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Review

The Role of Gut Microbiome in Psoriatic Arthritis—A Literature Review

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Abstract: Psoriatic arthritis is a heterogeneous chronic autoimmune disorder characterized principally by skin lesions, arthritis, dactylitis and enthesitis. The exact etiology of the disease is yet to be discovered, with genetic predisposition alongside environmental factors being a well-known theory. In recent years, new discoveries have emphasized the role of gut microbiome in perpetuating inflammation in spondylarthritis. The exact mechanism through which dysbiosis underlies the pathophysiology of psoriatic arthritis is not defined. One of the current areas of focus in rheumatic research with new studies emerging annually is the link between microbiome and psoriatic arthritis. In this review, we synthesized the recent knowledge on intestinal microbiome and psoriatic arthritis. We screened two databases for articles, PubMed and Medline, using the following keywords: "microbiome", "microbiota" and "psoriatic arthritis". We described the current expertise on diversity and composition of gut microbiome in psoriatic arthritis, comparing the results with other inflammatory diseases. In the future, preventing the dysbiosis process that leads to the development of psoriatic arthritis could open the door to new therapeutic modalities. Moreover, fecal microbiota transplantation and probiotics' benefits in modulating the gut microbiome are being intensively researched at the moment.

Keywords: gut microbiome; microbiota; psoriatic arthritis; spondylarthritis; dysbiosis

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1. Introduction

Psoriatic arthritis (PsA) is a heterogeneous, chronic inflammatory disorder characterized principally by axial and/or peripheral arthritis, dactylitis, enthesitis and psoriasis, with clinical symptoms in line with other spondyloarthritis (SpA). In the last few decades, intestinal involvement with microscopic gut inflammation in over 50% of SpA patients without gastrointestinal conditions has been verified [1,2]. Additionally, approximately 20–30% of people with psoriasis will develop psoriatic arthritis [3,4]. Although the nature of the pathology is still undetermined, hypotheses claim that the main cause is a combination of genetic predispositions and environmental influences [5]. Moreover, investigations on animals have shown that HLA-B27 rats grown in a microbe-free environment do not acquire SpA; rather, they show symptoms when exposed to a certain intestinal population [6].

Recently, a new theory has emerged, focusing on the gastrointestinal barrier, which can contribute to the production of inflammatory cytokines such as interleukin (IL)-23 and IL-17, with the microbiota playing an important role in this process [7–9]. The increased risk of Crohn's disease in PsA and psoriasis patients provides additional evidence that the gut microbiota is involved in these conditions [10]. The human microbiome encompasses the microorganisms existing in, on, and within a human body (such as bacteria, archaea, viruses and eukaryotes) together with their genetic components and their habitat [5,11]. Every anatomical region is made up of distinct microbial communities with an important contribution to the host physiology [10,12]. The taxonomic characterization of these microbial communities has been recently identified owing to important progress in sequencing techniques [13]. Moreover, as a result of the research advances, it seems that the human microbiome is a dynamic community influenced by numerous factors such as genetics, age, dietary customs, antibiotic use and geography [14]. It is well-known that interactions between a host and a microbe are important in the development of a healthy organism [15]. Disturbances of the intestinal flora, dysbiosis, can be associated with different forms of inflammation in the organism and therefore with various autoimmune diseases [16]. Dysbiosis may be caused by a decrease in commensal bacteria such as *lactobacilli*, *bifidobacterial* and *Faecalibacterium prausnitzii* and/or an increase in pathogens such as *Escherichia coli*, *Salmonella*, and *Helicobacter* [17,18]. In patients diagnosed with psoriatic arthritis, a lower consistency of multi-gut bacteria was observed; however, the exact characteristics of the microbial components and their influence on immune diseases activity is yet to be discovered [5,16].

Interleukin-22, tumor necrosis factor (TNF), interferon gamma and IL-23/IL-17 axis are the key cytokines involved in the pathophysiology of PsA, with the latter playing the primary role in this condition [19,20]. The central role of IL-23/IL-17 and increased levels of lymphocyte T helper, mainly Th17, have been proven in patients with inflammatory bowel disease [21–23]. Activated macrophages and dendritic cells regulate the synthesis of IL-23, as a result of environmental variables such as various infections, but also the existence of self-molecules identified as autoantigens by CD4+ and CD8+ T cells [4].

Recent studies have highlighted the importance of innate lymphoid cells (ILCs), which are a subtype derived from natural killers' cells, but are not yet fully described [24]. ILCs have the ability to secrete cytokine, resulting in the initiation and perpetuation of inflammation [25,26]. Furthermore, the relationship between the microbiome and spondyloarthritis is backed up by research, showing that individuals with ankylosing spondylitis (AS) had higher blood and synovial fluid concentrations of gut-derived ILCs that secrete IL-17 and IL-22 [23,27]. Moreover, the strong relation between psoriatic arthritis and inflammatory bowel diseases supports the role of gut dysbiosis in the pathophysiology of PsA, even though the main structures affected in this disorder are the enthesis and joints [28].

There is a commensal and mutualistic link between specific intestinal flora and immune system. Since the gut flora contains the greatest variety of bacteria, the involvement of the intestinal microbiota in autoimmune disorders has attracted increasing study interest [14]. Genetic, epigenetic factors, but also factors related to the external environment, especially diet and the probiotic intake recently analyzed, determine the profile of the intestinal microbiota [15,29]. Recently, studies have been focusing on the existence of a bidirectional signaling pathway between the gut microbiome and the osteoarticular system [30]. The concept of the skin–joint–gut axis describes the relationship between the intestinal microbiota and the function of the skin, joints, relevant especially in spondyloarthritis, such as PsA [11,16]. Unrelated to non-steroidal anti-inflammatory medicines, increased intestinal permeability caused by epithelial barrier dysfunction has been linked to SpA. This increased permeability is also linked to bacterial translocation, which starts and maintains inflammation [31].

Moreover, in dermatology, it has also been demonstrated that inflammatory skin diseases are associated with disruption of the skin and gut microbiota; the main diseases with this implication are psoriasis, rosacea and atopic dermatitis [32]. The function and

differentiation of T cells with the imbalance of regulatory T cells, mostly Th17, are involved in the mechanism of the gut–skin axis in psoriasis. The interaction between pattern recognition receptors expressed by the host cell and the bacterial antigen are important factors in this mechanism [33]. Commensal bacteria play a crucial role in the balance of effector and regulatory T cells, the induction of immunoglobulin A that activates B cells, and the subsequent generation of particular immunoglobulin A antibodies. These processes all have an impact on adaptive immunity [16].

Gut dysbiosis is involved in Th17-mediated skin inflammation and in metabolite production, which results in an anti-microbial signaling changing immune cell activation through the IL-23/IL-17 signaling pathway through IL-22 and interferon gamma production [23]. The result of this mechanism is the hyperproliferation of keratinocytes, as illustrated in Figure 1 [34].

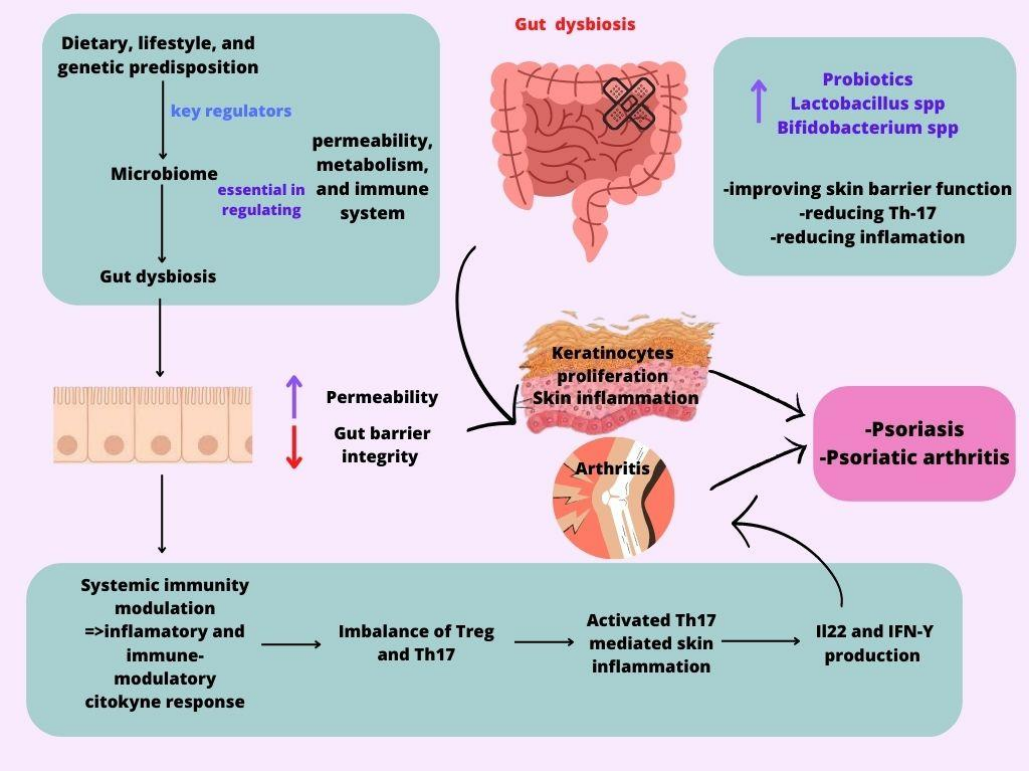

Figure 1. Gut microbiota relationship with psoriasis disease. Dietary, genetic and environmental factors are key regulators of the microbiome. If there is no balance of these factors, it can lead to dysbiosis; this, by increasing permeability and destabilizing the integrity of the intestinal barrier, leads to inflammation and an aberrant cytokine response. The result is inflammation of the skin with keratocyte proliferation and the appearance of psoriatic arthropathy.

The effects of probiotics in rheumatic disorders, particularly PsA, have drawn considerable scientific attention. Probiotics might improve the quality of life of patients with psoriasis disease by promoting specific bacteria and reshaping the composition of the intestinal microbiome; however, further research is needed to establish the beneficial effects of this therapeutic option for autoimmune conditions [35,36].

Studies examining the role of the microbiome in inflammatory diseases are proliferating, with an emphasis on AS, inflammatory bowel disease (IBD) and psoriasis, with PsA being a recently considered disease in this topic. The goal of this narrative review is to compile pertinent data available on gut microbiome heterogeneity and its potential link to the inflammatory pathway in psoriatic arthritis.

2. Results

In this review, we have included a total of five studies relevant to gut microbiota in PsA published until December 2022. One study is a double-blind trial on fecal microbiome transplantation and its impact on PsA; one study focuses on the probiotic intake, analyzing the effect on the disease activity; and three studies are on gut microbiota components, using 16S rRNA sequencing from fecal samples. In the description of the results section, we included one study realized on mice, due to the valuable information provided by the authors on the chosen theme. The main characteristics of the results are illustrated in Table 1.

Table 1. Results on gut microbiome in PsA.

Studies on Microbiota				
Study	**Year**	**Cohort**	**Method**	**Results**
CY Lin et al. [16]	2022	9 PsA patients 10 No-PsA patients	16S rRNA amplicon sequencing from fecal sample	• Increased Family: XIII_AD3011in No-PsA > PsA. • Increased *Megasphaera elsdenii*, *Bacteroides, Firmicutes, Proteobacteria* and *Actinobacteria* in PsA > No-PsA.
A Haidmayer et al. [35]	2020	10 PsA patients who received probiotics	*Fecal zonulin*, α1-antitrypsin and calprotectin Peripheral immune phenotyping	• Increased enteric permeability marker (zonulin) correlated with Th17 cells frequency. • Elevated Calprotectin. • Reduction in disease activity.
J. Manasson et al. [37]	2020	15 patients PsA/AS treated with TNFi vs. 14 patients treated with anti-interleukin-17A vs. controls.	16S rRNA gene sequencing from fecal sample	Comparison to controls before treatment: • Increased in Clostridiales and Erysuoelotrichales. • Reduction in Bacteroidales. Comparison after treatment: • Reduction in Bacteroidales in all TNFi group, and in thirt of anti-IL-17A group. Reduction in *Ruminococcaceae* in TNFi. • Increased *Candida albicans* and *Clostridiales* after treatment with anti-IL-17A. • Increased *Saccharomycetales* after both therapies. • Increased *Saccharomyces cerevisiae* in TNFi.
J. Scher et al. [28]	2015	16 PsA patients 15 PsO patients 17 controls.	16S ribosomal RNA pyrosequencing from fecal samples	• Microbiota less diverse in PsA and PsO than controls. • Decreased *Coprococcus* sp. in PsA and PsO. • Decreased *Akkermansia*, *Ruminococcus*, *Clostridia* and *Pseudobutyrivibrio* in PsA.
Studies on Fecal Microbiota Transplantation				
Study	**Year**	**Cohort Sample**	**Score Used**	**Results**
MS Kragsnaes et al. (Double-blind study) [38]	2021	31 patients 15 FMT group vs. 16 sham group	Side effects ACR20 score HAQ-DI	• No adverse effects. • Sham group had better improvement of disease activity than FMT.

Abbreviations: PsA = psoriatic arthritis; No-PsA = controls without psoriatic arthritis; TNFi = tumor necrosis factor inhibitors; AS = Ankylosis spondylitis; PsO = psoriasis; IL = interleukin; sp. = species; FMT = fecal microbiota transplantation; ACR20 = American College of Rheumatology 20% score; HAQ-DI = The Health Assessment Questionnaire Disability Index.

In a recent study, Chun-Yu Lin et al. analyzed the fecal samples from a small cohort of 9 PsA patients, compering the results with a control group [16]. They showed that PsA patients had a specific microbiome species ($p = 0.048$) and a different microbial density ($p < 0.05$). *Bacteroides*, *Firmicutes*, *Proteobacteria* and *Actinobacteria* were the bacterial communities more frequent in PsA, with significantly increased levels for *Actinobacteria* compared to those in No-PsA. Moreover, as regards symptomatology, dactylitis and enthesitis are especially associated with a specific microbiome, and this theory is supported by a higher frequency of *Megasphaera elsdenii* among patients with PsA with dactylitis and/or enthesitis compared with the No-PsA group. Another finding was the negative association of *Magasphaera elsdenii* and *Bifidobacterium longum* with eosinophil count. Additionally, they carried out a metagenome sequencing and showed bacterial phylotypes differences between the two groups. Across the groups, they reported various microbial compositions for multiple

species, including *Actinobacteria Phylum, Fusobacteriales Order, Acidaminococcaceae Family, Erysipelotrichaceae Family, Clostridium innocuum Genus,* with *Family: XIII_AD3011* being significantly higher for No-PsA controls, $p = 0.039$.

In a small study, the authors examined the impact of probiotic intake for 12 weeks on PsA activity, analyzing the enteric permeability, gut inflammatory marker, calprotectin and possible correlations with peripheral Th17 cells frequency [35]. The results showed that probiotic intake, by influencing the gut microbiome, can interfere with the immune process and significantly ameliorate the disease activity. Moreover, they brought to light the association of Th17 cells levels, suggesting that patients with a positive effect of the probiotic usage are those with lower levels of Th17 peripheral cells. Regarding the gut permeability, analyzing fecal zonulin and α1-antitrypain, the results showed higher levels of those markers. Gut inflammation was investigated using fecal calprotectin, and 60% of patients in this study had high levels of calprotectin. After probiotic intake, the markers analyzed significantly decreased. Thus, this paper stated that PsA has an increase degree of gut permeability and inflammation, and that probiotic usage has a beneficial effect [35]. However, the effects of probiotic treatment are not long-lasting; however, further investigations are needed to establish a correct correlation.

J. Manasson and colleagues characterized the gut microbiome in PsA/AS patients before and after biological therapy with TN necrosis factor inhibitors (TNFi) and with anti-interleukin-17A agents [37]. In this study, all 14 patients treated with TNFi were diagnosed with PsA, while only 64.3% (N = 9) of patients treated with anti-interleukin-17A had their PsA faecal samples analyzed before treatment with a biological agent and compared with controls. They reported an increase in *Clostridiales* and *Erysuoelotrichales*, and a reduction in *Bacteroidales* compared to controls. Comparing the groups with pre- and post-exposure to biologic therapy, the results showed a reduction in all subjects from TNFi group and in one-third of anti-IL17 group for *Bacteroidales*. For the anti-IL17 patients, there was expansion and reduction in *Clostridiales* levels throughout the therapy; these changes not identified in the TNFi treatment. Regarding fungal perturbation after biological treatment, the authors observed increased levels of *Saccharomycetales* after therapy. Moreover, 29% of the cohort had an expansion of *Candida,* while a reduction in *Candida* was registered in 14% of cohort treated with anti-IL17 [37]. The shift in *Candida albicans* in patients treated with anti-IL17 was significantly higher than TNFi treatment, $p < 0.005$. 40% of TNFi cohort showed an enlargement in *Saccharomyces cerevisiae*, which was significantly higher than that in anti-IL17.

The first study that analyzed gut microbiome in PsA patients was carried out by J. Scher et al. in 2015 [28]. They compared the gut microbiome in recent-onset PsA patients, naïve to treatment and psoriasis patients, further comparing the results to controls. PsA subjects had an important decrease in *Coprococcus* sp., *Akkermansia*, *Ruminococcus* and *Pseudobutyrivibrio*. The results also showed a reduction in *Clostridia* in PsA patients. In contrast, reduced levels of *Parabacteroides* and *Coprobacillus* were registered in psoriatic patients. Furthermore, they analyzed the levels of proinflammatory markers in fecal samples and serum IgA and the results showed an increased fecal IgA level ($p = 0.06$) and a significant decreased in RANKL level ($p < 0.005$) with no difference in OPG levels between PsA and controls, but significantly lower osteoprotegerin levels in psoriasis ($p < 0.005$). Analyzing the fatty acids in those patients, these evidenced that medium chain fatty acids have lower quantities in samples from PsA group. Comparing the fecal and serum levels of inflammatory cytokines, no differences were registered in the study.

In 2020, Miguens Blanco et al. published a study protocol for a multicentric, prospective, observational study (Mi-PART study) with the aim of identifying changes in the gut microbiome using 16S rRNA gene sequencing and manopore sequencing from fecal sample [39]. In order to complete this research, they enrolled 65 PsA patients, 30 ankylosis spondylitis patients and 30 healthy controls. The principal aims of this paper are to link disease activity to microbiota, to identify new biomarkers from gut microbiome and a potential mechanism in order to better understand how microbiome drives the immune

disease. These findings could enrich not only the knowledge of physiological role of gut microbiota in PsA, but also some new therapy options [39].

In our review, we included one trial on fecal microbiota transplantation (FMT) in psoriatic arthritis patients, conducted by MS Kragsnaes et al. and published in 2020 [38]. They realized a randomized double-blind trial on 31 patients with PsA which underwent FMT or sham transplantation. Their results showed no significant side effects of the procedure. Furthermore, they investigated the disease activity using ACR20 score and HAD-DI score. In contrast to the sham group, FMT patients registered more frequent treatment failure (p = 0.018) and slightly less improvement of the HAQ-DI score (by 0.23 points, p = 0.031). For a certain conclusion of the FMT effect regarding the disease activity, a bigger cohort is needed.

P. Lin et al., in a study from 2014, analyzed the gut microbiota in HLA-B27 rats [40]. This paper revealed that HLA-B27 gene expression is associated with gut microbiome disfunction. *Clostridia* and *Helicobacter* had similar levels in HLA-B27 rats and wild rats. There was a reduction in the *Rikenellaceae family* for HLA-B27 group, while *Paraprevotella* registered an increase. A more abundant *Bacterioides vulgatus* and a reduction in *Akkermansia muciniohila* are the principal changes observed in HLA-B27 rats [40].

3. Discussion

The intestine constitutes an internal barrier, acting similarly to a semipermeable structure, which allows the uptake of beneficial nutrients while restricting the passage to toxic substances and pathogens [41]. The skin is the largest organ of the human body and constitutes an external barrier between the body and the environment. There are many factors contributing to the integrity of this barrier, one of them being the human microbiome, both cutaneous and intestinal.

The interaction between the host and the intestinal microorganisms is essential for maintaining human health since intestinal microorganisms are involved in various processes such as digestion, synthesis of vitamins or adaptive immune homeostasis [42]. Perturbation of this interaction can lead to intestinal dysbiosis, further contributing to the pathogenesis of various diseases such as psoriatic disease [43], but also other well-established comorbidities of psoriatic disease such as spondylarthritis [44], diabetes mellitus [45], cardiovascular disease [46] and inflammatory bowel disease [47].

Psoriasis can affect an individual in various ways, and this is why psoriatic disease would be a more appropriate term that encompasses its manifestations. Therefore, psoriatic arthritis and psoriasis (PsO) should be considered part of the spectrum of psoriatic disease [48], developing from an intricate interaction between genetic predisposition and environmental factors. It is now well-known that the intestinal microbiome is a major regulator of this complex interaction as an important component of the skin–joint–gut axis, a concept that perfectly describes the relationship between the intestinal microbiome, PsO and PsA, but also the development of other comorbidities [18].

The interaction between human microbiome, both cutaneous and intestinal, and the development of PsO and PsA has been a popular research topic recently, as proven by the high number of papers regarding this subject. The findings of these studies can be confounding and the purpose of the present review is to focus on the major findings regarding PsA patients.

It is well-established that the major driver of PsO and PsA is the IL-23/IL-17 signaling pathway [49]. It seems that the intestinal dysbiosis is involved in the Th17-mediated skin inflammation and in metabolite production, resulting in an anti-microbial signaling changing immune cell activation through the IL-23/IL-17 signaling pathway through IL-22 and interferon gamma production [34]. Increased intestinal permeability was reported in spondyloarthritis and Crohn's disease patients, as demonstrated by the elevated serum zonulin levels [50,51]. Nevertheless, there was no correlation found between disease activity and intestinal permeability in AP patients [52,53]. Gut microbiome in autoinflammatory disease can open up new therapeutical developments in the future. Probiotics are live

organisms that help to restore the balance of the intestinal microbiome, thus increasing the function of the intestinal barrier [54,55]. The influence of this off-label treatment is yet undefined in immune diseases such as SpA. Another therapeutic option increasingly researched is fecal microbiota transplantation, which had a beneficial effect in IBD and some metabolic syndrome patients [56,57].

3.1. The Intestinal Microbiome in Psoriatic Arthritis

At the phylum level, the intestinal microbiome of PsA patients is composed predominantly of *Bacteroides*, *Firmicutes*, *Proteobacteria* and *Actinobacteria*, the latter being more represented compared to patients with undifferentiated arthritis. Furthermore, *Megasphaera elsdenii* was more frequently found among patients with dactylitis and/or enthesitis [16]. These findings complement the previous information stating that PsA patients have an important decrease in *Coprococcus*, *Akkermansia*, *Ruminococcus* and *Pseudobutyrivibrio*, with a global decrease in *Clostridia* class. Moreover, this study was among the first to demonstrate the lower concentration of medium chain fatty acids in PsA patients' stools [28].

Furthermore, questions have arisen regarding the intestinal microbiome dynamics in relation to biological therapies. Fecal samples of the PsA and AS patients treated with tumor necrosis factor inhibitors and with anti-interleukin-17 inhibitors were analyzed before and after treatment [37]. In the pre-TNFi phase, there were two clusters dominated by *Bacteroides* and *Ruminococcaceae* that became less prominent after treatment. In the pre-IL-17i phase, there was a strong positive correlation between *Bacteroides* and *Ruminococcaceae*, with nodes arranged in a linear structure that separated into two negatively correlated clusters after treatment. Quite uniquely, the mycobiome was analyzed as well and an increase in *Saccharomycetales* was found in both groups, in addition to the expansion of *Candida* and *C. albicans* in a subgroup of patients of varying clinical phenotypes, with a few subjects demonstrating a reduction in the IL-17i group.

Regarding the impact of probiotic intake on PsA activity, the authors concluded that PsA patients suffer from enhanced enteric permeability and inflammation (by measuring fecal zonulin, α1-antitrypsin and calprotectin, as well as peripheral immune phenotyping) and that probiotics may ameliorate disease activity in PsA by targeting these alterations [35].

Fecal transplantation appeared to be inferior to sham in treating active peripheral PsA since treatment failure occurred more frequently in the FMT group than in the sham group and the improvement in HAQ-DI was in favor of sham, with no difference in the proportion of ACR20 responders between the groups [38].

3.2. The Intestinal Microbiome in Psoriasis

Regarding the microbiome composition, the most frequently reported findings are the reduction in *Bacteroides* and *Akkermansia*, with the increase in *Firmicutes* and *Actinobacteria* [29,58]. Altered intestine leads to bacterial translocation triggering inflammation, which is able to influence extra-intestinal sites [59]. It is well-known that psoriasis can be associated with inflammatory bowel diseases, as patients with Crohn's disease have a five-fold risk of developing psoriasis [60]. Moreover, in these patients, *Faecalibacterium praunitziiis* is reduced, limiting its anti-inflammatory effect through the inhibition of the NFkB pathway [33].

Comparison between the PsA and PsO patients revealed that *Akkermansia* and *Ruminococcus* (including *Firmicutes*/*Clostridiales* and *Verrucomicrobiales*, respectively) were significantly less abundant in PsA patients, whereas the Bacteroidetes phylum and *Coprobacillus* genus were less abundant in PsO patients [28].

Antibiotics used to treat intestinal dysbiosis can lead to improvements in PsO activity; however, it cannot be a long-term solution since it eradicates beneficial microbial communities [33,61].

Analogously to PsA patients, probiotics can decrease PsO activity, but can also provide a better response to treatment, lower the need for steroids and lower the risk of relapse [29].

Prebiotics and symbiotics can be used as adjunctive therapies in psoriasis due to their role in immunomodulation [12].

3.3. The Cutaneous Microbiome in Psoriasis

It seems that *Firmicutes*, *Actinobacteria* and *Proteobacteria* are the predominant phyla identified in the cutaneous plaques. Furthermore, there is a decrease in *Actinobacteria* and *Bacteroides* and an increase in *Coprobacillus*, *Ruminococcus* and *Streptococcus* [33,62].

There is also an important increase in the number of *Staphylococcus* in both non-lesional (more precisely, *S. sciuri* and *S. aureus*) and lesional skin (*S. aureus* and *S. ptettenkoferi*) when compared to the skin of healthy individuals [63,64]. *S. aureus* can be identified in the cutaneous lesions of 60% of PsO patients and its colonization is linked to an inflammatory Th17 response [63]. Moreover, in up to 60% of cases, *S. aureus* can secrete enterotoxins and toxic shock syndrome toxin-1. *S. pyogenes* is also frequently identified as a trigger for both the development and the exacerbations of PsO [60].

3.4. The Gut Microbiome in Ankylosing Spondylitis

The strong link between ankylosing spondylitis and dysbiosis is supported by recent research, which verified composition changes of microbial components. B Liu et al., in analyzing the microbiome in AS patients, have showed increased levels of *Cyanobacteria*, *Deinococcota*, *Patescibacteria* and *Actinobacteria* and decreased levels of *Acidobacteria*, *Proteobacteria*, *Campyobacteria* when compared to the those of healthy controls [65]. The diversity of AS microbiota is demonstrated in another study investigating the stool of 127 AS patients in comparison with 123 healthy controls [66]. The authors showed that microbiome in AS patients consisted of increased levels of *Clostridiales bacterium*, *Clostridium bolteae* and *Clostridium hatheway* and decreased levels of *Bifidobacterium*, *Coprococcus*, *Lachnospiraceae* and *Roseburia*. Additionally, they examined the impact of TNFi on microbial alterations, and their findings demonstrated that patients who had never had TNFi therapy were significantly different from healthy controls; however, there was no distinction between patients treated with TNFi and controls, indicating that the medication can restore the balance of the intestinal microbiota. [66]. Similar to IBD, *Fecalibacterium prausnitzii*, a species with a crucial role due to the anti-inflammatory properties, is deficient in AS patients. It is interesting to note that following TNFi therapy, *Fecalibacterium prausnitzii* levels reverted to normal [66]. *Dialister* sp. are more frequent among AS, being significant correlated with this disease, compared not only with healthy individuals, but with non-inflammatory intestinal biopsy from AS patients as well [67].

The link between gut dysbiosis and disease activity was analyzed, and a recent study showed a strong correlation of dysbiosis with an active disease and physical dysfunction in axial-SpA [68]. Regarding therapeutic improvements, although there is some evidence that probiotic intake in rats reduced arthritis and the levels of pro-inflammatory cytokines, the usefulness of probiotics in ankylosing spondylitis has not been yet established [69,70].

3.5. The Gut Microbiome in Inflammatory Bowel Disease

More research has been conducted on the influence of gut microbiota in IBD than on PsA; currently being investigated is not only the presence of dysbiosis, but also the potential increased intestinal bacterial translocation [18]. The results from animal and human studies have revealed the indisputable and critical role of the gut microbiome in the pathophysiology of inflammatory bowel disease. Dysbiosis in IBD is supported by the disturbance of microbial distribution with decreased beneficial pathogens and increased harmful ones. Aberrant microbial composition was observed in IBD patients, mainly represented by reduced levels of *Firmicutes* and *Faecalibacterium,* and increased amounts of *Bacteroidetes*, *Enterobacteriaceae* and *Escherchia*, which has been connected to NOD2 mutations [18,71,72]. *Fecalibacterium prausnitzii*, from the *Clostridium leptum* subgroup, has increased levels in normal microbiota, having a beneficial role by producing a protein with anti-inflammatory properties that is able to inhibit the nuclear factor-κB pathway. Quevrain et al. showed that

Faecalibacterium prausnitzii has decreased levels in the microbiome from Crohn's disease patients [73]. Similar to AS and PsA patients, *Bifidobacterium adolescentis* and *Coprococcus* levels are depleted in IBD patients [66,74].

Even though probiotics can enhance the diversity and richness of the microbiome and promote intestinal barrier function, a certain probiotic effect on IBD has not been determined, and more research is required to determine the therapeutic benefits of probiotics for use in day-to-day care [55]. On the other hand, FMT can improve the diversity of gut microbial components in IBD patients; however, at present, there are mixed results regarding this therapeutic option in Crohn's disease or ulcerative colitis [75–77].

This narrative review highlights the new data about the microbiota in psoriatic arthritis, a rheumatic pathology that has been less researched on this topic until now. The principal limitation of this literature research is the small number of studies conducted on this subject, especially the small number of enrolled patients in each study. Second, it is more difficult to compare and validate the findings across studies due to the variety of the gut microbiota and various component analysis.

4. Materials and Methods

This review was conducted by searching two databases, PubMed and Embase, using the combinations of words "gut microbiota" or "microbiome" and "psoriatic arthritis", until December 2022. A total of 175 articles were generated. After excluding the duplicates, we analyzed the article content, applying the inclusion and exclusion criteria. The inclusion criteria were as follows: original studies, written in English, that focused on the importance of gut microbiota in PsA. Exclusion criteria were: reviews, studies with a focus only on psoriasis, not PsA, studies without significant information on gut microbiome in PsA, and studies conducted on animals (although we described a relevant study in the Results section, we did not include it in the Results table). The research strategy is illustrated in Figure 2.

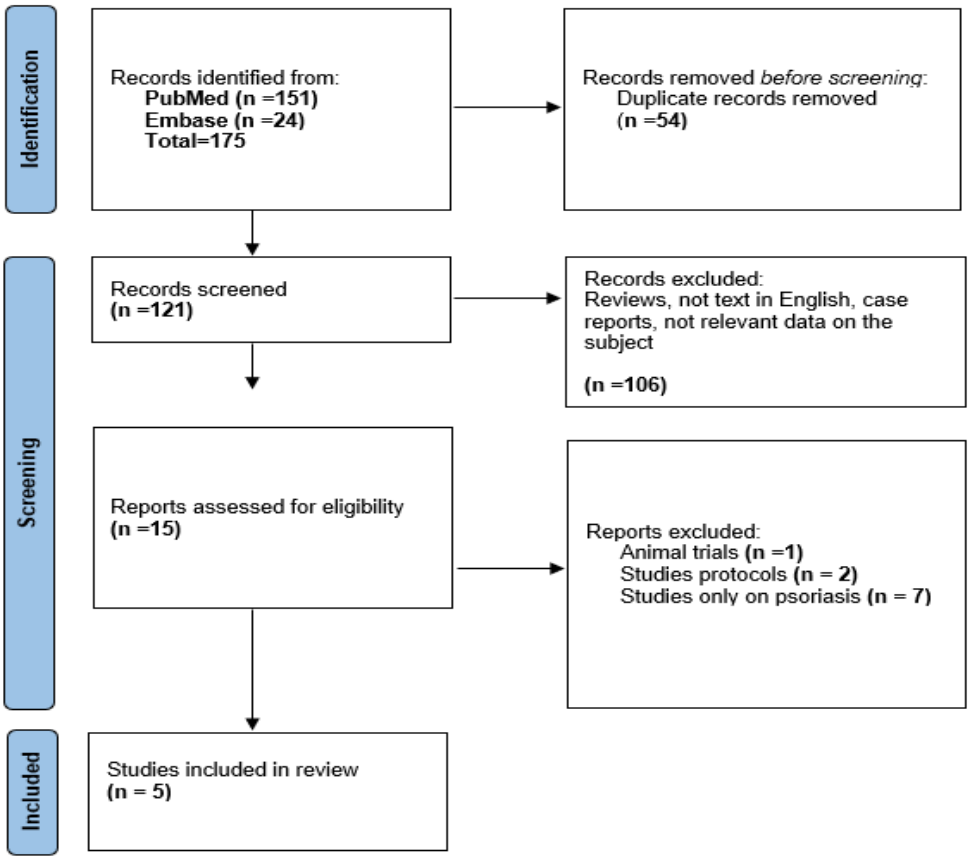

Figure 2. Database search for gut microbiota in psoriatic arthritis.

5. Conclusions

According to recent research, the microbiome has a role in the development and progression of psoriatic arthritis. The composition and diversity of the gut microbiome are different in psoriatic arthritis patients compared to healthy people. Studies have revealed that alterations in the gut microbiota may be related to a specific inflammatory disease, with differences between psoriatic arthritis and psoriasis, ankylosis spondylitis and inflammatory bowel disease. Furthermore, there is evidence that various microbial components are associated with specific symptoms such as enthesitis and dactylitis. As this is still subject under investigation, more research is required to completely understand the gut microbiota's role in the pathophysiology of psoriatic arthritis. The effects of biologic therapy on the microbiome and the association of HLA-B27 and dysbiosis are arguments to support the importance of gut microbiota in Spondylarthritis. Moreover, the possibility of fecal transplantation and the scarce evidence of beneficial probiotic usage in treating chronic inflammatory diseases such as psoriatic arthritis encourage the development of novel therapeutic options targeting microbiome.

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