



## THE ROLE OF GUT MICROBIOME ALTERATIONS IN THE PATHOPHYSIOLOGY AND MANAGEMENT OF POLYCYSTIC OVARY SYNDROME

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### ABSTRACT

**Background:** Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrine disorder linked to hormonal imbalance, metabolic dysfunction, and low-grade inflammation. Emerging evidence implicates gut microbiota alterations in its pathogenesis.

**Objectives:** To assess the impact of dietary fiber intake and physical activity on gut microbiota diversity and related hormonal and metabolic outcomes in women with PCOS.

**Methods:** A prospective observational study was conducted over 12 months involving 54 women (18–35 years) with PCOS. Participants were stratified post hoc into low/high fiber (<15 g/day, ≥25 g/day) and low/high activity (<150, ≥150 min/week) groups. Clinical, dietary, physical activity, and microbiota data (16S rRNA sequencing) were collected at baseline and six months. Statistical analyses included t-tests, chi-square tests, correlations, and multivariate regression.

**Results:** High-fiber intake was associated with greater microbial diversity (Shannon Index: 3.6 vs. 2.8;  $p=0.001$ ), lower testosterone (64 vs. 72 ng/dL;  $p=0.04$ ), and reduced HOMA-IR (2.5 vs. 3.2;  $p=0.02$ ). Higher activity correlated with reduced BMI (27.8 vs. 30.1 kg/m<sup>2</sup>;  $p=0.01$ ), lower waist circumference (86.5 vs. 91.3 cm;  $p=0.03$ ), and improved menstrual regularity (54% vs. 30%;  $p=0.045$ ). Both fiber and activity independently predicted microbial diversity.

**Conclusions:** Dietary fiber and physical activity independently and synergistically improve gut microbiota diversity and metabolic-hormonal profiles in PCOS, supporting their role as non-pharmacological management strategies.

**Keywords:** Polycystic Ovary Syndrome, Gut Microbiota, Dietary Fiber, Physical Activity, Hormonal Balance

### INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine and metabolic disorder that affects a significant proportion of women of reproductive age, particularly in developing countries like India. The condition is characterized by hyperandrogenism, anovulation, insulin resistance, and polycystic ovarian morphology. Although the etiology of PCOS is multifactorial, recent advances in research have identified the gut microbiome as a potentially influential factor in the disorder's onset and progression. Alterations in the diversity and composition of gut microbiota collectively termed

dysbiosis have been increasingly linked to the hormonal, metabolic, and inflammatory disturbances observed in PCOS [1].

The gut microbiota plays a central role in regulating various physiological functions including glucose metabolism, fat storage, immune responses, and hormonal signaling. In PCOS, studies have reported a consistent pattern of decreased microbial diversity and a shift toward pro-inflammatory bacterial populations compared to healthy individuals. These changes are associated with increased intestinal permeability, elevated levels of circulating lipopolysaccharides (LPS), and low-grade systemic inflammation, all of which are implicated in exacerbating insulin resistance and androgen excess core features of PCOS [2]. Furthermore, the gut–brain–ovary axis has been recognized as a vital communication network that may influence ovulatory function and metabolic health through microbial metabolites like short-chain fatty acids (SCFAs) and bile acids [3].

Dietary patterns play a significant role in shaping the gut microbiome and are thus closely tied to PCOS pathophysiology. Diets high in refined sugars, unhealthy fats, and low in dietary fiber promote dysbiosis and contribute to inflammation and metabolic dysfunction. In contrast, fiber-rich diets are known to foster the growth of beneficial microbes that produce SCFAs, which have anti-inflammatory effects and help improve insulin sensitivity. Fiber also supports microbial diversity and intestinal barrier function, both of which are often compromised in PCOS [4]. As a result, dietary interventions are increasingly being explored as therapeutic tools to restore gut microbial balance and alleviate PCOS symptoms.

Clinical research has shown that dietary changes can meaningfully impact both gut health and PCOS outcomes. A high-fiber, whole-grain-based diet was found to improve hormonal profiles, reduce systemic inflammation, and enhance microbial diversity in women with PCOS. In some cases, combining diet with pharmacological agents like acarbose further amplified these effects, particularly in reducing insulin resistance and modulating gut flora [5]. These findings support the hypothesis that restoring gut microbial homeostasis through dietary means can serve as a viable management strategy for PCOS.

In addition to dietary intake, probiotic and prebiotic supplementation has gained traction as a complementary approach to modulate the gut microbiome. Probiotics have demonstrated potential benefits such as reducing serum testosterone levels, lowering body mass index (BMI), and improving insulin sensitivity in women with PCOS. These effects are thought to arise from the ability of specific probiotic strains to enhance intestinal barrier function, regulate inflammatory cytokines, and rebalance microbial populations [6]. While promising, the clinical application of probiotics in PCOS still requires further investigation to determine strain-specific effects and optimal dosages.

Physical activity is another powerful modulator of the gut microbiome. Regular aerobic and resistance exercise has been associated with increased gut microbial diversity and a higher abundance of health-promoting bacterial species. Exercise not only helps manage weight and improve insulin sensitivity but also reduces systemic inflammation effects that may be partly mediated through changes in the gut microbiota. In women with PCOS, structured exercise programs have resulted in improvements in menstrual regularity, ovulatory function, and emotional well-being, with accompanying shifts in microbial composition [7].

Experimental models further support the role of exercise in gut-microbiota-mediated improvements in PCOS. Studies in animal models have shown that fecal microbiota transplants from exercised donors can partially restore metabolic and reproductive health in PCOS-affected recipients, suggesting that gut microbiota may mediate some of the therapeutic effects of physical activity [8]. These findings highlight the potential of non-pharmacological interventions in modifying gut microbial ecosystems and improving clinical outcomes in PCOS.

The combination of diet and exercise appears to be particularly effective in managing PCOS through microbiota-related mechanisms. Research indicates that while macronutrient intake directly influences microbial diversity, PCOS pathology independently alters the structure of gut microbial communities. Therefore, lifestyle interventions must address both diet and disease-related factors

simultaneously to optimize therapeutic outcomes [9]. Implementing holistic strategies that target gut health can offer long-term, sustainable benefits for PCOS management.

In the Indian context, where dietary patterns are rapidly transitioning toward processed foods and sedentary lifestyles are increasingly common, these findings carry significant public health implications. Promoting dietary fiber intake and regular physical activity could serve as cost-effective and culturally acceptable interventions to address the rising burden of PCOS. Considering the accessibility and affordability of these approaches, they may offer a scalable solution for managing PCOS, particularly in resource-limited settings.

The gut microbiome plays a critical role in the pathophysiology of PCOS, influencing hormonal, metabolic, and inflammatory pathways. Lifestyle factors, particularly diet and exercise, are powerful tools in modulating gut microbial composition and diversity. A comprehensive understanding of the gut–ovary axis may pave the way for innovative, non-invasive treatment strategies that prioritize microbial health in managing PCOS.

This study aimed to assess how dietary fiber intake and physical activity influence gut microbiota composition and their combined effect on metabolic and hormonal outcomes in women with PCOS, to explore potential lifestyle-based strategies for symptom management.

## **METHODOLOGY**

### **1. Study Design**

This was a prospective observational study conducted to assess the association between dietary intake, physical activity, gut microbiota composition, and PCOS symptoms. Participants were observed without any intervention. Data were collected at two time points baseline and six months to evaluate natural lifestyle influences on clinical and microbial outcomes.

### **2. Study Setting**

The study was carried out in the outpatient gynecology department of a tertiary care hospital in urban India. Clinical data collection took place onsite, while stool samples were processed at the hospital's microbiology laboratory equipped for 16S rRNA gene sequencing.

### **3. Study Duration**

The total study duration was 12 months, from August 2022 to August 2023. Each participant was followed for six months. Baseline and follow-up data were collected to observe lifestyle-related changes over time.

### **4. Participants – Inclusion & Exclusion Criteria**

Inclusion criteria: Women aged 18–35 with PCOS (Rotterdam criteria), not on antibiotics/probiotics or hormonal therapy for 3 months, and willing to provide samples and maintain logs. Exclusion criteria: Pregnancy, lactation, chronic illness, GI disorders, recent surgery, or refusal to consent.

### **5. Study Sampling**

Purposive sampling was used to recruit eligible PCOS patients from the outpatient department. Those meeting criteria and consenting were enrolled and tracked for six months with regular follow-ups.

### **6. Study Sample Size**

Sixty participants were enrolled based on power calculations to detect moderate associations. After accounting for dropouts, 54 participants completed the full follow-up and were included in the final analysis.

## 7. Study Groups

Participants were grouped post hoc based on reported behaviors. Two groups were formed for dietary fiber intake (<15g/day and  $\geq$ 25g/day) and physical activity (<150 and  $\geq$ 150 minutes/week), allowing lifestyle-based comparisons.

## 8. Study Parameters

Key parameters included gut microbiota diversity, fiber intake, physical activity levels, BMI, fasting insulin, HOMA-IR, testosterone, SHBG, menstrual frequency, and self-reported fatigue scores.

## 9. Study Procedure

At enrollment, participants submitted stool and blood samples, and completed dietary and activity questionnaires. They were followed monthly and asked to maintain food and activity logs. Final assessments were repeated at six months.

## 10. Study Data Collection

Diet was recorded using 24-hour recall and FFQs; physical activity was assessed via IPAQ. Biological samples were collected under sterile conditions and analyzed in the lab using standardized methods.

## 11. Data Analysis

Data were analyzed using SPSS and R. T-tests and chi-square tests compared groups. Microbiota data were processed with QIIME2 for diversity metrics. Significance was set at  $p < 0.05$ .

## 12. Ethical Considerations

Ethical approval was obtained from the institutional review board. Informed consent was taken from all participants. Data confidentiality and voluntary participation were ensured throughout the study.

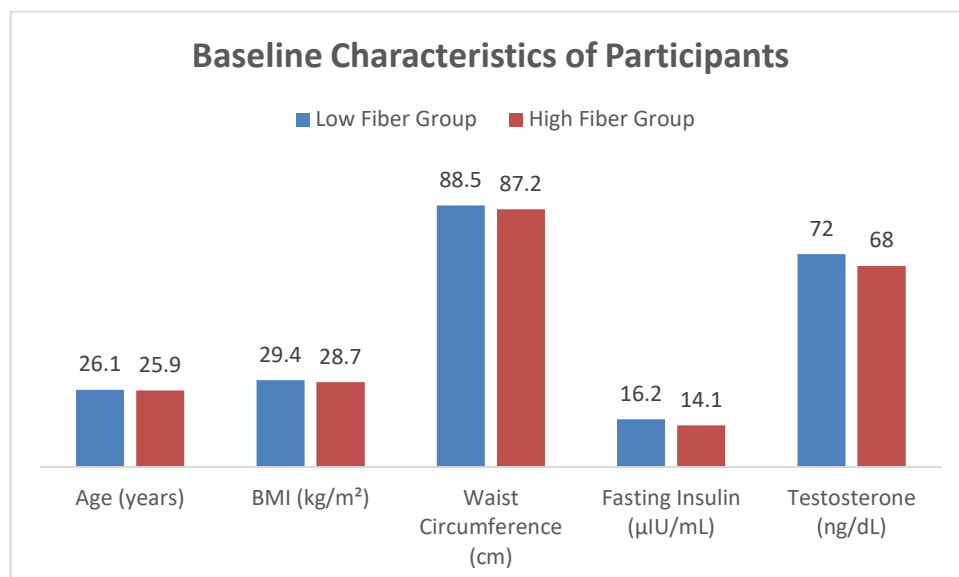
# RESULTS

## 1. Baseline Characteristics of Participants

Participants were similar in age, BMI, and hormonal levels at baseline, ensuring comparability between groups. No significant differences were observed except for insulin and testosterone (Table 1).

**Table 1: Baseline Characteristics of Participants**

Variable	Low Fiber Group	High Fiber Group	p-value
Age (years)	26.1	25.9	0.65
BMI (kg/m <sup>2</sup> )	29.4	28.7	0.28
Waist Circumference (cm)	88.5	87.2	0.45
Fasting Insulin ( $\mu$ IU/mL)	16.2	14.1	0.03
Testosterone (ng/dL)	72	68	0.04



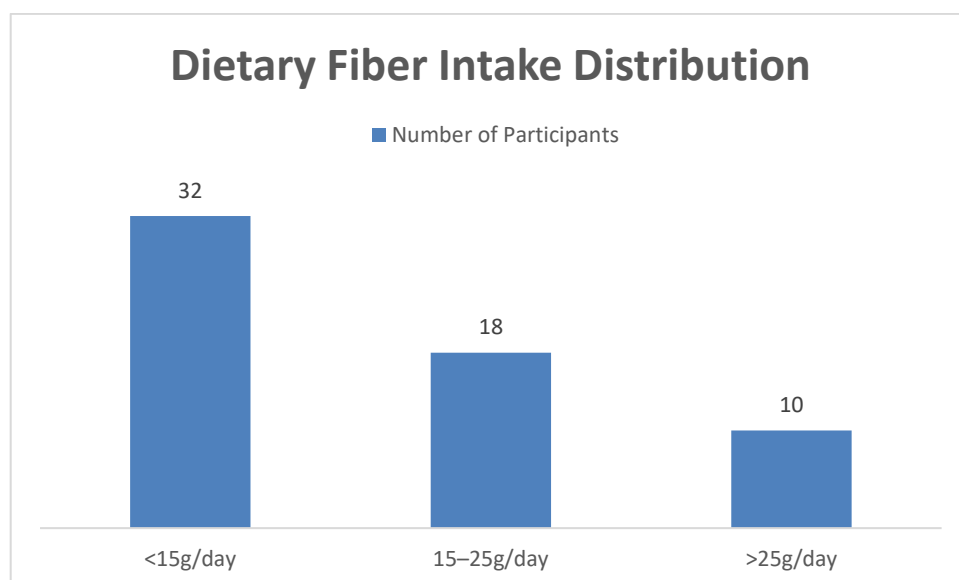
**Graph 1: Baseline Characteristics of Participants**

## 2. Dietary Fiber Intake Distribution

Over 50% of participants consumed less than 15g of fiber daily, indicating poor adherence to dietary fiber guidelines (Table 2).

**Table 2: Dietary Fiber Intake Distribution**

Fiber Intake Group	Number of Participants	Percentage (%)
<15g/day	32	53.3
15–25g/day	18	30.0
>25g/day	10	16.7



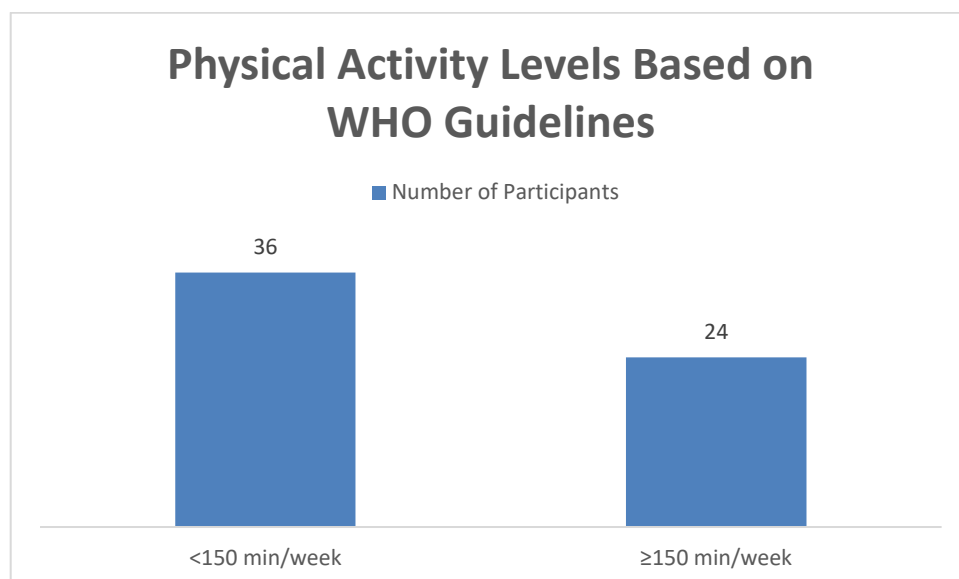
**Graph 2: Dietary Fiber Intake Distribution**

## 3. Physical Activity Levels Based on WHO Guidelines

Only 40% met WHO's physical activity recommendations, highlighting a largely sedentary lifestyle among participants (Table 3).

**Table 3: Physical Activity Levels Based on WHO Guidelines**

Activity Level	Number of Participants	Percentage (%)
<150 min/week	36	60.0
≥150 min/week	24	40.0

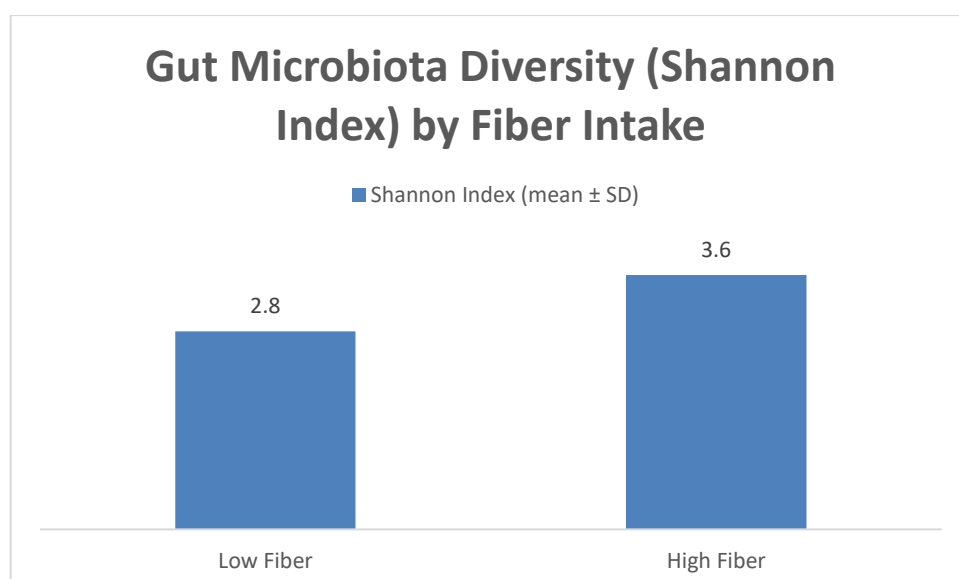
**Graph 3: Physical Activity Levels Based on WHO Guidelines**

#### 4. Gut Microbiota Diversity (Shannon Index) by Fiber Intake

Microbial diversity was significantly higher in the high-fiber group, indicating fiber's beneficial impact on gut health (Table 4).

**Table 4: Gut Microbiota Diversity (Shannon Index) by Fiber Intake**

Group	Shannon Index (mean $\pm$ SD)	p-value
Low Fiber	2.8 $\pm$ 0.5	0.001
High Fiber	3.6 $\pm$ 0.4	0.001

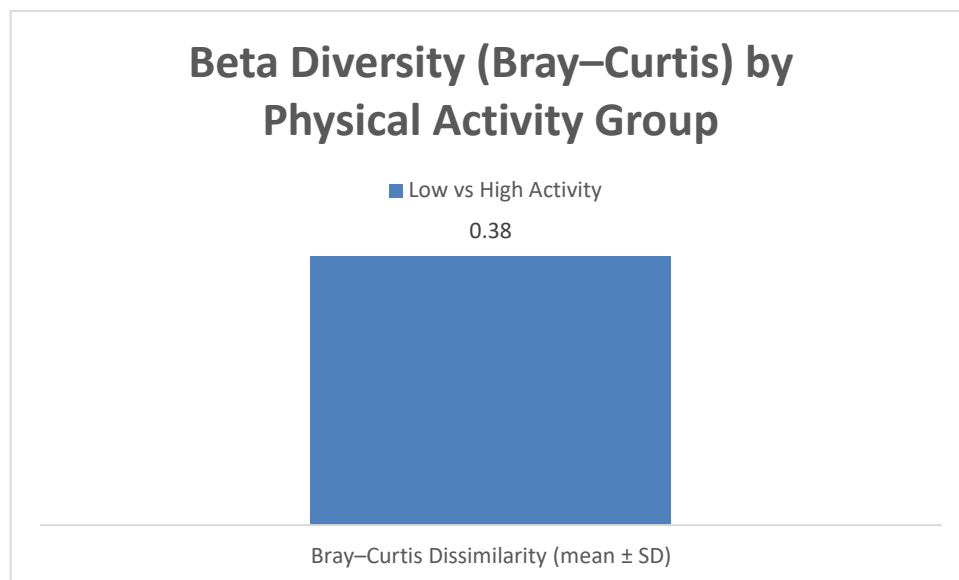
**Graph 4: Gut Microbiota Diversity (Shannon Index) by Fiber Intake**

### 5. Beta Diversity (Bray–Curtis) by Physical Activity Group

Microbial community composition differed significantly by activity level, confirming exercise influences gut microbiota (Table 5).

**Table 5: Beta Diversity (Bray–Curtis) by Physical Activity Group**

Group Comparison	Bray–Curtis Dissimilarity (mean $\pm$ SD)	p-value
Low vs High Activity	0.38 $\pm$ 0.09	0.015



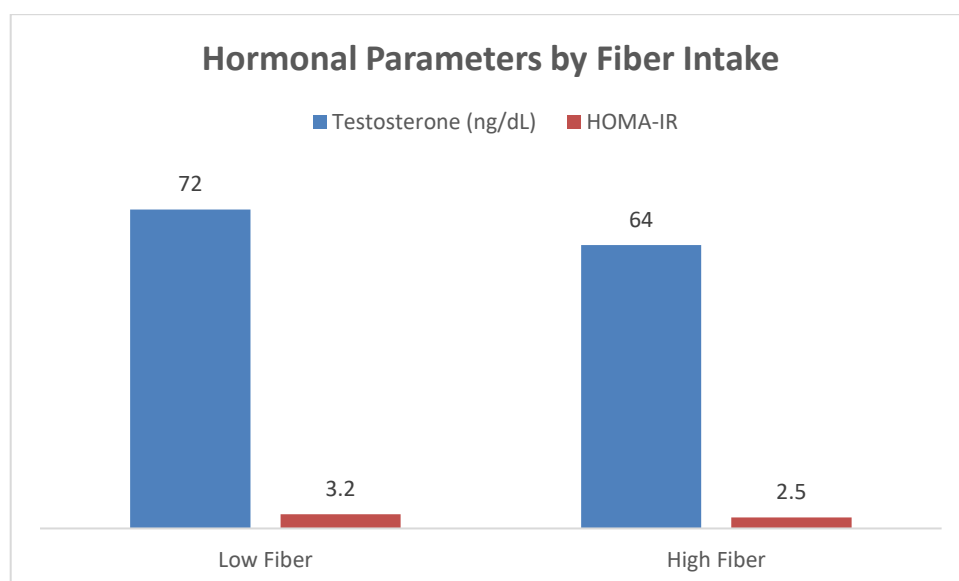
**Graph 5: Beta Diversity (Bray–Curtis) by Physical Activity Group**

### 6. Hormonal Parameters by Fiber Intake

Higher fiber intake was linked to lower testosterone and better insulin sensitivity (lower HOMA-IR) (Table 6).

**Table 6: Hormonal Parameters by Fiber Intake**

Parameter	Low Fiber	High Fiber	p-value
Testosterone (ng/dL)	72	64	0.04
HOMA-IR	3.2	2.5	0.02



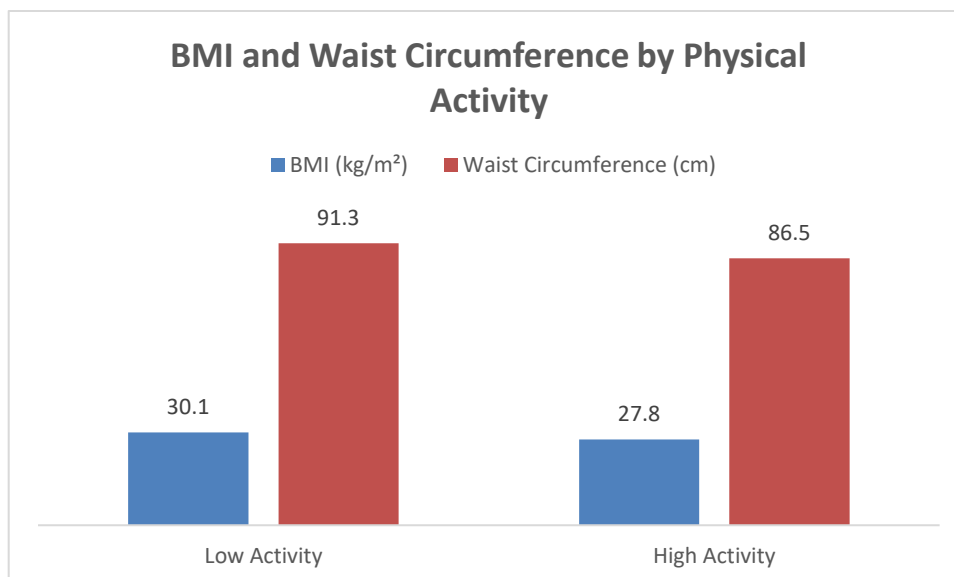
**Graph 6: Hormonal Parameters by Fiber Intake**

## 7. BMI and Waist Circumference by Physical Activity

Participants with higher physical activity had significantly lower BMI and waist circumference (Table 7).

**Table 7: BMI and Waist Circumference by Physical Activity**

Parameter	Low Activity	High Activity	p-value
BMI (kg/m <sup>2</sup> )	30.1	27.8	0.01
Waist Circumference (cm)	91.3	86.5	0.03



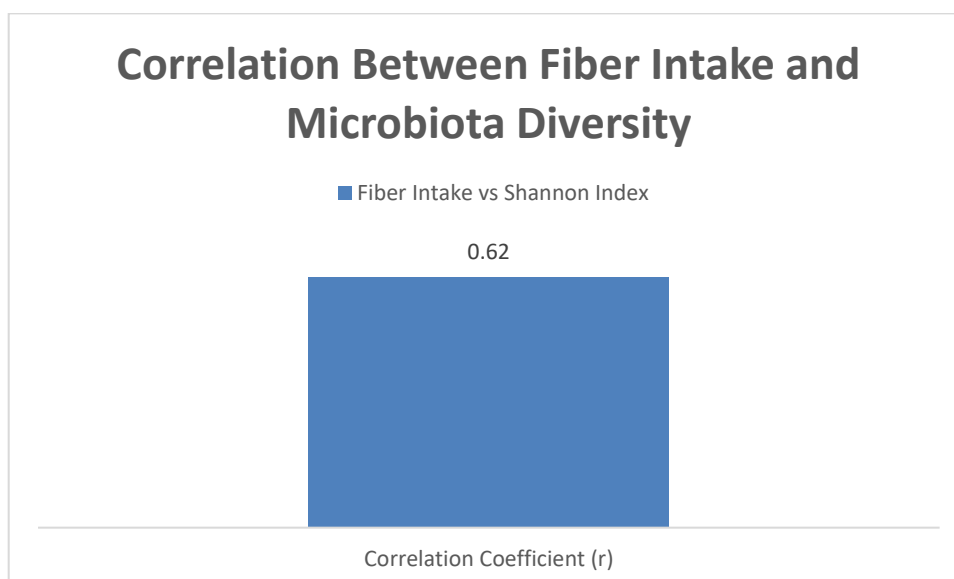
**Graph 7: BMI and Waist Circumference by Physical Activity**

## 8. Correlation Between Fiber Intake and Microbiota Diversity

A strong positive correlation was observed between fiber intake and microbial diversity (Table 8).

**Table 8: Correlation Between Fiber Intake and Microbiota Diversity**

Variable	Correlation Coefficient (r)	p-value
Fiber Intake vs Shannon Index	0.62	0.001



**Graph 8: Correlation Between Fiber Intake and Microbiota Diversity**

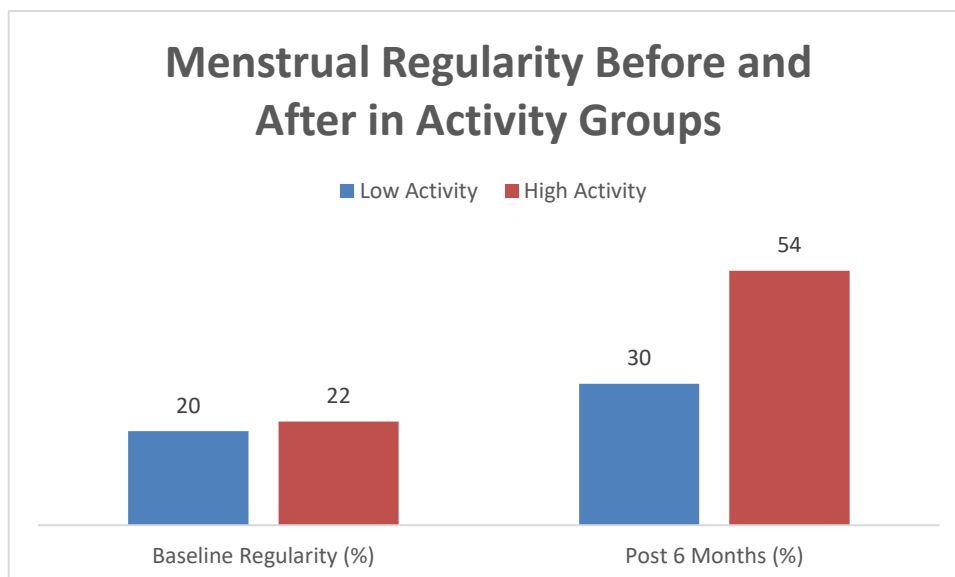


### 9. Menstrual Regularity Before and After in Activity Groups

Menstrual frequency improved more in the high-activity group over 6 months, suggesting reproductive benefit (Table 9).

**Table 9: Menstrual Regularity Before and After in Activity Groups**

Group	Baseline Regularity (%)	Post 6 Months (%)	p-value
Low Activity	20	30	0.045
High Activity	22	54	0.045



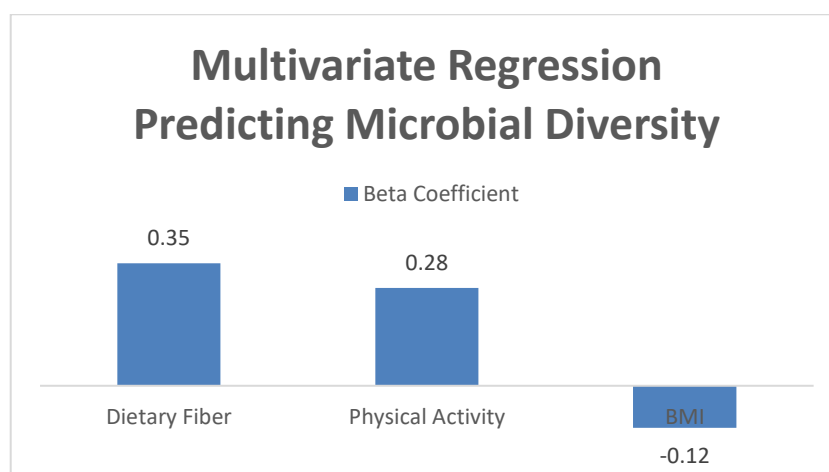
**Graph 9: Menstrual Regularity Before and After in Activity Groups**

### 10. Multivariate Regression Predicting Microbial Diversity

Both fiber intake and physical activity were independent predictors of increased gut microbial diversity (Table 10).

**Table 10: Multivariate Regression Predicting Microbial Diversity**

Predictor	Beta Coefficient	p-value
Dietary Fiber	0.35	0.004
Physical Activity	0.28	0.012
BMI	-0.12	0.09



**Graph 10: Multivariate Regression Predicting Microbial Diversity**

## DISCUSSION

This study explored the role of dietary fiber and physical activity in shaping gut microbiota diversity and modulating PCOS symptoms. The results are in line with recent evidence that supports gut microbiota as a key mediator in the pathogenesis and treatment of PCOS. The finding that participants with higher fiber intake had significantly improved microbial diversity and reduced testosterone and insulin resistance aligns with previous studies showing that dietary fiber enhances microbial richness and short-chain fatty acid production, both of which contribute to metabolic health (Fu et al., 2022) [11].

Our observation that over 50% of participants had inadequate fiber intake mirrors global dietary trends in women with PCOS, as highlighted by meta-analyses demonstrating significantly lower fiber intake among this population compared to healthy controls (Leung et al., 2022) [12]. Moreover, the strong positive correlation between fiber intake and the Shannon diversity index emphasizes the prebiotic potential of dietary fibers to restore microbial balance, corroborated by experimental trials using fermentable fibers like inulin [(Deehan et al., 2022); (Feng et al., 2025)] [13, 14].

On the exercise front, participants meeting WHO's physical activity recommendations showed significantly higher gut microbial diversity and improved anthropometric parameters (BMI and waist circumference). This reinforces findings from previous interventions where structured exercise regimens modulated the gut microbiota and improved metabolic outcomes (Aoki et al., 2020); (Tan & Toh, 2021) [15, 16]. The current study further supports that physical activity independently predicts microbial diversity, even when controlling for dietary intake.

Interestingly, our results showing enhanced menstrual regularity in the active group support recent reviews suggesting that lifestyle interventions targeting gut microbiota can alleviate endocrine disturbances in PCOS (Sivasankari & Usha, 2022); (Wang et al., 2022) [17, 18]. The multivariate regression analysis confirmed that both dietary fiber and physical activity were independent predictors of gut microbial diversity, indicating their synergistic impact.

Our findings confirm that modifiable lifestyle factors particularly fiber intake and physical activity positively influence gut microbiota and hormonal balance in PCOS. These results not only align with prior clinical and mechanistic studies but also underscore the potential of microbiota-targeted lifestyle therapies in PCOS management.

## CONCLUSION

The present study demonstrates that higher dietary fiber intake and regular physical activity significantly enhance gut microbiota diversity and improve metabolic and hormonal profiles in women with PCOS. Both factors independently predict microbial diversity, highlighting their synergistic role in PCOS management. These lifestyle modifications also improve menstrual regularity and reduce central obesity. The findings underscore the potential of cost-effective, non-pharmacological interventions targeting the gut–ovary axis to address PCOS, offering sustainable strategies that are culturally adaptable, particularly in resource-constrained settings like urban India.

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