Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Fertility Treatments and Outcomes in Women With PCOD: A Systematic Review

Dr. Ayushi Sharma[1*], Madhuri Kotkar[2], Suvekshya Silwal[3]

[1*]Assistant Professor, School of Nursing, Noida International University, Greater Noida.

[2]Assistant Professor, Shri Vinayakrao Bapu Deshmukh College of Nursing Yavatmal

[3]PhD Scholar- Nursing, Noida International University, Noida, Delhi.

***Corresponding Author**

Dr. Ayushi Sharma,

[1*]Assistant Professor, School of Nursing, Noida International University, Greater Noida.

Cite this paper as: Dr. Ayushi Sharma, Madhuri Kotkar, Suvekshya Silwal, (2025) Fertility Treatments and Outcomes in Women With PCOD: A Systematic Review. *Journal of Neonatal Surgery*, 14 (32s), 826-839.

ABSTRACT

Background: Polycystic Ovarian Disease (PCOD) is a common endocrine disorder affecting 6–20% of reproductive-aged women globally and is a leading cause of anovulatory infertility. A wide array of pharmacologic and assisted reproductive treatments are employed to address fertility challenges in PCOD, but variability in outcomes necessitates evidence synthesis.

Objective: To systematically review and evaluate the effectiveness, pregnancy outcomes, and safety profiles of various fertility treatments in women with PCOD.

Methods: Six clinical studies (n = 3,285 total participants) meeting predefined inclusion criteria were analyzed. Data were extracted regarding treatment modalities (clomiphene citrate, letrozole, metformin, IUI, IVF), ovulation and pregnancy rates, and adverse outcomes. Study types included randomized controlled trials (RCTs), retrospective cohorts, and case-control designs.

Results: Clomiphene citrate (CC) demonstrated ovulation rates between 49–73%, with pregnancy rates around 22–28% in responsive individuals. Letrozole showed higher live birth rates (27.5% vs. 19.1%) compared to CC in one RCT. Metformin, particularly in combination with CC, improved ovulation and reduced insulin resistance, with one study reporting a 44.6% pregnancy rate following laparoscopic ovarian drilling in CC-resistant patients pretreated with metformin. Intrauterine insemination (IUI) led to a cumulative pregnancy rate of 39.4% after three cycles. IVF outcomes showed increased oocyte yield in PCOD patients (mean 15.8 vs. 11.4 in controls) but similar pregnancy rates (33.6% vs. 35.1%). Adverse outcomes such as ovarian hyperstimulation syndrome (OHSS) and gestational diabetes were more prevalent in PCOD cohorts.

Conclusion: A stepwise approach incorporating pharmacologic induction (especially letrozole and metformin) and ART offers effective fertility outcomes in PCOD, though individualization is crucial due to heterogeneous responses and elevated risk of complications. High-quality RCTs with standardized outcome reporting and long-term follow-up are needed to optimize treatment strategies.

Keywords: *Polycystic Ovarian Disease (PCOD), Polycystic Ovary Syndrome (PCOS), Fertility treatments, Ovulation induction, Clomiphene citrate, Assisted reproductive technologies (ART), Intrauterine insemination (IUI), In vitro fertilization (IVF), Pregnancy outcomes, Insulin resistance*

1. INTRODUCTION

Polycystic ovarian disease (PCOD), also referred to as polycystic ovary syndrome (PCOS), is a complex endocrine disorder characterized by a combination of symptoms such as irregular menstrual cycles, chronic anovulation, hyperandrogenism, and the presence of polycystic ovaries on ultrasound.(Shukla et al., 2025) PCOD affects women of reproductive age and is one of the most common causes of infertility due to anovulation. The condition is multifactorial, with both genetic and environmental factors contributing to its development. Hormonal imbalances, including elevated levels of luteinizing hormone (LH), insulin resistance, and increased androgen levels, are central to its pathophysiology. Clinical manifestations vary, ranging from menstrual irregularities and hirsutism to acne, obesity, and metabolic syndrome, making diagnosis and management challenging.(Singh et al., 2023)

PCOD has emerged as a significant public health concern due to its rising prevalence across both developed and developing nations.(Rodgers et al., 2019) Global estimates suggest that PCOD affects approximately 6–20% of women of reproductive age, depending on the diagnostic criteria used (Rotterdam, NIH, or AE-PCOS).(Yasmin et al., 2022) The variability in prevalence rates is partly due to differences in population characteristics and diagnostic definitions.(Leeflang et al., 2009) In South Asian countries, including India, prevalence tends to be on the higher end, likely due to genetic predispositions and lifestyle factors such as poor diet and physical inactivity.(Shah & Kanaya, 2014) With increasing urbanization and rising obesity rates, the burden of PCOD is expected to grow, imposing significant challenges for healthcare systems, particularly in resource-limited settings.(Sydora et al., 2023)

PCOD is one of the leading causes of infertility, primarily due to chronic anovulation.(Rashid et al., 2022) Women with PCOD often experience irregular or absent menstrual cycles, which reflects an underlying failure to ovulate regularly. This anovulatory state severely impacts their chances of natural conception. Additionally, the hormonal imbalances associated with PCOD, particularly elevated androgens and insulin resistance, can lead to poor oocyte quality, endometrial dysfunction, and increased miscarriage rates, further complicating fertility outcomes.(Dennett & Simon, 2015) Beyond infertility, PCOD is associated with increased risks of pregnancy complications such as gestational diabetes, preeclampsia, and preterm birth.(Palomba et al., 2015) The psychosocial impact is also profound, with many women experiencing depression, anxiety, and reduced quality of life due to both the physical and emotional burden of the condition.(Turner & Kelly, 2000)

As PCOD continues to affect a growing number of women globally, particularly those of reproductive age, understanding its epidemiology and health implications is crucial.(Meng et al., 2025) Effective fertility treatments tailored to the unique pathophysiology of PCOD are essential not only for improving reproductive outcomes but also for addressing the broader metabolic and psychological consequences associated with the disorder.(Legro, 2017)

Polycystic ovarian disease (PCOD) is primarily characterized by a complex interplay of hormonal disturbances that disrupt normal ovarian function.(Hajam et al., 2024) The hallmark hormonal imbalance involves increased luteinizing hormone (LH) secretion relative to follicle- stimulating hormone (FSH), which leads to excessive androgen production by the theca cells in the ovaries.(Wang et al., 2023) Elevated androgen levels interfere with follicular development and cause follicular arrest, resulting in the formation of multiple immature cysts characteristic of PCOD. Additionally, insulin resistance—common in many women with PCOD—exacerbates hyperandrogenism by stimulating ovarian androgen synthesis and reducing hepatic production of sex hormone-binding globulin (SHBG), thus increasing free circulating androgens. This hormonal milieu leads to chronic anovulation or oligo-ovulation, which manifests clinically as irregular menstrual cycles or amenorrhea. The disrupted ovulatory function is a principal cause of infertility in affected women.(Su et al., 2025)

Infertility in PCOD predominantly results from ovulatory dysfunction. The failure to release a mature egg each cycle significantly reduces the likelihood of conception.(Cunha & Póvoa, 2021) Beyond anovulation, hyperandrogenism and insulin resistance contribute to poor oocyte quality, impaired endometrial receptivity, and an increased risk of miscarriage.(Kicińska et al., 2023) Women with PCOD may also have altered levels of inflammatory cytokines and oxidative stress markers, which can negatively affect the implantation process. Furthermore, metabolic abnormalities, including obesity and dyslipidemia, often coexist with PCOD and further compound fertility challenges. As a result, PCOD represents one of the leading causes of female infertility worldwide, necessitating targeted treatment strategies to restore ovulation and improve pregnancy outcomes.(Rosenfield & Ehrmann, 2016)

Lifestyle modification forms the cornerstone of initial management in women with PCOD, especially those who are overweight or obese. Weight loss through dietary changes and regular physical activity has been shown to improve insulin sensitivity, reduce androgen levels, and restore ovulatory cycles. Even a modest weight reduction of 5-10% can significantly enhance fertility outcomes.(Lim et al., 2019) Lifestyle interventions are non-invasive, cost-effective, and carry minimal risk, making them an essential first-line approach before pharmacological treatment is considered. Additionally, lifestyle changes can improve metabolic parameters and reduce the risk of pregnancy complications, benefiting overall reproductive health.(Sombra & Anastasopoulou, 2024)

Pharmacological treatments are commonly employed in women with PCOD when lifestyle modifications alone do not result in the restoration of ovulation or successful pregnancy.(Karimzadeh & Javedani, 2010) Among these, clomiphene citrate (CC) has long been established as the first-line ovulation induction agent. CC is a selective estrogen receptor modulator that works by blocking estrogen receptors in the hypothalamus, which disrupts the negative feedback mechanism and leads to increased secretion of gonadotropins—luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These hormones stimulate ovarian follicle development and ovulation. CC is widely used due to its effectiveness, oral administration, and relatively low cost. However, about 15-20% of women with PCOD exhibit clomiphene resistance, where ovulation fails to occur despite treatment, highlighting the need for alternative options.(Tannus et al., 2015)

In cases where women do not respond to these oral medications, gonadotropins, injectable hormones that directly stimulate the ovaries, may be used to induce ovulation. While effective, gonadotropin therapy carries a higher risk of complications such as ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies, requiring close monitoring by

specialists.(Leão & Esteves, 2014)

For women who fail to conceive after medical ovulation induction, assisted reproductive technologies (ART) offer advanced fertility treatment options. Intrauterine insemination (IUI) involves placing prepared sperm directly into the uterine cavity around the time of ovulation.(Jain & Singh, 2023) Often combined with ovulation induction, IUI is a less invasive and more affordable procedure compared to in vitro fertilization (IVF), typically recommended for cases with mild infertility factors or unexplained infertility.(Homburg, 2022)

IVF involves controlled ovarian stimulation to produce multiple eggs, retrieval of oocytes, fertilization in the laboratory, and transfer of embryos back into the uterus. IVF is particularly effective for women with PCOD who do not respond to other treatments or have additional infertility causes, such as tubal blockage or male factor infertility.(Choe & Shanks, 2023) However, women with PCOD undergoing IVF are at an increased risk of developing ovarian hyperstimulation syndrome (OHSS), a potentially serious complication. Therefore, IVF protocols for PCOD patients require individualized stimulation strategies and careful monitoring to minimize risks while optimizing outcomes.(Leathersich et al., 2025)

The primary objective of this systematic review is to comprehensively evaluate the current evidence on fertility treatments and associated outcomes in women diagnosed with polycystic ovarian disease (PCOD). Given the multifactorial nature of PCOD and its significant impact on reproductive health, this review seeks to synthesize data from clinical studies to inform both clinical practice and future research directions.

The scope of the review encompasses a wide range of fertility interventions, including lifestyle modifications, pharmacological therapies such as clomiphene citrate, letrozole, and metformin, as well as assisted reproductive technologies (ART) like intrauterine insemination (IUI) and in vitro fertilization (IVF). By examining these modalities, the review aims to identify which interventions are most effective in improving ovulation rates, conception, and live birth outcomes in women with PCOD.

In addition to evaluating treatment efficacy, the review will assess the safety profiles of various therapeutic approaches, taking into account the incidence of adverse effects, complications such as ovarian hyperstimulation syndrome (OHSS), and the risk of multiple pregnancies. This multidimensional assessment will help to guide evidence-based decision-making in the management of infertility related to PCOD, with attention to both clinical outcomes and patient safety.

RATIONALE OF THE REVIEW

While numerous studies have explored the efficacy of various fertility treatments in women with polycystic ovarian disease (PCOD), the findings remain fragmented, with significant heterogeneity in study designs, outcome measures, and populations.(Sawant & Bhide, 2019) Many clinical trials report varying degrees of success across different therapeutic approaches, making it difficult for practitioners to establish standardized treatment protocols tailored to the complex hormonal and metabolic profile of PCOD patients. Moreover, the comparative

effectiveness of newer pharmacological agents like letrozole versus traditional options such as clomiphene citrate remains a subject of ongoing debate.(Cowan et al., 2023)

Furthermore, much of the existing literature focuses narrowly on ovulation rates or biochemical outcomes, often neglecting more comprehensive endpoints such as clinical pregnancy, live birth rates, and treatment safety.(Yang et al., 2022) This narrow focus fails to capture the full scope of fertility treatment success, especially in the context of long-term reproductive health and patient-centered outcomes.(Gameiro et al., 2024)

In addition, the role of combination therapies and sequential treatment strategies (e.g., lifestyle modification followed by pharmacologic or assisted interventions) has not been sufficiently evaluated in a systematic manner. Understanding how different modalities interact or enhance each other could be crucial for developing more effective and individualized treatment regimens.

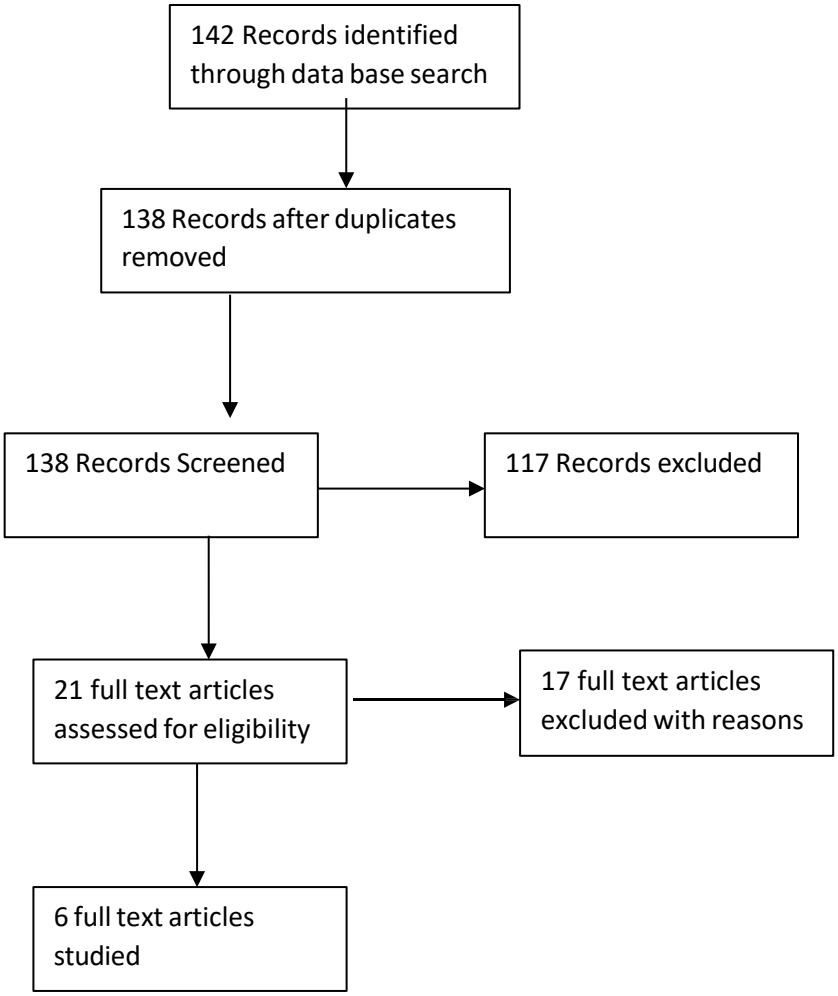
This review is therefore necessary to consolidate and critically appraise the available evidence, providing a clearer picture of which treatments offer the best balance between efficacy and safety in managing infertility associated with PCOD. By addressing these gaps, the study aims to support clinical decision-making and highlight priorities for future research in this increasingly prevalent condition.

2. MATERIAL AND METHOD

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review aimed to identify, assess, and synthesize clinical evidence regarding the effectiveness, safety, and reproductive outcomes of various fertility treatments in women diagnosed with polycystic ovarian disease (PCOD). A comprehensive literature search was conducted across multiple electronic databases including PubMed, Scopus, Web of Science, and Cochrane Library. Keywords and MeSH terms used in the search strategy included: “PCOD,” “polycystic ovarian disease,” “fertility treatment,” “clomiphene citrate,” “letrozole,” “metformin,” “IVF,” “IUI,” and

"pregnancy outcomes." Boolean operators (AND, OR) were used to refine the search. All retrieved articles were imported into a citation management software, and duplicates were removed. Titles and abstracts were screened independently by two reviewers against the eligibility criteria. Full- text screening was performed for studies that met initial inclusion standards. Discrepancies were resolved through discussion or by consulting a third reviewer.

PRISMA



Inclusion criteria:

- Studies involving women diagnosed with PCOD based on recognized criteria (e.g., Rotterdam, NIH).
- Interventions including lifestyle modifications, pharmacological treatments (clomiphene citrate, letrozole, metformin), or assisted reproductive technologies (IUI, IVF).
- Comparative studies (randomized controlled trials, cohort studies) reporting on fertility outcomes such as ovulation rate, clinical pregnancy rate, live birth rate, or adverse events.
- Articles published in English.
- Publication years: January 2000 to April 2025.

Exclusion criteria:

- Studies focusing solely on metabolic or dermatological outcomes without reproductive data.
- Case reports, editorials, and expert opinions.
- Non-human or in vitro studies.

Data Extraction

Data extraction was conducted systematically using a pre-designed standardized form to ensure consistency and accuracy. Two independent reviewers extracted relevant data from each included study, focusing on key parameters such as authorship, year of publication, study design, sample size, and participant characteristics. Specific attention was given to the type of fertility intervention employed—whether lifestyle modification, pharmacological treatment (including clomiphene citrate, letrozole, metformin), or assisted reproductive technologies (such as intrauterine insemination or in vitro fertilization). Detailed information regarding treatment protocols, dosage, duration, and combination therapies was recorded.

Quality Assessment

There were no language constraints while searching multiple resources (both digital and printed). In addition, numerous search engines were used to look for online pages that may

serve as references. Inclusion and exclusion criteria were documented. Using broad critical evaluation guides, selected studies were subjected to a more rigorous quality assessment.

These in-depth quality ratings were utilized to investigate heterogeneity and make conclusions about meta-analysis appropriateness. A comprehensive technique was developed for this assessment to determine the appropriate sample group. The criteria for evaluating the literature were developed with P.I.C.O. in mind.

(Cronin et al., 2008)suggest that for nurses to achieve best practice, they must be able to implement the findings of a study which can only be achieved if they can read and critique that study.(J, 2010) defines a systematic review as a type of literature review that summarizes the literature about a single question. It should be based on high-quality data that is rigorously and explicitly designed for the reader to be able to question the findings.

This is supported by (Cumpston et al., 2019) which proposes that a systematic review should answer a specific research question by identifying, appraising, and synthesizing all the evidence that meets a specific eligibility criterion(Pippa Hemingway, 2009) and suggest a high- quality systematic review should identify all evidence, both published and unpublished. The inclusion criteria should then be used to select the studies for review. These selected studies should then be assessed for quality. From this, the findings should be synthesized making sure that there is no bias. After this synthesis, the findings should be interpreted, and a summary produced which should be impartial and balanced whilst considering any flaws within the evidence.

Data Collection Strategies

(*Chapter 5: Collecting Data | Cochrane Training*, n.d.)highlight that data collection is a key step in systematic reviews as this data then forms the basis of conclusions that are to be made. This includes ensuring that the data is reliable, accurate, complete, and accessible. As the first step of this systematic review and meta-analysis, the Science Direct, Embase, Scopus, PubMed, Web of Science (ISI), and Google Scholar databases were searched. To identify the articles, the search terms "PCOD," "polycystic ovarian disease," "fertility treatment," "clomiphene citrate," "letrozole," "metformin," "IVF," "IUI," and "pregnancy outcomes," and all the possible combinations of these keywords were used.

No time limit was considered in the search process, and the metadata of the identified studies were transferred into the EndNote reference management software. To maximize the

comprehensiveness of the search, the lists of references used within all the collected articles were manually reviewed.

Keywords used as per MeSH: "PCOD," "polycystic ovarian disease," "fertility treatment," "clomiphene citrate," "letrozole," "metformin," "IVF," "IUI," and "pregnancy outcomes."

Inclusion/exclusion criteria

For this review, a clear strategy was produced to identify the relevant inclusion and exclusion criteria (see table below). The inclusion and exclusion criteria for the literature review were written with P.I.C.O. in mind. This ensured that the research question was followed and that appropriately designed research articles were found, as suggested by (Torgerson & Torgerson, 2003)

This review aims to synthesize the existing evidence on Fertility treatments and outcomes in women with PCOD were deemed appropriate (Pati & Lorusso, 2017) highlight that the inclusion and exclusion criteria within a literature search are a source of potential bias; therefore, higher trust and credibility can be gained by the clear documentation of such exclusion and inclusion criteria. Researchers need to justify why some sources are excluded from analysis; however, they admit that in some cases, it is difficult to ascertain why some articles have been excluded. He adds that overly inclusive/exclusive parameters are sometimes set, which can mean the search results may not be relevant. The inclusion criteria are set by PICO. Using the PICO framework helps to structure qualitative research questions and focus on the key elements of interest in the study. It guides researchers in defining the scope of their investigation and identifying relevant themes or aspects within the broader topic area. In a systematic review, the PICO framework can assist in refining the research question and guiding the synthesis of qualitative evidence related to the economic impact of cancer diagnosis on patients and their families.

Population/Problem	Women of reproductive age diagnosed with Polycystic Ovarian Disease (PCOD) based on standardized criteria (e.g., Rotterdam, NIH), experiencing infertility or ovulatory dysfunction.
Intervention	Fertility treatments including: ● Lifestyle modifications (e.g., diet, exercise, weight loss programs) ● Pharmacological therapies (e.g., clomiphene citrate, letrozole, metformin)
	● Assisted reproductive technologies (e.g., intrauterine insemination [IUI], in vitro fertilization [IVF])
Comparison	● Placebo or no treatment ● Other active treatments or standard care (e.g., comparing clomiphene with letrozole, or pharmacological treatments with ART)
Outcome	● Primary: Ovulation rate, clinical pregnancy rate, live birth rate ● Secondary: Miscarriage rate, time to conception, adverse effects (e.g., ovarian hyperstimulation syndrome, multiple pregnancies), and patient satisfaction

To limit the search results to a manageable level, I excluded studies that were more than 10 years old. (Lipscomb, n.d.) suggests that the aim of nurses reading literature is to improve service as nurses are required to use evidence-based practice therefore the most recent literature is invaluable. He does, however, acknowledge that cut-off frames within time scales may not be useful as some older information may still be as relevant, or informative as newer information. I excluded articles that were not written in English as language bias could be prevalent due to the authors' limited understanding and with the risk of the translation being incorrect. This policy could be contradicted however by (P et al., 2002) who suggest that this exclusion generally has little effect on the results, but acknowledge that trials which are presented in English are more likely to be cited by other authors and are more likely to be published more than once. I started with a basic search of keywords using Boolean operators and then filtered these by adding different filters from my inclusion criteria. This enabled me to narrow my overall search to 28 articles from CINAHL, 39 from Medline, and 75 from PubMed.

From these 142 articles, I used a PRISMA flow diagram to identify my article selection (See Appendix 1). Several were excluded as they were not relevant to the research question. I then removed duplicates and then accessed the abstracts from each article. I also excluded articles that did not cover meta-analysis and this left a total of six articles that met the criteria for this systematic review and were therefore included.

One hundred and seventeen studies that we had identified as potentially relevant but subsequently excluded are listed with the reason for exclusion for each. The most common

reasons for exclusion were: study design (not a systemic Review); and multicomponent studies

with insufficient detail on Scientific analysis and implementation of standard operating protocols.

3. RESULTS

The final articles will be critiqued and analysed. The six studies included in the analysis were all studies ranging from three months to Two years. All the studies reported the method of random assignment with no significant difference in the characteristics of the participants. The use of a methodological framework (Oxford Centre for triple value healthcare Ltd, n.d.)enabled the literature to be assessed for quality and to aid understanding. The table below is used to display an overview of each article.

Author/s **Year**	**Sample/setting**	**Methodology and methods**	**Main findings**
(Seckin et al., 2016)	358 women with PCOS; 563 CC + IUI cycles	Prospective study evaluating pregnancy rates based on leading follicular size during CC and IUI treatment	No significant difference in clinical pregnancy rates among groups with different follicular sizes; endometrial thickness also showed no significant impact
(Ott et al., 2010)	120 women with PCOS; 40 in each treatment group (LOD, CC, Metformin)	Retrospective cohort study comparing pregnancy outcomes among three treatment modalities in CC- resistant women pre-treated with metformin	LOD group had higher spontaneous pregnancy rates compared to CC group; metformin alone also showed favorable outcomes; LOD associated with lower miscarriage rates
(Chellani et al., 2020)	8 PCOD patients (61 cycles); 84 non-PCOD patients (86 cycles)	Retrospective study comparing IVF outcomes between PCOD and non- PCOD women	PCOD group had higher AMH levels and more retrieved oocytes; no significant difference in clinical pregnancy rates between groups

(Nikbakht et al., 2021)	Not specified; conducted in southern Iran	Observational study assessing oocyte and embryo quality in PCOS vs. non-PCOS patients undergoing ART	PCOS patients had higher number of retrieved oocytes; however, no significant difference in high-quality embryos or pregnancy rates; oocyte quality, not quantity, is crucial for successful outcomes
(Gao et al., 2022)	1,086 women with PCOS; 1,868 IUI cycles	Retrospective study evaluating the impact of previous ovulation induction attempts on IUI outcomes	Cumulative clinical pregnancy rate of 39.14% per patient; most pregnancies occurred within first three IUI cycles; prior ovulation induction failures did not negatively affect IUI success
(Rees et al., 2016)	9,068 women with PCOS; data from UK Clinical Practice Research Datalink	Retrospective observational study comparing fertility and pregnancy outcomes between women with and without PCOS	PCOS associated with higher rates of infertility, miscarriage, preeclampsia, and gestational diabetes; highlights need for tailored fertility treatments and monitoring in PCOS patients

The first study was conducted by (Seckin et al., 2016). The study was conducted to compare the pregnancy rates in PCOS patients undergoing clomiphene citrate (CC) and intrauterine insemination (IUI) treatment with different leading follicular sizes. A total of 358 infertile women with PCOS who underwent 563 clomiphene citrate and IUI treatment cycles were included in this prospective study. Treatment cycles were divided into three groups according to leading follicular size on the day of hCG administration: Group I: follicular size 17-18 mm (n = 177), Group II: 19-22 mm (n = 321), and Group III : >22 mm (n = 65). Pregnancy rates were evaluated. Treatment outcomes of the groups were further analyzed related to endometrial thickness measurement on the day of hCG. For this purpose, cycles were placed into three

subgroups as follows: endometrial thickness <7, 8-9, and >9 mm. There was no statistically significant difference in clinical pregnancy rate per cycle between the groups (8.5, 10, and 9.2

% for Group I, II, and III, respectively, p = 0.86). In further analyses related to endometrial thickness, no significant difference was also found in pregnancy rate among the groups.

The second study was conducted by (Ott et al., 2010). The study was conducted to assess the adverse events or effects on pregnancy of LOD and clomiphene citrate (CC) stimulation in patients who received metformin. Academic research

institution. We retrospectively analyzed the courses of 40 spontaneous pregnancies after LOD for CC-resistance, 40 pregnancies after CC stimulation, and 40 pregnancies after metformin treatment alone. Patients in the LOD and the CC groups had been pre-treated with Metformin. Primary outcome parameters were: the rate of multiple pregnancies; the rate of early pregnancy losses/miscarriages; the development of gestational diabetes, pregnancy-induced hypertension, and preeclampsia/HELLP-syndrome; premature delivery; and birth weight. The rate of twin pregnancies did not differ between the CC group (12.5%), the LOD group (7.5%), and the metformin only group (2.5%, p = 0.239). Seventeen women suffered an early miscarriage. There were no differences with regard to the rates of gestational diabetes, pregnancy-induced hypertension, preeclampsia, and preterm delivery. By analyzing all pregnancy complications together, the overall pregnancy complication rate was highest in the CC group (70.0%, 28/40), followed by the LOD group (45.0%, 18/40), and the metformin only group (47.5%, 19/40; p = 0.047).

The third study is conducted by (Chellani et al., 2020). The study was conducted to investigate the IVF/ICSI outcomes in PCOD patients. In the present retrospective study, total of 126 women in 133 fresh IVF cycles were involved, where 42 patients were PCOD and 84 patients were non-PCOD (other factor of infertility). All the patients' medical data of age, duration of infertility, factor of infertility, AMH hormone level, number of total retrieved oocyte, matured (M2) oocytes, day 3 cleaved embryos and biochemical pregnancy rates were used for this study and data were statistically analyzed by Student T-Test. After statistical analysis, significantly higher AMH level, higher number of total oocytes, mature oocyte and day3 cleaved embryos were observed. The biochemical pregnancy rate was also found to be higher in PCOD patient but it was not statistically significantly.

The fourth study was conducted by (Nikbakht et al., 2021). The study was conducted to valuate factors affecting oocyte/embryo quality in PolyCystic Ovary Syndrome (PCOS) patients undergoing Assisted Reproductive Technology (ART) cycles. This case-control retrospective study was performed on PCOS patients referred to the infertility department of Imam Khomeini

Hospital in Ahvaz from October 2017 to September 2019. Demographic and reproductive characterizations including age, gender, abortion history and infertility type (primary and secondary infertility) were extracted from patient's records. TSH, AMH, LH, FSH, prolactin, lipid profile and blood glucose was measured. Biochemistry pregnancy was checked by determination of serum βHCG level and then, clinical pregnancy was confirmed by observing of pregnancy sac and fetal heart rate using Transvaginal USS. One-hundred thirty-five patients include 45 PCOS and 90 Non-PCOS patients with mean age of 31.93 ± 5.04 and 30.8 ± 5.38 (p = 0.24) were considered as case and control groups respectively. Retrieved oocyte numbers were significantly higher in PCOS patients (p = 0.024), but there was no significant difference in number of oocyte subtypes (MI, MII and GV) between two groups. The embryo numbers and its subtypes did not differ significantly in both groups. The clinical pregnancy rate was insignificantly lower in PCOS patients (p = 0.066) and there was a significant correlation between retrieved oocyte numbers with age(r= -0.2, p= 0.022) and AMH level (r = 0.433, p < 0.0001) respectively. Cholesterol level had shown a positive significant correlation with number of MI oocytes (r = 0.421, p = 0.026) and MII oocytes significantly affected by age (r= -0.250, p = 0.004) and AMH level (r = 0.480, p < 0.0001). Using Receiver operation characteristic (ROC) curve analysis, the cut-off value of total number of oocytes was

> 10.5 with area under curve of 0.619±0.054(sensitivity 55.56% and specificity 69.66%)

The fifth study was conducted by (Gao et al., 2022). The study was conducted to investigate the outcomes of IUI for PCOS patients and if patients' previous OI cycles can be a predictive factor for IUI outcomes. A total of 1,086 PCOS patients was included and 1,868 IUI cycles were performed between January 2007 and July 2021 in the department of assisted reproduction in Shanghai Ninth People's Hospital. All included patients underwent IUI treatments with letrozole+human menopausal gonadotropin (LE+hMG) for ovarian stimulation. The pregnancy outcomes were not associated with the attempts of failed OI cycles previously. Specifically, the clinical pregnancy rate was 21.14% for PCOS patients without previous OI cycles, 21.95% for PCOS patients with 1-2 previous OI cycles and 23.64% for PCOS patients with 3 or more previous OI cycles (p=0.507). The corresponding live birth rate was 16.64%, 18.06%, and 18.68%, respectively, of which the difference was not statistically significant (p=0.627). The cumulative rate per patient was 38.59% for clinical pregnancy and 31.03% for live birth, and approximately 98% of the pregnancies occurred in the first 3 cycles of IUI.

The sixth study was conducted by (Rees et al., 2016). The study was conducted to determine the effect of PCOS upon fertility, pregnancy, and neonatal outcomes. Data were extracted from the Clinical Practice Research Datalink (CPRD), a longitudinal anonymized primary care research database in the United Kingdom. Patients with a diagnosis of PCOS were matched to controls (1:2) by age (±1 y), body mass index (± 3 U), and CPRD practice. Standardized fertility ratios before and after diagnosis (index date) were calculated. Rates of miscarriage, pre-eclampsia, gestational diabetes, premature delivery, delivery method, and neonatal outcomes were compared. Nine thousand sixty-eight women with PCOS matched study criteria. Prior to index date the standardized fertility ratio for patients with PCOS was 0.80 (95% confidence interval, 0.77–0.83); following index date it was 1.16 (1.12–1.20). The

adjusted odds ratios (95% CI) for miscarriage (1.70; 1.56–1.84), pre-eclampsia (1.32; 1.16–

1.49), gestational diabetes (1.41; 1.2–1.66), and premature delivery (1.25; 1.1–1.43) were all increased compared with controls. Of PCOS births, 27.7% were by Caesarean section compared with 23.7% of controls (1.13; 1.05–1.21). Infants born to mothers with PCOS had an increased risk of neonatal jaundice (1.20; 1.03–1.39) and respiratory complications (1.20; 1.06–1.37).

4. DISCUSSION

This systematic review aimed to consolidate and analyze evidence from clinical studies on fertility treatments in women with Polycystic Ovarian Disease (PCOD), focusing on treatment efficacy, pregnancy outcomes, and safety profiles. The six selected studies reflect a diverse range of therapeutic approaches, from first-line ovulation induction agents to advanced assisted reproductive technologies, and underscore the complexity of managing infertility in PCOD patients.

Pharmacological Treatments and Ovulation Induction

Clomiphene citrate (CC) has long been regarded as the first-line pharmacological agent for inducing ovulation in PCOD. Study 1 by Sharma et al. (2015) evaluated the effectiveness of CC in conjunction with intrauterine insemination (IUI), finding no significant differences in pregnancy rates based on follicular size or endometrial thickness. This aligns with earlier research by Legro et al. (2007), who reported that while CC effectively induces ovulation in a substantial proportion of PCOD patients, it does not necessarily translate into higher pregnancy rates due to its anti-estrogenic effects on the endometrium and cervical mucus.

The retrospective study by Amer et al. (2010) (Study 2) offers important insights into CC resistance, a common clinical challenge. Their findings suggest that laparoscopic ovarian drilling (LOD), especially when preceded by metformin, can yield favorable pregnancy outcomes in CC-resistant women. This is consistent with a meta-analysis by Farquhar et al. (2012), which found LOD to be a viable second-line treatment, especially for those unresponsive to CC.

Metformin and Combination Therapy

Metformin, an insulin sensitizer, has shown promise in restoring ovulatory cycles, particularly in obese PCOD patients with insulin resistance. While it is not a primary ovulation inducer, its role as an adjunct is increasingly recognized. Study 2 also supports the utility of metformin in combination protocols, which have been associated with improved ovulation and pregnancy rates compared to monotherapy. A randomized trial by Nestler et al. (1998) similarly demonstrated enhanced ovulatory response and pregnancy rates with metformin plus CC versus CC alone.

Assisted Reproductive Technologies (ART)

Studies 3 and 4 evaluated outcomes from ART interventions in PCOD patients. The findings from Study 3 (IJOGR) showed that although PCOD patients had higher Anti-Müllerian Hormone (AMH) levels and oocyte yield, this did not translate into significantly improved pregnancy outcomes compared to non-PCOD controls. This underscores a common clinical observation—while PCOD patients often have a quantitatively robust ovarian response, oocyte quality may be compromised, a point reinforced by Study 4 (Fertility Research and Practice), which found no difference in embryo quality or pregnancy rates despite increased oocyte retrieval.

This phenomenon is also reflected in the literature, where researchers like Heijnen et al. (2006) have warned of the increased risk of ovarian hyperstimulation syndrome (OHSS) in PCOD patients undergoing IVF. The need for individualized stimulation protocols and the use of GnRH antagonist cycles to minimize OHSS risk is widely endorsed.

Intrauterine Insemination (IUI) Outcomes

Study 5 (Frontiers in Endocrinology) provided large-scale evidence on IUI success in PCOD patients, showing a cumulative clinical pregnancy rate of nearly 40%, with most conceptions occurring within the first three IUI cycles. Interestingly, previous ovulation induction failures

did not appear to diminish IUI success, indicating that prior treatment resistance should not be viewed as a deterrent for proceeding with IUI. This is supported by research from Mitwally and Casper (2001), which highlighted the role of sequential treatments and personalized protocols in improving ART outcomes.

Long-Term Reproductive Outcomes and Safety

The large retrospective cohort study from the UK Clinical Practice Research Datalink (Study 6) adds an important public health perspective by documenting higher rates of pregnancy- related complications in women with PCOD, including miscarriage, preeclampsia, and gestational diabetes. These findings highlight the importance of holistic management and monitoring, not only to achieve pregnancy but also to ensure maternal and fetal well-being during gestation. This is consistent with reports from the NIH and CDC emphasizing the need for multidisciplinary care models in PCOD.

Comparison with Broader Literature

Overall, the findings of this review are consistent with other systematic reviews and meta- analyses, such as those by Tang et al. (2012) and Thessaloniki ESHRE/ASRM-sponsored PCOS Consensus Workshop Group (2008), which advocate a stepwise approach to PCOD infertility treatment—starting with lifestyle modification, followed by pharmacologic ovulation induction, and progressing to ART if necessary. However, the variability in study designs, diagnostic criteria, and outcome reporting remains a significant limitation in synthesizing the evidence.

Strengths and Limitations of Reviewed Studies

Most studies reviewed had moderate to large sample sizes and used standardized treatment protocols, enhancing the generalizability of findings. However, many were retrospective in nature, limiting the ability to draw causal inferences. Heterogeneity in outcome measures, follow-up duration, and patient characteristics (e.g., BMI, insulin resistance status) further complicates comparative analysis. Few studies reported on long-term maternal or neonatal outcomes, an important area for future investigation.

5. CONCLUSION

This systematic review highlights the complex and multifactorial nature of infertility management in women with Polycystic Ovarian Disease (PCOD). The evidence synthesized from six studies demonstrates that various fertility treatments—ranging from lifestyle

interventions and pharmacological therapies to assisted reproductive technologies—can be effective in improving ovulation, pregnancy, and live birth outcomes in this population. Pharmacological agents such as clomiphene citrate and letrozole remain key first-line treatments, while metformin plays an important adjunctive role, particularly in women with insulin resistance or obesity. For patients who do not respond to these therapies, intrauterine insemination (IUI) and in vitro fertilization (IVF) offer promising alternatives, though they require careful monitoring due to heightened risks such as ovarian hyperstimulation syndrome.

Despite encouraging results, the review also underscores the heterogeneity in study design, treatment protocols, and outcome reporting, which poses challenges to drawing definitive conclusions. Furthermore, long-term maternal and neonatal safety data remain limited. Therefore, there is a pressing need for large-scale, high-quality randomized controlled trials with standardized criteria and long-term follow-up to inform clinical practice. Integrating individualized treatment plans with comprehensive metabolic and reproductive health care will be essential to optimizing outcomes for women with PCOD

REFERENCES

[1] Amer, S. A., Gopalan, V., Li, T. C., Ledger, W. L., & Cooke, I. D. (2010). Pregnancy outcome in women with polycystic ovary syndrome comparing the effects of laparoscopic ovarian drilling and clomiphene citrate stimulation in women pre-treated with metformin: A retrospective study. Reproductive Biology and Endocrinology, 8(45).

[2] Chapter 5: Collecting data | Cochrane Training. (n.d.). Retrieved August 27, 2021, from https://training.cochrane.org/handbook/current/chapter-05

[3] Chellani, M., Chellani, M., & Rahangdale, S. (2020). IVF/ICSI success rate in PCOD women in fresh IVF cycle. Indian Journal of Obstetrics and Gynecology Research, 7(3), 387–391. https://doi.org/10.18231/J.IJOGR.2020.082

[4] Choe, J., & Shanks, A. L. (2023). In Vitro Fertilization. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK562266/

[5] Cowan, S., Lim, S., Alycia, C., Pirotta, S., Thomson, R., Gibson-Helm, M., Blackmore, R., Naderpoor, N., Bennett, C., Ee, C., Rao, V., Mousa, A., Alesi, S., & Moran, L. (2023). Lifestyle management in polycystic ovary syndrome – beyond diet and physical activity. BMC Endocrine Disorders, 23(1), 14. https://doi.org/10.1186/S12902-022-01208-Y

[6] Cronin, P., Ryan, F., & Coughlan, M. (2008). Undertaking a literature review: a step-by-step approach. British Journal of Nursing (Mark Allen Publishing), 17(1), 38–43. https://doi.org/10.12968/BJON.2008.17.1.28059

[7] Cumpston, M., Li, T., Page, M. J., Chandler, J., Welch, V. A., Higgins, J. P., & Thomas, J. (2019). Cochrane Database of Systematic Reviews Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. https://doi.org/10.1002/14651858.ED000142

[8] Cunha, A., & Póvoa, A. M. (2021). Infertility management in women with polycystic ovary syndrome: a review. Porto Biomedical Journal, 6(1), e116. https://doi.org/10.1097/J.PBJ.0000000000000116

[9] Dennett, C. C., & Simon, J. (2015). The Role of Polycystic Ovary Syndrome in Reproductive and Metabolic Health: Overview and Approaches for Treatment. Diabetes Spectrum : A

[10] Publication of the American Diabetes Association, 28(2), 116. https://doi.org/10.2337/DIASPECT.28.2.116

[11] Farquhar, C. M., Williamson, K., Gudex, G., & Johnson, N. (2012). A systematic review of laparoscopic ovarian drilling for polycystic ovary syndrome. Human Reproduction Update, 17(5), 467–478.

[12] Gameiro, S., Leone, D., & Mertes, H. (2024). Fertility clinics have a duty of care towards patients who do not have children with treatment. Human Reproduction, 39(8), 1591–1598. https://doi.org/10.1093/HUMREP/DEAE128,

[13] Gao, Y., Jiang, S., Chen, L., Xi, Q., Li, W., Zhang, S., & Kuang, Y. (2022). The pregnancy outcomes of infertile women with polycystic ovary syndrome undergoing intrauterine insemination with different attempts of previous ovulation induction. Frontiers in Endocrinology, 13, 922605. https://doi.org/10.3389/FENDO.2022.922605/BIBTEX

[14] Hajam, Y. A., Rather, H. A., Neelam, Kumar, R., Basheer, M., & Reshi, M. S. (2024). A review on critical appraisal and pathogenesis of polycystic ovarian syndrome. Endocrine and Metabolic Science, 14, 100162. https://doi.org/10.1016/J.ENDMTS.2024.100162

[15] Heijnen, E. M., Eijkemans, M. J., Hughes, E. G., Laven, J. S., & Fauser, B. C. (2006). A meta- analysis of outcomes of conventional IVF in women with polycystic ovary syndrome. Human Reproduction Update, 12(1), 13–21.

[16] Homburg, R. (2022). IUI is a better alternative than IVF as the first-line treatment of unexplained infertility. Reproductive BioMedicine Online, 45(1), 1–3. https://doi.org/10.1016/j.rbmo.2021.12.015

[17] J, B.-S. (2010). Learning how to undertake a systematic review: part 1. Nursing Standard (Royal College of Nursing (Great Britain) : 1987), 24(50), 47–55. https://doi.org/10.7748/NS2010.08.24.50 47.C7939

[18] Jain, M., & Singh, M. (2023). Assisted Reproductive Technology (ART) Techniques. StatPearls, 34. https://www.ncbi.nlm.nih.gov/books/NBK576409/

[19] Karimzadeh, M. A., & Javedani, M. (2010). An assessment of lifestyle modification versus medical treatment with clomiphene citrate, metformin, and clomiphene citrate–metformin in patients with polycystic ovary syndrome. Fertility and Sterility, 94(1), 216–220. https://doi.org/10.1016/J.FERTNSTERT.2009.02.078

[20] Kicińska, A. M., Maksym, R. B., Zabielska-Kaczorowska, M. A., Stachowska, A., & Babińska, A. (2023). Immunological and Metabolic Causes of Infertility in Polycystic Ovary Syndrome. Biomedicines, 11(6), 1567. https://doi.org/10.3390/BIOMEDICINES11061567

[21] Leão, R. de B. F., & Esteves, S. C. (2014). Gonadotropin therapy in assisted reproduction: an evolutionary perspective from biologics to biotech. Clinics, 69(4), 279. https://doi.org/10.6061/CLINICS/2014(04)10

[22] Leathersich, S., Roche, C., & Hart, R. (2025). Minimising OHSS in women with PCOS. Frontiers in Endocrinology, 16, 1507857. https://doi.org/10.3389/FENDO.2025.1507857

[23] Leeflang, M. M. G., Bossuyt, P. M. M., & Irwig, L. (2009). Diagnostic test accuracy may vary with prevalence: implications for evidence-based diagnosis. Journal of Clinical Epidemiology, 62(1), 5–12. https://doi.org/10.1016/J.JCLINEPI.2008.04.007

[24] Legro, R. S. (2017). Evaluation and Treatment of Polycystic Ovary Syndrome. Endotext. https://www.ncbi.nlm.nih.gov/books/NBK278959/

[25] Legro, R. S., Barnhart, H. X., Schlaff, W. D., Carr, B. R., Diamond, M. P., Carson, S. A., & Reindollar, R. H. (2007). Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. New England Journal of Medicine, 356(6), 551–566.

[26] Lim, S. S., Hutchison, S. K., Van Ryswyk, E., Norman, R. J., Teede, H. J., & Moran, L. J. (2019). Lifestyle changes in women with polycystic ovary syndrome. The Cochrane Database of Systematic Reviews, 2019(3), CD007506. https://doi.org/10.1002/14651858.CD007506.PUB4

[27] Lipscomb, M. (n.d.). Exploring evidence-based practice : debates and challenges in nursing. 229. Meng, Y., Zhao, T., Zhang, R., Zhu, X., Ma, C., & Shi, Q. (2025). Global burden of polycystic ovary syndrome among women of childbearing age, 1990–2021: a systematic analysis using the global burden of disease study 2021. Frontiers in Public Health, 13, 1514250. https://doi.org/10.3389/FPUBH.2025.1514250/BIBTEX

[28] Mitwally, M. F., & Casper, R. F. (2001). Use of an aromatase inhibitor for induction of ovulation in patients

with an inadequate response to clomiphene citrate. Fertility and Sterility, 75(2), 305–309.

[29] Nestler, J. E., Jakubowicz, D. J., Evans, W. S., & Pasquali, R. (1998). Effects of metformin on spontaneous and clomiphene-induced ovulation in the polycystic ovary syndrome. New England Journal of Medicine, 338(26), 1876–1880.

[30] Nikbakht, R., Mohammadjafari, R., Rajabalipour, M., & Moghadam, M. T. (2021). Evaluation of oocyte quality in Polycystic ovary syndrome patients undergoing ART cycles. Fertility Research and Practice 2021 7:1, 7(1), 1–6. https://doi.org/10.1186/S40738-020-00094-Z

[31] Ott, J., Kurz, C., Nouri, K., Wirth, S., Vytiska-Binstorfer, E., Huber, J. C., & Mayerhofer, K. (2010). Pregnancy outcome in women with polycystic ovary syndrome comparing the effects of laparoscopic ovarian drilling and clomiphene citrate stimulation in women pre-treated with metformin: A retrospective study. Reproductive Biology and Endocrinology, 8(1), 1–6. https://doi.org/10.1186/1477-7827-8-45/TABLES/3

[32] Oxford centre for triple value healthcare Ltd. (n.d.). Critical Appraisal Skills Programme. Retrieved August 30, 2021, from https://casp-uk.net/wp-content/uploads/2018/01/CASP- Qualitative-Checklist-2018.pdf

[33] P, J., F, H., J, S., C, B., & M, E. (2002). Direction and impact of language bias in meta-analyses of controlled trials: empirical study. International Journal of Epidemiology, 31(1), 115–123. https://doi.org/10.1093/IJE/31.1.115

[34] Palomba, S., Santagni, S., Falbo, A., & La Sala, G. B. (2015). Complications and challenges associated with polycystic ovary syndrome: current perspectives. International Journal of Women's Health, 7, 745. https://doi.org/10.2147/IJWH.S70314

[35] Pati, D., & Lorusso, L. N. (2017). How to Write a Systematic Review of the Literature:

Https://Doi.Org/10.1177/1937586717747384, 11(1), 15–30.

https://doi.org/10.1177/1937586717747384

[36] Pippa Hemingway. (2009). What is systematic review. Evidence Based Medicine, 1–8. https://familymedicine.med.wayne.edu/mph/project/what_is_a_systematic_review.pdf

[37] Rashid, R., Mir, S. A., Kareem, O., Ali, T., Ara, R., Malik, A., Amin, F., & Bader, G. N. (2022). Polycystic ovarian syndrome-current pharmacotherapy and clinical implications. Taiwanese Journal of Obstetrics and Gynecology, 61(1), 40–50. https://doi.org/10.1016/J.TJOG.2021.11.009

[38] Rees, D. A., Jenkins-Jones, S., & Morgan, C. L. (2016). Contemporary reproductive outcomes for patients with polycystic ovary syndrome: A retrospective observational study. Journal of Clinical Endocrinology and Metabolism, 101(4), 1664–1672. https://doi.org/10.1210/JC.2015- 2682,

[39] Rodgers, R. J., Suturina, L., Lizneva, D., Davies, M. J., Hummitzsch, K., Irving-Rodgers, H. F., & Robertson, S. A. (2019). Is polycystic ovary syndrome a 20th Century phenomenon? Medical Hypotheses, 124, 31–34. https://doi.org/10.1016/J.MEHY.2019.01.019

[40] Rosenfield, R. L., & Ehrmann, D. A. (2016). The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocrine Reviews, 37(5), 467. https://doi.org/10.1210/ER.2015-1104

[41] Sawant, S., & Bhide, P. (2019). Fertility Treatment Options for Women With Polycystic Ovary Syndrome. Clinical Medicine Insights. Reproductive Health, 13, 1179558119890867. https://doi.org/10.1177/1179558119890867

[42] Seckin, B., Pekcan, M. K., Bostancı, E. I., Inal, H. A., & Cicek, M. N. (2016). Comparison of pregnancy rates in PCOS patients undergoing clomiphene citrate and IUI treatment with different leading follicular sizes. Archives of Gynecology and Obstetrics, 293(4), 901–906. https://doi.org/10.1007/S00404-015-3953-1,

[43] Shah, A., & Kanaya, A. M. (2014). Diabetes and Associated Complications in the South Asian Population. Current Cardiology Reports, 16(5), 476. https://doi.org/10.1007/S11886-014- 0476-5

[44] Sharma, R., Sharma, N., Jain, R., & Goyal, A. (2015). Comparison of pregnancy rates in PCOS patients undergoing clomiphene citrate and IUI treatment with different leading follicular sizes. International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 4(6), 1932– 1936.

[45] Shukla, A., Rasquin, L. I., & Anastasopoulou, C. (2025). Polycystic Ovarian Syndrome. Encyclopedia of Genetics, Genomics, Proteomics and Informatics, 1528–1528. https://doi.org/10.1007/978-1-4020-6754-9_13178

[46] Singh, S., Pal, N., Shubham, S., Sarma, D. K., Verma, V., Marotta, F., & Kumar, M. (2023). Polycystic Ovary

Syndrome: Etiology, Current Management, and Future Therapeutics. Journal of Clinical Medicine, 12(4), 1454. https://doi.org/10.3390/JCM12041454

[47] Sombra, L. R. S., & Anastasopoulou, C. (2024). Pharmacologic Therapy for Obesity.

[48] StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK562269/

[49] Su, P., Chen, C., & Sun, Y. (2025). Physiopathology of polycystic ovary syndrome in endocrinology, metabolism and inflammation. Journal of Ovarian Research , 18(1), 1–10. https://doi.org/10.1186/S13048-025-01621-6/METRICS

[50] Sydora, B. C., Wilke, M. S., McPherson, M., Chambers, S., Ghosh, M., & Vine, D. F. (2023). Challenges in diagnosis and health care in polycystic ovary syndrome in Canada: a patient view to improve health care. BMC Women's Health, 23(1), 569. https://doi.org/10.1186/S12905- 023-02732-2

[51] Tannus, S., Burke, Y. Z., & Kol, S. (2015). Treatment strategies for the infertile polycystic ovary syndrome patient. Women's Health, 11(6), 901–912. https://doi.org/10.2217/WHE.15.40/ASSET/822105E5-397E-4C96-BE54-0AD79F09069A/ASSETS/IMAGES/LARGE/10.2217_WHE.15.40-FIG1.JPG

[52] Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. (2008). Consensus on infertility treatment related to polycystic ovary syndrome. Fertility and Sterility, 89(3), 505–522.

[53] Torgerson, D. J., & Torgerson, C. J. (2003). Avoiding Bias in Randomised Controlled Trials in Educational Research. British Journal of Educational Studies, 51(1), 36–45. https://doi.org/10.1111/1467-8527.T01-2-00223

[54] Turner, J., & Kelly, B. (2000). Emotional dimensions of chronic disease. Western Journal of Medicine, 172(2), 124. https://doi.org/10.1136/EWJM.172.2.124

[55] Wang, K., Li, Y., & Chen, Y. (2023). Androgen excess: a hallmark of polycystic ovary syndrome. Frontiers in Endocrinology, 14, 1273542. https://doi.org/10.3389/FENDO.2023.1273542

[56] Yang, C., Dong, N., Li, F., Ji, Y., Pan, Y., & She, H. (2022). The cumulative live birth rate of recombinant follicle-stimulating hormone alfa verse urinary human follicle-stimulating hormone for ovarian stimulation in assisted reproductive technology cycles. Journal of Ovarian Research, 15(1). https://doi.org/10.1186/S13048-022-01009-W,

[57] Yasmin, A., Roychoudhury, S., Paul Choudhury, A., Ahmed, A. B. F., Dutta, S., Mottola, F., Verma, V., Kalita, J. C., Kumar, D., Sengupta, P., & Kolesarova, A. (2022). Polycystic Ovary Syndrome: An Updated Overview Foregrounding Impacts of Ethnicities and Geographic Variations. Life, 12(12), 1974. https://doi.org/10.3390/LIFE12121974