Short Report

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EGOI-PCOS survey on the prevalence of respiratory disorders associated with polycystic ovary syndrome

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ABSTRACT

Background: Polycystic Ovary Syndrome (PCOS) is a multifaceted disorder that has also recently been associated with chronic respiratory diseases (CRDs). While several studies have highlighted that pulmonary health is frequently altered in women with PCOS and *vice versa,* no mechanistic investigation has elucidated an overlapped etiology, so far. Thus, in the present survey we explored the frequency of respiratory issues in a population of PCOS patients, and the medical characteristics that possibly link the two diseases.
Results: A total of 353 women participated in the survey. CRDs affected 27.4% of the surveyed PCOS patients, with asthma representing the most prevalent respiratory problem in 61.5% of cases. In 59.3% of women, respiratory and PCOS onset appaired at the same age and in 68% of cases first symptoms appeared in adolescence.
Conclusions: While several authors have linked respiratory issues and menstrual disturbances, there are no available surveys that investigate the frequency of CRDs in PCOS patients. Despite their qualitative nature, our results sustain previous indications on a possible link between CRDs and PCOS. In future, appropriate studies may elucidate possible etiological mechanisms joining respiratory health to PCOS.

Key words: asthma, menstrual disturbances, chronic respiratory diseases, polycystic ovary syndrome, PCOS

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Introduction

Polycystic Ovary Syndrome (PCOS) is a metabolic-endocrine disorder affecting women of reproductive age with a prevalence of 10-13% [1], that exhibits a wide spectrum of psychological, dermatologic, and reproductive issues [2]. We recently conducted a survey that pointed out that PCOS often challenges the quality of life and the financial well-being of patients. Indeed, the interviewees indicated that many facets of PCOS make diagnosis a

painfully long process, which leads to distrust in medical specialists and to resort to poorly reliable sources of information [3].

From a practitioner point of view, diagnosis is complicated by currently debated clinical guidelines and limited knowledge of the comorbidities that can be associated with PCOS [4, 5]. Indeed, besides endocrine and metabolic alterations, recent evidence uncovered a likely correlation between PCOS and pulmonary affections [6]. As a matter of fact, women are more susceptible to pulmonary issues than men [7], and menstrual disturbances (MDs) represent one of the most frequent comorbidity, present in up to 40% of patients having chronic respiratory diseases (CRDs) [8, 9]. Under the epidemiological point of view, recent studies have observed that asthma have greater incidence in women suffering from endometriosis or premenstrual syndrome (PMS) that present a three-time higher likelihood of having asthma and allergic rhinitis [10]. Conversely, women with MDs demonstrate an increased odd for lung affections, and particularly for asthma [11]. In addition, given that PCOS and asthma often share similar clinical features (e.g., insulin resistance (IR), obesity, and elevated androgen levels) [12, 13], we recently proposed the existence of the "asthma-polycystic ovary overlap syndrome" [14], suggesting that in some patients reproductive and respiratory health may be disrupted by common or somewhat related etiological factors. While the exact underlying molecular mechanisms are still unclear, we decided to conduct a survey on patients with PCOS to collect further information on their medical history of respiratory diseases. To the best of our knowledge, this is the first time a self-evaluating survey has explored the respiratory experience of PCOS patients.

Materials and methods

A Google Form-based questionnaire was released on the communication channels of the web-based community NoiPCOS between the 7th and the 28th of February 2025. The questionnaire was in Italian and composed of 14 either open or multiple-choice questions (available as supplementary material – Table S1). The interviewees included in the present study agreed to the General Data Protection Regulation (GDPR - UE 2016/679) and maintained anonymity; self-reported PCOS diagnosis; and responded to all questions.

Chi-Square test was used to compare proportion between groups.

In order to assess any risk factors associated with the presence of CRD, a stepwise multivariate logistic regression was performed.

Statistical analyses were carried out at two-sided with a 0.05 significance level, using SAS® (Version 9.4, SAS Institute Inc., Cary, NC, USA) and STATA™ version 8.2 (Stata Corporation, College Station, Texas, United States).

Results

A total of 353 women participated in the survey; 347 reported to have PCOS. Among the 347 PCOS patients, 332 completed the entire questionnaire. Table 1 summarizes characteristics self-reported by the responders.

Out of these 332, 106 (31.9%) reported having also respiratory issues, with 91 (27.4%) with diagnosis of Chronic Respiratory Disease, CRD (Figure 1 – panel A). In detail, reported CRDs included any type of asthma (n=56, 61.54%), recurrent

Table 1. Characteristics of responders. CRDs, chronic respiratory diseases; BMI, body mass index.

Entry	Category	Responses N (%)
Age	14-19 years old	5 (1.51)
	20-25 years old	53 (15.96)
	26-30 years old	69 (20.78)
	>30 years old	205 (61.75)
BMI	<18.5	32 (9.64)
	≤24.9	107 (32.23)
	≤29.9	120 (36.14)
	≤34.9	45 (13.55)
	≤39.9	12 (3.61)
	>40	16 (4.82)
Familiarity with CRDs	-	103 (31.24)
Smokers	Ex	26 (7.8)
	Current	19 (5.72)

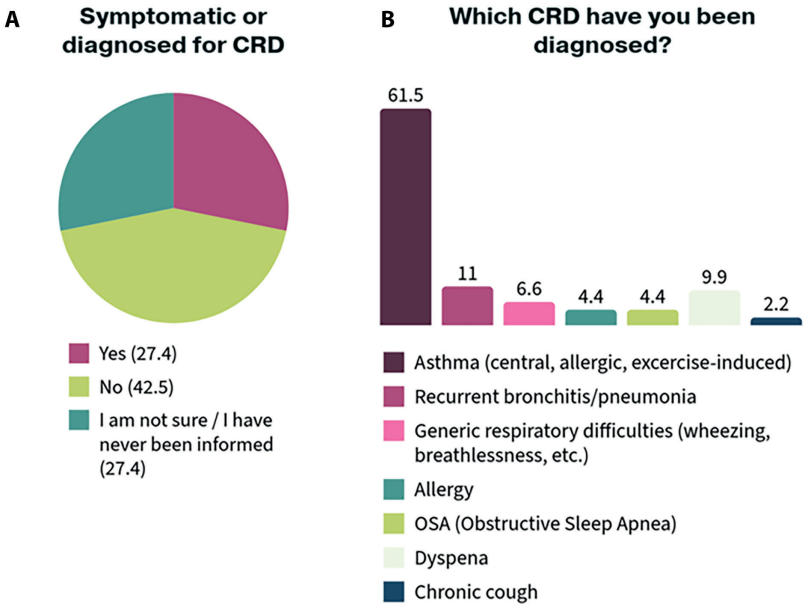

Figure 1. A) Prevalence of CRDs in PCOS patients; B) Types of CRD concomitantly diagnosed among respondents with PCOS.

bronchitis or pneumonia (n=10, 10.99%); generic respiratory issues (e.g. wheezing or breathlessness; n=6, 6.59%) and obstructive sleep apnea, OSA (n=4, 4.40%) (Figure 1 – panel B). According to responses given at questions 1.1 and 5.2 (Supplementary Table 1), 59.3% (n=54) of patients experienced the onset of PCOS and respiratory symptoms around the same age.

The BMI profile of all PCOS patients who completed the questionnaire was stratified, as reported in Figure 2 panel - A. The percentage of patients also having CRDs is reported for each BMI subgroup in bold. Of the 91 (27.4%) patients with diagnosis for CRD, the exposure to possible risk factors for pulmonary affections is reported in Figure 2 – panel B. Panel C of Figure 2 depicts the BMI distribution of participants that do not present any known risk factor for CRDs. In this subset of patients, the onset of CRDs occurred during adolescence (10-19 years old) in 62 (68.1%) cases, and 55 of them referred to that both PCOS and CRD symptoms appeared at the same time.

Comparison of participants with or without CRDs showed that the ones with CRDs were older than those without CRDs (71% vs 57% 30+ years, p=0.0283), have been diagnosed with PCOS when they were younger (81% vs 70% diagnosed before age 20, p=0.0513), showed higher BMI levels (67% vs 47% with BMI <25, p=0.0041) and reported more frequently familiarity for CRDs (45% vs 23%, p<0.0001) (Table 2).

Table 3 reports the multivariate logistic regression model showing that older age, higher body weight and family history of CRDs are risk factors associated with the development of both PCOS and CRDs.

Pharmacological treatments included antihistamines, corticosteroids, bronchodilators, or leukotriene inhibitors for CRDs; inositol, insulin sensitizers and hormonal treatment, both alone and in combination, for PCOS. The efficacy of these therapies falls outside the scope of this survey, and the data collected does not allow any analysis in this regard.

Discussion

Prevalence of CRDs in our sample of women with PCOS

As reported in Figure 1 – panel A, we found that around one third (27.4%) of the interviewed PCOS patients were diagnosed also with CRD (27.4%). Despite this result refers to a selected population, these results highlight a marked difference with respect to

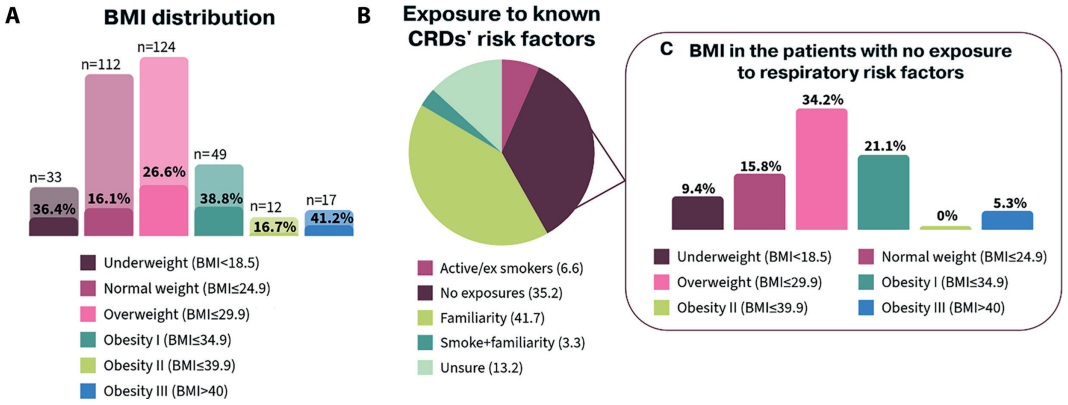

Figure 2. A) BMI distribution and percentage of PCOS patients also having CRDs for different BMIs (bold); B) Risk factors for CRD in PCOS patients; C) BMI distribution of patients with PCOS and CRD, but without exposure to known risk factors for respiratory diseases.

Table 2. Comparison of participants with or without CRDs.

Entry	Category	PCOS+CRD	Only PCOS	p value*
		n (%)	n (%)	
Age	*<30*	26 (28.6)	64 (42.7)	0.0283
	30+	65 (71.4)	86 (57.3)	
Age PCOS	*<20*	74 (81.3)	105 (70.0)	0.0513
	20+	17 (18.7)	45 (30.0)	
BMI	*<25*	30 (33.0)	79 (52.7)	0.0041
	(25.0–29.9)	33 (36.2)	47 (31.3)	
	30+	28 (30.8)	24 (16.0)	
Familiarity with CRD	*no*	38 (41.8)	108 (72.0)	<0.0001
	yes	41 (45.0)	34 (22.7)	
	unknown	12 (13.2)	8 (5.3)	

* Chi square test.

the prevalence of CRDs in the Italian general population of 9% [15].

The simultaneous presence of gynecological and respiratory disorders has recently led researchers to hypothesize possible common etiological factors. Indeed, they noted that women with PCOS often have a low pulmonary function and frequently exhibit reduced lung capacity or obstructions of the airways [16]. Moreover, epidemiological studies highlighted that CRDs, and MDs often coexist. Yang and colleagues observed that young girls with asthma have higher likelihood of developing MDs in the adult age, compared to healthy subjects [17]. In addition, some observational studies have stated that acute respiratory failure or uncontrolled asthma attacks are the primary cause of hospitalization for non-gynecological reasons in PCOS patients [18]. Nevertheless, only observations based on clinical evidence have been reported so far, and mechanistic studies are required to better understand the link between alterations in ovarian physiology and respiratory diseases.

Table 3. Multivariate logistic regression for the risk of developing both PCOS and CRDs.

Entry		OR	95% CI
Age	<30	1	
	30+	1.74	(0.96-3.16)
BMI	<25	1	
	(25.0–29.9)	1.69	(0.88-3.21)
	>=30	2.68	(1.30-5.53)
Familiarity for CRD	no	1	
	yes	3.34	(1.83-6.11)
	unknown	3.84	(1.43-10.31)

OR, Odds Ratio; 95% CI, 95% Confidence Interval.

In addition, the findings of our study highlight that age, family history of CRDs, and BMI may be key risk factors for developing CRDs in PCOS patients. In particular, the multivariate logistic regression of our data shows that overweight and obese subjects respectively have 69% and almost 3 times increased risk for developing CRDs with respect to healthy-weight women (Table 3). Elevated body weight is known to be a critical factor both in CRDs and PCOS. Indeed, high body fat may induce metabolic syndrome and low-grade systemic inflammation [19], which are the prominent drive factors for PCOS or pulmonary affections [13, 20]. However, CRDs and BMI, as well as PCOS and BMI, have mostly been studied separately, and future clinical studies should explore the relationships that may connect the two frameworks.

Age of onset for ovarian and pulmonary symptoms

The temporal manifestation of PCOS and CRD in the same person is another aspect worth discussing. Particularly, 59.3% of the interviewed women experienced symptoms for PCOS and CRD at the same age. Furthermore, these symptoms first appeared during adolescence in around 68% of cases.

Epidemiological studies pointed out that the prevalence of CDRs during adolescence is higher in females than males [21] . Some authors ascribe the reason of such difference to distinct hormonal fluctuations between genders during puberty [22], some others suggest a possible genetic cause [23]. Despite reasons still being in debate, our results indicate that higher attention should be devoted to female adolescents with gynecological disorders, to promptly tackle respiratory problems.

Asthma in PCOS patients

Asthma was reported by more than half of the interviewed PCOS patients with CRDs (Figure 1 – panel B). One plausible link with PCOS may reside in the physiological role of steroid hormones [24]. Fluctuations in estrogens and progesterone, as observed during menstrual cycle, can downregulate pulmonary adrenoceptors beta 2 reducing airway conductance and lung capacity [25]. Additionally, sexual hormones may regulate histamine release, eosinophil adhesion, and Th2 polarization [26, 27]. As hormonal alterations are a hallmark of PCOS, they may concur to increase the risk for asthma, but also obesity and IR may play a role. Accumulated visceral fat, as well as systemic IR, is known to affect cytokine production causing long-term phlogosis, characteristics of both PCOS and asthma [28].

Although IR is not generally considered among the diagnostic criteria for PCOS, it is strictly connected with the condition. Up to 80% of PCOS patients, indeed, have IR, possibly explaining the higher likelihood of respiratory issues [29, 30].

Moreover, IR proved to influence fibroblast deposition and muscarinic modulation in the pulmonary parenchyma [12], worsening spirometry parameters such as Forced Expiratory Volume (FEV_1), Forced Vital Capacity (FVC), and Forced Expiratory Flow over the middle half of the FVC (FEF_{25-75}%) [31].

Does the effect of inositol supplementation strengthen the hypothesis of a relationship between PCOS and CRDs?

Despite PCOS guidelines indicate hormonal substitutes (e.g., oral contraceptives) as therapeutic option, most participants to our survey reported inositol as treatment of choice. Myo-inositol (MYO), which is the most abundant isomeric form of inositol, is an endogenous compound that acts as cell membrane component, osmotic regulator, and second messenger

of several hormones including insulin and follicle stimulating hormone (FSH) [32]. Due to its endocrine effect, the dietary supplementation with MYO has proven to increase ovarian sensitivity to FSH, thus counteracting alterations of the menstrual cycles in women with PCOS [33]. Moreover, a recent metanalysis stated that inositol ameliorates insulin responsiveness in PCOS patients with IR in a comparable manner to metformin, which is commonly used as an off-label treatment in PCOS [34].

Beside its popular application in PCOS, MYO exhibits beneficial effects on pulmonary health. Indeed, early clinical studies demonstrated for the first time that intravenous administration of MYO to premature infants with respiratory distress syndrome (RDS) decreases the occurrence of bronchopulmonary disorders, and improves the development of newborns [35]. In fact, MYO is a key component of pulmonary surfactant, the alveolar biofilm that reduces surface tension and prevents alveoli to collapse during breathing, and that is not fully developed in preterm infants [36]. Based on such results, MYO was also administered to patients with chronic obstructive pulmonary disease (COPD), who experienced overall recovery from respiratory issues [37].

In addition, more recent studies have observed marked MYO depletion in lung fibroblasts of patients with idiopathic pulmonary fibrosis (IPF), connected with the overactivation of myo-inositol oxygenase (MIOX) and the downregulation of inositol co-transporters, respectively responsible for MYO catabolism and intracellular uptake [38]. Researchers observed that MYO deficiency is a constant finding in arginine-dependent fibroblasts of patients with IPF, which always exhibit a downregulation of arginosuccinate synthase 1 (ASS1) that leads to increased production of extracellular matrix (ECM) [39]. Despite not yet clarified the relationship between inositol and pro-fibrotic consequences of ASS1 downregulation, some experiments have suggested that the supplementation of MYO holds promises to treat IPF. Li et al. indeed demonstrated that fibroblasts from patients with IPF treated with inositol display significant reduction of the expression of pro-fibrotic agents. Furthermore, the same authors observed remarkable reduction of fibrotic lesions and overall improvement of mice health, when they supplemented MYO to animal models of IPF treated with bleomycin [38].

The use of MYO in CRDs still remains a hypothesis that further strengthens the link with PCOS. However, the use of MYO as dietary supplement in CRDs especially when PCOS is present as comorbidity needs of future and careful evaluations.

Limitations

The present survey on the prevalence of CRDs in PCOS patients was based on responses to a questionnaire, therefore our results lack clinical verification and are to be considered as informative; they only suggest that properly designed epidemiological studies and correlation analyses including a non-PCOS control group should be undertaken. The survey consisted of volunteers taking part in social-based communities, introducing a potential selection bias that limits the generalizability of our findings.

Conclusion

To our knowledge, no previous survey has investigated the frequency of CRDs in PCOS patients, thus the present work provides an original perspective on the problem, and it offers insights for future multidisciplinary research in gynecology and pneumology. The collected responses confirm previous indications of a link between PCOS and respiratory diseases. We observed in our sample a prevalence of chronic pulmonary conditions that appears about three times higher than that reported for the general population in Italy.

Despite their preliminary and totally qualitative nature, our results fuel the hypothesis of a possible sharing clinical background that may potentially involve endocrine or metabolic alteration of PCOS and respiratory conditions.

List of abbreviations

ASS1: Arginosuccinate synthase 1
COPD: Chronic obstructive pulmonary disease
CRD: Chronic respiratory diseases

ECM: Extracellular matrix
FEF_{25-75}%: Forced expiratory flow over the middle half of the FVC
FEV_1: Forced expiratory volume
FSH: Follicle stimulating hormone
FVC: Forced vital capacity
IPF: Idiopathic pulmonary fibrosis
IR: Insulin resistance
MDs: Menstrual disturbances
MIOX: Myo-inositol oxygenase
MYO: Myo-inositol
PCOS: Polycystic ovary syndrome
PMS: Premenstrual syndrome
RDS: Respiratory distress syndrome

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Appendix

Supplementary files

Table S1. Submitted questions and given responses.

N	Question	Option	Responses
1	Do you have polycystic ovary syndrome (PCOS)?	Yes	347
		No	6
1.1	If you answered yes to the previous question, when did you first experience symptoms?	Adolescence (10-19 years old)	259
		Post-adolescence (20-25 years old)	53
		Maturity (26-30 years old)	22
		After 30 years old	13
2	Age	14-19 years old	5
		20-25 years old	54
		26-30 years old	74
		>30 years old	214
3	Height (Select the range that best represents your height)	<150 cm	11
		150-159 cm	111
		160-169 cm	172
		170-179 cm	50
		≥180 cm	3
4	Weight (Select the range that best represents your weight)	<45 Kg	6
		45-54 Kg	55
		55-64 Kg	107
		65-74 Kg	77
		75-84 Kg	36
		85-94 Kg	37
		≥95 Kg	29
5	Have you ever been diagnosed with a respiratory disease or experienced breathing difficulties?	Yes	106
		Unsure	91
		No	150
5.1	If you answered yes to the previous question, which disease?	Allergy	4
		Sleep obstructive apnea	4
		Asthma	41
		Allergic asthma	13
		Asthma exercise-induced	2
		Recurrent bronchitis/pneumonia	10
		Generic respiratory difficulties	6
		Dyspnea	9
		Chronic cough	2
		Other	11
5.2	If yes, when did you first experience symptoms?	Adolescence (10-19 years old)	55
		Post-adolescence (20-25 years old)	16
		Maturity (26-30 years old)	13
		After 30 years old	7
5.3	What treatments are you following for your respiratory condition?	Antihistamines	7
		Corticosteroids, bronchodilators, leukotriene inhibitors	30
		Others	3
		No therapy	51

(*Continued*)

N	Question	Option	Responses
6	Does anyone in your family have a diagnosis of asthma or other chronic respiratory diseases?	Yes	41
		No	38
		I don't know	12
7	Are you or have you ever been a smoker?	Yes, I'm currently a smoker	5
		Yes, I have been a smoker	5
		No, I have never smoked	81
8	What treatment are you following for polycystic ovary syndrome? (Select all that apply)	Inositols	29
		Inositols + insulin sensitizers	11
		Inositols + hormonal therapy	5
		Inositols + insulin sensitizers + hormonal therapy	2
		Insulin sensitizers	4
		Insulin sensitizers + hormonal therapy	6
		Hormonal therapy	11
		Others (dietary supplements, life-style changing)	2
		No treatment	21
8.1	Since starting this treatment, have you noticed any improvements in your respiratory symptoms?	Yes	10
		No	60
		Un-responded	21
8.2	If yes, which of the following symptoms have improved?		