientific investigation. Among these, Long COVID has come forward as a syndrome with multisystemic manifestations involving persistent symptoms of multiple organ systems, such as the gastrointestinal tract and central nervous system (Gang et al., 2022). Cumulating evidence indicates that gut microbiota can potentially contribute to the emergence, maintenance, and severity of these extended symptoms since SARS-CoV-2 is established to infect the gastrointestinal tract by ACE2 receptors that are expressed highly in enterocytes (F. Zhang et al., 2023). In addition, an understanding of this relationship holds promise for innovative microbiota-targeted therapies—in the form of probiotics, prebiotics, synbiotics, and fecal microbiota transplantation—to assist in Long COVID prevention or treatment and underlying metabolic dysfunctions (Biazzo and Deidda, 2022). Therefore, the present review aims to incorporate the current information, highlight limitations in the existing literature, and establish a premise for future investigation of the role of gut microbiota in the recovery from and long-term implications of COVID-19. Considering the unprecedented size of the pandemic and its continued strain on

healthcare systems, the subject matter is both urgent and necessary for guiding clinical practices and public health policy.

COVID-19 elicits a dysregulated and frequently multifaceted immune response with a critical role to play in governing the clinical path of SARS-CoV-2 infection. Having entered the host through angiotensin-converting enzyme 2 (ACE2) receptors, the virus is picked up by innate immune receptors such as toll-like receptors (TLRs), with inflammatory signal cascades activation and the induction of pro-inflammatory cytokines and chemokines being triggered (Manfrini et al., 2024; Kulshrestha et al., 2020; Bandyopadhyay et al., 2025). In its less stringent forms, such natural response substantially prevents viral multiplication and allows adaptive immunity activation in the form of virus-specific T cell response as well as B cell generation of neutralizing antibodies. Yet, in severe to critical cases, a hyperimmune response—described as a “cytokine storm” of increased levels of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other inflammatory mediators—is capable of leading to enormous tissue damage, acute respiratory distress syndrome (ARDS), multi-organ failure, and death (Pantaleo et al., 2022). Notably, severe COVID-19 is often associated with lymphopenia, and particularly of $CD4^+$ and $CD8^+$ T cells, which compromises the body to effectively respond with an antiviral response.

Further, the virus seems to hijack crucial components of immune control, such as interferon signaling, to promote antiviral protection (Minkoff and tenOever, 2023). Even the adaptive immune system seems heterogeneous post-infection; some people become highly developed and persistent immunity, but some experience weak or lagged antibody and T-cell immunity, potentially leading to the virus becoming chronic and taking an extended time for the symptoms to be eliminated. Furthermore, increasingly, evidence indicate that immune dysregulation may be lasting after the initial phase of infection and cause chronic inflammation, autoimmunity, and Long COVID symptoms (R. C. Wang and Wang, 2023). For this reason, it is significant to identify mechanisms of the immune response to SARS-CoV-2 to organize proper treatment, vaccines, and long-term care protocols for COVID-19 and post-acute sequelae.

The metabolic effect of COVID-19 forms the foundation and is multi-factorial and wide-ranging outside of the acute phase of inflammatory response to infection and contributes to the exacerbation of pre-existing metabolic disease and generates novel-onset metabolic derangements (Table 1). SARS-CoV-2 infection can derange glucose and lipid homeostasis, exacerbate insulin resistance, and induce systemic inflammation—all the key constituents of metabolic syndrome (Steenblock et al., 2021). Existing conditions such as obesity, T2DM, and cardiovascular disease not only have a high risk of developing severe COVID-19 disease but also tend to exacerbate these comorbid conditions independently. Mechanistically, interaction of the virus with the angiotensin-converting enzyme 2 (ACE2) receptor that occurs in metabolic tissues such as the pancreas, adipose tissue, liver, and skeletal muscle can cause direct tissue damage and disruption of metabolic regulation (Bigdelou et al., 2022; Bandyopadhyay et al., 2025). In addition, the acute inflammatory response from COVID-19, with the characteristic cytokine storm, leads to insulin resistance and beta-cell injury, potentially to hyperglycemia even in metabolically normal subjects (Fig. 1).

Indeed, an abrupt rise in the incidence of new-onset diabetes and hyperglycemia after COVID-19 has been reported, and it is postulated that the virus can act as a diabetogenic agent (Khunti et al., 2021; Prasad et al., 2021). Long COVID also worsens metabolic health by continuing to fuel chronic

inflammation, disrupting hormonal homeostasis, and inducing reduced physical activity and enhanced psychological stress—both of which are risk factors for worsening of metabolism. Also, gut microbiota that is responsible for energy metabolism as well as insulin sensitivity is often altered in patients with COVID-19, which may be responsible for microbial dysbiosis leading to post-infection metabolic consequences (Naidu et al., 2024). Together, these results highlight the necessity for monitoring and intervention in metabolic status during recovery from COVID-19, even in the event of initial mild illness, to prevent long-term health impacts and to decrease the continued burden of chronic non-communicable disease in the post-pandemic period.

The gut microbiota, a highly diverse and densely populated community of trillions of bacteria that reside in the gastrointestinal tract, plays a role in the regulation of metabolic health and body homeostasis. These microorganisms—archaea, bacteria, fungi, and viruses—are known to play a role in numerous metabolic functions, including vitamin K and B vitamin metabolism as well as the degradation of fiber in the diet, and the fermentative metabolism of carbohydrates not absorbed to produce short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate that are vital energy sources with anti-inflammatory effects (Kovatcheva-Datchary et al., 2013; Jain et al., 2024a). The gut microbiota is also involved in lipid metabolism control, glucose homeostasis, and insulin sensitivity and, thus, influences the risk of metabolic diseases such as obesity, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD) (Pavithra et al., 2025; Parua et al., 2025). Dysbiosis, or interference with gut microbiota function or gut microbiota balance, has always been associated with metabolic syndrome and comorbidities, most typically represented by reduced microbial diversity, pathobiont enrichment, and reduction in commensal species like *Faecalibacterium prausnitzii and Akkermansia muciniphila* (J. Wu et al., 2021).

In addition, microbial metabolites have also been shown to interact with host receptors, regulate the immune system, and regulate systemic inflammation, a powerful amplifier of metabolic derangement (Adhikary et al., 2024). Additional evidence, in recent years, has allocated the gut-brain axis, whereby the microbiota indirectly regulates metabolic health through neuroendocrine mechanisms and behavioral changes, such as appetite and energy expenditure (Ullah et al., 2023). Diet, antibiotic use, lifestyle, and early-life exposure profoundly influence the stability and structure of gut microbiota, suggesting that some interventions like prebiotics, probiotics, dietary intervention, and even fecal microbiota transplantation (FMT) are promising for prevention or therapy of metabolic diseases (Karim et al., 2024).

The composition and functionality of the gut microbiome is tightly regulated by epidemiological and lifestyle factors, critically influencing its resistance against infections and associated metabolic disorders. Variation in geography also drives microbial diversity through divergent dietary intakes, sanitation, and environmental influences High fiber, plant-based diets are associated with more *Prevotella and Bifidobacterium* species whereas a “western” diet high in fats and sugars as well as low in microbial diversity is linked with higher abundance of Bacteroides (Jain et al., 2023). Other approaches including physical activity and sleep patterns, as well as the psychological stress may also influence gut composition by the way of promoting pro-inflammatory lifestyles, like sedentary lifestyle or chronic stress. Given the high prevalence of patients with COVID-19 and Type 2 Diabetes, these lifestyle factors can either worsen the gut dysbiosis associated with this infection or impair recovery. These factors are crucial for the design of personal therapeutics and microbiome-related

treatments that take into account both monolayer conditions and sociocultural aspects. Therefore, shedding light on the complex relationships between gut microbiota and metabolic well-being is significant not only for the disentanglement of the pathophysiology of current disease but also for the creation of novel, microbiome-focused therapies.

Type 2 Diabetics have been shown to experience unique modifications to the gut microbiota with post-COVID patients in recent studies. This, however, is contradicted by an increase in pro-inflammatory and opportunistic taxa (i.e. *Streptococcus* spp., *Clostridium* spp., *Candida* spp.) during the acute phase of infection that are significant contributors to prolonged viral shedding and systemic inflammation. On the other hand, beneficial commensals like *Faecalibacterium prausnitzii, Bifidobacterium* spp., *Lactobacillus* spp. well diminished thus potentially compromising gut barrier integrity and immune modulation. Similarly, the genus *Blautia* spp., which is associated with anti-inflammatory effects, presented a biphasic pattern; it was depleted during acute illness and became enriched in the convalescent state, and thus it could play a role in microbial recovery. Bacteroides spp. in metformin-treated T2D subjects vs. dominate host metabolism, which may in turn impact host metabolic pathways (Jain et al., 2024b). These microbial alterations likely reflect the central interaction between viral infection, host immune response and metabolic state, and emphasize patterns of redirection the microbiota that may need to be addressed by more directed microbiome-based therapeutic strategies in post-COVID diabetic management (Talath et al., 2024).

The gut microbiota is a complex metabolic system that regulates glucose metabolism and insulin sensitivity through microbial metabolite signaling to host tissues, immune modulation, and control of enteric hormone activity. The best-studied process is the fermentation of dietary fiber by bacteria in the gut into SCFAs, primarily acetate, propionate, and butyrate, which regulate glucose homeostasis by several mechanisms. SCFAs cause the release of peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) from enteroendocrine cells, which promotes insulin release and causes satiety (Y.-D. Zhou et al., 2023). SCFAs also act on G-protein-coupled receptors GPR41 and GPR43 to enhance insulin sensitivity and to limit systemic inflammation, which is the primary stimulus for insulin resistance. A healthy, balanced gut microbiota also supports the preservation of intestinal barrier function and inhibits translocation of lipopolysaccharides (LPS) and other endotoxins into the bloodstream, which can potentially cause chronic low-grade inflammation and metabolic endotoxemia—both of which are established to interfere with insulin signaling (Wachsmuth et al., 2022). Certain bacteria species, such as *Akkermansia muciniphila*, have been linked to improved glucose tolerance and metabolic well-being, potentially by maintaining gut barrier integrity and modulating host immunity. Dysbiosis with diminished microbial diversity and increased pro-inflammatory species levels has been associated with the pathogenesis of T2DM and obesity, typically with elevated circulating LPS levels, lower SCFA production, and greater insulin resistance [43]. These findings suggest that modulation of the gut microbiota by dietary interventions, prebiotics, probiotics, or even fecal microbiota transplantation may have new therapeutic roles to enhance insulin sensitivity and control metabolic diseases (Fig. 2).

Certain studies indicated that T2DM patients possessed reduced abundance of symbiotic microbiota like *Akkermansia muciniphila, Faecalibacterium prausnitzii*, and other butyrate producers and elevated abundance of opportunistic pathogens and inflammatory bacteria like *Ruminococcus gnavus* and *Bacteroides caccae* (Longo et al., 2024). This microbiome shift results in decreased SCFAs,

butyrate, production necessary to ensure intestinal integrity and initiate anti-inflammatory response. Moreover, diabetics' dysbiosis transmits dysregulation to bile acid metabolism but also reduces insulin sensitivity and exacerbates glucose regulation by deregulation from receptors such as FXR and TGR5 (Młynarska et al., 2024). The gut microbiome also regulates glucose absorption, suppression of satiety, and hormonal signaling through the gut-brain axis, again involving microbial composition in metabolic derangement.

Post-COVID-19 microbiome changes have become an area of study to focus on, as they have explained how SARS-CoV-2 infection has effects that reach far beyond the respiratory tract. Rising evidence indicates that COVID-19 has the capacity to significantly disrupt the gut microbiota, causing persistent dysbiosis that can contribute to long-term symptoms, immune dysregulation, and metabolic derangements in recovered patients. Research has shown that SARS-CoV-2-infected patients undergo a significant loss of healthy commensal bacteria, including *Faecalibacterium prausnitzii, Eubacterium rectale,* and *Bifidobacterium adolescentis*, which have anti-inflammatory functions and functions in gut epithelial integrity maintenance (Yaghmaei et al., 2024; Righi et al., 2024). Concurrently, there is an increase in opportunistic pathogens such as Enterococcus, Escherichia coli, and Rothia, which might worsen the intestinal inflammation and enhance vulnerability to secondary infection.

Even after the resolution of respiratory symptoms, such microbial imbalances may last for months, implying long-term disruption of the gut ecosystem. One possible mechanism is that the gut-lung axis enables systemic inflammation caused by SARS-CoV-2 to impact gastrointestinal function, resulting in compromised gut permeability and microbial translocation, which propagates further inflammation and immune dysfunction (Druszczynska et al., 2024; Bhattacharya et al., 2021; Uti et al., 2025). In addition, the administration of broad-spectrum antibiotics and antiviral medications in acute COVID-19 can also worsen dysbiosis by eliminating helpful microbes and promoting resistant strains to take over (Fig. 3).

Importantly, post-COVID microbiome changes have been linked to long COVID symptoms, including fatigue, cognitive dysfunction, and gastrointestinal complaints. A study by Li et al. (2022) found that individuals with persistent symptoms months after infection had distinct gut microbial signatures compared to those who fully recovered, including reduced microbial richness and altered metabolite profiles affecting tryptophan metabolism, bile acids, and SCFAs. This dysbiotic condition can impair mucosal immune function and systemic metabolic control, leading to glucose dysregulation, inflammation, and mental symptoms—all of which are frequently encountered in long COVID (J. Zhang et al., 2024).

These results place the gut microbiome as both a therapeutic target and option in the treatment of post-COVID sequelae (Chhotaray and Jal, 2023). Dietary modification, probiotics, and fecal microbiota transplantation (FMT) are being investigated as methods to achieve microbial homeostasis and palliate long-term symptoms. Insight into the breadth and functional effects of microbiome disruption in patients with post-COVID is important for the construction of thorough, gut-directed interventions in post-viral recovery.

Especially in patients with Type 2 Diabetes do co-morbidities play a major role for the composition of the gut microbiome response to COVID-19. Obesity, hypertension, cardiovascular disease and

chronic respiratory disorders are often set against pre-existing gut dysbiosis with decreased diversity and expanded profiles of pro-inflammatory bacteria. Overweight, reporting excessive *Firmicutes/Bacteroidetes* ratio and impoverishment of SCFA-producing bacteria in obese subjects, behaviors that might increase inflammation posterior to SARS-CoV-2 infection along with metabolic disarrays. Enterobacteriaceae and Streptococcus spp., which were enriched in patients with cardiovascular disease, have systemic inflammation or a poor prognosis in COVID-19. Chronic respiratory diseases may also affect the gut-lung axis, and this immune cross-talk far from the lungs causes changes in microbial composition. These comorbidities that predispose patients to severe COVID-19 can also delay recovery of the microbiome and prolong symptoms, a problem common in developing post-acute sequelae of SARS-CoV-2 (PASC) or protracted course of SARS-CoV-2. These interactions must be considered to design precision microbiome-based interventions across the spectrum of patient health.

Viral infections can significantly disrupt the composition and functionality of gut microbiota, destabilizing its finely tuned homeostasis and triggering downstream effects on host immunity, metabolic regulation, and overall health. Homeostasis in the gut microbiota is developed through digestion, secretions of metabolites, and host immune interaction. If there is a viral infection present—whether gut-limited or systemic—it can also be inflammatory, induce death of enteric epithelial cells, and disrupt the local environment, all of which have the potential to alter microbial abundance and diversity (Alwin and Karst, 2021; Ramakoti et al., 2024). Norovirus, rotavirus, and influenza viruses have been shown to decrease the richness of commensals like Lactobacillus and Bifidobacterium and induce opportunistic pathogens like *Enterobacteriaceae* and *Clostridium difficile* (Helmy et al., 2023).

One of the ways in which viruses are known to affect the microbiota is by eliciting host immune reactions like interferon and pro-inflammatory cytokine production that can make the gut environment unhelpful for favorable bacteria. This immune-mediated disruption of microbial homeostasis also undermines barrier integrity further, causing augmented gut permeability (“leaky gut”) and translocation of microbial products like lipopolysaccharides (LPS) into systemic circulation, provoking inflammation (Wirusanti et al., 2022). Viral infections also interfere with bile acid metabolism, mucus secretion, and nutrient uptake, all of which control microbial survival and colonization patterns (Table 2).

Most importantly, viral infections can cause chronic or delayed microbiome disturbance following virus clearance. HIV, influenza, and SARS-CoV-2 research has, for instance, identified long-term alterations in the gut microbiome that are associated with disease severity, immune suppression, and risk of increased comorbidity (Cyprian et al., 2021). COVID-19 has been linked to decreases of protective bacteria like *Faecalibacterium prausnitzii* and overproduction of inflammatory-related genera like Rothia and Streptococcus, which last months and lead to long COVID syndromes. In addition, virus-bacteria gut interactions are reversible: some bacteria can inhibit or facilitate viral infection. Some commensals exert an anti-viral protective role against viral pathogens by inducing innate immunity or competition for nutrients, while others can permit virus entry and replication by metabolic byproducts (Zheng et al., 2020). Such intricate interactions form the basis that gut microbiome dynamics need to be considered in modulating viral disease. Therapeutic interventions

to restore microbial homeostasis—i.e., probiotics, supplementation with dietary fiber, or FMT—might reverse the systemic symptoms of viral infections and permit recovery.

Diets are one of the most potent regulators of the gut microbial community; short and long-term dietary intake modulate overall diversity and metabolic output. Fiber-rich diets (found in whole grains, legumes, fruits and vegetables) are all utilized by beneficial taxa such as *Bifidobacterium, Faecalibacterium prausnitzii, and Roseburia* which produce short-chain fatty acids (SCFAs), which promote an intact gut barrier and control of inflammation (F. Zhang et al., 2023). Conversely, Western-style diets rich in saturated fats, refined sugars and processed foods are associated with an increased abundance of *Bacteroides and Alistipes* coupled with low microbial diversity reinforcing the pro-inflammatory state. An imbalance in gut flora (dysbiosis) could be exacerbated or attenuated, depending on dietary choices both during and following COVID-19 infection; this is particularly the case in patients with Type 2 Diabetes who suffer from metabolic as well as immune imbalances. The converging data there suggest potential roles for specific populations, prebiotic and probiotic foods or supplements in modulating microbe number and species abundance following COVID infection which could have substantial impacts on glycemic skewing post-COVID.

Probiotics, prebiotics, and nutritional therapies are now potent gut microbiome modulators with efficacious approaches towards the prevention and treatment of metabolic diseases such as T2DM and gut healing following COVID-19 infection. Probiotics are live microorganisms, taking them in sufficient quantities, confer beneficial effects on the host by the mechanism of the shift in gut microbiota, refinement of the barrier function, and immune system modulation (Markowiak and Śliżewska, 2017). Most frequently employed probiotic genera—Lactobacillus, Bifidobacterium, and *Saccharomyces boulardii*—have been shown to dampen systemic inflammation, improve insulin sensitivity, and modulate lipid profiles and glucose management in favor in animal models and human clinical studies (Zikou et al., 2023). The strains increase production of health-imparting metabolites like SCFAs that improve glucose metabolism, increase satiety, and inhibit pro-inflammatory cytokine release. As part of post-COVID-19 recovery therapy, probiotics have also been demonstrated to recover microbiome homeostasis and reverse gastrointestinal long.

COVID symptoms, albeit stronger controlled trial evidence is currently needed (Facchin et al., 2024). Prebiotics, which are designed to induce the activity or growth of beneficial colonic bacteria and are not digestible food ingredients, complement probiotic action. Prebiotic fiber such as inulin, galacto-oligosaccharides (GOS), and fructo-oligosaccharides (FOS) serves to feed commensal bacteria, i.e., SCFA-producing genera such as *Bifidobacterium and Faecalibacterium prausnitzii*. These compounds inhibit gut permeability, inhibit pro-inflammatory mechanisms, and increase metabolic effect. Clinical trials demonstrated that prebiotic supplementation was effective in lowering fasting glucose, improving lipid metabolism, and regulating the appetite hormones such as ghrelin and GLP-1 in patients with T2D or those who are obese (Kaur et al., 2021). In addition, when prebiotics and probiotics are mixed as synbiotics, synergistic effects are further amplified by increasing microbial colonization and activity, especially in metabolically disadvantaged individuals.

1. Nutraceutical interventions, particularly high in polyphenols, fiber, and unsaturated fatty acids, significantly influence gut microbiota composition and function. The Mediterranean diet has been extensively researched to enhance microbial diversity, increase SCFA production, and reduce inflammation and insulin resistance markers

(Perrone and D'Angelo, 2025). Dietary patterns dominated by high consumption of refined sugars, saturated fats, and processed foods, on the other hand, cause gut dysbiosis, endotoxemia, and metabolic derangement. There is also increasing evidence to propose that personalized nutrition according to unique microbiome signatures can also enhance the efficacy of diet interventions even further, allowing for targeted modulation of certain microbial mechanisms that play a role in glucose homeostasis and immune function (Hitch et al., 2022).

Finally, probiotics, prebiotics, and tailored dietary treatments are low-cost, non-drug, evidence-based therapies with enormous potential to modulate gut microbiota, promote metabolic well-being, and facilitate immune reconstitution—especially among T2D patients or COVID-19 survivors [60]. Future research needs to emphasize the development of standardized guidelines for strain selection, dose, and treatment duration and establishment of microbiome-based biomarkers to optimize and personalize these treatments (Chhotaray and Jal, 2025).

Therapeutic Implications and Future Directions for dysregulation of gut microbiome, metabolic health, and COVID-19 recovery emphasize an increased appreciation for the gut as a potential site of new intervention to restore immune-metabolic homeostasis (Chhotaray and Jal, 2024). In view of the mounting evidence favoring gut dysbiosis as a common aetiology of type 2 diabetes (T2D) and post-acute COVID-19 syndrome (PACS), treatments that can alter the composition of gut microbiota —such as probiotics, prebiotics, synbiotics, postbiotics, dietary therapies, and FMT—are becoming more and more explored (Mukherjee et al., 2018). Certain probiotic strains like *Lactobacillus rhamnosus, Bifidobacterium longum,* and *Akkermansia muciniphila* have been shown to possess the ability to inhibit systemic inflammation, enhance insulin sensitivity, and strengthen gut barrier function, thus resulting in improved glycemic control in diabetic patients (Si et al., 2022).

To address the COVID-19 pandemic, the reestablishment of gut microbial homeostasis in previously recovered patients—particularly in individuals with long COVID or underlying metabolic syndromes —is currently a treatment priority. FMT represents a promising yet still investigational treatment for inducing quick reconstituting of gut microbiota and lowering inflammatory markers in both gastrointestinal and extraintestinal illness (F. Zhang et al., 2023). Furthermore, nutritional intervention with high-fiber, polyphenolic, and Mediterranean-type diets has been demonstrated to have profound impacts on microbiota structure and metabolic well-being, proposing a straightforward, non-surgical intervention to reduce long-term COVID-associated metabolic risk (Randeni et al., 2024). Pharmacologic treatments that act on the microbiome-host interface—e.g., TLR4 antagonists, SCFA analogs, or bile acid modulators—are also being explored for their ability to break the inflammatory feedback cycle between the metabolic tissues and the gut (Ramos Meyers et al., 2022).

In addition, precision medicine strategies are under development to individualize microbiome-directed therapies based on microbial profiles, genetics, and comorbidities (Table 3). Disease course and response to treatment can be predicted using metagenomic sequencing, metabolomics, and machine learning algorithms (Kashyap et al., 2017). Future studies need to be long-term clinical trials that examine the efficacy, safety, and durability of these interventions in diverse populations. Inclusion into the mainstream of microbiome science would revolutionize the control of chronic

metabolic disease and post-viral syndromes and confirm the gut microbiota as a biomarker and a modifiable therapeutic target for the combat against T2D and COVID-19 complications.

The application of drugs, including antibiotics and corticosteroids in the treatment of COVID-19 heavily sculpts gut microbiome constellation. Empiric anti-infectives, mainly broad-spectrum antibiotics to prevent secondary infections can disturb the normal microbial diversity and lead to an overgrowth of opportunistic pathogens such as *Enterococcus* spp.*, and Bilophila* spp. while downregulating *Roseburia, Agathobacter, and Barnesiella* as well. In addition, treatment with corticosteroids and some antiviral agents (including hydroxychloroquine and lopinavir/ritonavir) is associated with a reduced abundance of symbiotic bacteria and increased gut permeability, further promoting systemic inflammation. Such perturbation of metabolism and immune competence could further deteriorate convalescence post-COVID which is already troubled with metabolic and immune dysregulation in Type 2 Diabetes.

As our understanding of the gut microbiome's intricate dance with immune and metabolic health keeps improving, particularly for COVID-19 and type 2 diabetes (T2D), it is clear that future research must aim towards mechanistic, longitudinal, and personalized studies to set robust therapeutic targets and optimize treatment strategies. One of the pressing requirements is to clarify causal mechanisms through which post-COVID-19 microbiome alterations are associated with deteriorated glycemic control and chronic inflammation in diabetic patients. While some studies have demonstrated correlations between gut dysbiosis and worsened metabolic outcomes after infection (Hussain et al., 2021), causality remains under-investigated, especially in humans. New multi-omics approaches—metagenomics, metabolomics, and transcriptomics—coupled with machine learning can potentially enable the identification of microbial biomarkers with prognostic potential for T2D development and COVID-19 recovery to aid early diagnosis and risk stratification (Pang et al., 2024).

Furthermore, future studies must assess the long-term efficacy and safety of therapies targeting microbiomes, such as fecal microbiota transplantation (FMT), postbiotics, synbiotics, probiotics, and prebiotics, especially in post-COVID diabetics. Despite their promise, there is generalizability hindered by clinical heterogeneity and suboptimality because of the absence of standardization concerning strain, dose, and mode of administration (Bloom and Chung, 2025). Extended follow-up randomized controlled trials (RCTs) are needed to ascertain treatment effect durability and potential side effects. Precision nutrition, tailored to an individual's microbiome and metabolic profile, has shown early potential for improving glycemic control (Mehta et al., 2024) and needs to be taken to larger and more diverse populations to determine evidence-based recommendations.

Another key line of inquiry involves investigating the roles of microbial metabolites, such as short-chain fatty acids (SCFAs), bile acids, and tryptophan metabolites, that occupy the intersection between host energy regulation, immune regulation, and brain-gut communication (Kim, 2024). Understanding how COVID-19 disrupts such mechanisms could be the source of novel intervention targets. In addition, second-generation probiotics containing recently characterized therapeutic strains like *Akkermansia muciniphila and Faecalibacterium prausnitzii* are also worth exploring as anti-inflammatory combatants and promoters of insulin sensitivity (Gautier et al., 2021).

Within treatment development, engineered probiotics and microbiome-derived drug leads with the capability to specifically regulate host metabolism are of growing interest. These would be capable, potentially, of allowing targeted alterations of some specific bacterial processes with minimal impact upon the greater microbial community. Coincidentally, immune-modifying treatments that deal with chronic COVID post-virus-induced inflammation perhaps through the altering of microbiota profiles are an additional area in which tremendous anticipation lies. Interdisciplinary collaboration among microbiologists, endocrinologists, immunologists, and data scientists will be critical in driving these therapeutic innovations and translating them into commercially available, mass-accessible products for global populations most affected by both COVID-19 and diabetes. Forthcoming research may go beyond correlation to uncover causality, validate the efficacy of interventions within clinical care, and embrace personalized, systems-level interventions for treating post-COVID metabolic disease. As microbiome science evolves, it has unparalleled ability to transform the prevention and treatment of chronic diseases like diabetes in the post-pandemic world.

Section snippets

Conclusion

The crosstalk between COVID-19 infection and gut microbiome dysbiosis in type 2 diabetes patients is a key, albeit yet insufficiently appreciated, aspect of post-viral metabolic derangement. This review highlights how SARS-CoV-2–mediated inflammatory cascades, immune modulation, and direct gastrointestinal involvement lead to chronic dysbiosis, hence exacerbating insulin resistance and undermining glycemic control. The two-way interaction of the gut microbiota with metabolic health implies that …

CRediT authorship contribution statement

Nilanjana Bose: Writing – original draft, Resources, Data curation. **Deepa Bisht:** Writing – original draft. **M. Vinod Kumar:** Writing – original draft, Supervision, Resources. **Kazi Anika Nawar:** Software, Resources, Data curation. **Benjo Chalissery:** Writing – original draft, Software, Resources, Investigation. **D. Neha:** Writing – original draft, Software, Data curation. **Nikita Dung Dung:** Software, Resources, Methodology. **Shivani Rawat:** Supervision, Software, Resources. **Deepika Ahuja:** Writing – review …

Ethics statement

No ethical permission was applicable. …

Declaration

Authors declared no conflict of interest. …

Funding statement

No funds were utilized during this review work. Besides those, it is clearly declared that none of the Authors have any kind of conflict of interests for the current study. …

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. …

Acknowledgement

We are thankful to the institute for providing all facilities to write this article. Scientific partner Probecell Scientific Pvt. Ltd. India assisted in proofreading and editing this article. …

References (127)

A. Alwin *et al.*
The influence of microbiota-derived metabolites on viral infections
Curr. Opin. Urol. (2021)

U. Bandyopadhyay *et al.*
Interplay of calcium, vitamin D, and parathormone in the milieu of infections and immunity: reassessed in the context of COVID-19
J. Steroid Biochem. Mol. Biol. (2025)

P.P. Bloom *et al.*
The future of clinical trials of gut microbiome therapeutics in cirrhosis
JHEP Reports Innovat. Hepatol (2025)

S.R. Bornstein *et al.*
Practical recommendations for the management of diabetes in patients with COVID-19
Lancet Diabetes Endocrinol. (2020)

Y. Cai *et al.*
Fasting blood glucose level is a predictor of mortality in patients with COVID-19 independent of diabetes history
Diabetes Res. Clin. Pract. (2020)

R.L. Cloutier *et al.*
A dangerous pandemic pair: covid19 and adolescent mental health emergencies
Am. J. Emerg. Med. (2021)

A.C. Codo *et al.*
Elevated glucose levels favor SARS-CoV-2 infection and monocyte response through a HIF-1α/Glycolysis-Dependent axis
Cell Metab. (2020)

F. Cyprian *et al.*
SARS-CoV-2 and immune-microbiome interactions: lessons from respiratory viral infections
Int. J. Infect. Dis. (2021)

T.C.A. Hitch *et al.*
Microbiome-based interventions to modulate gut ecology and the immune system
Mucosal Immunol. (2022)

A. Jain *et al.*
Chemoprofiling and antioxidant activity of edible curcuma species
Food Humanit. (2023)

View more references

Cited by (0)

View full text