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# Microbiome Alterations in Patients with Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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## ABSTRACT

**Background:** Chronic Prostatitis/ Chronic Pelvic Pain Syndrome (CP/CPPS) is a widespread disease among men, featuring persistent pelvic discomfort and urinary symptoms in the absence of infection. Recent studies suggest that gut microbiota may influence systemic inflammation and pain signaling pathways, thus offering clues into the possible pathophysiology of CP/CPPS. 'To compare the gut microbiome profile of patients with CP/CPPS to that of healthy individuals, and to explore possible associations with clinical symptoms and lifestyle factors'.

**Methods:** A case-control study was carried out over the span of a year, from May 2023 to December 2024, with a sample size of 51 men. This included 26 patients diagnosed with CP/CPPS and 25 health matched controls. Relevant demographic information such as age alongside clinical history with symptoms severity scoring was captured systematically. Stool samples were gathered and analyzed via DNA sequencing for the 16S rRNA gene. Intergroup comparison of microbial diversity indices and taxonomic composition was carried out using appropriate statistical approaches.

**Results:** Patients diagnosed with CP/CPPS exhibited decreased alpha diversity in comparison to the controls (Shannon index $p = 0.004$; Simpson index $p = 0.006$). In this group, increased relative abundance of Escherichia/Shigella together with decreased levels of some beneficial genera such as Lactobacillus and Faecalibacterium were noted. Such microbial changes were coupled with an increase in recent antibiotic use and lower fiber intake among patients.

**Conclusion:** Patients with CP/CPPS exhibit signs of gut dysbiosis, marked by reduced microbial diversity and an imbalance in bacterial composition. These findings suggest a possible link between the gut microbiome and the persistence of pelvic pain symptoms, highlighting the potential of microbiome-targeted strategies in the management of CP/CPPS.

***Keywords:*** *CP/CPPS, chronic prostatitis, gut microbiome, pelvic pain, microbial diversity, dysbiosis, 16S rRNA sequencing*

## 1. INTRODUCTION

Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) is a complicated urological problem which affects a significant number of younger males, especially those below the age of 50. The condition manifests as pelvic and perineal discomfort lasting longer than three months along with urinary or sexual difficulties in the absence of any detected bacterial infection. The condition has no cause, and both patients and medical professionals face continuing challenges in its management [1-3].

The prostate gland has long been regarded as the focal point of importance for this condition, but new evidence suggests it could be an accessory to what is a systemic process. Within the last decade, researchers have begun examining the microbiome the sophisticated ecosystem of microorganisms inhabiting humans as potentially relevant to chronic inflammatory and pain syndromes. More specifically, the gut microbiome has been linked with modulating immune response, inflammation, and pain perception [4-6].

Several researchers have suggested that changes in the body's microbial equilibrium, termed 'dysbiosis,' might cause or worsen symptoms of conditions like irritable bowel syndrome, chronic fatigue syndrome, and interstitial cystitis. Considering the overlapping symptomatology among these features along with other systemic manifestations it seems plausible to consider CP/CPPS may also have a distinctive microbial component [7-9].

This study was designed to investigate 'whether men with CP/CPPS exhibit differences in gut microbial composition compared to healthy controls'. By analyzing stool samples and comparing microbial diversity and taxonomic structure, we aimed to uncover potential microbial signatures that may help explain the persistence of symptoms and suggest new directions for treatment.

## 2. METHODOLOGY

This was a prospective, observational, case-control study conducted over a one-year period from May 2023 to December 2024. The study was performed at Pir Abdul Qadir Shah Institute of Medical Sciences Gambat, Pakistan, after receiving the institutional ethics committee's approval. All subjects provided informed written consent prior to participation.

A total of 51 'adult male participants were enrolled in the study'. The sample included 26 patients with clinically diagnosed CP/CPPS and 25 age matched healthy controls. Patients were ascertained according to the National Institutes of Health (NIH) criteria for Category III prostatitis, commonly referred to as CP/CPPS which entails chronic pelvic pain greater than three months without evidence of urinary tract infection on standard culture.

**Inclusion Criteria**

Participants in the CP/CPPS group were:

- Aged between 20 and 60 years,
- Experiencing pelvic or perineal discomfort for ≥3 months,
- Scoring positively on the NIH Chronic Prostatitis Symptom Index (NIH-CPSI),
- Free of active urinary tract infection at the time of sampling.

Healthy controls were:

- Age-matched males with no history of urogenital disorders,
- Free from antibiotic or probiotic use within the last three months,
- Asymptomatic and not currently under medical treatment.

**Exclusion Criteria**

Exclusion criteria for both groups included:

- Recent antibiotic use (<3 months),
- Active gastrointestinal disease or inflammatory bowel disease,
- Recent urological surgery or catheterization,
- Diagnosed metabolic or immunological disorders,
- Ongoing cancer treatment, and
- Use of any immunosuppressive or microbiome-altering medications.

Detailed demographic and lifestyle information was collected through structured interviews and validated questionnaires. This included data on age, BMI, smoking and alcohol use, physical activity levels, dietary habits, and recent antibiotic exposure. In the patient group, clinical assessment was conducted using the NIH-CPSI, capturing data on pain severity, urinary symptoms, and quality of life.

Each participant provided a fresh stool sample, collected using sterile containers and transported immediately under cold chain conditions. Samples were stored at –80°C until DNA extraction. Microbial DNA was isolated using a standardized extraction kit, ensuring high-quality yield.

The '16S rRNA gene sequencing done for the V3–V4 segment utilized Next Generation Sequencing (NGS) tools'. Analysis of alpha and beta diversity, 'as well as taxonomic composition at phylum, genus, and species levels were performed using bioinformatic frameworks'. All analyses in this research were conducted on QIIME2 and validated with statistical tools in R software.

Statistical comparisons between groups were conducted using SPSS (version 25). 'Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent sample t-test or Mann–Whitney U test as appropriate'. 'Categorical variables were analyzed using the chi-square test or Fisher's exact test'. For microbiome diversity and composition, PERMANOVA was used for beta diversity comparison, and p-values <0.05 were considered statistically significant.

## 3. RESULTS

The study enrolled a total of 51 participants, including 26 patients diagnosed with CP/CPPS and 25 healthy control individuals. The mean age of patients in the CP/CPPS group was 39.8 years, while that of the controls was 38.2 years ($p$ = 0.56), indicating no significant difference. Body mass index (BMI) also did not differ substantially between the groups ($p$ = 0.31). In terms of lifestyle habits, smoking was more prevalent among CP/CPPS patients (50.0%) compared to controls (40.0%), although this was not statistically significant. Alcohol consumption rates were nearly the same in both groups. Notably, 61.5% of patients reported low dietary fiber intake compared to 36.0% of controls, a difference approaching statistical significance ($p$ = 0.06). A greater proportion of CP/CPPS patients had used antibiotics in the recent past (30.8% vs. 12.0%, $p$ = 0.09), which may be relevant given the impact of antibiotics on microbial communities.

**Table 1: Demographic and Lifestyle Characteristics of Study Participants (n = 51)**

| Variable | CP/CPPS (n=26) | Controls (n=25) | *p*-value |
|---|---|---|---|
| Age (mean ± SD, years) | 39.8 ± 8.7 | 38.2 ± 9.4 | 0.56 |
| BMI (mean ± SD) | 25.9 ± 3.2 | 24.8 ± 3.5 | 0.31 |
| Smoking status (Yes, %) | 13 (50.0%) | 10 (40.0%) | 0.45 |
| Alcohol use (Yes, %) | 9 (34.6%) | 8 (32.0%) | 0.84 |
| Physical activity (Active, %) | 10 (38.5%) | 15 (60.0%) | 0.12 |
| Dietary fiber intake (Low, %) | 16 (61.5%) | 9 (36.0%) | 0.06 |
| Recent antibiotic use (Yes, %) | 8 (30.8%) | 3 (12.0%) | 0.09 |

Among patients diagnosed with CP/CPPS, the average duration of symptoms was 10.2 months (±4.8). Pain levels, measured using the NIH-CPSI pain domain, averaged 13.5 (±3.2), indicating moderate discomfort. Urinary symptoms were also present, with a mean score of 7.4 (±2.5). Over half of the patients (65.4%) reported some degree of sexual dysfunction, and 53.8% had a previous history of prostatitis. The mean quality-of-life score was 6.8 (±1.9), highlighting the significant burden of disease in these patients.

**Table 2: Clinical and Symptom Profiles of CP/CPPS Patients (n = 26)**

| Variable | Mean ± SD / n (%) |
|---|---|
| Duration of symptoms (months) | 10.2 ± 4.8 |
| Pain score (NIH-CPSI) | 13.5 ± 3.2 |
| Urinary symptoms (NIH-CPSI) | 7.4 ± 2.5 |
| Sexual dysfunction reported | 17 (65.4%) |
| Past prostatitis episodes | 14 (53.8%) |
| QoL score (NIH-CPSI) | 6.8 ± 1.9 |

Significant differences in microbial diversity were observed between the CP/CPPS and control groups. Alpha diversity metrics, including the Shannon index and Simpson index, were markedly reduced in the CP/CPPS group ($p$ = 0.004 and $p$ = 0.006, respectively), suggesting a less diverse gut microbial environment. The Chao1 richness estimator was also significantly lower among CP/CPPS patients ($p$ = 0.02). Beta diversity analysis using Bray-Curtis distance further confirmed

distinct clustering between groups, with a statistically significant *p*-value of 0.01 from PERMANOVA testing. These findings support the hypothesis that microbial diversity is compromised in patients with CP/CPPS.

**Table 3: Microbiome Diversity Measures in CP/CPPS Patients and Controls**

| Diversity Metric | CP/CPPS (n=26) | Controls (n=25) | *p*-value |
|---|---|---|---|
| Shannon diversity index | 2.83 ± 0.45 | 3.21 ± 0.39 | 0.004 |
| Simpson index | 0.71 ± 0.12 | 0.81 ± 0.09 | 0.006 |
| Chao1 richness estimator | 132 ± 22 | 148 ± 19 | 0.02 |
| Beta diversity (Bray-Curtis, p) | – | – | 0.01[1] |

[1] *PERMANOVA test for group separation.*

At the genus level, notable shifts were identified in microbial composition. 'The relative abundance of *Escherichia/Shigella* was significantly higher in CP/CPPS patients (8.6%) than in controls (3.4%, $p < 0.001$), indicating possible overgrowth of pro-inflammatory bacteria'. 'Conversely, beneficial genera such as *Lactobacillus* and *Faecalibacterium* were reduced in the CP/CPPS group, both showing statistically significant differences ($p = 0.002$ and $p < 0.001$, respectively)'. While *Bacteroides* and *Prevotella* were slightly lower in CP/CPPS patients, these differences were not statistically significant. These alterations suggest a dysbiotic microbial profile in CP/CPPS, potentially contributing to inflammation or immune dysregulation.

**Table 4: Relative Abundance of Selected Gut Bacteria (Genus Level)**

| Genus | CP/CPPS (%) | Controls (%) | *p*-value |
|---|---|---|---|
| *Escherichia/Shigella* | 8.6 ± 3.2 | 3.4 ± 1.9 | <0.001 |
| *Lactobacillus* | 1.8 ± 0.7 | 4.5 ± 1.6 | 0.002 |
| *Bacteroides* | 23.7 ± 6.4 | 26.1 ± 5.9 | 0.22 |
| *Faecalibacterium* | 9.4 ± 2.5 | 13.8 ± 3.1 | <0.001 |
| *Prevotella* | 5.1 ± 1.7 | 6.4 ± 2.0 | 0.07 |

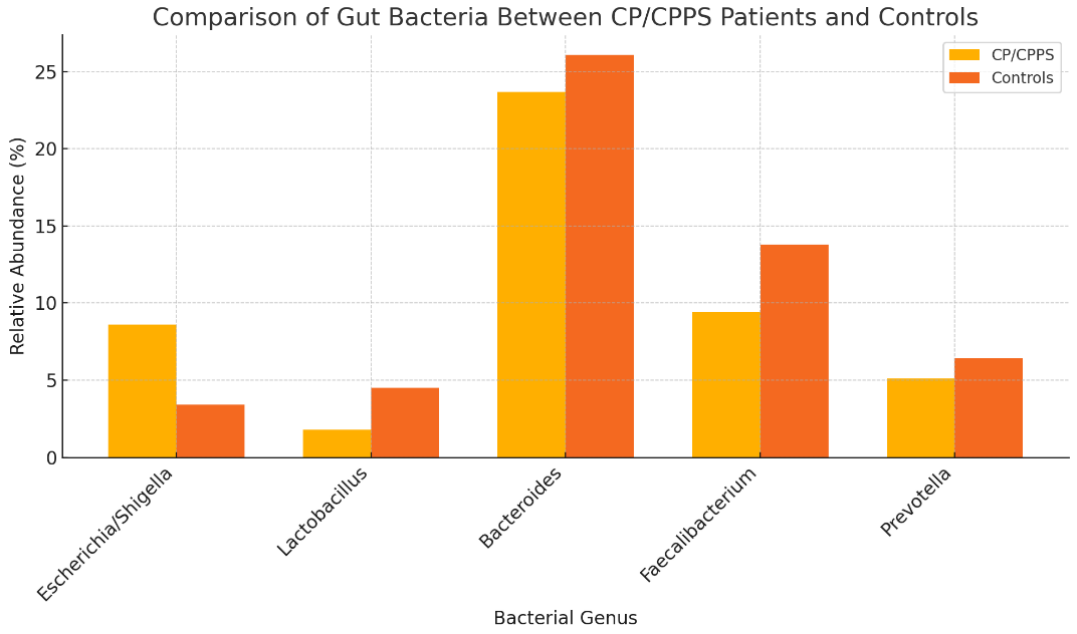


**Figure 1: A bar chart depicting the comparison of key gut bacteria between CP/CPPS patients and healthy controls visually emphasizes dysbiosis, showcasing elevated Escherichia/Shigella alongside decreased Lactobacillus and Faecalibacterium in the CP/CPPS group.**

## 4. DISCUSSION

This study highlights significant disparities in the composition of gut microbiota between individuals diagnosed with CP/CPPS and healthy counterparts. It supports the hypothesis that dysbiosis microbial imbalance may contribute substantially to the underlying processes of chronic pelvic pain syndromes, particularly when infection is not present [10-12].

Our research indicates that there is a markedly lower reduction in microbial diversity CP/CPPS patients harbored when measured with the Shanon and Simpson scores. The literature has linked this loss of microbail variety to immune dysregulation alongside chronic inflammation which is thought to contribute to the enduring pelvic pain some of these patients experience. These findings correspond to studies that reported a reduced gut microbial richness in CP/CPPS patients, thus implying the possible relation between gastrointestinal microbiota and urological symptoms [13-15].

This study noted a greater relative abundance of Escherichia/Shigella spp. in CP/CPPS cases, suggesting possible pro-inflammatory alterations which might have occurred. These genera are known to cause immune response and barrier dysfunction activation in chronic diseases. Simultaneously, beneficial genera Lactobacillus and Faecalibacterium showed significantly lower levels in affected individuals. Faecalibacterium decreases was highlighted due to its anti-inflammatory functions along with preserving intestinal epithelium health. Decreased levels may indicate increased translocation of microbial antigens through a deregulated gut epithelial barrier [15-17].

Dietary patterns, such as lower fiber intake observed in the CP/CPPS group, could partially explain these shifts. Fiber is a primary nutrient source for many beneficial bacteria, and its deficiency may favor the overgrowth of opportunistic or inflammatory species. The trend toward more frequent antibiotic use among CP/CPPS patients also raises concerns about repeated disruption of microbial communities, potentially contributing to the chronicity of symptoms [18-20].

Although this study focused primarily on gut microbiota, it is worth noting that pelvic pain may also be influenced by local urogenital microbial changes. The gut-bladder axis is increasingly recognized as a two-way system in which gastrointestinal bacteria can influence urinary tract immune tone and vice versa. This broader ecosystem model may help explain why a gastrointestinal intervention, such as diet modification or probiotic therapy, has shown promise in some small clinical trials.

However, ‘this study has some limitations the sample size was modest, and while statistically significant differences were observed, larger multicenter trials are needed to confirm these findings’. Moreover, only stool samples were analyzed; future work could incorporate prostatic secretion, urine microbiome, and blood inflammatory markers for a more comprehensive view. Longitudinal studies would also help determine whether the observed dysbiosis is a cause or a consequence of chronic symptoms.

## 5. CONCLUSION

The current study shows a definitive alteration in the gut microbiome of individuals with CP/CPPS as opposed to the healthy controls. Reduced microbial diversity, along with specific taxonomic imbalances particularly the rise in pro-inflammatory and decline in beneficial bacterial genera suggest a potential microbial contribution to symptom persistence and severity. These findings underscore the importance of considering gut health in the management of CP/CPPS and open the door for microbiome-targeted interventions as part of a broader, multi-system treatment strategy.

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