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Systematic Review

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Systematic Review on the Various Clinical Features of Polycystic Ovary Syndrome (PCOS) Patients

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ABSTRACT

Background: Oligoanovulation, hyperandrogenism, and polycystic ovaries are signs of Polycystic Ovary Syndrome (PCOS). Genetic and environmental factors cause this diverse illness. Androgen excess disrupts follicular development, causing histopathological abnormalities. Dysregulated luteinizing hormone (LH) secretion causes hyperandrogenism. Oestrogen synthesis is affected by feedback mechanisms, which are worsened by obesity. Lifestyle adjustments, hormonal contraceptives, metformin for glucose intolerance, clomiphene citrate for infertility, and metformin in IVF to reduce risks are used to manage. This systematic review aims to thoroughly examine and summarise the many clinical characteristics of PCOS patients.

Methods: Researchers who studied the physical traits of PCOS patients used a variety of search engines, such as PubMed and Google Scholar, as well as Boolean logic, to find relevant studies. In addition to clinical data, authentic websites included extra information. PRISMA analysis was used to guide the selection of journals, which resulted in eliminating duplicates and identifying ten relevant journals for further examination.

Results: PCOS is characterized by several clinical characteristics, the most prevalent of which are raised levels of androgens, hirsutism, and an elevated ratio of luteinizing hormone to follicle-stimulating hormone (LH/FSH). The menstrual cycle can be restored with metformin medication, which has a noteworthy therapeutic effect. Studies highlight the intricacy of PCOS highlighting the importance of individualized care strategies for its myriad symptoms.

Conclusion: The systematic review highlights the multifaceted clinical features of PCOS and underscores the importance of tailored management strategies for addressing its complexity.

Key-words: Polycystic ovary syndrome (PCOS), Genetic, LH/FSH, Metformin medication, Menstrual cycle

INTRODUCTION

Women are affected mainly by the common endocrine condition known as polycystic ovary syndrome. Stein and Leventhal reported on an anovulation-related symptom complex in 1935. Diagnosing PCOS is based on the presence of oligomenorrhea, obesity, hirsutism, and an enlarged polycystic ovary. This issue is now recognized as stemming from continuous anovulation with various causes and clinical presentations [1]. No universally accepted definition of PCOS exists. The clinical appearance is historically considered a trio of oligomenorrhea, obesity, and hirsutism. It is currently understood as a heterogeneous condition that leads to excessive synthesis of androgens, mainly from the ovaries and is connected to insulin resistance. In 1921, Archard and Thiers first recognized the relationship between glucose intolerance and hyperandrogenism (HA) through their description of a diabetic woman with excessive facial hair [2,3].

PCOS is an endocrine abnormality that might predispose individuals to different illnesses. It remains a prevalent factor in causing infertility in women. The three primary factors linked to PCOS are irregular ovulation, elevated androgen levels, and the presence of cystic ovaries

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despite variations in signs and symptoms. Most women with PCOS experience issues with ovulation and increased androgen levels. Hirsutism, alopecia, and acne are linked to high levels of androgens, and approximately 70% of people with PCOS had polycystic ovaries on pelvic ultrasound [4,5].

PCOS can manifest with the absence of menstruation, symptoms of excessive male hormones (hyperandrogenemia), infertility, and indications of metabolic conditions, including dyslipidemia and insulin resistance. The likely cause is prolonged anovulation. Various endocrine disorders can cause anovulation, resulting in the development of polycystic ovaries. Consequently, PCO might be seen as a functional disorder. PCOS can manifest many dysfunctional states through its clinical presentation and ovarian status [6].

Functional ovarian hyperandrogenism PCOS is characterized by hyperandrogenism, oligo anovulation, as well as polycystic ovarian anatomy. Several hereditary and environmental factors contribute to functional ovarian hyperandrogenism. Excessive androgen levels boost the early selection of primordial follicles for development [7]. It starts early luteinization, which prevents the dominant follicle from being selected simultaneously. This leads to typical histopathological and macroscopic alterations in classical PCOS, forming PCOM: Although increased LH levels do not cause PCOS, they sustain them. Hyperandrogenemia stimulates excess LH production, affecting the theca and luteinized granulosa cells, supporting the menstrual cycle [8].

Ovarian hormonal dysregulation disrupts LH synthesis and may increase secretion in response to the pulsatile secretion of gonadotropin-releasing hormone (GnRH) instead of LH promoting the ovaries' generation of androgens. Nevertheless, the appropriate stimulation of aromatase in granulosa cells is impeded by the reduced amount of FSH, leading to a decrease in the conversion of androgens to potent estrogen estradiol [9].

High levels of androgens in the bloodstream are transformed into estrogens, primarily estrone, in the outer regions of the body. Conversion mainly takes place in the adipose tissue's stromal cells, causing obese PCOS patients to produce more estrogen. This transformation leads to persistent feedback at the pituitary and hypothalamus, as opposed to the typical variations in feedback seen during the development, Showing a follicle with varying amounts of estradiol. Endometrial hyperplasia may arise from the endometrium's unchecked estrogen stimulation [9].

Exercise and calorie-restrictive diets are the primary therapies recommended to help overweight and obese women & adolescents having PCOS lose weight and improve their glucose tolerance. The primary treatment for monthly irregularities, excessive hair growth (hirsutism), and acne is a hormonal contraception, such as a vaginal ring, patch, or oral contraceptive [8]. The Endocrine Society recommends that individuals with polycystic ovarian syndrome who have poor glucose tolerance or type 2 diabetes start using metformin and have not responded to lifestyle changes. The first-line therapy for PCOS-afflicted women who are infertile is clomiphene citrate. Metformin is recommended as a supplementary treatment for infertility to reduce the risk of the condition known as ovarian hyperstimulation syndrome among an IVF patient [9].

MATERIALS AND METHODS

Search strategy- The search technique is one of the critical parts of performing research projects. diverse clinical characteristics of patients with PCOS. Compared to the current study, the search method has been centered on gathering useful information regarding the clinical characteristics of PCOS patients. Authentic websites have been utilised to gather PCOS-related clinical data. PubMed and Google Scholar were utilised to find study-related papers and articles. The Boolean technique has been utilised to search and retrieve documents examining PCOS patients' diverse clinical characteristics.

Furthermore, the search approach has focused on finding articles that emphasise the different clinical characteristics of PCOS patients. Study-relevant journals were chosen using PRISMA analysis. A database search excluded duplicate journals and chose 10 real ones for further examination (Fig. 1).

Inclusion and exclusion criteria

Inclusion

- In order to conduct this research, journals that were published after 2000 and are the latest were selected.
- This study selected those participants who were suffering from PCOS.

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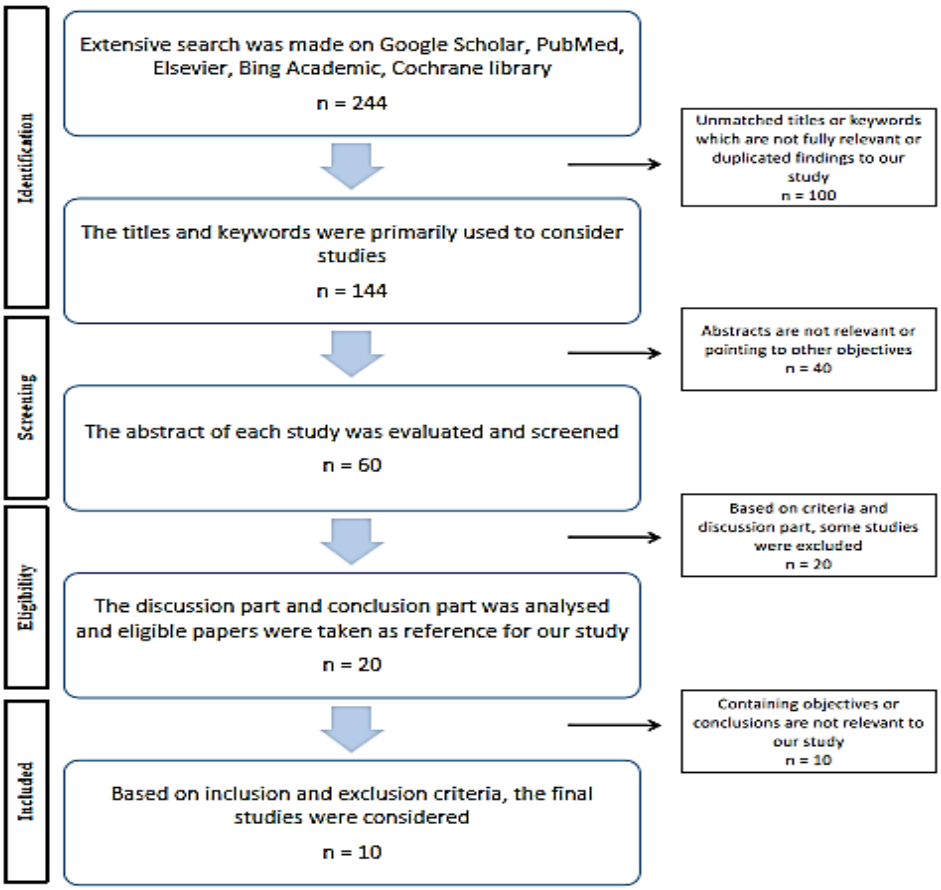

Fig. 1: PRISMA Flowchart

Exclusion

- This study did not include before 2000 journal papers.
- Patients with underlying gynecologic conditions other than PCOS

RESULTS

Fig. 2 shows the analysis of ten studies examining various clinical features associated with PCOS reveals noteworthy findings. Increased androgen levels were the most frequently observed among the investigated features, appearing in 70% of the studies. Hirsutism, a common manifestation of androgen excess, was also prevalent across the studies, being noted in 60% of them. The ratio of LH to FSH, often indicative of hormonal imbalances, was also found to be elevated in 60% of the studies. Other features such as increased waist-to-hip ratio, indicating central obesity, and elevated lipid levels were each reported in 50% of the studies. Serum testosterone levels and acne, though slightly less prevalent, were still notable in 30% of the studies. Restoration of regular menstrual cycles with metformin therapy, a significant therapeutic outcome, was observed in 10% of the studies.

However, certain features such as increased plasma estradiol (E2) levels, alopecia, and male pattern hair loss were comparatively less frequently documented, each appearing in only 20% of the studies. Acanthosis nigricans, a skin condition often associated with insulin resistance, was also reported in 30% of the studies. These findings collectively underscore the multifaceted nature of PCOS and highlight the diverse clinical features that clinicians and researchers must consider in its diagnosis and management.

Table 1 presents a comprehensive overview of clinical features observed in various studies investigating PCOS. Kataoka et al. (2022) conducted a prospective cohort study involving 246 women, revealing that oligo-/amenorrhea was predominant among women with PCOS, with 62 out of 63 individuals exhibiting this condition. Additionally, total testosterone levels correlated positively with anti-Müllerian hormone (AMH) levels, indicative of hormonal imbalance characteristic of PCOS.

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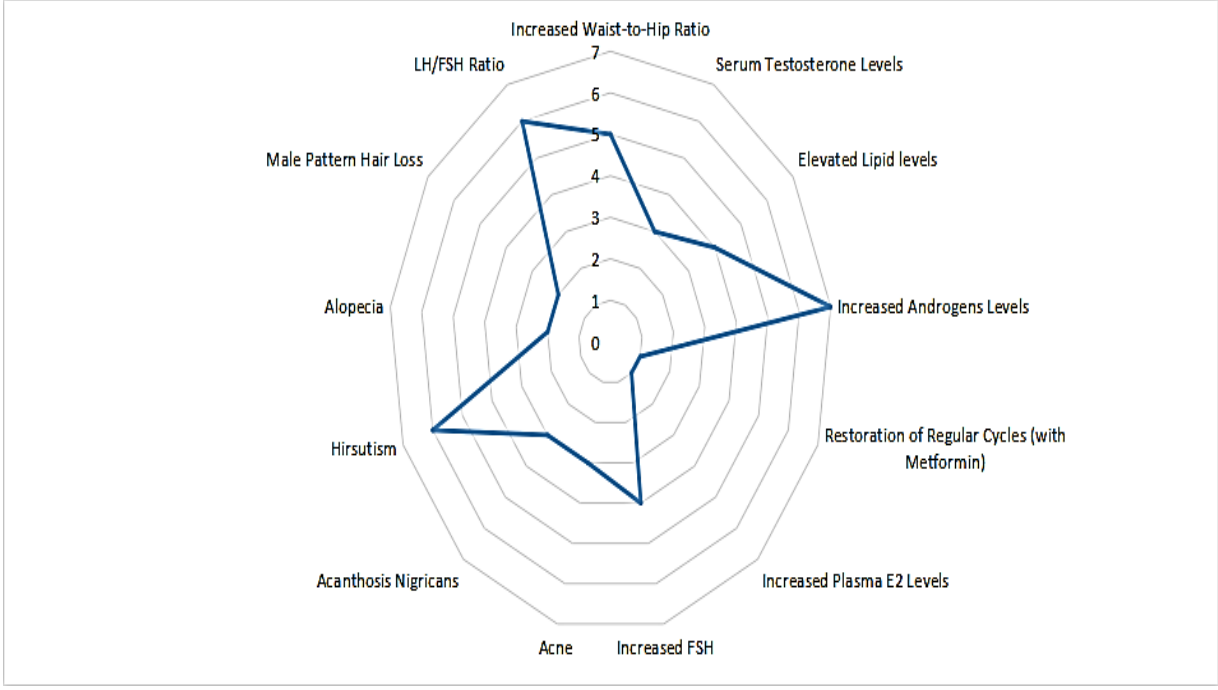

Fig. 2: Clinical features as found in the studies included in this systematic review

Similarly, Trummer et al. (2018) conducted a randomized controlled trial (RCT) with 123 participants, demonstrating a high prevalence of menstrual irregularity, with oligomenorrhea being the most common manifestation. Pereira-Eshraghi et al. (2019), through an RCT involving 50 subjects, found significant associations between PCOS and elevated levels of free testosterone, total testosterone, obesity, and insulin resistance.

Furthermore, Jungari et al. (2023), in a retrospective cohort study of 130 women, observed a notable restoration of regular menstrual cycles in 91% of participants, alongside a decrease in the volume and appearance of polycystic ovaries on ultrasound in 86% of cases. Li et al. (2019) conducted a prospective randomized controlled trial with 185 individuals, reporting significant improvements across various parameters including menstrual cycle duration, hirsutism score, acne severity, body weight, and lipid profiles following treatment. Romualdi et al. (2009) found a decrease in testosterone levels and restoration of regular cycles in about 70% of patients after metformin treatment, based on a randomized double-blind study involving 28 participants.

Furthermore, Fruzzetti et al. (2002) observed increased plasma estradiol levels and significantly higher levels of free testosterone, androstenedione, dehydro-epiandrosterone sulfate, and follicle-stimulating hormone in an open, controlled clinical study with 10 subjects. Romero-Ruiz et al. (2019) noted a decrease in basal follicle-stimulating hormone levels in a clinical study with 60 participants. Thathapudi et al. (2014) conducted a prospective case-control study involving 204 individuals, reporting high percentages of hirsutism, acne, alopecia, male pattern hair loss, and acanthosis nigricans. Lastly, Dravecká et al. (2016), in an RCT with 39 participants, observed a decrease in the LH/FSH ratio and serum testosterone levels. Overall, these studies collectively highlight the diverse range of clinical features associated with PCOS, including menstrual irregularities, hormonal imbalances, metabolic disturbances, and dermatological manifestations. The findings underscore the complexity of PCOS and emphasize the importance of tailored management approaches to address its multifaceted nature.

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Table 1: Findings of the included studies in this review

Study	Type of study	Study Population	Findings of Clinical Features
Kataoka *et al.* [1]	Prospective cohort-study	246	Oligo-/amenorrhea was observed in the majority of women with PCOS (62 out of 63). Total testosterone levels were positively correlated with AMH levels in women with PCOS, indicating a hormonal imbalance characteristic of PCOS. AMH was higher in women with PCOS (5.47 ± 4.89 µg/L) compared with non-PCOS (2.66 ± 3.71 µg/L).
Trummer *et al.* [2]	RCT	123	89.4% of patients had menstrual irregularity, with 71.7% experiencing oligomenorrhea, 2.2% hypermenorrhea, and 15.6% amenorrhea.
Pereira-Eshraghi *et al.* [3]	RCT	50	This study found the nature of PCOS which had Free testosterone (pg/mL), mean (SD) 8.26 (4.6) and Testosterone (ng/dL), mean (SD) 45.4 (19.5), Obesity (p = 0.03) and HOMA-IR (p = 0.02).
Jungari *et al.* [4]	Retrospective cohort study	130	The menstruation cycle became regular in 91% of the women while volume, theca, and appearance of polycystic ovaries on ultrasound decreased in 86%.
Li *et al.* [5]	Prospective randomized controlled trail	185	The menstrual cycle duration decreased significantly, Ferriman–Gallwey (mF-G) score, which assesses hirsutism, decreased in all groups after treatment, Global Acne Grading System (GAGS) scores decreased, Body weight, BMI, waist circumference, and waist-to-hip ratio (WHR) all decreased, Serum testosterone levels decreased, Total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and TC/HDL and LDL/HDL ratios also decreased.
Romualdi *et al.* [6]	Randomized double-blind study	28	Decrease in testosterone (T) levels with metformin. Ovarian and adrenal androgens levels were at the upper limit of or above the normal range. menstrual abnormalities, with a restoration of regular cycles in about 70% of patients after 6 months of metformin treatment.
Fruzzetti *et al.* [7]	Open, controlled, clinical study	10	Plasma E2 levels increased, free testosterone, androstenedione (A), dehydroepiandrosterone sulfate (DHEAS), and follicle-stimulating hormone (FSH) were significantly higher
Romero-Ruiz *et al.* [8]	Clinical studies	60	Decrease in basal FSH level.
Thathapudi *et al.* [9]	Prospective case-control study	204	95%; hirsutism, 92%; acne, 88%; alopecia, 65%; male pattern of hair loss, 18%; and acanthosis nigricans, 7% were noted.
Dravecká *et al.* [10]	RCT	39	Decreased LH/FSH ratio, decreased serum fTST, and significantly decreased serum TST levels.

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DISCUSSION

A study was done to assess the clinical result after a 2-year hiatus in teenage females with established irregular menstruation, whether or not polycystic ovaries were identified by ultrasonography. The study's findings endorse obesity, the screening of irregular menses, and symptoms of clinical hyperandrogenism to facilitate early identification of PCOS and enhance the reproductive wellness of adolescent girls [8-10].

Hyperandrogenemia is linked to irregular menstrual cycles, excessive hair growth, acne, and a possible increased susceptibility to PCOS. The results validate that monthly irregularity and/or increased androgen levels are evident throughout adolescence in females with PCOS and infertility in the future, emphasizing the significance of early detection of irregular menstruation [11-13].

PCOS, or polycystic ovarian syndrome, is a multifaceted illness characterized by irregular menstrual cycles, persistent lack of ovulation, excessive hair growth, male-pattern baldness, and acne [11]. Patients can present with various presentations at diagnosis, depending on the patient's age, disease phenotype, and lifestyle. Most individuals seek medical care due to the symptoms of PCOS, such as irregular menstruation, hyperandrogenism, and infertility. The review aimed to examine infertility caused by PCOS and the treatment options available, along with how COVID-19 infection affects the outcome of fertility treatments. Ultimately, employing particular therapeutic medications and patients' commitment to lifestyle adjustments can aid in the restoration of individuals' metabolic and reproductive well-being [12-14].

The cause of this syndrome is primarily unknown. However, increasing evidence indicates that PCOS may be a complex illness influenced by multiple genes, as well as influential epigenetic and environmental variables such as nutrition and lifestyle [15-17]. PCOS is commonly linked with insulin resistance, metabolic issues, abdominal fat accumulation, obesity, and cardiovascular risk factors. Diagnosing and treating PCOS involves using standardized diagnostic tools and appropriate therapy approaches to address ovarian dysfunction outcomes, hyperandrogenism, and associated metabolic diseases [13].

Women diagnosed individuals with PCOS are considerably more vulnerable to metabolic abnormalities [18-20]. The goal was to provide up-to-date information on PCOS, obesity, and insulin resistance, concentrating on the difficulties faced in diagnosis and methodology in research and clinical settings. Insulin resistance is typical among PCOS-afflicted individuals, yet there significant heterogeneity in reported cases due to not differentiating subgroups that affect insulin resistance and limited methods to assess it. There is a favorable correlation between inflammatory indicators and testosterone levels, although specific interactions require further investigation [21-24]. The main treatment is weight management. Providing special guidance to decrease the glycaemic load of the diet and reduce the intake of advanced glycation and pro-inflammatory saturated fatty acids (SFA) end products has shown encouraging outcomes. Women with PCOS should be informed about their heightened susceptibility to metabolic problems to facilitate prompt and suitable lifestyle adjustments [14].

Hyperandrogenism is the main indication of PCOS in clinical terms. Excess androgen has a major effect on granulosa cell function and the development of follicles through intricate pathways that result in obesity and resistance to insulin. Many individuals with PCOS who experience excessive levels of male hormones have issues with the production of steroids, leading to irregular development of ovarian follicles and the failure to choose a dominant follicle. Hyperandrogenism causes obesity, excessive hair growth, acne, and male-pattern baldness [24]. These symptoms can cause significant psychological distress for women. Medications including combination oral contraceptive pills, low-dose spironolactone, pioglitazone, and metformin enhance pregnancy rates by reducing testosterone levels in the body. PCOS is diverse, and hyperandrogenism is not the sole causative factor. Obesity and resistance to insulin worsen the symptoms of hyperandrogenism, creating a harmful cycle that contributes to the formation of PCOS [25].

CONCLUSIONS

The systematic review of ten studies exploring clinical features associated with PCOS presents a comprehensive understanding of the multifaceted nature of this condition. Analysis revealed that increased androgen levels were the most frequently observed feature in 70% of the studies. Hirsutism, often indicative of androgen

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excess, was prevalent in 60% of the studies, along with an elevated LH/FSH ratio, suggesting hormonal imbalances. Notably, features such as increased waist-to-hip ratio and elevated lipid levels were each reported in 50% of the studies, indicating the metabolic implications of PCOS. Serum testosterone levels and acne, though slightly less prevalent, were still significant in 30% of the studies.

Additionally, the therapeutic outcome of restoring regular menstrual cycles with metformin was observed in 10% of the studies, highlighting its clinical relevance. Conversely, features like increased plasma estradiol levels, alopecia, and male pattern hair loss were less frequently documented, appearing in only 20% of the studies. Acanthosis nigricans, a marker of insulin resistance, was reported in 30% of the studies. Overall, these findings underscore the diverse clinical manifestations associated with PCOS and emphasize the importance of tailored management approaches to address its complex nature effectively.

CONTRIBUTION OF AUTHORS

Research concept- Jifang Shi
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Supervision- Jifang Shi
Materials- Ayesha Akter Farhana
Data collection- Jifang Shi
Data analysis and Interpretation- Ayesha Akter Farhana
Literature search- Ayesha Akter Farhana
Writing article- Ayesha Akter Farhana
Critical review- Jifang Shi
Article editing- Ayesha Akter Farhana
Final approval- Jifang Shi

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