Original Article

Physicians' agreement with evidence-based guidelines for polycystic ovary syndrome management: implications for future policy and practice

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ABSTRACT

Background

Polycystic ovary syndrome(PCOS) is a frequently prevalent health issue that significantly affects women's reproductive health. The prompt diagnosis and suitable treatment methods employed by medical professionals determine favorable clinical outcomes of the disease.

Objective

The present study aimed to explore physicians' agreement with the standard guidelines for PCOS diagnosis and treatment.

Methods

The cross-sectional study was conducted using a self-administered 36-item questionnaire at four public and three private tertiary care hospitals and different clinics in Karachi, Pakistan.

Results

The overall response rate of the present study was 77.3%, with a mean age of 36.1±11.9 years. The Rotterdam criteria were the most commonly used measure for the diagnosis of PCOS by (n=112, 71.3%) respondents; however, the response rate varied significantly with their experience ($p<0.001$). Lifestyle modifications (n=149, 94.9%) and metformin (n=142, 90.4%) were the treatments most commonly prescribed by the respondents. Almost all the respondents (n=150, 95.5%) consider obesity, infertility, and hirsutism when prescribing hormonal medications for PCOS.

Conclusions

The outcomes revealed a disparity in the diagnostic approaches of PCOS among the respondents. The findings can be used to establish strategies to raise knowledge among primary care physicians, shorten the time it takes to diagnose cases, and, ultimately, better manage women who have the condition.

Keywords

Polycystic ovary syndrome; Gynecology; Endocrinology; Diagnosis; Pakistan.

INTRODUCTION

Polycystic ovary syndrome(PCOS) is a commonly prevalent endocrinological disorder that adversely affects women's reproductive, psychological, and metabolic health [1]. PCOS affects people throughout their lives by increasing their cardiovascular risk, causing infertility and diabetes. The etiology of PCOS is not known,

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though insulin resistance (IR), follicular irregularities, and hyperandrogenemia are assumed to be the major causes. IR is a major pathophysiological component of PCOS, with excess weight worsening PCOS symptoms [1]. More than 60% of PCOS patients have IR and 10% of PCOS women have chances to develop type-2 diabetes by the age of 40. Moreover, the increased incidence of PCOS can be associated with genetic factors, environmental variables, and intermarriages [2]. Increased levels of anti-Müllerian hormone (AMH) and luteinizing hormone are associated with PCOS-related ovulation problems [3]. Weight control should be considered for all women with PCOS because the international evidence-based guidelines consider lifestyle management as the first-line treatment [4, 5].

As PCOS has a range of symptoms, it cannot be treated or managed by a single treatment approach, and interdisciplinary treatment should be recommended when appropriate [6]. Hence, treatment interventions include educating adolescent women about the signs and consequences of the condition, encouraging a healthy lifestyle, providing therapy for psychological stress, and using the medication as necessary [4]. PCOS patients can seek treatment from general practitioners, endocrinologists, obstetricians, and gynecologists. The guidelines also emphasize that a healthy lifestyle and a healthy weight are the collective efforts of all health professionals working with those who have PCOS [7].

Regarding the diagnosis of PCOS, it has a wide range of clinical signs; no single test can identify the disorder, and diagnosis might be difficult at times. According to previous studies, PCOS patients are often dissatisfied with their diagnosis and treatment, with a delayed diagnosis being one of their most serious concerns [8, 9]. They are typically diagnosed when they have irregular periods, are unable to naturally conceive, or have metabolic abnormalities such as dyslipidemia or IR. Late diagnosis can be due to several factors, including the complexities of PCOS symptoms and the lack of integrated diagnostic standards [10]. The diagnosis was initially dependent on the National Institutes of Health (NIH) criteria but it was later changed to add polycystic ovaries on ultrasonography as a crucial diagnostic criterion [11]. The Rotterdam Criteria, which is currently the standard diagnostic criteria globally, involves the identification of two of three indications: PCO (P), hyperandrogenism (H), or anovulation (A) (O) [12].

PCOS is commonly prevalent among Asian women (52%) as compared to Western Caucasian women (20%–25%) [13]. In Pakistan, there are currently no statistics reported on gynecologists' or physicians' comprehension of PCOS diagnosis criteria. Despite the rapid advancement of Pakistan's healthcare services in recent decades, the reproductive endocrinology specialty is still in its early stages and it is not a subspecialty in most Pakistani hospitals [14]. Hence, the present study aimed to explore physicians' agreement with the standard guiding principles for PCOS diagnosis and treatment.

METHODOLOGY

Study design and setting:

A cross-sectional, quantitative study was carried out in the Pakistani metropolis of Karachi between November 2021 and April 2022. A self-administered questionnaire was used to survey physicians at 4 public and 3 private tertiary care hospitals and different clinics in Karachi, Pakistan. The study population includes obstetricians, gynecologists, endocrinologists, and residents. The survey was distributed among the respondents via official email addresses or personal contacts.

Inclusion and Exclusion Criteria

Obstetricians, gynecologists, endocrinologists, and other physicians or residents involved in providing therapeutic care to women of reproductive age and willing to contribute to the study were considered the target population. The physicians who declined to participate or did not complete the informed consent form were excluded from the study.

Sampling Technique

The G Power program, version 3.0.10, used a Chi-square goodness of fit test with an effect size of 0.2, an alpha error of 0.05, and a power of test of 0.8(9) to calculate the study sample size [15]. The calculated sample size was 197. The respondents were chosen using a convenient sampling technique.

Research Instrument Development and Piloting

A 36-item study tool was developed after a thorough evaluation of the prior studies on the topic as well as the evidence-based guiding principles for the diagnosis and management of PCOS [6, 16, 17]. Three gynecologists from the Dow University of Health Sciences evaluated the developed questionnaire for its face, content,

and convergent validity. The survey forms were then distributed to n=30 respondents to evaluate the consistency and acceptability of the initial version of the survey instrument. After the pilot testing, a minor adjustment was required. By calculating the Cronbach's alpha value, the internal consistency of the study tool was assessed, and it was found to be acceptable (α = 0.7). The final analysis excluded the data that was collected during the pilot survey. The questionnaire was circulated to the potential respondents via email or personal contacts once its reliability and validity had stabilized.

The survey form included 36 closed-ended questions in addition to the six that inquired about respondents' baseline data. The questions explored the frequency of PCOS patients that respondents consult in their clinics, the most common diagnostic criteria for PCOS used by them, biochemical parameters used for the diagnosis of hyperandrogenism, long-term health concerns, and, finally, the treatments that respondents preferred for the management of PCOS. All of the questions had "yes," "no," and "don't know" options to measure respondents' agreement with the evidence-based diagnosis and management of PCOS.

Data analysis

The respondents' initial characteristics were evaluated using descriptive statistics. Using the Kolmogorov-Smirnov test, the type of data distribution was determined. Mann-Whitney U and Kruskal Wallis tests were employed to investigate statistical variances between groups, with a p-value <0.05 being considered significant. Data analysis was done using SPSS for Windows version 24.0.0 (SPSS, IBM Inc., Chicago, IL, USA).

Ethical clearance:

The study approval was received from the ERC of Sohail University having protocol # 000138/21. Before the study, every respondent provides written consent for participation in the study.

RESULTS

Demographic Information

In the current research, 203 survey forms were distributed; however, 157 completed questionnaires were used in the study, as some of the forms were not returned and some were not duly filled out by the respondents. Hence, the overall response rate was 77.3%.

The respondents' mean age was 36.1±11.9 years. Only n= 16(10.1%) were males and n= 141(89.8%) were females. More than 75% were working in public sector hospitals. Table 1 shows the detailed demographics of the respondents.

Table 1: Baseline characteristics of study population

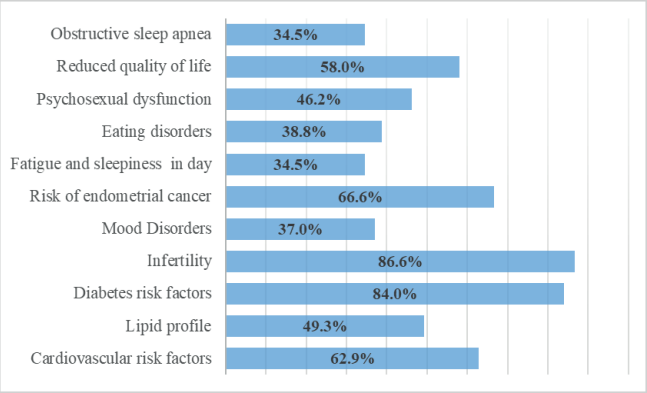
Baseline characteristics	Frequency (%)
Age	36.1±11.9
Gender	
Male	16(10.1)
Female	141(89.8)
Working organization	
Private	35(22.2)
Public	122(77.7)
Practice area	
Primary patient care	15(9.5)
Secondary patient care	24(15.2)
Tertiary patient care	118(75.1)
Experience	
< 1 year	22(14)
1-5 years	41(26.1)
6-10 years	38(24.2)
11-20 year	26(16.5)
>20 years	30(19.1)
Number of PCOS patients treated annually	
>200	44(28)
1-50	51(32.4)
50-200	62(39.4)

Respondents' compliance with the diagnostic and risk assessment of PCOS:

The respondents (n=152, 96.8%) believed that when irregular menstrual periods are observed, a PCOS diagnosis should be evaluated following the criteria. The respondents (n=72, 45.8%) define irregular menstrual cycles as < 8 cycles per year whereas (n=54, 34.3%) define it as primary amenorrhea by age 15. More than half of the respondents (n=96, 61.1%) opined that the approximate prevalence (frequency) of PCOS in Pakistan is 20-40%. More than 75% of the respondents stated 20-30 years as the most frequent age of PCOS diagnosis in their practice. Rotterdam criteria that necessitate the manifestation of oligo/anovulation, hyperandrogenism or polycystic ovaries on ultrasound were the most commonly used measure for the diagnosis

of PCOS by (n=112, 71.3%) respondents; however, the response rate varied significantly with their experience (p<0.001). Irregular menstrual cycles (n=144, 91.7%), biochemical hyperandrogenism (n=130, 82.8%), ultrasound and polycystic ovarian morphology (n=112, 71.3%) were the most commonly examined symptoms for the diagnosis of PCOS by the respondents. The most commonly used biochemical parameters by the respondents for diagnosing hyperandrogenism in patients were free testosterone (n= 95, 60.5%) and dehydroepiandrosterone sulfate (n=61, 38.8%). More than 55% of the respondents preferred the transvaginal ultrasound approach in the diagnosis. Infertility (n=136, 86.6%) and diabetes risk factors (n=132, 84%) were the respondents' perceived most important long-term concerns with PCOS. (Figure 1) Of those patients diagnosed with PCOS, menstrual disturbances (n=150, 95.5%) and infertility (n=133, 84.7%) were the most frequent justifications for visiting a clinic.

Figure 1: Respondents' perceived important long-term concern in PCOS patient



Respondents' approach to PCOS treatment:

Lifestyle modifications (n=149, 94.9%) and metformin (n=142, 90.4%) were the treatments most commonly prescribed for PCOS patients by the respondents. Lifestyle modifications (n=145, 92.3%) and clomiphene citrate plus metformin (n=131, 83.4%) were the treatments most commonly recommended for PCOS patients regarding fertility. Almost all the respondents (n=150, 95.5%) consider obesity, infertility, and hirsutism when prescribing hormonal medications for PCOS. The major factor whenever they prescribed metformin was to start at a low dose of 500mg to minimize adverse effects (n=33, 21%) (Figure 2)

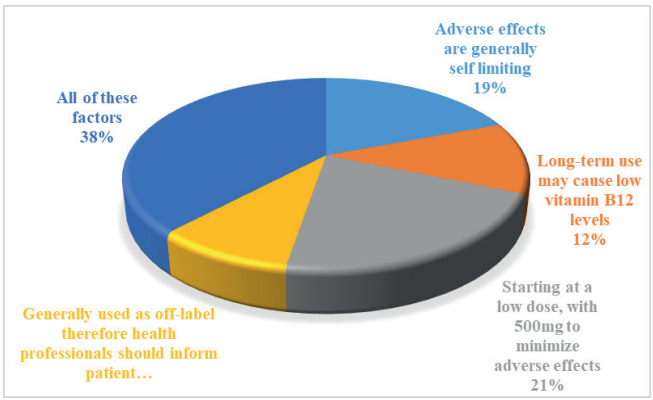


Figure 2: Respondents' consideration when prescribe metformin

The respondents (n=155, 98.7%) inquired about their patients' family histories of cardiovascular disease, diabetes and PCOS during the diagnosis. (Table 2) More than 90% of the respondents adopted a multidisciplinary approach for patients with PCOS. Almost all the respondents suggested lifestyle intervention (especially a multicomponent approach that includes diet, exercise, and behavioral techniques) for all PCOS patients and considered factors such as obesity, infertility, and hirsutism while prescribing hormonal medicines.

The majority (n=137, 87.2%) of the respondents informed patients about the potential risks and adverse effects of using metformin, combined oral contraceptive pills (COCPs) and other pharmacological therapies; though the responses differed considerably with age (p=0.001) and practice area (p=0.012). Around 40% of the respondents denied using COCPs to treat clinical hyperandrogenism and irregular menstrual cycle responses, with this negation varying considerably with their experience (p=0.006), age (p<0.001) and practice area (p=0.002). Around 70% of the respondents consider COCP in adolescents with a definite diagnosis of PCOS; the response varies significantly with their practice area (p=0.002). More than 90% of the respondents recommend metformin together with lifestyle changes in PCOS; the response varying significantly with the number of patients treated annually (p=0.002), the age (p<0.001) and experience (p=0.001) of the respondents. Metformin was considered more beneficial in high metabolic risk groups by respondents (n=142, 90.4%); the response varied significantly with their experience (p=0.007) and the number of patients annually treated (p=0.003).

Table 2: Respondents' preferences and practices for the PCOS treatment

Statement	Yes	No	May be/ sometimes
Do you ask patients regarding the history of PCOS, cardiovascular disease and diabetes in family?	155(98.7)	2(1.2)	0
Do you adopt a multidisciplinary approach for PCOS patients?	147(93.6)	3(1.9)	7(4.4)
Do you suggest lifestyle interventions for all PCOS patients?	156(99.3)	0	1(0.6)
Do you consider factors such as obesity, infertility, and hirsutism while prescribing hormonal medicines for PCOS?	155(98.7)	0	2(1.2)
Do you inform patients about the potential risks and adverse effects of pharmacological therapies that are widely used off-label in PCOS?	137(87.2)	6(3.8)	14(8.9)
Do you consider COCP in a definite diagnosis of PCOS?	109(69.4)	23(14.6)	25(15.9)
Do you use COCP in women 'at risk' of PCOS?	51(32.4)	64(40.7)	42(26.7)
Do you recommend metformin in individuals with PCOS?	149(94.9)	4(2.5)	4(2.5)
Do you believe that metformin may be more useful in high metabolic risk groups?	142(90.4)	4(2.5)	11(7)
Do you suggest anti-obesity medications to improve fertility?	48(30.5)	78(49.6)	31(19.7)
Do you use anti-androgens to treat hirsutism and androgen-related alopecia?	90(57.3)	33(21)	34(21.6)
Do you use inositol as an experimental therapy in PCOS?	87(55.4)	49(31.2)	21(13.3)
Do you give special consideration in monitoring women with PCOS during pregnancy?	129(82.1)	5(3.1)	23(14.6)
Do you utilize letrozole for inducing ovulation?	88(56)	39(24.8)	30(19.1)
Do you think that letrozole appears to reduce the chance of multiple pregnancies when compared to clomiphene citrate?	101(64.3)	24(15.2)	32(20.3)
Do you recommend patients to use gonadotropins as a second-line pharmacological agent?	75(47.7)	22(14)	60(38.2)
Do you think that laparoscopic ovarian surgery is a considerable second-line treatment?	66(42)	48(30.5)	43(27.3)
Do you recommend bariatric surgery as an exploratory therapy in PCOS women to conceive?	24(15.2)	86(54.7)	47(29.9)
Do you recommend IVF as an option when all other ovulation induction therapies have failed?	104(66.2)	12(7.6)	41(26.1)

Around half of the respondents did not suggest anti-obesity medications to improve fertility; however, the age ($p<0.001$), experience ($p=0.001$) and practice area ($p=0.03$) of the respondents significantly affected their responses. The respondents (n=90, 57.3%) propose anti-androgens to treat hirsutism and androgen-related alopecia; their responses statistically varied with their experiences ($p=0.006$). More than 80% give special consideration to monitoring women with PCOS during pregnancy. More than half of the respondents use letrozole as the first-line treatment strategy for inducing ovulation, whereas more than 60% think that letrozole appears to reduce the chance of multiple pregnancies when compared to clomiphene citrate. The respondents (n=66, 42%) think that laparoscopic ovarian surgery is a considerable treatment option in clomiphene citrate resistant women; however, the response varied significantly with the respondents'' age ($p<0.001$) and experience ($p<0.001$). The respondents (n=104, 66.2%) recommend IVF when other ovulation induction treatments have been unsuccessful.

More than half of the respondents considered the cost, expertise, clinical efficacy, monitoring and risks of multiples when they prescribed gonadotropins. (Figure 3) The majority of respondents (n=93, 59.2%) consider comparative cost, the expertise required, intra and post-

operative risks, and the possibility of lower ovarian reserve or ovarian function loss as the factors needed to be considered when laparoscopic ovarian surgery is to be recommended.

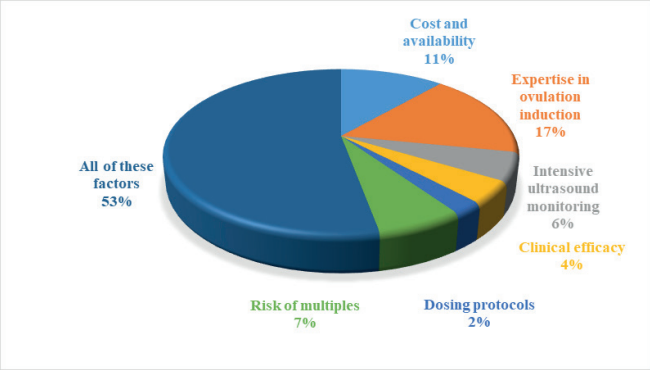


Figure 3: Respondents' consideration when prescribe gonadotropins

DISCUSSION

The present study examined physicians' approaches to diagnosing and treating PCOS in Pakistan. In contrast to many other types of research, which explore patients' knowledge, the present study represents the viewpoint of physicians [18, 19]. In the present study, the Rotterdam criteria were the most commonly used measure for the diagnosis of PCOS. Another study reported a significant association between endocrinologists and gynecologists (p= 0.001) in their consideration of hyperandrogenism in PCOS diagnosis [20]. A Nordic study revealed that Rotterdam diagnostic criteria were used by more than two-thirds of the physicians who responded to the survey [21]. Anuja et al., reported that 27.7% of physicians were uncertain about the PCOS diagnostic criteria they were using [22]. A Chinese study reported that the Androgen Excess and Polycystic Ovary Syndrome Society (AE-PCOS) criteria were most commonly employed (48.2%), other criteria followed were the Rotterdam criteria (35.7%), and the NIH criteria (12.1%) [23]. The majority of the respondents opined that the frequency of PCOS in Pakistan is 20-40%. Compared to western countries, PCOS is far more common in South Asian women, especially among Pakistani women [24]. More than 75% of the respondents stated 20-30 years as the most frequent age of PCOS diagnosis in their practice. It is reported that primary care physicians are least confident in diagnosing PCOS when compared to other healthcare professionals in the survey [25]. PCOS is typically noticed by women when they are unable to conceive, however, it can also present in early 20s or 30s. It may also often present a few months following the first menstrual period, at age 11 or 12 [26]. In the present study, infertility and diabetes risk factors were the respondents' perceived most important long-term concerns. A Chinese survey found disparities in the assessment and management of obesity in PCOS among various specialties [27].

Another study conducted by members of the European Society of Endocrinology, reported that 64% of endocrinologists identified diabetes and obesity as the main long-term PCOS concerns, while 20% of endocrinologists recognized infertility, 12% cardiovascular diseases, 3% considered psychological issues, and 1% considered endometrial cancer as the major long-standing PCOS concerns [28].

More than 90% of the respondents stated that they would adopt a multidisciplinary approach and suggest lifestyle interventions for all PCOS patients. Younger respondents more often suggested lifestyle management for PCOS patients to overcome infertility issues than more experienced respondents, which is consistent with the protocol of the International PCOS guidelines [4]. Similar outcomes were reported by another study [21]. Another study reported that women with PCOS were frequently identified by their clinical characteristics, lifestyle management, and comorbidities; the impairment of their psychosocial well-being was less well recognized [21]. It is well-documented that PCOS patient exhibit greater rates of depression, anxiety, and psychological stress than their non-PCOS counterparts, even after they have passed the reproductive age [29].

The hormonal, metabolic, and psychosocial factors that affect PCOS women get worse with obesity [31]. Losing weight can help with metabolic symptoms like IR and factors associated with cardiovascular disease, diabetes mellitus and psychiatric issues. Therefore, the primary line of treatment for PCOS women is multidisciplinary therapy [30]. A study from Pakistan reported that the most typical signs of PCOS in the Pakistani community were weight gain following abnormal hair growth and identified a family history of diabetes mellitus as a major risk factor for developing PCOS [31]. IR is a significant pathophysiological hallmark of PCOS. Even in lean women with PCOS, IR exists in a form that is thought to be mechanistically different from obesity-associated IR [32].

The healthcare provider's choice of therapy is likely to be influenced by the patient's awareness of the most recent treatment guidelines [33]. The current study reported the respondents' inclination towards recommending metformin in addition to lifestyle changes. Dokras et al., reported that oral contraceptives and lifestyle changes were the most often advised therapies for women who weren't trying to conceive, and the majority of the respondents prescribed metformin alone to treat fertility and infertility problems [22]. Metformin was considered to be more beneficial in high metabolic risk groups by respondents. The guidelines advise using Metformin in addition to a healthy lifestyle to help manage weight and reduce cardiometabolic risk factors, especially in people who are overweight or obese [34]. A study reported no significant association between lifestyle management and metformin for the clinical results, such as an increase in menstruation frequency and pregnancy outcomes. Besides, there were no appreciable improvements in lowering BMI by adding metformin with lifestyle management [35].

The respondents of the present study consider that preconception obesity, hyperandrogenism, and probably increased gestational weight gain all increase the risk of pregnancy and birth difficulties in PCOS-positive women during pregnancy. Breastfeeding difficulties are common following delivery, and pregnant PCOS women face long-term cardiovascular and psychological issues. The international evidence-based guidelines advise monitoring a woman with PCOS's blood sugar, blood pressure, diet, weight, sleep pattern, exercise, and emotional, sexual and mental health [34]. More than half of the respondents utilize letrozole for inducing ovulation whereas more than 60% think that letrozole appears to reduce the chance of multiple pregnancies when compared to clomiphene citrate. Letrozole is the first choice for anovulatory infertility in PCOS. However, a customized approach should be taken into account when managing pregnancy in PCOS [35]. A randomized controlled trial (RCT) comparing letrozole to placebo or no therapy found inadequate evidence to support letrozole, though letrozole was associated with a greater ovulation rate per woman in PCOS patients [36]. Another study reported that a gonadotropin antagonist with an estrogen or a combination of estrogen and progesterone pretreatment was the most often used treatment approach by doctors (for 44.9% of patients) [37]. Women with PCOS who are clomiphene-resistant have an increased ovarian reserve, longer cycles, more unpredictable metabolic profiles, and much higher levels of hyperandrogenism. When choosing the ovulation induction protocol, these discrepancies should be taken into consideration [38]. The gold-standard medication for PCOS ovulation induction is clomiphene citrate, yet 15–40% of women with PCOS experience CC resistance [39]. However, a considerable number of respondents assumed laparoscopic ovarian surgery as a worthy option for clomiphene citrate-resistant women. When first and second-line medications have failed to treat women with PCOS and anovulatory infertility, the majority of respondents advise IVF as a third-line treatment option. Before beginning treatment, PCOS patients having IVF or ICSI should get counseling on their elevated risk of ovarian hyperstimulation syndrome (OHSS) [36].

CONCLUSIONS

The outcomes of the present study highlight the need for standardized diagnostic and management strategies, as the different approaches could delay the diagnosis and the initiation of adequate treatment. The findings could assist in establishing policies to increase knowledge of PCOS among primary care physicians, shorten the time it takes to diagnose cases, and, ultimately, better manage women who have the condition.

Conflict of Interest None.

Funding None

Authors' contribution

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