Original paper

Study of gut microbiome alterations in plaque psoriasis patients compared to healthy individuals

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Adv Dermatol Allergol 2024; XLI (4): 378–387
DOI: https://doi.org/10.5114/ada.2024.142394

Abstract

Introduction: Many studies have shown significant alterations in the gut microbiome of patients with psoriasis compared to healthy controls.

Aim: The primary objective of the current research was to explore the impact of gut microbiome composition on the progression and severity of plaque psoriasis.

Material and methods: A total of 20 patients with moderate-to-severe psoriasis and 20 healthy individuals were recruited and provided a stool sample to assess the gut microbiome. After the samples were prepared according to the NGS library preparation workflow, they were sequenced using the Illumina platform and the report was generated that underwent statistical analysis.

Results: The microbiome profiles of psoriasis patients exhibited significant differences compared to healthy controls as evidenced by the statistical analysis of various bacterial genera, with the median abundance significantly lower in psoriasis patients compared to healthy controls ($p = 0.033$). The analysis of the Firmicutes-to-Bacteroidetes ratio, a commonly evaluated marker of dysbiosis, did not reach statistical significance ($p = 0.239$). However, there was a noticeable trend towards a higher median ratio in psoriasis patients compared to healthy controls. The ratio did not show significant associations with PASI or BSA but trends towards significance with DLQI ($B = –12.11$, $p = 0.095$).

Conclusions: Overall, the above findings underscore the importance of the gut microbiome in psoriasis and suggest that modulation of specific bacterial genera, especially that with significant differences, could be a potential strategy for therapeutic intervention. Targeting these depleted genera through microbiome-based interventions, such as probiotic supplementation or faecal microbiota transplantation, could potentially help to restore gut homeostasis and alleviate the inflammatory burden in psoriasis.

Key words: gut microbiome, dysbiosis, psoriasis.

Introduction

The term microbiome was coined by Nobel Prize laureate Joshua Lederberg. It refers to the community of microorganisms that typically inhabit a given habitat, including commensal, symbiotic and pathogenic bacteria, archaea and eukaryotes within the human body. Essentially, it encompasses the entire microbial ecosystem, rather than just their genomes [1]. Many studies have shown significant alterations in the gut microbiome of patients with psoriasis compared to healthy control groups, including inter alia reduction in overall microbial diversity, increased number of Firmicutes and a reduction in Bacteroidetes phyla (marked as Firmicutes/Bacteroidetes; F/B ratio). It may result in short-chain fatty acids (SCFAs) and medium-chain fatty acids (MCFAs) production alteration and increased production of pro-atherogenic trimethylamine-N-oxide (TMAO) [2, 3]. Also, in several studies psoriasis was found to be related to "leaky gut syndrome", resulting in the translocation of bacteria occurring through the intestinal wall, resulting in low-grade, chronic inflammatory status that can promote the formation of psoriatic plaques [4, 5].

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Received: 13.05.2024, **accepted:** 15.06.2024, **online publication:** 21.08.2024.

Aim

The primary objective of the current study is to explore the impact of gut microbiome composition on the progression and severity of plaque psoriasis.

We assumed the following hypothesis: the gut microbiota composition in patients suffering from plaque psoriasis varies significantly from that of healthy subjects and has a significant impact on the disease severity.

The goal of this study is to gain deeper insights into how gut microbial profiles may influence the clinical manifestations of psoriasis by exploring the complex relationship between the gut microbiome and psoriasis, aiming to uncover mechanisms that could guide future treatments.

Material and methods

The study was part of the project "Bacterial dysbiosis in psoriasis vulgaris", carried out in accordance with the guidelines of the Declaration of Helsinki. It received approval from the local research Ethical Committee of the Medical University of Silesia with the decision number PCN/0022/KB1/47/20, issued on 30 June 2020. In this research, a total of 20 patients with moderate-to-severe plaque psoriasis and 20 age-matched healthy controls who attended the outpatient clinic for dermoscopic evaluation of pigmental nevus but without diseases were recruited. The participants met the inclusion and exclusion criteria outlined in Table 1. The recruitment process focused on patients admitted to the Dermatology Clinic between 2022 and 2023 due to their psoriasis condition. On the initial day of patients' admission, detailed information was collected, including sex, age, psoriasis duration, concomitant diseases, former smoking habits, body mass Index (BMI). Each patient was assessed using Psoriasis Area and Severity Index (PASI), Body Surface area (BSA) and Dermatology Life Quality Index (DLQI).

The day after admission, the authors collected a 10 g stool sample to assess the gut microbiome. The specimens were obtained using sterile collection sets, following the recommended procedure for safe sample collection. The collected stool samples were frozen in a freezer at –18°C and then collectively transported to the A&A Biotechnology Laboratory in a container with a cooling cartridge. Genomic DNA was isolated using a modified method based on the Genomic Mini kit AX Bacteria + (A&A Biotechnology). Mechanical lysis of samples was used in the device type FastPrep-24 using zirconium balls. DNA concentration was measured using the fluorometric method on a Qubit 4 device Fluorometer. The presence of bacterial DNA in the tested samples was confirmed using Real-Time PCR. The Real-Time PCR reaction was performed in a CFX Connect thermal cycler (Biorad) using SYBR Green dye as a fluorochrome. Universal primers were used in the reaction, amplifying a fragment of the bacterial gene 16S rRNA. After the samples were prepared according to NGS library preparation workflow, they were sequenced using Illumina platform (library protocol 16S Metagenomic Sequencing Library Preparation Part # 15044223 Rev. B; library kit Herculase II Fusion DNA Polymerase Nextera XT Index V2

Table 1. Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. Confirmed diagnosis of plaque psoriasis, with no other types of psoriasis ever recognized. 2. The patient fulfilled the criteria for moderate-to-severe plaque psoriasis, including PASI (Psoriasis Area and Severity Index) score of ≥ 10 and Body Surface Area (BSA) involvement of ≥ 10%. 3. Age range between 18 and 40 years old. 4. The patient has not received any systemic therapies (such as antibiotics, probiotics, or non-steroidal anti-inflammatory drugs) in the last 60 days.	1. Patients who did not provide consent for evaluation. 2. Pregnancy or breastfeeding. 3. Recent infections: bacterial, viral, or fungal infections of the skin, mucous membranes, upper respiratory tract, or gastrointestinal tract within the last 60 days. 4. Current tobacco smokers. 5. Patients with alcohol or drug addiction. 6. Individuals who have received systemic immunosuppressive therapy in the past. 7. Concomitant psoriatic arthritis: patients with a diagnosis or suspicion of concomitant psoriatic arthritis. 8. Inflammatory Bowel Disease (IBD): patients with a diagnosis of inflammatory bowel disease, which includes e.g. Crohn's disease and ulcerative colitis. 9. Menstruation in females (to avoid contamination of faecal samples with blood). 10. Any special dietary restrictions or dietary supplements, including pre-, pro- or synbiotics. 11. Other relevant concomitant diseases or drug intake that, in the opinion of the authors, might have a relevant impact on the gut microbiome composition. 12. Individuals with a history of gastrointestinal tract diseases that affect frequency or may result in problems with defecation (e.g., irritable bowel syndrome, haemorrhoids, etc.).

Table 2. Demographic characteristics of the study groups

Characteristic	*N*	Total sample[a]	Group		*P*-value[c]
			Psoriasis[a] $n_1 = 20$	Control[a] $n_2 = 20$	
Sex:	40				1.000
Women		14.00 (35.00%)	7.00 (35.00%)	7.00 (35.00%)	
Men		26.00 (65.00%)	13.00 (65.00%)	13.00 (65.00%)	
Age [years]	40	35.50 (32.75, 39.00)[b]	35.50 (32.00, 39.00)[b]	35.00 (33.75, 39.00)[b]	0.924[d]
BMI [kg/m^2]	40	28.77 (25.52, 31.17)[b]	29.24 (26.01, 30.72)[b]	28.22 (25.52, 31.46)[b]	0.808[d]
Prevalence of overweight/obesity	40	30.00 (75.00%)	15.00 (75.00%)	15.00 (75.00%)	1.000
Smoking habits:	40				1.000[e]
Former		9.00 (22.50%)	4.00 (20.00%)	5.00 (25.00%)	
No		31.00 (77.50%)	16.00 (80.00%)	15.00 (75.00%)	

[a]n (%), [b]Mdn (Q1, Q3), [c]Pearson's χ^2 test, [d]Wilcoxon rank sum test, [e]Fisher's exact test. N – sample size, n – group size, Mdn – median, Q1 – the first quartile (25%), Q3 – the third quartile (75%), p – the p-value of statistical test.

Table 3. Psoriatic patients' characteristics concerning the disease duration and intensity

Characteristic	Psoriasis[a] $n = 20$
Disease duration [years]	10.00 (4.75, 16.00)
According to categories:	
Below 5 years	6.00 (30.00%)[b]
5–10 years	5.00 (25.00%)[b]
Over 10 years	9.00 (45.00%)[b]
PASI score	11.00 (10.18, 15.00)
BSA score	14.50 (11.25, 34.25)
DLQI score	12.00 (6.00, 18.25)

[a]Mdn (Q1, Q3), [b]n (%), n – group size, Mdn – median, Q1 – the first quartile (25%), Q3 – the third quartile (75%).

Kit). The NGS library report was generated, which further underwent biostatistical and then statistical analysis. The detailed statistical method characteristics are provided in the Annex.

Results

The demographic characteristics of the analysed plaque psoriasis and healthy control groups are presented in Table 2. Each cohort included 20 adults. The characteristics included age, sex distribution, BMI, the prevalence of overweight/obesity and smoking habits. The demographic and health status analysis, evenly split between those with plaque psoriasis and healthy controls, revealed no statistically significant differences across all measured parameters, suggesting comparable baseline characteristics between the two groups. The median BMIs were slightly higher in the psoriasis group compared to the controls, but this difference was not statistically significant ($p = 0.808$). Smoking habits were also similar between the groups, with no significant differences in the proportion of former smokers and non-smokers.

Table 3 offers a comprehensive overview of psoriasis-specific data for study participants diagnosed with plaque psoriasis. The median duration of psoriasis was 10 years (interquartile range: 4.75–16 years) with 45% of patients living with psoriasis for over 10 years. The PASI score had a median value of 11 (interquartile range: 10.18–15), the medium BSA score of 14.50 (interquartile range: 11.25–34.25), the median DLQI score of 12 (6–18.25), classifying all patients as moderate-to-severe psoriasis with a substantial effect on the quality of life.

In Table 4, we present the microbiome profiles that have been successfully detected in both psoriasis patients and healthy controls. By examining the differences and similarities in the microbial communities, we aim to identify specific microbes which presence correlates with the clinical manifestations of psoriasis. The abundances of specific bacterial genera, as well as the Firmicutes and Bacteroidetes phyla and their ratio, were used as predictors, while the Psoriasis Area and Severity Index (PASI), Body Surface Area (BSA), and Dermatology Life Quality Index (DLQI) were used as outcome measures of psoriasis severity. The microbiome profiles of psoriasis patients exhibit significant differences compared to healthy controls, with median abundance of the Bacteria kingdom (undifferentiated genus) significantly lower (4.49×10^{-5} vs. 10.35×10^{-5}, $p = 0.033$), showing lower biodiversity of gut microbiome composition in psoriasis patients. Also, the number of Bacteroides (3.35×10^{-5} vs. 42.77×10^{-5}, $p = 0.011$), Lachnospira (38.31×10^{-5} vs. 145.08×10^{-5}, $p = 0.001$), Lachnospiraceae UCG-008 (1.91×10^{-5} vs. 3.52×10^{-5}, $p = 0.008$), Marvinbryantia (10.44×10^{-5} vs.

Table 4. Comparison of detected microbiome profiles between psoriasis patients and healthy controls

Characteristic	Group				*P*-value[a]
	Psoriasis		Control		
	n_1	Mdn (Q1, Q3)	n_2	Mdn (Q1, Q3)	
Bacteria kingdom undifferentiated genus [× 10^{-5}]	7	4.59 (2.31, 7.55)	10	10.35 (6.40, 19.16)	**0.033**
Bacteroides [× 10^{-3}]	18	3.35 (0.48, 17.14)	19	42.77 (8.22, 88.66)	**0.011**
Frisingicoccus [× 10^{-5}]	5	17.44 (11.66, 22.19)	5	74.57 (61.84, 132.45)	0.056
Lachnospira [× 10^{-5}]	15	38.31 (25.01, 65.17)	12	145.08 (78.66, 340.69)	**0.001**
Lachnospiraceae UCG-008 [× 10^{-5}]	11	1.91 (1.56, 2.54)	11	3.52 (2.34, 8.33)	**0.008**
Marvinbryantia [× 10^{-4}]	15	10.44 (2.87, 18.10)	15	18.39 (14.82, 31.14)	**0.037**
Olsenella [× 10^{-5}]	3	24.41 (21.22, 27.66)	3	8.61 (4.87, 11.08)	0.100
Streptococcus [× 10^{-3}]	20	6.46 (1.32, 17.17)	20	17.38 (11.00, 48.00)	**0.007**
UCG-002 [× 10^{-5}]	17	29.18 (3.46, 231.74)	16	150.90 (37.32, 316.95)	0.179
Granulicatella [× 10^{-5}]	10	1.80 (1.06, 3.01)	15	1.52 (0.98, 2.99)	0.765
Pygmaiobacter [× 10^{-5}]	9	1.84 (1.21, 3.50)	6	1.73 (0.45, 4.07)	0.456
UCG-003 [× 10^{-5}]	7	1.53 (1.40, 4.25)	12	4.02 (0.96, 8.88)	0.711
Bifidobacterium [× 10^{-4}]	19	28.37 (7.28, 53.20)	19	27.62 (7.30, 62.45)	0.817
[Eubacterium] brachy group [× 10^{-5}]	15	12.12 (5.92, 15.79)	13	5.03 (3.05, 14.18)	0.254
Faecalibacterium [× 10^{-5}]	19	16.59 (3.75, 51.00)	20	27.40 (12.29, 76.89)	0.258
Oscillibacter [× 10^{-5}]	12	1.88 (0.88, 4.46)	13	3.18 (1.74, 6.59)	0.376
UCG-010 Family Unknown Genus [× 10^{-5}]	10	4.46 (2.67, 12.97)	15	3.44 (1.10, 25.33)	0.849
Subdoligranulum [× 10^{-5}]	19	52.85 (33.74, 75.02)	20	36.76 (25.21, 69.71)	0.296
Clostridia Class Unknown Genus [× 10^{-5}]	17	3.71 (1.17, 5.77)	17	3.61 (1.94, 6.86)	0.919
Parabacteroides [× 10^{-5}]	14	4.77 (3.73, 56.96)	18	8.25 (2.35, 56.22)	0.837
Coriobacteriales Incertae Sedis Family Unknown Genus [× 10^{-5}]	15	43.34 (13.21, 90.44)	12	40.40 (5.64, 90.19)	0.648
Family XIII UCG-001 [× 10^{-5}]	10	3.23 (0.46, 8.46)	11	11.03 (2.44, 23.28)	0.152
Gemella [× 10^{-5}]	13	2.02 (1.12, 2.83)	15	2.30 (1.66, 3.56)	0.413
Firmicutes (phylum)	20	0.85 (0.70, 0.93)	20	0.82 (0.75, 0.90)	0.678
Bacteroidetes(phylum)	19	0.02 (0.01, 0.05)	20	0.04 (0.01, 0.12)	0.228
Firmicutes-to- Bacteroidetes ratio phylum	18	38.98 (19.53, 255.10)	20	25.27 (5.97, 91.20)	0.239

[a]*Wilcoxon rank sum test. n – group size, Mdn – median, Q1 – the first quartile (25%), Q3 – the third quartile (75%), p – the p-value of statistical test.*

18.39 × 10^{-5}, $p = 0.037$) and Streptococcus (6.46 × 10^{-3} vs. 17.38 × 10^{-3}, $p = 0.007$) is lower in patients suffering from plaque psoriasis.

Table 5 presents the results of the univariate analyses, demonstrating the impact of various bacterial genera and phyla on PASI, BSA, and DLQI scores. No statistically significant correlation was found between the general biodiversity as well as the genera Bacteroides, Frisingicoccus, Lachnospira, Lachnospiraceae UCG-008, Marvinbryantia, Olsenella, and Streptococcus and PASI, BSA, and DLQI values. However, a correlation between BSA score and Bacteroidetes (B = 1.24 × 10^{-3}, $p = 0.024$), Parabacteroides ($B = 1.64$, $p = 0.044$) and Faecalibacterium ($B = 1.73$, $p < 0.001$) abundance was present. The PASI score was correlated with the abundance of Faecalibacterium ($B = 3.58$, $p = 0.021$), Parabacteroides ($B = 13.12$, $p < 0.001$) and Firmicutes ($B = 0.01$, $p = 0.037$). DLQI was found to correlate with the number of bacteria from Family XIII UCG-001 ($B = –0.56$, $p = 0.035$) and Pygmaiobacter ($B = 0.15$, $p = 0.004$). No statistically significant correlation was found between the Firmicutes-to-Bacteroidetes ratio and PASI, BSA, and DLQI values.

Discussion

The analysis, which examined the characteristics of both individuals with plaque psoriasis and healthy controls, found no statistically significant differences across all measured parameters. This suggests that the two groups have comparable baseline characteristics. It was important to investigate the gut microbiome composi-

Table 5. The results of the univariate analysis (RLM) assessing the impact of microbiome composition on psoriasis severity levels

Predictor	Outcome	B	95% CI	*P*-value
Bacteria kingdom undifferentiated genus [× 10^{-5}]	PASI	–0.28	–1.48–0.92	0.574
	BSA	–0.10	–0.38–0.19	0.430
	DLQI	0.04	–0.64–0.72	0.892
Bacteroides [× 10^{-3}]	PASI	0.10	–1.69–1.90	0.905
	BSA	0.26	–0.20–0.72	0.255
	DLQI	0.05	–1.06–1.17	0.920
Frisingicoccus [×10^{-5}]	PASI	0.40	–2.81–3.61	0.721
	BSA	0.35	–0.11–0.80	0.093
	DLQI	2.90	–0.98–6.78	0.098
Lachnospira [× 10^{-5}]	PASI	1.90	–5.13–8.93	0.569
	BSA	0.72	–0.59–2.03	0.256
	DLQI	1.94	–0.76–4.63	0.144
Lachnospiraceae UCG-008 [× 10^{-5}]	PASI	–0.09	1.56–4.77	0.144
	BSA	0.00	–0.03–0.03	0.997
	DLQI	–0.02	–0.10–0.06	0.613
Marvinbryantia [× 10^{-5}]	PASI	–0.57	–1.85–0.70	0.349
	BSA	–0.03	–0.73–0.67	0.926
	DLQI	–0.53	–1.49–0.44	0.258
Olsenella [× 10^{-5}]	PASI	–1.25	–10.54–8.04	0.337
	BSA	–0.23	–4.36–3.89	0.601
	DLQI	1.09	–2.63–4.82	0.167
Streptococcus [× 10^{-3}]	PASI	–0.50	–1.73–0.73	0.404
	BSA	–0.26	–0.63–0.10	0.143
	DLQI	–0.30	–1.12–0.52	0.449
UCG-002 [× 10^{-5}]	PASI	–4.20	–24.62–16.22	0.667
	BSA	–0.61	–6.84–5.63	0.838
	DLQI	–2.64	–17.83–12.55	0.717
Granulicatella [× 10^{-5}]	PASI	0.03	–0.16–0.23	0.710
	BSA	0.02	–0.04–0.08	0.441
	DLQI	0.01	–0.15–0.18	0.852
Pygmaiobacter [× 10^{-5}]	PASI	–0.65	–1.53–0.22	0.119
	BSA	–0.04	–0.19–0.11	0.550
	DLQI	0.15	0.07–0.24	**0.004**
UCG-003 [× 10^{-5}]	PASI	0.15	–0.48–0.77	0.577
	BSA	0.10	–0.06–0.26	0.167
	DLQI	0.01	–0.49–0.51	0.969
Bifidobacterium [× 10^{-4}]	PASI	–1.93	–5.46–1.59	0.263
	BSA	–0.93	–2.29–0.42	0.165
	DLQI	–1.26	–3.80–1.28	0.309
[Eubacterium] brachy group [× 10^{-5}]	PASI	–0.46	–1.43–0.51	0.323
	BSA	–0.18	–0.51–0.14	0.241
	DLQI	0.11	–0.63–0.86	0.751

Table 5. Cont.

Predictor	Outcome	B	95% CI	*P*-value
Faecalibacterium [× 10^{-5}]	PASI	3.58	0.62–6.54	**0.021**
	BSA	1.73	0.84–2.62	**< 0.001**
	DLQI	0.14	–2.54–2.81	0.916
Oscillibacter [× 10^{-5}]	PASI	–0.07	–0.49–0.34	0.694
	BSA	–0.03	–0.16–0.10	0.616
	DLQI	–0.07	–0.53–0.40	0.761
UCG-010 Family Unknown Genus [× 10^{-5}]	PASI	–1.17	–2.65–0.32	0.108
	BSA	–0.15	–0.48–0.18	0.332
	DLQI	–0.64	–1.54–0.26	0.140
Subdoligranulum [× 10^{-5}]	PASI	1.37	–1.52–4.27	0.331
	BSA	0.76	–0.02–1.54	0.056
	DLQI	1.65	–0.22–3.51	0.079
Clostridia Class Unknown Genus [× 10^{-5}]	PASI	–0.33	–0.90–0.23	0.228
	BSA	–0.10	–0.25–0.006	0.200
	DLQI	–0.19	–0.47–0.08	0.155
Parabacteroides [× 10^{-5}]	PASI	13.12	10.00–16.25	**< 0.001**
	BSA	1.64	0.05–3.22	**0.044**
	DLQI	1.44	–2.93–5.81	0.487
Coriobacteriales incertae sedis family unknown genus [× 10^{-5}]	PASI	–0.41	–8.74–7.93	0.917
	BSA	–1.22	–4.36–1.92	0.415
	DLQI	1.31	–4.19–6.82	0.614
Family XIII UCG-001 [× 10^{-5}]	PASI	–0.17	–1.17–0.83	0.703
	BSA	–0.21	–0.54–0.13	0.191
	DLQI	–0.56	–1.07–-0.05	**0.035**
Gemella [× 10^{-5}]	PASI	–0.18	–0.60–0.23	0.350
	BSA	–0.01	–0.11–0.08	0.784
	DLQI	0.12	–0.08–0.33	0.207
Firmicutes (phylum)	PASI	0.01	0.00–0.03	**0.037**
	BSA	3.30×10^{-3}	0.00–0.01	0.128
	DLQI	-1.97×10^{-3}	–0.01–0.01	0.661
Bacteroidetes (phylum)	PASI	2.08×10^{-3}	0.00–0.01	0.179
	BSA	1.24×10^{-3}	0.2×10^{-3}–2.3×10^{-3}	**0.024**
	DLQI	5.45×10^{-4}	-1.5×10^{-3}–2.6×10^{-3}	0.584
Firmicutes-to-Bacteroidetes ratio phylum	PASI	–5.58	–23.63–12.47	0.521
	BSA	–1.32	–5.28–2.64	0.490
	DLQI	–12.11	–16.56–2.35	0.095

B – regression coefficient, CI 95% – confidence interval 95%; p – p-value od statistical test.

tion in patients with similar BMIs and obesity statutes as obesity and dietary habits may have an impact on the course of psoriasis [6].

The microbiome profiles of psoriasis patients exhibit significant differences compared to healthy controls as evidenced by the statistical analysis of various bacterial genera. The median abundance of Bacteria kingdom undifferentiated genus was significantly lower in psoriasis patients compared to healthy controls with $p = 0.033$. This suggests a possible reduction in microbial diversity or a specific depletion of this unidentified bacterial group in psoriasis. These findings remain consistent with other studies claiming lower biodiversity in moderate-to-severe psoriasis patients [2, 7, 8].

Similarly, the genus Bacteroides, known for its role in maintaining gut barrier integrity and immunomodulation [9], was found in significantly lower abundance ($p = 0.011$) in psoriasis patients compared to controls. The reduction of Bacteroides in psoriasis patients could contribute to an impaired barrier function and increased intestinal permeability, possibly leading to systemic inflammation that exacerbates skin lesions [4].

Conversely, Lachnospira, a genus potentially involved in the production of short-chain fatty acids that regulate inflammation and immune responses [10], showed a significantly reduced median abundance in psoriasis patients compared to controls ($p = 0.001$). The depletion of such beneficial bacteria could exacerbate the inflammatory processes underlying psoriasis.

Furthermore, the genus Lachnospiraceae UCG-008 also presented a lower median abundance in psoriasis patients compared to controls ($p = 0.008$), supporting the notion of a disrupted microbial environment in psoriasis [11]. In a study by Matsumoto *et al*., which investigated the effects of nutrients consumed on the entire gut microbiome in healthy Japanese monozygotic twins, Lachnospiraceae UCG-008 abundance had a negative correlation with the saturated fatty acid intake [12]. This finding remains important as saturated fatty acids were found to increase the cardiovascular risk in many studies [13] and patients with psoriasis in general are up to 50% more likely to develop cardiovascular disease with the risk increasing along with the skin involvement severity [14]. Marvinbryantia, another genus potentially important for gut health, was significantly less abundant in psoriasis patients than in controls ($p = 0.037$). In mice, Marvinbryantia was shown to play an important role in consuming oligosaccharides and boosting the yield of succinate [15]. In humans, it was positively associated with fibre intake and lower risk of type 2 diabetes [16]. Many studies showed that the risk of type 2 psoriasis is higher in psoriatic patients, especially in late-onset psoriasis [17], which may indicate similar gut microbiome alterations and the important role of diet in these diseases.

Conversely, the genus Olsenella, which produces inosine [18], although not reaching statistical significance ($p = 0.100$), showed an increased median abundance in psoriasis patients compared to controls. Inosine is a nucleoside that plays an essential role in the purine biosynthesis and degradation. There is a link between inosine, gut microbiota composition and the pathways involved in many anti-tumour, anti-inflammatory and antimicrobial responses [19] as the inosine influences the Th1 differentiation and antitumor immunity by activating the T cell adenosine 2A receptor (A2AR)/CREB pathway. However, this effect (either boosting or inhibiting) depends on the presence of inter alia IFN-γ [18] that in general shows a higher concentration in the serum of psoriatic patients [20]. Yet, this link needs further investigation.

Notably, the genus Streptococcus showed a statistically significant lower median abundance in psoriasis patients compared to healthy controls, with $p = 0.007$. This finding is of particular interest as Streptococcus is often implicated in triggering immune responses which could either exacerbate or mitigate inflammatory conditions such as psoriasis [21]. The reduced levels in psoriasis patients may suggest a compromised ability to manage pathogenic interactions or modulate immune responses adequately.

The genus UCG-002 also presented interesting results, with a higher median abundance in healthy controls compared to psoriasis patients, although the difference did not reach statistical significance ($p = 0.179$). UCG-002 produces valeric acid and is associated with anti-inflammatory effect [22].

Other genera such as Granulicatella, which has a pro-inflammatory effect [23], and Pygmaiobacter, which in an animal model contributes to short-chain fatty acids (SCFAs) promotion [24], showed no significant differences in median abundance between psoriasis patients and controls, with $p = 0.765$ and 0.456, respectively. The absence of significant differences in these genera suggests that they may not play a critical role in the pathogenesis of psoriasis, or their impact might be overshadowed by more dominant microbial interactions and influences. For other genera such as UCG-003, Bifidobacterium, [Eubacterium] brachy group, Faecalibacterium, and Oscillibacter, no statistically significant differences were found.

Specifically, Bifidobacterium, known for its beneficial role in gut health [25], showed nearly identical median levels between psoriasis patients and controls with $p = 0.817$. This suggests that despite the systemic inflammation present in psoriasis, the levels of Bifidobacterium, which might play a role in maintaining mucosal integrity and modulating immune responses [25], remain comparable to those of healthy individuals.

The analysis of UCG-010 Family Unknown Genus, Clostridia Class Unknown Genus, Parabacteroides, Coriobacteriales Incertae Sedis Family Unknown Genus, Gemella, and the phyla Firmicutes and Bacteroidetes did not demonstrate significant differences in median abundance between psoriasis patients and healthy controls. The *p*-values ranged from 0.228 to 0.919, indicating a high likelihood that any observed differences could be due to random variation rather than a true difference between the groups. This suggests that these microbial components may not be distinctly altered in individuals with psoriasis, or their impact on disease pathophysiology might be less pronounced.

Subdoligranulum and Family XIII UCG-001 showed trends toward differences in median abundances, though these did not reach statistical significance ($p = 0.296$ and $p = 0.152$, respectively). Subdoligranulum, known for its potential anti-inflammatory properties [26], was higher in psoriasis patients, which might suggest a compensatory

response to systemic inflammation. Conversely, the lower abundance of Family XIII UCG-001 in psoriasis patients could indicate a reduction in certain beneficial microbes, potentially contributing to the inflammatory milieu characteristic of psoriasis.

Following the analysis of detected microbiomes, this subsection shifts focus to the microbial profiles that were not detected in the groups under study (zero values, which indicate no detection of individual bacteria in stool samples). The absence of certain microbes can be as informative as their presence, offering insights into microbial gaps that may influence health status. The analysis particularly highlighted that the majority of non-detected microbiome values occurred in Olsenella, with both groups showing high non-detection rates (85% in each group or $n_1 = n_2 = 17$). In contrast, no instances of non-detection were recorded for Streptococcus and within the entire Firmicutes phylum. Statistical analysis of these non-detection rates revealed no significant differences between the two groups, with *p*-values ranging from 0.102 to 1.000. These findings indicate that the frequency of undetectable bacteria is similar between patients with psoriasis and healthy controls under the conditions of this study.

The bacteria kingdom (undifferentiated genus) as well as the genera Bacteroides, Frisingicoccus, Lachnospira, Lachnospiraceae UCG-008, Marvinbryantia, Olsenella, and Streptococcus showed variations in their influence across PASI, BSA, and DLQI, but none reached statistical significance.

Faecalibacterium stands out with significant associations observed with both PASI and BSA scores. The coefficients indicate a positive relationship, suggesting that higher levels of Faecalibacterium are associated with increased severity of psoriasis, as evidenced by PASI ($B = 3.58$, $p = 0.021$) and BSA ($B = 1.73$, $p < 0.001$). This finding is particularly notable as Faecalibacterium is generally considered a beneficial commensal bacterium associated with anti-inflammatory properties in other contexts [27]. The observed association might suggest a complex, context-dependent role in psoriasis or it could reflect underlying disease mechanisms not previously appreciated.

In contrast, other bacteria such as UCG-002, Granulicatella, Pygmaiobacter, UCG-003, Bifidobacterium, and the [Eubacterium] brachy group did not show significant impacts on PASI or BSA scores. However, Pygmaiobacter, which promotes SCFAs production [24], exhibited a statistically significant association with DLQI ($B = 0.15$, $p = 0.004$), suggesting that it may influence the quality of life aspects of psoriasis rather than the clinical severity measured by PASI and BSA. This could imply that Pygmaiobacter has a role in the psychosocial or symptomatic dimensions of psoriasis, such as itch, which are not captured by PASI and BSA.

The taxa Oscillibacter, UCG-010 (Family Unknown Genus), Subdoligranulum, Clostridia Class Unknown Genus, Coriobacteriales incertae sedis (family unknown genus), Family XIII UCG-001, and Gemella mostly show non-significant effects across all three psoriasis severity outcomes (PASI, BSA and DLQI). This suggests that, individually, these microbial entities may not play a prominent role in influencing the severity of psoriasis as measured by these indices. However, this does not preclude their involvement in more complex microbial interactions that could influence disease or their effects on other unmeasured aspects of psoriasis.

Notably, Parabacteroides, which in general regulate immunity, relieve inflammation and produce SCFAs [28], exhibit a statistically significant and strong association with PASI scores ($B = 13.12$, $p < 0.001$) and a significant, albeit smaller, effect on BSA scores ($B = 1.64$, $p = 0.044$). These results suggest a potentially impactful role for Parabacteroides in exacerbating psoriasis severity, which remains in contrast with general findings [28]. The magnitude and significance of the association with PASI are particularly compelling, indicating that increases in Parabacteroides are associated with worsening of psoriasis severity. The biological mechanisms behind this association could involve inflammatory pathways as Parabacteroides may influence immune responses, which are critical in the pathogenesis of psoriasis.

Family XIII UCG-001 shows a significant association with DLQI, albeit with a negative coefficient ($B = –0.56$, $p = 0.035$), suggesting that higher levels of this bacterial group could be linked to a slight improvement in the DLQI, or at least does not exacerbate it. This could indicate a potential protective or mitigating effect on the quality of life impairments typically associated with psoriasis, which is consistent with previous findings as this family plays a protective role in certain inflammatory conditions, e.g. eczema [29].

The other bacteria, including UCG-010 (Family Unknown Genus) and Subdoligranulum, despite showing suggestive trends towards significance in some outcomes, did not reach statistical significance in this analysis. This could be due to limited power, variability in the microbial data, or the complex nature of interactions in the microbiome that are not captured in a univariate model.

Bacteroidetes and Firmicutes are the two most dominant phyla in gut microbiome composition, secreting SCFAs [2]. Concerning the phylum level, the analysis showed a statistically significant positive association of Firmicutes with the PASI, with a regression coefficient $B = 0.01$ ($p = 0.037$). This suggests that an increase in Firmicutes is associated with a mild increase in psoriasis severity as measured by PASI. The influence of Firmicutes on BSA and DLQI was not statistically significant, suggesting that the effect of Firmicutes might be more localized to the factors that PASI measures, possibly inflammation and the extent of skin lesions.

Bacteroidetes, on the other hand, showed a significant association with BSA ($B = 1.24 \times 10^{-3}$, $p = 0.024$) but not with PASI or DLQI. This indicates that Bacteroidetes may play a role in influencing the extent of skin area affected by psoriasis but does not significantly impact the severity per PASI or the quality of life impairments per DLQI. The specific mechanism by which Bacteroidetes influences BSA remains unclear but could involve factors related to skin barrier functions or local immune responses.

The analysis of the Firmicutes-to-Bacteroidetes ratio, a commonly evaluated marker of dysbiosis [7, 30–33] also did not reach statistical significance ($p = 0.239$), although there was a noticeable trend towards a higher median ratio in psoriasis patients compared to controls. Despite lacking statistical significance, this finding is in line with previous studies suggesting that psoriasis might be associated with gut dysbiosis, characterized by an increased Firmicutes-to-Bacteroidetes ratio [7, 30–33].

Interestingly, the Firmicutes-to-Bacteroidetes ratio did not show significant associations with PASI or BSA but trends towards significance with DLQI ($B = –12.11$, $p = 0.095$). Although this association did not reach statistical significance, it suggests a potential inverse relationship between this microbial ratio and quality of life, where a higher ratio might correlate with a lesser quality-of-life impact. This observation could imply that the balance between these two phyla, rather than their individual abundances, might influence the systemic effects of psoriasis or its psychosocial burdens.

Also, the authors would like to discuss the limitations of the study. A small study group was caused by restrictive inclusion and exclusion criteria as well as limited funding. Also, no standard microbiome model was established in order to compare the results as various factors modulate it [2].

These findings collectively underscore a complex interaction between microbiome composition at the phylum level and psoriasis severity. Patients with plaque psoriasis seem to demonstrate lower microbiome biodiversity then healthy controls. While Firmicutes and Bacteroidetes are individually associated with specific clinical outcomes (PASI and BSA, respectively), their ratio appears to potentially relate to broader quality-of-life effects. This suggests that interventions aimed at modifying the microbiome in psoriasis might need to consider the balance of microbial communities, in addition to the presence of specific microbes. Overall, the above findings underscore the importance of the gut microbiome in psoriasis and suggest that modulation of specific bacterial genera (especially those with significant differences) could be a potential strategy for therapeutic intervention. Targeting these depleted genera through microbiome-based interventions, such as probiotic supplementation [34] or faecal microbiota transplantation [2], could potentially help restore gut homeostasis and alleviate the inflammatory burden in psoriasis, as well as some of the associated risks.

Acknowledgments

The study was conducted in the Chair and Department of Dermatology, Medical University of Silesia, 20-24 Francuska Street, 40-027 Katowice, Poland.

Funding

Funding was provided as a part of funding statutory works by the Medical University of Silesia.

Ethical approval

Approval numer: PCN/0022/KB1/47/20.

Conflict of interest

The authors declare no conflict of interest.

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Annex

Detailed characteristics of the statistical methods

The statistical significance threshold was set at $\alpha = 0.05$. Shapiro-Wilk test was used to assess normality in order to establish the distribution characteristics of numerical data. Descriptive statistics using the median (Mdn) accompanied by the first (Q1) and third (Q3) quartiles was used in cases of numerical data that did not display normal distribution, and reported illustrating central tendency and dispersion. For categorical variables, the analysis involved reporting the counts (n) and percentages of each category. The Wilcoxon rank-sum test was used to compare differences between two independent groups concerning numerical variables, with the χ^2 test used as the primary method in cases where associations between two nominal (categorical) variables were examined. In cases, where the expected frequencies in any cell of the contingency table were less than five, Fisher's exact test was used instead. Spearman's rho correlation coefficients were used, with *p*-values calculated through the asymptotic *t* approximation to aid in assessing statistical significance for the analysis of correlation between two non-normal numeric variables. Our investigation into the impact of microbiome composition on the severity of psoriasis involved a robust statistical approach to accommodate potential outliers and non-normal data distributions. We employed a univariate regression model with a robust estimator (Robust Linear Model, RLM), which is particularly suitable for data that may not meet the assumptions required by ordinary least squares regression, such as the presence of outliers or heteroscedasticity. The 95% confidence intervals (CI) and *p*-values were estimated using the asymptotic *t* approximation. Analyses were conducted using the *R* Statistical language (version 4.3.1; R Core Team, 2023) on Windows 10 Pro 64 bit (build 19045), using the packages *parameters* (version 0.21.3; Lüdecke *et al*., 2020), *report* (version 0.5.7; Makowski *et al*., 2023), *gtsummary* (version 1.7.2; Sjoberg *et al*., 2021), *MASS* (version 7.3.60; Venables, Ripley, 2002), *dplyr* (version 1.1.3; Wickham *et al*., 2023) and *psych* (version 2.3.9; William Revelle, 2023).