RESEARCH

# Are patients with polycystic ovary syndrome more prone to irritable bowel syndrome?

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## Abstract

*Background:* Polycystic ovary syndrome (PCOS) encompasses endocrine, reproductive and metabolic disturbances. Abdominal pain and bowel movement disturbances are common complaints of PCOS patients. It remains uncertain whether the characteristic features of PCOS are associated with an increased incidence of irritable bowel syndrome (IBS).

*Methods:* In the study, 133 patients with PCOS diagnosed according to international evidence-based guidelines and 72 age- and BMI-matched eumenorrheic controls were enrolled. Anthropometric measurements and biochemical and hormonal characteristics were collected. The Rome IV criteria were used for IBS diagnosis. Quality of life (QoL) and depressive symptoms were also assessed.

*Results:* IBS symptom prevalence in PCOS was not significantly different than in controls. Hyperandrogenism and simple and visceral obesity did not appear to affect IBS prevalence in PCOS. There were no anthropometric, hormonal or biochemical differences between IBS-PCOS and non-IBS-PCOS patients, apart from IBS-PCOS patients being slightly older and having lower thyroid-stimulating hormone. Metabolic syndrome (MS) prevalence was higher in IBS-PCOS than non-IBS-PCOS. QoL appears to be significantly lower in IBS-PCOS compared to PCOS-only patients. The occurrence of depression was higher in IBS-PCOS vs non-IBS-PCOS patients. At least one alarm symptom was reported by 87.5% of IBS-PCOS; overall, this group experienced more alarm symptoms than the IBS-only group.

*Conclusions:* Since a link between PCOS and IBS comorbidity and increased MS prevalence was noted, patients presenting with both conditions may benefit from early MS diagnostics and management. The high incidence of alarm symptoms in PCOS women in this study highlights the need for differential diagnosis of organic diseases that could mimic IBS symptoms.

**Key Words**

- irritable bowel syndrome (IBS)
- Rome IV (diagnostic) criteria
- polycystic ovary syndrome (PCOS)
- constipation
- diarrhea

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## Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrinopathy characterized by chronic, low-grade inflammation with features such as clinical and/or biochemical hyperandrogenism, oligo- or anovulation and a characteristic image of ovaries on ultrasound (1, 2). It affects 4–21% of women worldwide depending on the

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region and nationality studied and the diagnostic criteria used (3, 4). PCOS is associated with an increased risk of insulin resistance (IR), hyperinsulinemia, type 2 diabetes mellitus (T2DM), dyslipidemia, obesity and cardiovascular diseases (CVDs) (5, 6). Studies on the complexity of this condition have suggested that PCOS patients present with gastrointestinal (GI) disturbances, including abdominal pain, constipation or bloating, more often than healthy women (7). A possible link between PCOS and increased intestinal permeability (IP) – the severity of which could be exacerbated by inflammation and IR – was also noted (8). Abdominal pain and discomfort are frequent complaints of PCOS women, although they may not be commonly considered issues relevant to this patient group (7).

Irritable bowel syndrome (IBS) affects around 10–20% of the general population, making it the most commonly diagnosed functional GI system disorder and one of the leading causes of absence from work (9). It is characterized by abdominal pain and changes in bowel habits, which allows classification of the condition into diarrhea- or constipation-predominant types, a mix of constipation and diarrhea, or an unspecified type (IBS-D, IBS-C, IBS-M or IBS-U, respectively) (10). According to the Rome IV criteria, IBS can be diagnosed when recurrent abdominal pain occurring at least once a week, on average, is related to defecation, associated with a change in the form of stool and/or its frequency, with such symptoms starting 6 months before diagnosis and being present for the previous 3 months (11). Clinical diagnosis necessitates the exclusion of underlying organic disease, history of an infection preceding symptoms or exposure to medications causing similar GI disturbances. Patients' family history of IBS, celiac disease and colorectal cancer should also be assessed (9). The fluctuating nature of the IBS and lack of a specific IBS biomarker render a IBS diagnosis challenging.

Although IBS may affect all ages and sexes, younger patients present with abdominal discomfort more frequently than older adults (12), with a 25% lower IBS prevalence in the latter group (10) and women suffer from this condition 1.5–3 times more often than men (10, 13). IBS-C or IBS-M seem to be more common in females, whereas men report more IBS-D symptoms (14, 15). Research shows that young females are most severely affected by IBS symptoms, which could inspire further investigations on the role of hormones in the pathogenesis of this condition (10, 12, 13, 16). Both PCOS and IBS are common disorders among women worldwide that affect their physical and mental wellbeing and quality of life (QoL); however, links between these two conditions and the possibility of finding better-targeted treatments for women with both PCOS and IBS have received limited attention in research thus far (17, 18).

### Aim

This study aimed to assess the IBS prevalence based on the Rome IV criteria in PCOS patient population and compare findings with anthropometric, biochemical, hormonal, depressive symptom and QoL data.

## Methods

Participants included 133 PCOS patients and 72 age- and BMI-matched eumenorrheic women, recruited to the study in the Department of Endocrinology, Metabolism and Internal Diseases at the Poznan University of Medical Sciences between years 2017 and 2020. The age range for both groups was 18–40 years. PCOS diagnosis was based on the latest international evidence-based guidelines (2, 19). It was made when at least two out of the following three features were present: oligoovulation or anovulation, clinical and/or biochemical signs of hyperandrogenism, or polycystic ovaries on ultrasound (2, 19). Healthy females had regular menstrual cycles and no evidence of androgen excess. Participants with known disorders such as Cushing's syndrome, hyperprolactinemia or congenital adrenal hyperplasia were not included in this study. None of the participants had diabetes, hypertension, severe acute or chronic renal or liver disease, cancer or previously known gastrointestinal disease. Individuals with celiac disease, extreme obesity (BMI >40 kg/m$^2$), diagnosed inflammatory bowel disease, heart defect, decompensated thyroid dysfunction, those who were on birth control pills, hormonal replacement therapy, ovulation-inducing agents, anti-androgens or metformin for up to 3 months before this study were also excluded from participation.

The 2016 Rome IV diagnostic criteria for IBS were used (11). Alarm symptoms such as a positive family history of colorectal cancer, anemia, dysphagia, vomiting, unintentional weight loss, gastrointestinal bleeding, nocturnal or progressive abdominal pain were noted. Data on non-celiac gluten sensitivity (NCGS) and lactose intolerance were collected from participants' medical histories. The presence of metabolic syndrome (MS) was evaluated with IDF-AHA/NHLBI criteria (2009) (20). Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R) and the participants' health-related QoL was estimated with the 15D instrument (21, 22). The CESD-R is a 20-item

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screening test assessing symptoms in nine different areas, in which a total score ≥16 suggests subthreshold depressive symptoms if the subject does not meet the major depressive episode criteria. The 15D instrument is a generic questionnaire designed to measure HRQoL, which consists of 15 different dimensions – mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality and sexual activity, each to be estimated on one of five ordinal levels which best relate to the patient's state of health (22). The total 15D score is calculated using a valuation algorithm and is a single index number on a 0–1 scale (0 = being dead, 1 = 'full' HRQoL, i.e., no problems of any dimension) (23).

Anthropometric and clinical examination included measurements of body weight (kg), height (cm), waist circumference (WC, cm) and hip circumference (HC, cm). WC was measured at the end of a normal expiration, in a horizontal plane midway between the inferior margin of the last palpable rib and the superior border of the iliac crest, using a stretch-resistant tape (24). Central obesity was determined using the waist-to-height ratio (WHtR), which was calculated by dividing WC by height (24). WHtR ≥ 0.5 was set as the cut-off point.

Transvaginal ultrasonography was performed by a single observer. The volume and morphology of each ovary were assessed, with thresholds set at 10 $cm^3$ for increased ovarian volume, ≥20 for the increased number of follicles in an ovary and 2–9 mm for follicle size (1, 2).

All participants gave informed written consent. The clinical examination protocol complied with the Declaration of Helsinki for Human and Animal Rights and its later amendments received ethical approval from the Board of Bioethics of the Poznan University of Medical Sciences (552/16; 986/17).

### Laboratory tests

Blood samples for biochemical analyses were collected from all participants in the morning between 8:00 and 9:00 h after an overnight fast in the follicular phase of spontaneous menstrual cycles. Glucose measurements were done in serum by the hexokinase method (Roche Diagnostics) with the coefficient of variation (CV) of ≤3%. Insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), DHEA sulfate (DHEAS), estradiol (E2), total testosterone (T), sex hormone-binding globulin (SHBG), anti-Müllerian hormone (AMH) and thyroid-stimulating hormone (TSH) measurements were performed using a Cobas 6000 analyzer (Roche Diagnostics) with kits provided by the manufacturer. The free testosterone index (FTI) was assessed with the following calculation: FTI = (T/SHBG) × 100 (25). Values of TT > 2.67 nmol/L and/or FTI > 5.5 were used as thresholds to define biochemical hyperandrogenism (26). Insulin resistance (IR) was diagnosed based on the homeostasis model assessment for insulin resistance (HOMA-IR) using the following calculation: HOMA-IR = (fasting plasma glucose (mg/dL) × fasting plasma insulin (mU/L))/405 (27). HOMA-IR > 2.5 was used as the threshold to determine IR (28).

The enzymatic colorimetric method was used to assess concentrations of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG). Low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald equation: LDL-C = TC – HDL-C – TG/5, where TG/5 served as an estimate of the VLDL-C concentration (29).

### Statistical analysis

Statistica v.13.1 software (StatSoft Polska Sp. z o.o, Kraków, Poland) was used for statistical analysis. Descriptive statistics of quantitative variables was presented as the median and interquartile range (IQR). The *t*-test of two independent samples was employed to calculate differences in measured parameters between the studied groups. Levene test was used for the testing of homogeneity of variances. For non-normal data distribution, the Mann–Whitney *U* test was used. The association between lipid and obesity indices and other parameters was assessed using Pearson's linear correlation coefficients. Two-tailed *P*-values of <0.05 were considered statistically significant for all analyses. For an alpha error of 0.05 and 100% statistical power to detect differences, a minimum of 48 women would be required in each group.

## Results

The general characteristics of the study sample, subdivided into subgroups with or without IBS symptoms, are shown in Table 1. Supplementary Table 1 (see section on supplementary materials given at the end of this article) presents anthropometric and laboratory data of PCOS patients and controls with no further subdivision. PCOS patients were characterized by higher levels of LH, DHEAS, T, FTI, LDL and AMH and lower SHBG concentrations vs controls (CON) ($P < 0.05$). The prevalence of IBS, according to the Rome IV criteria, was 24% (32/133) in PCOS patients vs 21% in CON (15/72) ($P = 0.60$). Among PCOS patients,

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**Table 1** Anthropometric and laboratory data of PCOS patients and controls including subgroups with and without IBS symptoms. Data are presented as the median and interquartile range (IQR) or number (percentage).

| Variable | **PCOS patients** ($n$ = 133) | | | **Controls** (CON) ($n$ = 72) | | | **IBS-PCOS vs IBS-CON** ($P$) |
|---|---|---|---|---|---|---|---|
| | IBS-PCOS ($n$ = 32) | non-IBS-PCOS ($n$ = 101) | $P$ | IBS-CON ($n$ = 15) | non-IBS-CON ($n$ = 57) | $P$ | |
| Age (years) | 26.96 (5.71) | 24.42 (5.00) | **0.01** | 28.25 (12.08) | 24.83 (8.17) | 0.21 | 0.88 |
| BMI (kg/m$^2$) | 23.57 (12.76) | 24.21 (6.97) | 0.58 | 22.04 (9.89) | 24.20 (6.93) | 0.99 | 0.28 |
| WC (cm) | 79.50 (31.00) | 82.00 (18.00) | 0.58 | 78.00 (25.00) | 80. 00 (18.00) | 0.74 | 0.72 |
| WHtR | 0.48 (0.18) | 0.48 (0.11) | 0.61 | 0.48 (0.20) | 0.47 (0.09) | 0.54 | 0.99 |
| AMH (pg/mL) | 47.48 (31.33) | 52.38 (47.84) | 0.54 | 20.35 (17.58) | 27.10 (9.07) | 0.83 | **0.005** |
| Glucose (mg/dL) | 89.00 (8.00) | 88.00 (10.00) | 0.39 | 86.00 (10.00) | 88.50 (8.00) | 0.49 | 0.24 |
| Insulin (mIU/mL) | 8.77 (10.33) | 9.54 (7.16) | 0.86 | 9.77 (3.98) | 8.07 (7.31) | 0.30 | 0.99 |
| HOMA-IR | 1.92 (2.08) | 2.19 (1.69) | 0.81 | 1.98 (0.89) | 1.80 (1.60) | 0.35 | 0.92 |
| TC (mg/dL) | 170.00 (31.00) | 171.00 (40.00) | 0.86 | 180.00 (55.00) | 164.00 (35.00) | 0.37 | 0.57 |
| TG (mg/dL) | 82.00 (59.00) | 70.00 (50.00) | 0.20 | 71.00 (61.00) | 81.00 (38.00) | 0.87 | 0.52 |
| HDL-C (mg/dL) | 59.00 (25.00) | 61.00 (20.00) | 0.41 | 63.00 (35.00) | 65.00 (25.00) | 0.93 | 0.23 |
| LDL-C (mg/dL) | 92.20 (28.50) | 90.60 (35.00) | 0.77 | 77.20 (43.70) | 83.55 (35.35) | 0.61 | 0.38 |
| TSH (µU/mL) | 1.80 (1.34) | 2.14 (1.32) | **0.02** | 2.18 (0.97) | 2.24 (1.25) | 0.34 | 0.31 |
| FSH (mU/mL) | 5.75 (2.20) | 5.80 (2.10) | 0.86 | 4.65 (3.80) | 5.50 (3.10) | 0.28 | 0.28 |
| LH (mU/mL) | 7.05 (6.30) | 8.45 (8.60) | 0.11 | 5.10 (2.55) | 6.50 (5.40) | 0.37 | 0.19 |
| DHEAS (µg/dL) | 331.00 (218.00) | 319.00 (181.00) | 0.55 | 226.00 (123.00) | 256 .00 (110.00) | 0.20 | **0.03** |
| T (nmol/L) | 1.46 (1.40) | 1.75 (1.00) | 0.44 | 1.20 (0.80) | 1.20 (0.80) | 0.68 | 0.31 |
| FTI (%) | 3.37 (3.44) | 3.37 (2.58) | 0.59 | 1.52 (1.83) | 1.75 (2.66) | 0.98 | 0.16 |
| E2 (pg/mL) | 40.00 (39.00) | 44.00 (42.00) | 0.18 | 87.00 (70.00) | 52.00 (75.50) | 0.79 | 0.29 |
| SHBG (nmol/L) | 50.90 (48.00) | 50.95 (32.95) | 0.83 | 69.50 (106.00) | 56.40 (26.90) | 0.44 | 0.19 |
| MS presence | 9/31 (29.0%) | 10/97 (10.3%) | **0.01** | 1/14 (7.1%) | 3/51 (5.9%) | 0.862 | 0.10 |

AMH, anti-Müllerian hormone; DHEAS, DHEA sulfate; E2, estradiol; FSH, follicle-stimulating hormone; FTI, free testosterone index; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment for insulin resistance; IBS-CON, controls with irritable bowel syndrome; IBS-PCOS, polycystic ovary syndrome patients with irritable bowel syndrome; LDL-C, low-density lipoprotein cholesterol; LH, luteinizing hormone; MS, metabolic syndrome; non-IBS-CON, controls without irritable bowel syndrome; non-IBS-PCOS, polycystic ovary syndrome patients without irritable bowel syndrome; SHBG, sex hormone-binding globulin; TC, total cholesterol; TG, triglycerides; TSH, thyroid-stimulating hormone; T, total testosterone; WC, waist circumference; WHtR, waist-to-height ratio.
Bold indicates statistical significance, $P < 0.05$.

6% (5/62) had previously diagnosed IBS compared to 8.1% (8/133) of CON ($P=0.60$). IBS-M was the most common subtype in both groups, with the prevalence of 46.9% (15/32) among PCOS subjects and 53.3% (8/15) among CON. The second most common type observed was the IBS-C, also in both groups – 27.5% (12/31) of PCOS and 13.3% (2/15) of CON subjects fell into this category. IBS-D could be diagnosed in 9.4% (3/32) of PCOS women and 13.3% (2/15) of CON. The least common type was IBS-U which was seen in 6.3% (2/32) of PCOS females but was not diagnosed in the CON group.

Results showed that TSH was significantly lower in PCOS women with IBS (IBS-PCOS) vs without IBS (non-IBS-PCOS) ($P < 0.05$). Age was slightly higher in IBS-PCOS patients than in PCOS-only individuals ($P=0.01$). Frequency of MS was higher in IBS-PCOS patients (9/31; 29%) than in non-IBS-PCOS patients (10/97; 10.3%) ($P=0.01$). There was no significant difference in MS occurrence when comparing CON with IBS symptoms (IBS-CON) and CON without IBS symptoms (non-IBS-CON) (7.1% vs 5.9%; $P=0.862$). Overall, PCOS patients and CON did not differ in terms of the prevalence of non-celiac gluten sensitivity (NCGS) and lactose intolerance. However, comparing subjects within the PCOS group, more IBS-PCOS patients had NCGS than non-IBS-PCOS (3/32, 9.4% vs 0/98, 0%; $P=0.02$). Among IBS-CON, 3/15 (20%) had lactose intolerance vs 1/56 (1.8%) of CON without IBS ($P=0.007$).

The prevalence of IBS differed neither between PCOS patients with and without overweight/simple obesity (BMI≥25 kg/m$^2$) (14/57, 24.6% vs 18/76, 23.7%; $P=0.91$) nor between PCOS patients with and without visceral obesity (13/52, 25% vs 19/79, 24.1%; $P=0.90$). No statistical difference was found in IBS occurrence between women with PCOS and biochemical hyperandrogenism and those with PCOS but no biochemical hyperandrogenism (9/35, 25.3% vs 23/95, 24.21%; $P=0.86$).

There was a significant difference between the occurrence of depressive symptoms in IBS-PCOS vs non-IBS-PCOS (54.2% vs 29.3%; $P=0.03$). No statistical difference was found in the incidence of depressive symptoms between IBS-CON and non-IBS-CON ($P > 0.05$).

15D scores measuring QoL were comparable between PCOS and CON. QoL appears to be significantly lower

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among IBS-PCOS patients compared to patients with PCOS only. Statistical differences were found in the total 15D score and dimensions of vision, sleeping, excretion, mental function, discomfort and symptoms, depression, vitality and sexual activity between IBS-PCOS vs non-IBS-PCOS patients. Interestingly, there were no differences between the assessed QoL of IBS-CON and non-IBS-CON, except in the distress dimension. Similarly, IBS-PCOS and IBC-CON did not differ in QoL scores (Table 2).

The occurrence of alarm symptoms was frequent in PCOS subjects and CON (Table 3). Only 4/32 (12.5%) of IBS-PCOS patients had no alarm features. The majority of IBS-PCOS patients had at least one alarm symptom (28; 87.5%). Only 2/15 (13.3%) of IBS-CON presented with no alarm signs; the rest of this group had at least one. A significant difference in the presence of alarm symptoms was observed in IBS-PCOS vs IBS-CON, where as much as 28.13% of the former group experienced two alarm symptoms, compared to only 6.67% of the latter (Table 3).

## Discussion

### IBS prevalence

This study points toward a comparably high prevalence of IBS complaints in PCOS patients (24%) and CON (21%). Similar results were obtained by Cañón *et al.* (2016) in a study on men and women aged 18–30 years, demonstrating a 24% IBS prevalence (Rome III Criteria) (30). The results of the current study suggest that IBS symptoms in the female population of reproductive age are a more frequent problem than what has been shown in several previous studies. In a meta-analysis on the global prevalence of IBS and its risk factors, 55 studies compared IBS prevalence among genders. Overall, the pooled prevalence among women was over 5% higher than in men, and the OR for IBS in women vs men was 1.67 (31). Significant variation in reported IBS prevalence exists among studies depending on the population, participants' age, diagnostic criteria used and geographic region studied. A 13% IBS prevalence was observed among both women and men by Ziółkowski *et al.* (2012) in a survey study on 850 Polish people (using the Manning criteria) (32). A markedly more frequent occurrence of IBS symptoms – of around 40%, based on the Rome III criteria – was described by Niemyjska *et al.* (2015) in a Polish population of female university students (33). To the best of the authors' knowledge, there have been no previous studies on IBS prevalence among the Polish population using the Rome IV criteria. As Palsson *et al.* (2016) noted, these wide differences in prevalence rates between populations may largely depend on the diagnostic criteria used (34). When employing the Rome III criteria, prevalence rates may be significantly higher (approximately twice as high) than those assessed with the Rome IV, which do not include the discomfort criterion and specify a more frequent symptom occurrence, as used in the current research (34, 35, 36).

Several studies have suggested an association between PCOS and a higher prevalence of IBS (37) with possible causal relationships between the two conditions (38). Mathur *et al.* found that as much as 41.7% of PCOS individuals

**Table 2** Health-related QoL scores of PCOS patients and controls, with and without IBS.

| Variable | PCOS patients | | | Controls | | | IBS-PCOS vs IBS-CON (*P*) | PCOS vs CON (*P*) |
|---|---|---|---|---|---|---|---|---|
| | IBS-PCOS | Non-IBS-PCOS | *P* | IBS-CON | Non-IBS-CON | *P* | | |
| Mobility | 0.07 (0.00) | 0.07 (0.00) | 0.53 | 0.07 (0.00) | 0.07 (0.00) | 0.64 | 0.66 | 0.64 |
| Vision | 0.05 (0.01) | 0.05 (0.00) | **0.04** | 0.05 (0.01) | 0.05 (0.00) | 0.51 | 0.96 | 0.88 |
| Hearing | 0.06 (0.00) | 0.06 (0.00) | 0.80 | 0.06 (0.00) | 0.06 (0.00) | 0.64 | 0.48 | 0.76 |
| Breathing | 0.07 (0.03) | 0.08 (0.03) | 0.11 | 0.06 (0.03) | 0.08 (0.03) | 0.15 | 0.49 | 0.84 |
| Sleeping | 0.05 (0.02) | 0.06 (0.03) | **0.02** | 0.05 (0.02) | 0.07 (0.03) | 0.10 | 0.94 | 0.23 |
| Eating | 0.07 (0.00) | 0.07 (0.00) | 0.59 | 0.07 (0.00) | 0.07 (0.00) | 0.98 | 0.98 | 0.94 |
| Speech | 0.07 (0.00) | 0.07 (0.00) | 0.98 | 0.06 (0.00) | 0.07 (0.00) | 0.68 | 0.36 | 0.63 |
| Excretion | 0.04 (0.02) | 0.06 (0.00) | **<0.001** | 0.05 (0.02) | 0.06 (0.00) | 0.20 | 0.27 | 0.63 |
| Usual activities | 0.07 (0.02) | 0.08 (0.00) | 0.16 | 0.07 (0.02) | 0.08 (0.00) | 0.26 | 0.48 | 0.54 |
| Mental function | 0.06 (0.04) | 0.09 (0.00) | **0.002** | 0.08 (0.00) | 0.09 (0.02) | 0.70 | 0.08 | 0.51 |
| Discomfort and symptoms | 0.04 (0.02) | 0.06 (0.02) | **0.004** | 0.04 (0.02) | 0.06 (0.02) | 0.86 | 0.12 | 0.30 |
| Depression | 0.04 (0.01) | 0.05 (0.01) | **0.02** | 0.04 (0.02) | 0.05 (0.01) | 0.43 | 0.89 | 0.79 |
| Distress | 0.05 (0.00) | 0.05 (0.01) | 0.09 | 0.04 (0.01) | 0.05 (0.01) | **0.002** | 0.06 | 0.65 |
| Vitality | 0.05 (0.02) | 0.06 (0.02) | **0.03** | 0.05 (0.02) | 0.06 (0.03) | 0.13 | 0.40 | 0.83 |
| Sexual activity | 0.05 (0.02) | 0.05 (0.01) | **<0.001** | 0.05 (0.01) | 0.05 (0.01) | 0.51 | 0.33 | 0.91 |
| Total 15D score | 0.83 (0.13) | 0.93 (0.08) | **<0.001** | 0.86 (0.07) | 0.95 (0.14) | 0.05 | 0.59 | 0.28 |

15D scores refer to subjects who completed the given questionnaire.
Bold indicates statistical significance, $P < 0.05$.

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**Table 3** The number of alarm symptoms present in PCOS patients with IBS and controls with IBS. Percentages refer to the subjects who completed the given questionnaire.

| No. of alarm symptoms | IBS-PCOS (%) | IBS-CON (%) |
|---|---|---|
| 0 | 4 (12.5) | 2 (13.3) |
| 1 | 11 (34.4) | 8 (53.3) |
| 2 | 9 (28.1) | 1 (6.67) |
| 3 | 5 (15.63) | 2 (13.3) |
| 4 | 2 (6.25) | 1 (6.67) |
| 5 | 1 (3.13) | 1 (6.67) |

IBS-CON, controls with irritable bowel syndrome; IBS-PCOS, polycystic ovary syndrome patients with irritable bowel syndrome.

may suffer from IBS compared to 10.3% of controls (38). PCOS may be linked to IBS as well as endometriosis more often than what could occur due to chance (39). Results of a recent Iranian study by Bazarganipour *et al.* (2020) showed a 29.7% prevalence of IBS in PCOS women but 11% in healthy controls ($P < 0.01$) when using Rome III criteria (40). However, the current results did not support these findings, as there were no statistically significant differences in IBS prevalence between PCOS patients and CON. Subsequent studies employing Rome IV criteria are needed in young women, including PCOS patients.

## IBS types

When it comes to the characteristics of IBS symptoms, the current observations suggest that IBS-M is the most common type among both PCOS and CON women, followed by IBS-C. Comparable results were obtained by Lee *et al.* for a general female population (14). However, Kim *et al.* indicated the highest pooled prevalence of IBS-C (40%), compared to 25.8% of IBS-M, among females (16). Bazarganipour *et al.* also reported that IBS-C was the most common IBS type among the studied population of PCOS women (40). As noted by Palsson *et al.*, the distribution of IBS subtypes is likely affected by the diagnostic criteria used, significantly reducing the proportional prevalence of IBS-M with the use of the Rome IV instead of Rome III criteria (34). Further studies on larger groups of PCOS women of different ethnic origins and nationalities are needed to better evaluate the prevalence of IBS subtypes.

## IBS, PCOS and QoL and depressive symptoms

According to previous research, IBS is a condition that may significantly affect patients' QoL (10, 14, 30). It was observed that IBS-PCOS women had significantly lower QoL scores than non-IBS-PCOS women. The current findings support Bazarganipour *et al.* who used the IBS-QOL scale to assess the dimensions of dysphoria, relationships, sexual concern, health worry, social reaction, body image, food avoidance and interference with activity and found the lowest IBS-QOL scores in the IBS-PCOS group. The PCOS-only patients, IBS-only patients and healthy women scored higher than women suffering from both studied conditions (40). QoL of PCOS patients was already reported as alarmingly low in previous studies (18, 41). For example, 85% of PCOS women received low QoL scores in research by Sidra *et al.*, in contrast to the observation in the current study that PCOS and CON have comparable QoL (42). Research suggests that complaints of non-gastrointestinal comorbidities are common among IBS patients. Moreover, those with concomitant somatic diseases may experience more severe IBS symptoms, lower QoL and more anxiety and depressive symptoms than IBS individuals with no comorbidities (43). The results of the current study add to the previous research on QoL in PCOS patient population by highlighting the importance of a careful diagnosis of possible concomitant conditions, such as IBS, which may further impair PCOS patients' QoL.

Moreover, mild to moderate depressive symptoms may be significantly more prevalent in this patient population (31%) compared to healthy women (17%), as seen by Cipkala-Gaffin *et al.* (44). The current results showed significant differences between depressive symptom occurrence in IBS-PCOS vs non-IBS-PCOS women, similar to the findings of a meta-analysis by Zhang *et al.*, who demonstrated a more frequent occurrence and greater severity of depressive symptoms in IBS patients compared to controls (17). This is also consistent with Jiang *et al.* who observed that participants with IBS experienced more severe depression than individuals with chronic abdominal discomfort only (13).

## IBS, PCOS and alarm symptoms

In the current study, it was observed that IBS-PCOS patients reported more alarm signs than IBS-CON. Evaluation of relevant alarm features is an essential element in the patient assessment that could help improve the IBS diagnostic yield (45). The high incidence of alarm symptoms seen in PCOS women in the current study (87.5% of IBS-PCOS reported ≥1 alarm symptom) highlights the need to pay closer attention to a range of potential alarming signs these patients may report and guide correct diagnosis of suspected organic diseases. Individuals with alarm symptoms were referred for further gastroenterological assessment and potential qualification for colonoscopy.

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### Anthropometric, biochemical and hormonal profile of IBS-PCOS and non-IBS-PCOS women

IBS-PCOS and non-IBS-PCOS patients did not differ anthropometrically, biochemically and hormonally, apart from the finding that those with IBS were slightly older and had lower TSH. Based on the observations in the current study, hyperandrogenism does not seem to impact IBS incidence in PCOS. Although IBS symptoms may fluctuate throughout the menstrual cycle, there is no clearly defined role of female hormones in IBS pathophysiology (38). Literature suggests that androgens may have a protective role in modulating visceral pain and inflammation by decreasing pro-inflammatory mediators, potentially limiting hyperalgesia occurrence (37). As Mulak *et al.* noted, this could be one reason why women are more prone to developing IBS than men (37). Seeing whether this may be true in hyperandrogenic PCOS vs non-hyperandrogenic PCOS and healthy women would require further research.

In the present study, overweight and obesity did not seem to influence IBS development in PCOS women either. Mathur *et al.* gathered contrary observations – they found that IBS-PCOS patients had a higher body fat percentage and BMI than healthy subjects and non-IBS-PCOS women (38). While obesity is a common finding among PCOS women, the potential links between obesity and IBS have not been well defined (46). Ziółkowski *et al.* suggest that BMI does not play a role in IBS development (32). However, Sadik *et al.* (2010) found that high BMI correlates positively with the severity of IBS symptoms (47). They noted that increased BMI is associated with increased rates of bowel transit, influencing stool-related IBS symptoms (47). Subsequent studies on the relationship between obesity and the severity of IBS in PCOS are needed.

The current research highlighted the importance of recognizing the potential coexistence of PCOS, IBS and MS. The results showed a higher MS prevalence in IBS-PCOS patients than non-IBS-PCOS patients. However, MS occurrence did not differ significantly between IBS-CON and non-IBS-CON. MS affects as much as 33% of PCOS patients (48). To prevent additional long-term health consequences, MS screening among PCOS patients, especially those of reproductive age, should be implemented to allow early diagnosis. Women should be advised on necessary lifestyle modifications which could help in MS prevention. When it comes to IBS and MS, links between the two syndromes have not been studied extensively. However, research by Guo *et al.* suggested that IBS is significantly associated with MS and its components, and thus, it could be beneficial to address IBS symptoms while aiming for MS prevention (49). A recent study by Bayrak also pointed to the significantly higher MS prevalence among IBS patients than controls (50). As both PCOS and IBS populations may be more prone to developing MS, patients presenting with both conditions could benefit from early MS diagnostics, prevention and management.

### Limitations of the study

IBS diagnosis can be challenging due to the resemblance of its symptoms to those of other GI disorders, such as lactose or fructose intolerance. It was suggested that 86% of IBS patients may also suffer from lactose intolerance (30). This could lead to an overestimation of IBS prevalence due to the similarity of symptoms characteristic for these conditions (30). In the current study, NCGS and lactose intolerance were evaluated only based on positive patient history. Therefore, future investigations should utilize objective tests to exclude the presence of food intolerance in patients. Future research on QoL should involve a larger study sample to accurately evaluate the potential influence of IBS symptoms on the QoL of both patients and CON.

## Conclusions

PCOS did not seem to influence IBS prevalence among the studied patient population, although many PCOS patients met the Rome IV criteria for IBS diagnosis. Hyperandrogenism, BMI and WHtR do not appear to affect IBS prevalence in PCOS. PCOS with concomitant IBS is associated with a decreased QoL and a more frequent occurrence of depressive symptoms than what could be observed in PCOS only. IBS-PCOS women may present with more warning signs than women with IBS only, which could signal a higher risk of organic disease. A relationship between comorbidity of PCOS and IBS and increased MS prevalence was also noted. Therefore, it would be advisable to expand the diagnostic process of affected women to manage the range of possible symptoms more effectively and improve patients' QoL.

**Supplementary materials**

This is linked to the online version of the paper at https://doi.org/10.1530/EC-21-0309.

**Declaration of interest**

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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