Background: Polycystic ovary syndrome (PCOS), the major endocrinopathy among reproductive-aged women, is not yet perceived as an important health problem in the world. It affects 4%–20% of women of reproductive age worldwide. The prevalence, diagnosis, etiology, management, clinical practices, psychological issues, and prevention are some of the most confusing aspects associated with PCOS. **Aim:** The exact prevalence figures regarding PCOS are limited and unclear. The aim of this review is to summarize comprehensively the current knowledge on the prevalence of PCOS. **Materials and Methods:** Literature search was performed through PubMed, ScienceDirect, Cochrane Library, and Google Scholar (up to December 2019). All relevant articles published in English language were identified following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. **Results:** Our analysis yielded 27 surveys with a pooled mean prevalence of 21.27% using different diagnostic criteria. The proportion of women with PCOS also increased in the last decade. **Conclusion:** The current review summarizes and interprets the results of all published prevalence studies and highlights the burden of the syndrome, thereby supporting early identification and prevention of PCOS in order to reverse the persistent upward trend of prevalence.

**Keywords:** Etiology, diagnostic criteria, polycystic ovary syndrome, prevalence, prevention

**INTRODUCTION**

Stein and Leventhal were the first to describe polycystic ovary syndrome (PCOS) more comprehensively in 1935.[1] With varied clinical manifestations, unknown etiology, complex pathophysiology, and poor diagnosis, it has produced considerable scientific debate.[2-11] The diagnosis of PCOS remains a controversy in clinical endocrinology. In order to create an extensive and descriptive definition for the diagnosis of PCOS, the National Institutes of Health (NIH) criteria came into existence in 1990.[12] Then, in 2003, a workshop in Rotterdam formulated a new diagnostic criterion named Rotterdam criteria.[13] This criterion requires the presence of two conditions out of the three: (1) oligomenorrhea/anovulation, (2) clinical/biochemical hyperandrogenism, and (3) polycystic ovaries (≥12 follicles in each ovary measuring 2–9 mm). In 2006, the Androgen Excess Society (AES) revised the diagnostic criteria. The AES requires the specific presence of clinical/biochemical hyperandrogenism in combination with either oligoanovulation or polycystic ovaries.[12,13] The process of standardization of diagnosis confronts certain obstacles. First, in early menarche, ovulation is often irregular. Thus, anovulation cannot be considered as a definite evidence of the existence of the syndrome.[14] Second, transvaginal ultrasonography is not routinely performed in adolescents, which restricts ovary visualization and therefore excludes any invasive technique.

**Address for correspondence:** Prof. Chandra S. Pundir, Department of Biochemistry, Faculty of Life Sciences, MD University, Rohtak, Haryana, India. E-mail: chandraspundir@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. J Hum Reprod Sci 2020;13:261-71.
diagnosis of polycystic ovarian morphology. Third, there is a lack of consensus on the biochemical levels of hyperandrogenism, and there is limited information regarding normal levels of androgens in adolescents. Therefore, determining androgen abnormality is a complex task. Fourth, multifollicular ovaries, which may be present normally in adolescent girls, are hard to extricate from polycystic ones. Thus, the Pediatric Endocrine Society has recommended certain guidelines for differential diagnosis of PCOS in adults and adolescence. The appropriate consensus (persistent hyperandrogenic oligoanovulation) based on age and stage appropriate standards for early diagnosis and management of PCOS is summarized in Supplementary Table 1.[15]

Multiple genetic and environmental factors play an important role in occurrence of PCOS. The consequences of this multifaceted disorder extend beyond the reproductive system affecting metabolic, cardiovascular, immune, and psychological health of affected women. Over the past decade, genome-wide association studies (GWASs) have greatly advanced the understanding of PCOS pathophysiology by identifying several critical genes involved in steroidogenesis, hypothalamic–pituitary pathways, gonadotrophin action, insulin action and secretion, adipose tissue disturbances, homeostasis, lipid metabolism, and chronic inflammation are considered as the most promising genes involved in PCOS. Some of these genes are LHR, FSHR, INSR, ERB, THADA, and HMGA2. [16-20] Azziz [21] reviewed the etiology of PCOS implicating genes involved in modulation of gonadotropin and neuroendocrine action, ovarian androgen biosynthesis, and possible insulin action, providing clues to the evolutionary path and potential evolutionary advantages of PCOS. The overexpression of DENND 1A isoform produced a PCOS theca phenotype, and causal mechanisms and balancing selection were inferred from genetic associations with PCOS. [22,23] Women with PCOS have considerable varied symptomatology across life span. Physical, biochemical, and radiographic evaluations along with medical history provide confirmatory PCOS-related evidences. Hallmark features of PCOS include anovulation, hyperandrogenism, and polycystic ovaries. Other major manifestations of PCOS are as follows: Luteinizing hormone hypersecretion, metabolic disturbances, hyperinsulinemia, insulin resistance, glucose intolerance, dyslipidemia, hirsutism, acne, obesity, diabetes mellitus type II, and infertility. Various long-term complications include cardiovascular events, endometrial cancer, and psychological disorders such as stress and depression. [24-26] Table 1 represents various symptomatologies associated with the disorder. In recent years, the geographic variations of PCOS prevalence have been studied worldwide. The prevalence of PCOS is frequently quoted between 2% and 26%. [27] The differences in diagnostic criteria, sample heterogeneity, socioeconomic level, medical care access, prevalence of influential risk factors, health and education/awareness were among the possible causes of substantial geographic disparities in the prevalence rate. [28] Based on ancestral or geographical segregation, the world’s populations vary in physical, social, and behavioral features due to natural selection and environmental adaptations, the conditions which then strongly influences the phenotype of the disease. It is now evident that race and ethnicity affect clinical presentation of PCOS due to different genetic and environmental predisposition to endocrine and metabolic aberrations. As reported in 2017, it was found that Hispanic PCOS women presented a higher degree of hyperandrogenism and metabolic aberrations as compared to non-Hispanic women. [29]

The need to improve the clinical and therapeutic management of PCOS patients has become increasingly evident in the last decade. Many treatment possibilities exist to correct the severity of clinical manifestations of PCOS patients. Every physician should be able to choose the most protocol in relation to PCOS and the possible prospect of a pregnancy. Table 2 includes the appropriate therapeutic techniques with pharmacological therapies in order to treat PCOS. [30-34] The key strategies for better management of PCOS included the need for specific biological markers, the use of more precise techniques for measuring circulating androgens, understanding the risk factor consequences of PCOS, and finally, treatment strategies based on individual-specific phenotype needs.

We therefore aimed to collate different prevalence studies conducted till date in order to explore key variables that may influence prevalence estimates. The present study highlighted past to present-day accepted guidelines used for PCOS diagnosis. This review also stressed on current treatment and screening guidelines used with specific emphasis on potential new therapies that can be used for better management of PCOS.

Materials and Methods

Search strategy

Two reviewers carried out a systemic computer-assisted literature search of all major databases including MEDLINE, PubMed, ScienceDirect, ISI Web of Knowledge, Embase, Google Scholar, and Wiley. The following search terms were entered as medical subject
headings for finding studies reporting the prevalence of PCOS: The search strategy used a combination of different terms “prevalence of PCOS,” “epidemiology of PCOS,” “PCOS in reproductive age,” and “polycystic ovary syndrome.” References in the identified studies were also investigated to identify additional studies. Any discrepancies regarding data extraction were resolved by mutual consensus.

### Table 1: Clinical features associated with polycystic ovary syndrome

| Clinical features               | Type of clinical feature | Parameters affected                                                                 |
|--------------------------------|--------------------------|---------------------------------------------------------------------------------------|
| **Directly related clinical features** |                          | Infrequent menstruation at intervals >35 days<br>Absence of menstruation<br>Heavy and prolonged menstrual periods |
| Menstrual irregularities       | Oligomenorrhea, Amenorrhea, Hypermenorrhea | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Clinical hyperandrogenism      | Hirsutism, Acne, Androgenic alopecia, Virilization | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Biochemical hyperandrogenism   | Elevated serum androgen level | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Polycystic ovaries             | Numerous small cysts in a “string-of-pearls” appearance | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| AN                             | Papillomatosis and hyperkeratosis of skin | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Acrochordons                   | Skin tags | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| **Reproductive consequences**  |                          | Infrequent menstruation at intervals >35 days<br>Absence of menstruation<br>Heavy and prolonged menstrual periods |
| Infertility                    | Primary infertility, Secondary infertility | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Endometrial cancer             | Endometrial hyperplasia | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| **Metabolic consequences**     |                          | Infrequent menstruation at intervals >35 days<br>Absence of menstruation<br>Heavy and prolonged menstrual periods |
| Metabolic syndrome             | NCEP Panel III criteria | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Obesity                        | Defined by body mass index | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Type 2 diabetes (DM2)          | Characterized by high blood sugar, insulin resistance, and relative lack of insulin | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| CVD                            | Group of disorders of heart and blood vessels | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Insulin resistance             | Impaired sensitivity to insulin-mediated glucose disposal | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Dyslipidemia                   | Abnormal amount of lipids | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| **Psychological features**     |                          | Infrequent menstruation at intervals >35 days<br>Absence of menstruation<br>Heavy and prolonged menstrual periods |
| Anxiety                        | BAI<br>0-21: Low anxiety<br>22-35: Moderate anxiety<br>36: Severe anxiety | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |
| Depression                     | BDI<br>0-9: Minimal depression<br>10-18: Mild depression<br>19-29: Moderate depression<br>30-63: Severe depression | Ferriman-Gallwey score ≥8<br>GAGS<br>Male pattern baldness<br>Thinning and diffuse hair loss |

GAGS=Global acne grading system, T=Testosterone, NCEP=National Cholesterol Education Program, TG=Triglycerides, LDL=Low-density lipoproteins, C=Cholesterol, BP=Blood pressure, BMI=Basal metabolic rate, HOMA-IR=Homeostatic model assessment-insulin resistance, BAI=Body adiposity index, BDI=Body density index, AN=Acanthosis nigricans, CVD=Cardiovascular disease
Eligibility criteria

Inclusion criteria

Studies meeting the following criteria were included: (1) cross-sectional, case–control, or cohort studies including PCOS women aged 15–45 years and age-matched controls of any ethnicity; (2) PCOS was diagnosed based on either Rotterdam, NIHCD, AES criteria, or all three; (3) studies containing original data (independent of other studies); (4) design where the prevalence of PCOS with sample size was presented; and (5) publications in full text written in English.

Exclusion Criteria

The studies were excluded, if these (1) contained data overlapping data with other studies (2) reported in language other than English (3) epidemiological studies reporting prevalence in family members of affected cases (4) letters, abstracts and conference proceedings, which are not fully published in peer reviewed journals or published with limited access.

Data extraction

A data extraction form consists of information needed for the study (name of first author, year of publication, country, study design, study population size and description, age group, diagnostic criteria used, and prevalence rates). 95% confidence intervals (CIs) were calculated from the available data. The analysis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Table 2: Different approaches for treatment of polycystic ovary syndrome

| Category                                           | Drug (commercial/scientific name) | Side effects                                      |
|----------------------------------------------------|-----------------------------------|--------------------------------------------------|
| Medical therapy for irregular menstruation        |                                   |                                                  |
| Oral contraceptive pill                           | Diane/Brenda/Juliet/Estelle/Yasmin/Valette | May increase insulin resistance and weight       |
| Combined oral contraceptives                       | Ethinylestradiol, desogestrel, gestodene | Mood changes, bloating, acne, hair loss          |
| Progestins and progesterone                        | Provera/Prometrium/Aygestin       | Increase risk of heart disease                   |
| Medical therapy for insulin resistance and diabetes|                                   |                                                  |
| Insulin-sensitizing drugs                          | Metformin, thiazolidinediones     | Nausea, abdominal bloating, vomiting, and loss of appetite |
| Insulin secretion drugs                            | Sulfonylureas, meglitinides, incretin mimetics | Weight gain, hypoglycemia                        |
| Insulin resistance                                 | Corticosteroids - Rayos, orlistat | Weight gain, increased appetite                  |
| GLP-1                                              | Bydureon, Byetta, Victoza         | Headache, nausea, and diarrhea                    |
| Medical treatment for fertility                    |                                   |                                                  |
| Ovulation induction                                | Clomiphene citrate/metformin      | Multiple births, ovarian cancer                   |
| Gonadotrophins                                     | FSH/LH/hCG                        | Multiple pregnancies                              |
| Assisted reproductive technology                   | IVF                               | Cost and failure                                  |
| Medical therapy for acne, hirsutism, and hair loss  |                                   |                                                  |
| Antiandrogen                                        | Androcur/Aldactone/Proscar        | Birth defects, weight gain, depression            |
| Sebum-reducing cream                               | Isotretinoin/Rogaine              | Dry skin and eczema                               |
| Medical therapy for obesity                        |                                   |                                                  |
| Lipase inhibitors                                  | Orlstat, Loraserin, Liraglutide    | Risk for heart disease                           |
| Central nervous system stimulants/anorexiants      | Belviq/Qsymia/Adipex/Regimex/Diethylpropion | Dizziness, diarrhea, anxiety, hair loss         |
| Opioid receptor blockade                           | Naltrexone                        | Nausea, constipation                              |
| GLP-1                                              | Victoza/Saxenda                   | Nausea, abdominal pain, constipation             |
| Medical therapy for obesity                        |                                   |                                                  |
| Antidepressants                                     | Anafranil/Adapin/Aventyl/Elavil   | Fatigue, weight gain, tremors, bladder problems  |
| Antianxiety drugs                                   | Tranquilizers - Xanax/Valium      | Confusion, stomach upset, dizziness              |
| Lifestyle management                                |                                   |                                                  |
| Diet                                                | Wholegrain cereals, low glycemic index foods, less Na and sugar intake | -        |
| Physical activity                                   | Walk, running, aerobics           | -                                                |
| Natural supplements                                | Licorice root/Maca/Vitex/Chasteberry/inositol | -        |

GLP1=Glucagon-like peptide 1, FSH=Follicle-stimulating hormone, LH=Luteinizing hormone, hCG=Human chorionic gonadotropin
Quality assessment
The quality of included studies was assessed by QUADAS tool\(^{[26]}\) (quality assessment for studies of diagnostic accuracy). The quality scoring checklist includes the following: (i) objective clearly stated, (ii) study design clearly described, (iii) patient selection criteria clearly defined, (iv) details of control selection, (v) sample size, (vi) method of PCOS diagnosis was provided, (vii) inclusion and exclusion criteria, (viii) prevalence clearly provided, (ix) confounding variables measured in the analysis, and (x) statistical analysis appropriately described. Studies scoring >7, 4–6, and <4 are rated as good, fair, and poor quality, respectively.

RESULTS
Figure 1 outlines the detailed study screening and selection process. Database search yielded 2167 initial citations. All irrelevant studies (1136) were excluded. The studies describing other aspects of PCOS (polymorphism, prevalence of a particular comorbidity only, clinical trials, and reviews) were also excluded (551). A total of 480 articles had their full text reviewed for inclusion. Four hundred and seventeen articles were excluded after full-text review. Out of 68 included studies, 41 studies were omitted due to incomplete information. Twenty-seven prevalence involving 32,125 participants were therefore selected for inclusion in the review.

Baseline characteristics of studies
Table 3 provides a comprehensive portrait of the prevalence studies of PCOS across the globe including all three international diagnostic criteria\(^{[27,37-64]}\). The present review represented data based on random cross-sectional, prospective, cohort, case–control, and observational studies using all three different diagnostic criteria. The Rotterdam criteria are the most common one, included in 19 studies. The second most used criterion was NIH (11 studies). Twenty studies adopted cross-sectional study design. Only five studies include a large sample size (>1000). Southern China, Iran, and the USA reported a prevalence of 2.2%, 3%, and 4%, respectively. Beijing, Palestine, Brazil, Sri Lanka, the UK, Greek, and Spain found a prevalence rate in the range of 5%–10%. Australia, Turkey, and Denmark reported a higher prevalence (15%–20%). The prevalence rates differ with different criteria used. The Rotterdam criteria are the most acceptable diagnostic, as it includes broader evidences (oligomenorrhea/amenorrhea, clinical/biochemical hyperandrogenism plus polycystic ovaries) of PCOS. Studies adopting Rotterdam criteria as diagnostic methodology report higher prevalence rates when compared with the other two methods [Figure 2]. Today, 1 in every 10 women is diagnosed with PCOS across the world. Until the late 1990s, the studies regarding the prevalence of PCOS were rare. Most of the studies were carried out on small sample size. The number of random community surveys is also limited. Fourteen studies were conducted in Asia, with India being the country presenting maximum number of researches (five). Seven studies were conducted in Europe, two in Australia, one in Africa, two in North America, and one in South America [Figure 3].

Table 4 shows a comparison between the results of various PCOS-associated parameters using three different methods. The total number of PCOS patients included in these studies was 3434, 838, and 410 using RC, NIH, and AES criteria, respectively. Statistically significant differences were observed in polycystic ovaries on ultrasound (0.003%), hirsutism (0.001), and obesity (0.001) among PCOS cases when all three diagnostic criteria were compared. As expected, overall PCOS cases had

![Figure 1: Flowchart of study screening and selection procedure](image1)

**Figure 1:** Flowchart of study screening and selection procedure

![Figure 2: Prevalence (% of PCOS using different diagnostic criteria.](image2)

PCOS=Polycystic ovary syndrome, NIH=National Institutes of Health, AES=Androgen excess society
### Table 3: Prevalence studies of PCOS across the globe with different diagnostic criteria

#### (a) Random community-based prevalence of polycystic ovary syndrome across the globe

| Place                      | Population | Participant selection | Age | Criteria | Prevalence (95% CI) | Reference                  | QS |
|----------------------------|------------|------------------------|-----|----------|---------------------|-----------------------------|----|
| Prev. studies w/ cross-sectional study design |            |                        |     |          |                     |                             |    |
| India                      | 385        | City                   | 17-24 | RC       | 8.2% (±2.74)        | Gupta M et al., 2018        | 8  |
| India                      | 480        | University             | NR   | RC       | 8.1% (±2.76)        | Joseph N et al., 2016       | 7  |
| Rohtak, India              | 325        | Random                 | 16-45| RC       | 6.8% (±2.74)        | Deswal R et al., 2014       | 8  |
| India                      | 600        | Census block           | 15-24| RC       | 22.5% (±3.34)       | Joshi B et al., 2014        | 8  |
| Mumbai, India              | 778        | Census block of Mumbai | 15-24| RC       | 22.5% (±2.93)       | Srabani M et al., 2014      | 8  |
| Denmark                    | 863        | Hospital               | 20-40| RC       | 16.6% (±8.48)       | Lauritsen MP et al., 2014   | 7  |
| Kerala, India              | 200        | Medical college        | 18-31| RC       | 15% (±4.95)         | Vijayan CP et al., 2013     | 8  |
| Palestine                  | 137        | University             | 18-24| NIH      | 7.3% (±4.36)        | Musmar S et al., 2013       | 8  |
| Ankara, Turkey             | 392        | Female staff           | 18-45| NIH      | 6.1% (±2.37)        | Yildiz BO et al., 2012      | 9  |
| Darwin, Australia          | 248        | Indigenous women       | 15-44| NIH      | 15.3% (±4.8)        | Boyle JA et al., 2012       | 8  |
| Salvador, Brazil           | 859        | Women seeking primary health care | 18-45| RC       | 8.5% (±1.86)        | Gabrielli L., 2012          | 8  |
| Kerman, Iran               | 118        | Women with acne        | 14-38| NIH      | 60.2% (±8.83)       | Zandi S et al., 2010        | 7  |
| Isfahan, Iran              | 1000       | Females visiting premarriage screening clinic | 14-18| MI and H | 3% (±1.06)        | Hashempipur M et al., 2004  | 7  |
| Greek island, Lesbos       | 192        | Random                 | 17-45| H and OM | 6.77% (±3.55)      | Diamanti KE et al., 1999    | 8  |
| Prev. studies w/ community-based study design |            |                        |     |          |                     |                             |    |
| Beijing                    | 15,924     | Han Chinese women in community | 19-45| Rotterdam | 5.6% (±0.36)      | Rong Li et al., 2013        | 8  |
| Lucknow, India             | 1520       | Volunteer college girls | 18-25| MI or H or both | 3.7% (±0.95)  | Gill H et al., 2012        | 8  |
| Iran                       | 1126       | Random selection       | 18-45| NIH      | 7.1% (±1.50)        | Tehrani FR et al., 2011     | 8  |
| Sri Lanka                  | 3030       | Random community selection | 15-39| RC       | 14.6% (±2.06)      | Kumarapeli V, 2008          | 9  |

#### (b) Prospective, observational, and case-control prevalence studies of polycystic ovary syndrome

| Place                      | Population | Participant selection | Age | Criteria | Prevalence (95% CI) | Author, year | QS |
|----------------------------|------------|------------------------|-----|----------|---------------------|--------------|----|
| Prev. studies w/ prospective study design |            |                        |     |          |                     |              |    |
| India                      | 460        | College girls          | 15-18| RC       | 9.13% (±2.63)       | Nidhi R et al., 2011  | 7  |
| UK                         | 400        | Women visiting University of Alabama | 18-45| RC       | 6.6% (±2.43)       | Azziz R et al., 2004  | 9  |
| Spain                      | 154        | Caucasian women in blood donation camp | 18-45| NIH      | 6.5% (±3.89)       | Asuncion M et al., 2000 | 7  |

Contd...
Deswal, et al.: The prevalence of PCOS: A review

higher percentages of girls with oligomenorrhea. Infertility was significantly higher in women with polycystic ovary morphology (21.70%) using AES criteria, while Rotterdam criteria reported the presence of the same in minority of women (6%). Hirsutism was present among 58.12% of cases (Rotterdam diagnosis) and 52.68% of cases (AES diagnosis). Degree of hirsutism was less in women diagnosed with NIH criteria (25.77%). However, there was no statistical difference found in the prevalence of insulin resistance and metabolic syndrome profile of these women. PCOS is present in both obese and lean females. Rotterdam criteria report a low prevalence of insulin resistance (8.04%) as the condition was found to be more prevalent in obese PCOS cases.

**Table 3: Contd...**

| Place               | Population | Participant selection                                      | Age    | Criteria | Prevalence (95% CI) | Reference                  | QS |
|---------------------|------------|-----------------------------------------------------------|--------|----------|---------------------|----------------------------|----|
| USA                 | 100        | Self-reporting women with PCOS                            | 18-45  | NIH      | 53% (±9.78)         | Clark NM et al., 2014      | 6  |
|                     |            |                                                            |        | RC       | 70% (±8.98)         |                            |    |
|                     |            |                                                            |        | AES      | 62% (±9.51)         |                            |    |
| Tanzania            | 100        | Infertile women in hospital                               | 18-45  | RC       | 32% (±9.14)         | Pembe AM et al., 2009      | 7  |
| Germany             | 61         | Female-to-male transsexuals                               | 18-45  | NIH      | 11.5% (±8.01)       | Schötz SN, 2009            | 6  |
|                     |            |                                                            |        | RC       | 14.8% (±8.91)       |                            |    |
| China               | 915        | Medical examination center                                 | 18-45  | RC       | 2.2% (±0.95)        | Chen X et al., 2008        | 7  |
| Thailand            | 58         | Women with idiopathic intracranial hypertension           | 18-45  | NIH      | 15.5% (±9.31)       | Avisar I et al., 2012      | 8  |
| Australia           | 728        | Maternity hospital                                         | 27-34  | NIH      | 8.7% (±2.05)        | March WA et al., 2010      | 7  |
|                     |            |                                                            |        | RC       | 11.9% (±2.35)       |                            |    |
|                     |            |                                                            |        | AES      | 10.2% (±2.20)       |                            |    |
| Rotterdam, Utrecht  | 869        | WHO-II normogonadotropic, anovulatory infertility women in medical center | 18-45  | NIH      | 55% (±3.31)         | Broekmans FJ et al., 2006 | 7  |
|                     |            |                                                            |        | RC       | 91% (±1.90)         |                            |    |

CI=Confidence interval, NIH=National Institutes of Health, RC=Rotterdam criteria, AES=Androgen excess society, CLT=Chronic lymphocytic thyroiditis, QS=Quality score

**DISCUSSION**

PCOS is associated with multiple reproductive, reproductive, and psychological complications which are of serious concern. PCOS represents a significant socioeconomic burden to health care. It was during the mid-nineteenth century that headway was made in the understanding of PCOS by Stein and Leventhal. In India, it took almost a century for the prevalence of PCOS to come in the forefront in medical literature. To address this issue, few nationally representative surveys have been conducted in India from 2010 to 2014, reporting the variation in prevalence rate from 6% to 46.8%. Ganie et al. published the first Indian case-control study using Rotterdam criteria in 2010, which reported a high prevalence rate of 46.8% as
A meta-analysis conducted by Gupta et al. in 2011, conducted a prospective study involving 460 girls of 15–18 years from a residential college in South India and reported a prevalence rate of 9.13%.[54] A 2017 study conducted by Gupta et al. in 500 college girls aged 17–24 reported a prevalence rate of 8.2%.[55] Later, during 2017, Choudhary A et al. showed a higher prevalence of 41% in 170 women with menstrual irregularities by NIH criteria. Another study conducted in Mumbai among 600 girls of 15–24 years reported an estimated prevalence of 22.5%.[40] A meta-analysis conducted by Ding et al., in 2017, reviewed the prevalence of PCOS across different ethnic groups and concluded that Caucasian females are less likely to develop PCOS compared with middle east and non white female populations.[56] Accordingly, the prevalence of PCOS varies among different countries worldwide. Iran, China, and the USA reported a prevalence of 3%, 2.2%, and 4.7%, respectively. Brazil, Beijing, Sri Lanka, Palestine, Greece, the UK, and Spain found a prevalence rate in the range of 5%–10%. Denmark, Turkey, and Australia reported a higher prevalence range (15%–20%). In 2018, Wolf et al. reported the prevalence of PCOS in Mexico also.[66] In 2019, Ganie et al. concluded the prevalence of PCOS in India ranging from 3.7%–22.5% depending on the population studied and criteria used for diagnosis.[67] A report from this laboratory showed that overall 71% of the women with PCOS resided in urban regions, while 29% in rural regions in the Haryana state of India.[68] The discrepancies might be partly attributed to small sample sizes, socioeconomic differences, clinical heterogeneity, low statistical power, differing ethnic backgrounds among various populations, geographic variations, and interactions with other environmental plus genetic factors. Until today, five different GWASs have identified 16 candidate genes/loci associated with PCOS. These findings implicated the role of genes involved in gonadotropin action (LHR and FSHR), insulin signaling and type 2 diabetes (INSR, THADA, HMGA2), cell proliferation (YAP1 and SUMO1P1), and chromatin remodeling (TOX3) in the pathogenesis of PCOS.[15–19] Shim et al., 2015, conducted pathway-based GWAS to elucidate significant biological pathways and candidate genes involved in pathogenesis of PCOS.[20] The study identified three top rank pathways (ovulation, insulin secretion, and calcium signaling) associated with PCOS. INSNR gene was observed in all three pathways. Variations in INSNR gene could result in abnormal insulin regulation and disordered glucose homeostasis which enhances insulin resistance, type 2 diabetes, and obesity deteriorating metabolic profile of PCOS. To offer novel insights into the etiology, pathogenesis, and treatment of PCOS, future population-based prospective case–control studies in compliance with family-based linkage studies involving a large number of individuals in various populations are clearly warranted. CLT is known as chronic lymphocytic thyroiditis. Ganie et al.[64] have reported that 170 girls (46 years age) with euthyroid CLT had higher hirsutism score, the lower number of annual menstrual cycles as well as higher insulin resistance score as compared to control girls, under the high prevalence of PCOS.
CONCLUSION AND FUTURE PERSPECTIVES

It is undoubtedly one of the most perplexing disorders posing threat to women’s health, probably due to various manifestations of the disorder and lack of uniformly accepted diagnostic criteria. The pathogenesis of PCOS remains elusive, with contributions from insulin resistance, adipose tissue dysfunction, abnormal steroidogenesis, and hypothalamic–pituitary–ovarian dysregulation. Genetic variants and epigenetic environmental factors probably contribute to the dysregulation of these varied systems and raise new avenues of research investigation in the rapidly evolving field of PCOS. Despite rigorous research, certain questions are still unanswered so far. (i) As no single candidate gene has emerged as a convincing biomarker, so the future studies could be focused on selecting the appropriate genes as biomarkers for PCOS (ii) designing different therapeutic approaches to ameliorate additional complications such as metabolic syndrome, endometrial cancer, cardiovascular diseases, and mental health issues in later life; (iii) formulation of epigenetic studies to untangle the nature and nurture of the syndrome; (iv) need for globally agreed upon consensus on optimal diagnosis and management of PCOS; (v) conducting the large epidemiological studies worldwide to address the accurate burden of PCOS (vi) study of genetic polymorphism at wide scale to optimize individualized treatment; and (vii) increased awareness of PCOS and associated comorbidities to helps in early detection and management of PCOS. The possible roles of autoimmune phenomenon in the etiopathogenesis of PCOS and overexpression of certain genes of gonadotropin and neuroendocrine action, ovarian androgen biosynthesis, and insulin action in etiology of PCOS are suggested.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol 1935;29:181-91.
2. Azizz R, Carmina E, Dewailly D. Task force on the phenotype of the polycystic ovary syndrome of the androgen excess and PCOS society. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: The complete task force report. Fertil Steril 2009;91:456-88.
3. Tasali E, Van Cauter E, Ehrmann DA. Relationships between sleep disordered breathing and glucose metabolism in polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91:36-42.
4. Giudice LC. Endometrium in PCOS: Implantation and predisposition to endocrine CA. Best Pract Res Clin Endocrinol Metab 2006;20:235-44.
5. Cerda C, Pérez-Ayuso RM, Riquelme A, Soza A, Villaseca P, Sir-Petermann T, et al. Nonalcoholic fatty liver disease in women with polycystic ovary syndrome. J Hepatol 2007;47:412-7.
6. Hollinrake E, Abreu A, Maifeld M, Van Voorhis BJ, Dokras A. Increased risk of depressive disorders in women with polycystic ovary syndrome. Fertil Steril 2007;87:1369-76.
7. McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinaemia. Circulation 1993;87:152-61.
8. Misra A, Vikram NK. Insulin resistance syndrome (metabolic syndrome) and obesity in Asian Indians: Evidence and implications. Nutrition 2004;20:482-91.
9. Sultan C, Paris F. Clinical expression of polycystic ovary syndrome in adolescent girls. Fertil Steril 2006;86 Suppl 1:S6.
10. Huang A, Brennan K, Azizz R. Prevalence of hyperandrogenemia in the polycystic ovary syndrome diagnosed by the National Institutes of Health 1990 criteria. Fertil Steril 2010;93:1938-41.
11. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, authors Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19-25.
12. Franks S. Controversy in clinical endocrinology: Diagnosis of polycystic ovarian syndrome: In defense of the Rotterdam criteria. J Clin Endocrinol Metab 2006;91:786-9.
13. Azizz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Positions statement: Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An Androgen Excess Society guideline. J Clin Endocrinol Metab 2006;91:4237-45.
14. Khan U. Polycystic ovary syndrome in adolescents. J Pediatr Adolesc Gynecol 2007;20:101-4.
15. Rosenfeld RL. The diagnosis of polycystic ovary syndrome in adolescents. Pediatrics 2015;136:6.
16. Lee H, Oh JY, Sung YA, Chung H, Kim HL, Kim GS, et al. Genome-wide association study identified new susceptibility loci for polycystic ovary syndrome. Hum Reprod 2015;30:723-31.
17. Chen ZJ, Zhao H, He L, Shi Y, Qin Y, Shi Y, et al. Genome-wide association study identifies susceptibility loci for polycystic ovary syndrome on chromosome 2p16.3, 2p21 and 9q33.3. Nat Genet 2011;43:55-9.
18. Shi Y, Zhao H, Shi Y, Cao Y, Yang D, Li Z, et al. Genome-wide association study identifies eight new risk loci for polycystic ovary syndrome. Nat Genet 2012;44:1020-5.
19. Hayes MG, Urbanek M, Ehrmann DA, Armstrong LL, Lee JY, Sisk R, et al. Genome-wide association of polycystic ovary syndrome implicates alterations in gonadotropin secretion in European ancestry populations. Nat Commun 2015;6:7502.
20. Shim U, Kim HN, Lee H, Oh JY, Sung YA, Kim HL. Pathway analysis based on a genome-wide association study of polycystic ovary syndrome. PLoS One 2015;10:e0136609.
21. Azizz R. New insight into the genetics of polycystic ovary syndrome. Nature Rev Endocrinol 2016;12:74-5s.
22. MacAllister JM, Modi B, Miller BA, Bieglar J, Braggeman R, Legro RS, et al. Overexpression of DENND1A isoform produces a polycystic syndrome theca phenotype. Proc Natl Acad Sci USA 2014;111:E1519-27.
23. Day FR, Hinds DA, Tung JY, Stolk L, Styrkarsdottir U, Saxena R, et al. Casual mechanisms and balancing selection inferred from genetic associations with polycystic ovary syndrome. Nat Commun 2015;6:8464.
24. Hull MG. Epidemiology of infertility and polycystic ovarian disease: Endocrinological and demographic studies. Gynecol Endocrinol 1987;1:235-45.
25. Franks S, White DM. Prevalence of and etiological factors in...
polycystic ovarian syndrome. Ann N Y Acad Sci 1993;687:112-4.
26. Goldzieher JW, Axelrod LR. Clinical and biochemical features of polycystic ovarian disease. Fertil Steril 1963;14:631-53.
27. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab 2004;89:2745-9.
28. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod 2016;31:2841-55.
29. Lawrence E, Susan J, Fangbai S, Richard L, Alex P, Karl H, et al. Racial and ethnic differences in the polycystic ovary syndrome (PCOS) metabolic phenotype. Am J Obstet Gynecol 2017;216: 493.e1-13.
30. Moghetti P, Tosi F, Tosti A, Negri C, Misciali C, Perrone F, et al. Comparison of spironolactone, flutamide, and finasteride efficacy in the treatment of hirsutism: A randomized, double blind, placebo-controlled trial. J Clin Endocrinol Metab 2000;85:89-94.
31. Lumachi F, Rondinone R. Use of cyproterone acetate, finasteride, and spironolactone to treat idiopathic hirsutism. Fertil Steril 2003;79:942-6.
32. Kiddy DS, Hamilton-Fairley D, Bush A, Short F, Anyaoku V, Kiddy DM, Lehotay DC, Dodampahala SH. A simple screening approach for assessing aerobic exercise in obese women: A randomized trial. JAMA 1999;281:335-40.
33. Deswal R, Dang A, Nanda S. Prevalence of polycystic ovarian syndrome (PCOS) metabolic phenotype. Ann N Y Acad Sci 2017;1416:S389-92.
34. Yildiz BO, Bozdag G, Yapici Z, Esinler I, Yarali H. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum Reprod 2012;27:3067-73.
35. Boyd JA, Cunningham J, O’Dea K, Dunbar T, Norman RJ. Prevalence of polycystic ovary syndrome in a sample of Indigenous women in Darwin, Australia. Med J Aust 2012;196:62-6.
36. Gabrielli L, Aquino EM. Polycystic ovary syndrome in Salvador, Brazil: A prevalence study in primary healthcare. Reprod Biol Endocrinol 2012;10:96.
37. Zandi S, Farajzadeh S, Safari H. Prevalence of polycystic ovary syndrome in women with acne: Hormone profiles and clinical findings. J Pak Assoc Dermatol 2010;20:194-8.
38. Hashemipour M, Faghhiimani S, Zolfaghary H, Hovsepian S, Ahmadi F, Haghighi S. Prevalence of polycystic ovary syndrome in girls aged 14-18 years in Isfahan, Iran. Horm Res 2004;62:278-82.
39. Diamanti-Kandarakis E, Koulgi CR, Bergiele AT, Filandra FA, Tsianateli TC, Spina GG, et al. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: Hormonal and metabolic profile. J Clin Endocrinol Metab 1999;84:4006-11.
40. Li R, Zhang Q, Yang D, Li S, Lu S, Wu X, et al. Prevalence of polycystic ovary syndrome in women in China: A large community-based study. Hum Reprod 2013;28:2562-9.
41. Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. Indian J Endocrinol Metab 2012;16:S389-92.
42. Tehrani FR, Simbar M, Tohid M, Hosseinpanah F, Azizi F. The prevalence of polycystic ovary syndrome in a community sample of Iranian population: Iranian PCOS prevalence study. Reprod Biol Endocrinol 2011;9:39.
43. Kumarpalvi V, Seneviratne Rde A, Wijeyaratne CN, Yapa RM, Dodampahala SH. A simple screening approach for assessing community prevalence and phenotype of polycystic ovary syndrome in a semi-urban population in Sri Lanka. Am J Epidemiol 2008;168:321-8.
44. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol 2011;24:223-7.
45. Asunció M, Calvo RM, San Millán JL, Sancho J, Avila S, Escobar-Morreale HF. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab 2000;85:2434-8.
46. Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of polycystic ovary syndrome in unselected black and white women of the Southeastern United States: A prospective study. J Clin Endocrinol Metab 1998;83:3078-82.
47. Clark NM, Podolski AJ, Brooks ED, Chizen DR, Pierson RA, Lohotay DC, et al. Prevalence of polycystic ovary syndrome phenotypes using updated criteria for polycystic ovarian morphology: An assessment of over 100 consecutive women self-reporting features of polycystic ovary syndrome. Reprod Sci 2014;21:1034-43.
48. Pembe AB, Abed IS. Polycystic ovaries and associated clinical and biochemical features among women with infertility in a tertiary hospital in Tanzania. Tanzan J Health Res 2009;11:175-80.
49. Schötz SN. Die Häufigkeit des Syndroms der Polycystischen
Ovarien bei Frau – zu – Mann – Transsexuellen. Dissertation, Universität Erlangen; 2009.

60. Chen X, Yang D, Mo Y, Li L, Chen Y, Huang Y. Prevalence of polycystic ovary syndrome in unselected women from Southern China. Eur J Obstet Gynecol Reprod Biol 2008;139:59-64.

61. Avisar I, Gaton DD, Dania H, Stiebel-Kalish H. The prevalence of polycystic ovary syndrome in women with idiopathic intracranial hypertension. Scientifica (Cairo) 2012;2012:708042.

62. March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544-51.

63. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria: Change in prevalence among WHO-II anovulation and association with metabolic factors. BJOG 2006;113:1210-7.

64. Ganie MA, Marwaha RK, Aggarwal R, Singh S. High prevalence of polycystic ovary syndrome characteristics in girls with euthyroid chronic lymphocytic thyroiditis: A case-control study. Eur J Endocrinol 2010;162:1117-22.

65. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: A systematic review and meta-analysis. Oncotarget 2017;8:96351-8.

66. Wolf WM, Wattick RA, Kinkade ON, Olfert MD. Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. Int J Environ Res Public Health 2018;15:2589-605.

67. Ganie MA, Vasudevan V, Wani IA, Baba MS, Arif T, Rashid A. Epidemiology, pathogenesis, genetics & management of polycystic ovary syndrome in India. Indian J Med Res 2019;150:333-44.

68. Deswal R, Nanda S, Ghalaut VS, Roy PS, Dang AS. Cross-sectional study of the prevalence of polycystic ovary syndrome in rural and urban populations. Int J Gynaecol Obstet 2019;146:370-9.
**Supplementary Table 1: Differential diagnostic guidelines for diagnosis of polycystic ovary syndrome in adults and adolescence**

| Adult Phenotype | Adolescence Phenotype |
|-----------------|------------------------|
| Phenotype I: NIH criteria | AUB |
| Clinical and/or biochemical HA | Abnormal for age |
| Oligoanovulation | Persistent symptoms for 1-2 years |
| Phenotype II: RC | HA |
| Clinical and/or biochemical HA | Persistent testosterone elevation above normal levels |
| Polycystic ovary | Moderate-to-severe hirsutism |
| Oligomenorrhea/amenorrhea | Moderate-to-severe acne vulgaris to indicate HA |

Phenotype III: AES

- Clinical and/or biochemical HA

AUB=Abnormal uterine bleeding, HA=Hyperandrogenism, NIH=National Institutes of Health, RC=Rotterdam criteria, AES=Androgen excess society