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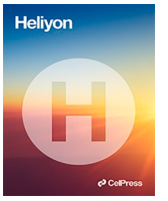

Research article

Prevalence of polycystic ovary syndrome among infertile women in the Gulf Cooperation Council (GCC) countries: A systematic review and meta-analysis

Zufishan Alam [a], Saleh Alseari [b], Mahra Alameemi [b], Mayytha Alzaabi [b], Reem Alkhoori [b], Linda Östlundh [c], Omar Melhem [d], Mohammed Altigani Abdalla [e], Rami H. Al-Rifai [a,1,*]

[a] Institute of Public Health, College of Medicine and Health Sciences, United Arab Emirates University, Abu Dhabi, United Arab Emirates
[b] College of Medicine and Health Sciences, United Arab Emirates University, Abu Dhabi, United Arab Emirates
[c] Örebro University, Örebro, Sweden
[d] Department of Nursing, Fatima College of Health Sciences, Abu Dhabi, United Arab Emirates
[e] Hull York Medical School, University of Hull, Hull, United Kingdom

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a significant contributor to female infertility and other various metabolic disorders. This systematic review estimates the prevalence of PCOS among infertile women in the Gulf Cooperation Council (GCC) countries.

Methods: The study searched five databases (PubMed, Embase, CINAHL, Web of Science, and SCOPUS), from their inception to 2022 for observational studies conducted in GCC countries. Eligible studies included data on PCOS prevalence among infertile women. A random-effects model assessed the pooled prevalence, stratified by age, BMI, and infertility type.

Results: Out of 855 records screened, seven studies were deemed eligible. Four (57.1 %) studies were conducted in Saudi Arabia, while the remaining three studies were carried out in Qatar, Kuwait, and Oman, respectively. The pooled prevalence of PCOS was 30.0 % (95 % CI: 29.0–38.0 %, I-squared: 91.98 %). PCOS prevalence was higher in obese (BMI: $\geq$30 kg/m^2) women (27.0 %, 95 % CI: 22.0–32.0 %) than those with normal (18.5–24.9 kg/m^2) BMI (18.0 %, 95 % CI: 11.0–26.0 %). Women aged 35 or older had a PCOS prevalence of 59.0 % (95 % CI: 45.0–72.0 %), compared to 30.0 % (95 % CI: 29.0–36.0 %) in age group 15–24 years old. Primary infertility was associated with higher PCOS prevalence (37.0 %, 95 % CI: 29.5–46.0 %) than secondary infertility (17.0 %, 95 % CI: 13.0–21.0 %).

Conclusion: In four out of six GCC countries, PCOS was diagnosed in three out of every ten infertile women. Older age, obesity, and primary infertility were linked to higher PCOS prevalence. Screening for PCOS in these high-risk groups could improve fertility outcomes.

* Corresponding author. Institute of Public Health, College of Medicine and Health Sciences, United Arab Emirates University, P.O. Box 15551, Al Ain, United Arab Emirates.
E-mail address: rrifai@uaeu.ac.ae (R.H. Al-Rifai).

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1. Introduction

Polycystic ovary syndrome (PCOS), alternatively known as Stein-Leventhal syndrome, is a complex hormonal disorder in women resulting in elevated levels of male sex hormones, morphological changes resulting in large cystic ovaries and/or ovulation disruption [1]. PCOS affects approximately one-quarter of women worldwide during their reproductive years. A recent study has estimated the pooled prevalence of PCOS on a global scale to be 21.3 % [2]. The exact root cause of PCOS remains unclear; however, it is suggested that a combination of genetic and environmental factors may lead to the dysregulation of sex hormones and elevated insulin levels, potentially contributing to the condition [3]. Common signs and symptoms of the condition encompass menstrual irregularities such as absence, prolonged, or heavy periods, as well as infertility, facial hair growth, acne, and thinning of scalp hair [1]. PCOS is a well-established risk factor for metabolic disorders, including type 2 diabetes mellitus, as well as cardiovascular diseases such as hypertension, dyslipidaemia, and atherosclerosis [4]. Furthermore, women affected by PCOS have shown a higher susceptibility to adverse mental health conditions, including depression, anxiety, bulimia nervosa, and a diminished health-related quality of life [5].

The diagnosis of PCOS relies on a comprehensive evaluation involving clinical, biochemical, and radiological assessments of its three primary characteristics: hyperandrogenism, anovulation, and ovary cysts. It is crucial to conduct a thorough history-taking and physical examination to assess irregular menstrual cycles, hirsutism, acne, and alopecia as essential components in PCOS diagnosis. Laboratory tests employed in the diagnostic process include estimation of blood testosterone levels and the calculation of the Luteinizing hormone/Follicle-stimulating hormone ratio. Additionally, pelvic ultrasonography is conducted to assess ovarian morphology. It is important to exclude other androgen-related disorders, such as thyroid disease, Cushing syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors as part of the diagnostic evaluation [6].

PCOS can be diagnosed using three widely recognized criteria, which include: [1] the Rotterdam criteria, which confirm PCOS if at least two out of the three following features (hyperandrogenism, cystic ovaries, and anovulation) are present [2], the National Institute of Health criteria, which confirm PCOS based on the presence of hyperandrogenism and anovulation, and [3] the Androgen Excess Society criteria, which confirm PCOS through the presence of hyperandrogenism, ovarian dysfunction, and the exclusion of disorders related to androgen excess [7,8]. Distinct phenotypes of PCOS have been identified, and these may exhibit variations based on the presence of diagnostic features, which can differ among individuals of different races and ethnicities [9]. The management of PCOS is customized based on the specific clinical goals required. For obesity management, lifestyle modifications are recommended. When addressing infertility, approaches such as ovulation induction or assisted conception may be pursued. Menstrual irregularities are typically addressed with oral contraceptives. In cases of hyperandrogenism symptoms like hirsutism, anti-androgen drugs are prescribed [6,10,11].

The adverse influence of PCOS on infertility has been well-documented in the existing literature. This impact is attributed to hormonal imbalances that disrupt the normal ovulatory pattern, hinder ovarian follicular maturation, and impede the release of eggs, ultimately resulting in anovulation [12]. PCOS has also been linked to poor pregnancy outcomes such as miscarriages [13]. Therefore, assessing the prevalence of PCOS among women experiencing infertility can be invaluable in comprehending its potential role in specific populations.

Global PCOS prevalence varies significantly. A recent meta-analysis examining PCOS prevalence in reproductive-aged women across different ethnic groups worldwide indicated that Middle Eastern women have one of the highest prevalence rates, standing at 16.0 % (95 % confidence interval: 13.8–18.6 %) [14]. Evidence suggests that overweight and obesity plays an important role in aggravating the signs and symptoms of PCOS [15]. Recent studies have documented the rising prevalence of obesity in the women in the GCC region particularly due to the influence of factors such as change in dietary patterns, lack of physical activity and urbanisation [16]. Thus, women in the GCC countries are likely to be at an increased risk of developing PCOS, as apparent from the study on burden of PCOS in the MENA region from 1990 to 2019 [17]. While there is no specific review summarizing infertility rates in the Gulf Cooperation Council (GCC) region, an analysis covering the broader Middle East and North African (MENA) region revealed a total clinical infertility prevalence of 7.2 % (95 % CI: 10.6–26.7 %) [18]. Studies have indeed been carried out to estimate the prevalence of PCOS in the general population of countries within the GCC region. However, there is currently no review that has comprehensively summarized the literature to shed a light on the prevalence of PCOS specifically among infertile women residing in the GCC countries. Consequently, the objective of this systematic review and meta-analysis is to consolidate the findings from studies conducted on the prevalence of PCOS within the infertile female population of the GCC countries.

2. Materials and methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines [19]. (See Supplementary File 1). Furthermore, the protocol for this systematic review was registered with International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42022355087) and subsequently peer-reviewed and published [20].

2.1. Study eligibility, source selection and search approach

To identify studies reporting on PCOS among infertile female populations in the GCC countries, we conducted a comprehensive search across five major databases: PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, and SCOPUS. This search encompassed articles published from the inception of the databases up to September 2022.

We included peer-reviewed observational epidemiological studies published in English and conducted within the six GCC countries

(Saudi Arabia, United Arab Emirates, Oman, Bahrain, Qatar, and Kuwait). Specifically, we focused on studies that examined infertile women, either diagnosed with PCOS or seeking infertility treatment. Studies reporting PCOS within non-infertile populations and those exploring infertility among individuals with PCOS were excluded. We considered studies for inclusion if they reported PCOS prevalence or if it could be calculated. Given the limited research available on this topic within the region, we included studies regardless of the setting or the specific diagnostic criteria used for PCOS.

We implemented a meticulous search strategy and in collaboration with an expert librarian (LÖ), which incorporated a pertinent combination of search terms and the Medical Subject Headings (MeSH). The comprehensive search strategy including search terms and MeSH used to search in all databases are provided in the Supplementary File 2.

In addition to articles, we also considered conference proceedings that provided complete data on outcome measures. Furthermore, we conducted a thorough examination of the reference lists in all included articles and performed citation tracking to ensure the inclusion of any pertinent studies that may have been overlooked.

To include potentially recently published studies, we updated our search just before manuscript submission to incorporate the most recent evidence. The resulting references were then imported into COVIDENCE, a software tool designed for record management and screening [21].

2.2. Study selection

Following the automated removal of duplicate records in COVIDENCE, a manual examination was conducted to eliminate any articles that duplicated results from a single study. The initial screening phase involved a review of the titles and abstracts of the included records against the eligibility criteria. This screening process was carried out independently by three reviewers (SA, MA, ZA).

Subsequently, the remaining records were assessed for full-text inclusion. In cases where disagreements arose, they were resolved through mutual discussion or, when necessary, the senior reviewer (RA) was consulted for resolution.

2.3. Data extraction and assessment of study quality

Data extraction from the retrieved full-text records was carried out independently by three reviewers (SA, MA, ZA) using a pre-designed and standardized data collection template, as detailed in the protocol [20]. This template encompassed various fields, including publication date and authorship, study duration, location, and setting, sample size, recruitment method, participant characteristics, and data collection methods. It also included information on how infertility and PCOS diagnoses were ascertained and the outcome measures. The primary outcome measure extracted was the overall PCOS prevalence reported in the respective study. Additionally, when available in the records, data on PCOS prevalence stratified by factors such as age, BMI, and infertility type among the participants was also extracted. In cases where complete data was lacking, authors were contacted for clarification.

To assess the quality and risk of bias (RoB) of the included studies, the National Institute of Health (NIH) quality assessment checklist for observational cohort and cross-sectional studies was utilized [22]. Five criteria within the checklist that were pertinent to our review were applied, including the clarity of the research question, specification of the study population, participation rate of recruited individuals, consistent application of eligibility criteria, provision of sample size justification, measurement of exposure and outcome with appropriate time frames, valid and reliable measurement of exposure (infertility) and its categories, valid measurement of outcome (PCOS), and blinding of outcome assessors.

Furthermore, to gauge the robustness of evidence from the included studies, we employed additional RoB assessment items. These items were based on criteria such as reliable ascertainment of PCOS (self-reported or clinical), sampling methodology (probability or non-probability based), response rate among the eligible infertile population (80 % or less), sample size of the study (100 individuals or less), and the appropriateness of the statistical analysis used.

2.4. Data synthesis and statistical analysis

We presented the characteristics of the included studies in a narrative format, summarizing estimate ranges for overall PCOS prevalence and categorizing them by geographical location, publication date, participants' age, Body Mass Index (BMI), and infertility type.

Subsequently, we conducted a random-effects meta-analysis to calculate the pooled prevalence of PCOS among infertile women. We employed the Inverse Variance method using the Metaprop command in STATA [23], which allowed us to determine the pooled prevalence along with its corresponding 95 % confidence interval (CI). Visual assessment of the pooled estimates was performed using forest plots, and we assessed heterogeneity by calculating Cochrane's Q statistic and tau-squared values. Additionally, we reported the predictive interval to provide a 95 % interval within which the true PCOS prevalence would fall in a new study [24]. A significance level of 0.1 was considered statistically significant for result interpretation.

We calculated the overall pooled prevalence as well as prevalence based on age categories (15–24 years, 25–34 years, 35–44 years, and 45 years and above), BMI classifications (normal, obese, and overweight), and infertility types (primary and secondary).

To detect any potential publication bias or small study effects, we visually inspected funnel plots where a study's effect size was plotted against its standard error. Furthermore, we confirmed this by conducting the Egger's test.

3. Results

3.1. Scope of the review

A total of 855 records were initially identified through the database search. Following the removal of duplicates (418 records), the titles and abstracts of the remaining 437 records were evaluated for eligibility. This assessment led to the identification of 33 articles that were subjected to further evaluation for full-text inclusion. Ultimately, seven articles met the eligibility criteria and were included in the review. One of these studies was obtained from the references cited within the included studies (Fig. 1).

The remaining 26 records were excluded for various reasons. These included studies that focused on the wrong population, specifically non-infertile women seeking healthcare (eight records), or addressed PCOS in the general population (five records). Additionally, studies involving women who had already been diagnosed with PCOS were excluded (3 records). We also excluded records related to non-GCC countries (four records) and those with incomplete data that prevented the calculation of PCOS prevalence (three records). Furthermore, records that merged outcome data with other health conditions, leading to ambiguity (two records), and records with unavailable full-text content (one record) were also excluded (Fig. 1).

3.2. Study characteristics

The seven studies that met the eligibility criteria and were reviewed, encompassed research conducted in four out of the six GCC countries. Among these studies, four (57.1 %) were conducted in Saudi Arabia [25–28] while the remaining three studies were each carried out in Qatar [29], Kuwait [30] and Oman [31] respectively. These seven studies included 2,033 infertile women and contributed a total of 25 overall and stratified (by age, BMI, and infertility type) prevalence estimates, all of which were extracted and included in the review (Table 1).

The seven studies in this review were conducted over a span of years, ranging from 2000 to 2022. Specifically, one study took place in 2000 [30] three were conducted between 2010 and 2019 [25,26,31], and three were carried out in the period from 2020 to 2022

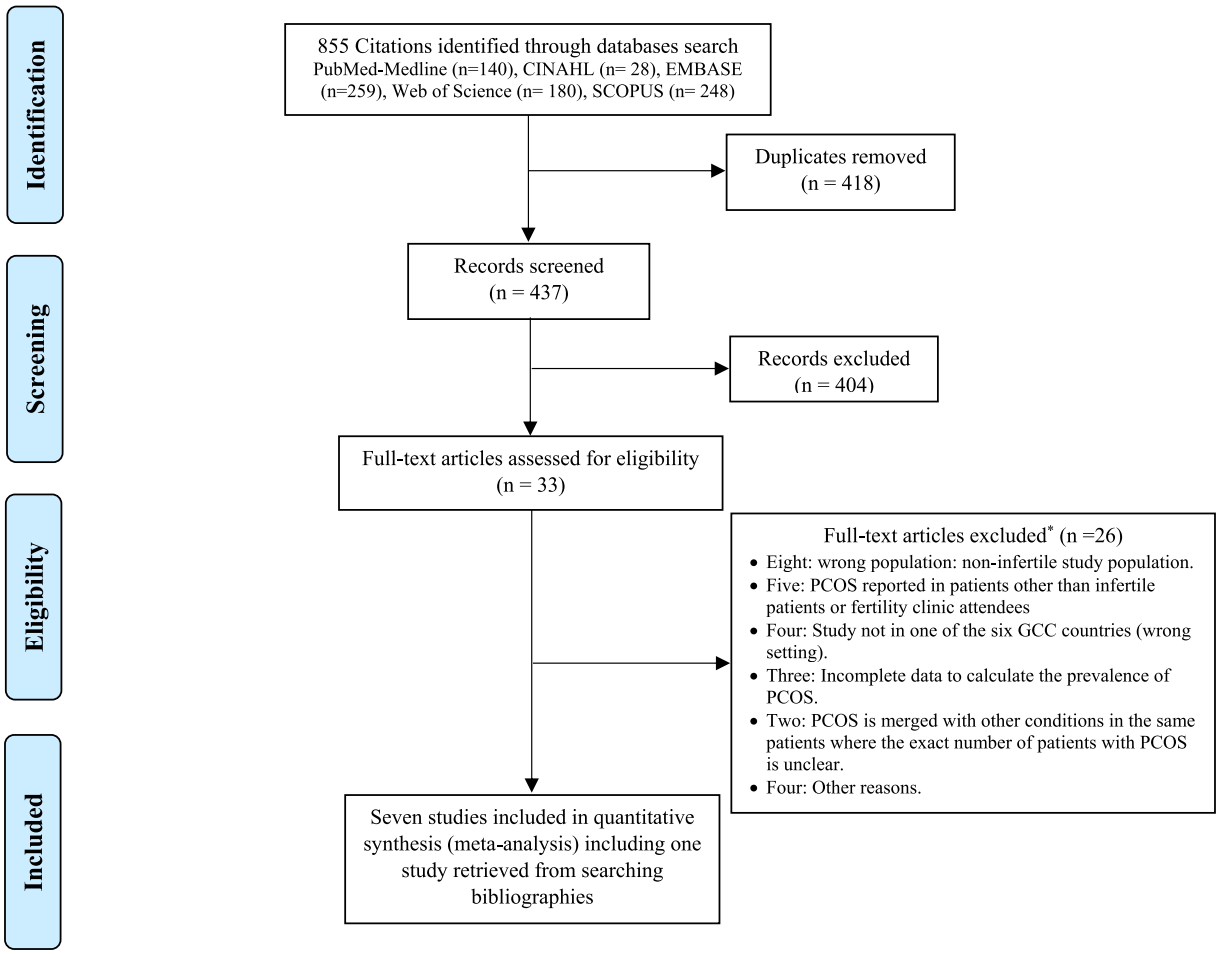

Fig. 1. Flow chart of databases search and eligible studies identification. Databases search date: 28.06.2022.

Table 1
Summary of studies reporting prevalence of PCOS in infertile patients in GCC countries.

Author, publication year [Ref]	Study design	Country, city	Study setting	Data collection duration	Sampling method	Studied population	PCOS diagnostic criteria	Basis of PCOS diagnosis	Strata	Sample size	PCOS positive	Prevalence (%)
Alexander EO. et al., 2000 [27]	Not specified	Kuwait	Infertility clinic, Kuwait University and Maternity Hospital	01-08-1994 to 01-07-1998	Consecutive	Couples unable to achieve conception for at least 12 months duration	Not specified	Menstrual history, hormone profile	All	600	129	21.5
Ahmed MI. et al., 2014 [22]	Prospective cohort	Saudi Arabia, Riyadh	Assisted conception unit, King Khalid hospital	01-01-2010 to 01-08-2011	Random	Infertile couples	Not specified	Menstrual history, hormone profile	All	303	70	23.10
Vaidyanathan G. et al., 2015 [28]	Cross-sectional	Oman, Muscat	Infertility clinic, Sultan Qaboos University Hospital	01-01-2006 to 01-01-2013	Random	Couples attending infertility clinic	Not specified	Hormonal profile	All	122	43	35.5
Amani AS. et al., 2017 [23]	Cross-sectional	Saudi Arabia, Tabuk	Infertility clinic, King Khalid hospital	01-02-2014 to 12-01-2014	Random	Infertile women with aged 15–45 years excluding women who were previously diagnosed with hypertension, diabetes mellitis, women under treatment with metformin or under any hormonal treatment	Rotterdam consensus	Menstrual history, clinical examination, transvaginal ultrasound examination, biochemical blood analysis	All	404	76	18.81
									15–24 years	68	20	29.41
									25–34 years	220	36	16.36
									35–45 years	116	20	17.24
									<18.5 kg/m^2	8	0	0.00
									18.5–24.9 kg/m^2	72	20	27.78
									25–29.9 kg/m^2	76	4	5.26
									≥30 kg/m^2	248	52	20.97
Aladin AA. et al., 2020 [25].	Cross-sectional	Saudi Arabia, Arar	Maternity and Children Hospital	01-12-2018 to 31-03-2019	Random	All women attending in and out patient department except those with chronic diseases affecting infertility.	Not specified	Menstrual history Health records for diagnosis	All	369	123	33.30
									Primary infertility	71	28	39.40
									Secondary Infertility	298	51	17.10
Nagla HK. et al., 2022 [24]	Cross-sectional	Saudi Arabia, Najran	Maternal and Childbirth Hospital	05-01-2020 to 05-01-2021	Random	Infertile women presenting with primary or secondary infertility aged 15–45 years	Not specified	Menstrual history, ultrasound examination	All	100	56	56.00
									Primary infertility	65	23	35.00

(*continued on next page*)

Table 1 (*continued*)

Author, publication year [Ref]	Study design	Country, city	Study setting	Data collection duration	Sampling method	Studied population	PCOS diagnostic criteria	Basis of PCOS diagnosis	Strata	Sample size	PCOS positive	Prevalence (%)
									Secondary infertility	35	7	21.00
									15–24 years	11	4	36.34
									25–34 years	31	18	58.10
									35–44 years	49	28	57.14
									≥45 years	9	6	66.67
Sufia A, 2022 [26]	Retrospective chart review/ Cross-sectional	Qatar, Al Wakra	Secondary Hospital	Not specified	Not specified	Infertile women receiving IVF/ICSI	Not specified	Not specified	All	135	42	31.10
									18.5–24.9 kg/m^2	40	2	4.76
									25–29.9 kg/m^2	25	5	20.00
									≥30 kg/m^2	70	35	50.00

[27–29]. In terms of study design, five of the studies (71.4 %) adopted a cross-sectional approach, one followed a prospective cohort design [22] while the design for one study was not explicitly specified [30] (Table 1).

Almost all of the studies employed random sampling methods, with one utilizing consecutive sampling [30] and the sampling method remaining unclear in another study [26]. Among the seven studies, four focused solely on females as the intended population [23–26], while three included both males and females, specifically couples [25,30,31] (Table 1). Infertility and PCOS diagnoses were confirmed through clinical, biochemical, and/or sonographic tests in six of the included records, while one study left the confirmation method unclear [29].

Regarding the settings for patient sampling, three major types were employed in the included records, which included infertility clinics or assisted conception units at hospitals or maternal and child hospitals. Out of the seven studies, three provided prevalence estimates based on the overall sample only [22,27,28], while the remaining four studies reported stratified prevalence, with two stratifying by age [23,24] two by BMI [23,26] and two by infertility type [24,25]. It's worth noting that only one study used the Rotterdam criteria as specific criteria for PCOS diagnosis [22]. Most of the studies (n = 6) except one [26] used menstrual history as a means for diagnosis of PCOS, whereas four used hormonal profile [22,23,27,28], and another two ultrasonography [23,24] in addition the history (Table 1).

3.3. PCOS prevalence

The prevalence of PCOS among infertile women varied across studies and countries. In Saudi Arabia, prevalence ranged from 18.0 % to 56.0 % in studies conducted between 2014 and 2022 [25–28]. Other countries in the GCC region reported PCOS prevalence as follows: 21.5 % in Kuwait (in 2000) [30], 31.1 % in Qatar (in 2022) [29] and 35.5 % in Oman (in 2015) [31].

The crude overall PCOS prevalence, calculated as an average, was estimated at 26.5 % based on data from a total of 2,033 infertile women of whom 539 were diagnosed with PCOS. Upon conducting a meta-analysis, the pooled prevalence of PCOS among 2,033 infertile women in the GCC countries was estimated to be 30.0 % (95 % CI: 29.0–38.0 %, I-squared: 91.98 %) (Fig. 2). It's noteworthy that the lowest (19.0 %) and highest (56.0 %) pooled prevalence rates were reported in studies conducted in Saudi Arabia [26,27]. In the other three countries, the pooled prevalence was as follows: 22.0 % (95 % CI: 18.0–25.0 %) in Kuwait [30], 31.0 % (95 % CI: 24.0–39.0 %) in Qatar [29]' and 35.0 % (95 % CI: 27.0–44.0 %) in Oman [31]. The predictive interval for the overall prevalence was reported to be in the range of 9.0 %–58.0 % (Fig. 2). The heterogeneity illustrated via *I*-squared (91.98 %) was high and the potential reasons could be difference in study designs and sampling methods as well as in PCOS diagnostic methods used.

In the subgroup analysis, the pooled prevalence of PCOS exhibited significant variations. Specifically, it was notably higher among

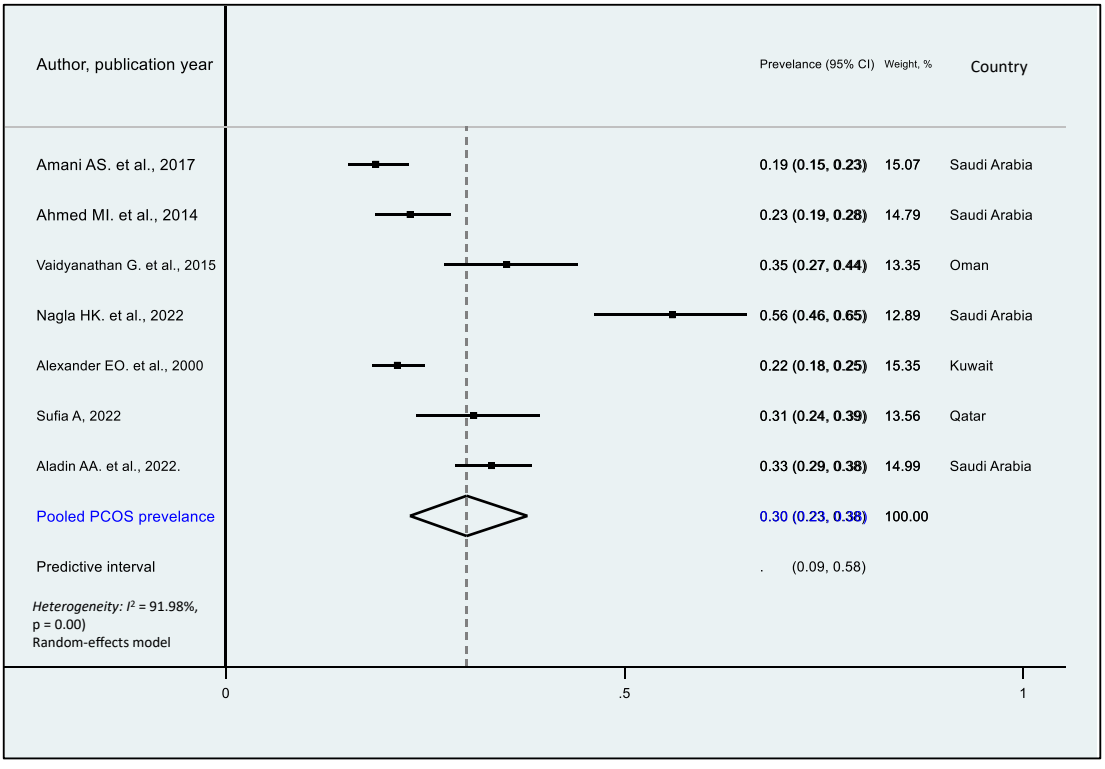

Fig. 2. Forest plot for the weighted pooled prevalence of PCOS among infertile women in four out of the six GCC countries. Heterogeneity I^2 = 91.98 %, p = 0.00). Heterogeneity between groups: p = 0.000.

women with an obese BMI (≥30 kg/m^2), estimated at 27.0 % (95 % CI: 22.0–32.0 %), compared to those with a normal BMI (18.5–24.9 kg/m^2), which was 18.0 % (95 % CI: 11.0–26.0 %), or an overweight BMI (25–29.9 kg/m^2), where it stood at 8.0 % (95 % CI: 3.0–14.0 %) (Fig. 3).

When considering age as a factor, PCOS prevalence was significantly higher among women aged 35 years or more, reaching 59.0 % (95 % CI: 45.0–72.0 %), in contrast to those aged 15–24 years (30.0 %, 95 % CI: 29.0–36.0 %) or 25–34 years (27.0 %, 95 % CI: 12.0–46.0 %) (Fig. 4).

Furthermore, women diagnosed with primary infertility exhibited a higher PCOS prevalence of 37.0 % (95 % CI: 29.5–46.0 %) compared to those with secondary infertility, where the prevalence was 17.0 % (95 % CI: 13.0–21.0 %) (Fig. 5). These pooled estimates were derived from only two studies for each subgroup.

3.4. Risk of bias

The results of the RoB assessment are depicted in Fig. 2. Overall, the RoB and quality of evidence indicated a significant low RoB, with domains such as the study population, research question, and PCOS ascertainment methodology achieving high-quality evidence scores of 100 %, 71.4 %, and 85.7 %, respectively. For only one study the ascertainment of PCOS was based on Rotterdam consensus criteria while in the other studies the exact criteria used to diagnose PCOS was not reported. Also, only two out of the seven studies provided a clear justification for the screened sample size (see Supplementary Fig. 1).

3.5. Publication bias

A small study effect was evident on inspection of funnel plot (see Supplementary Fig. 2), which suggests the potential presence of publication bias. Egger's test (P-value: 0.047).

4. Discussion

The current study offers a thorough and comprehensive evaluation of the available literature concerning PCOS among infertile

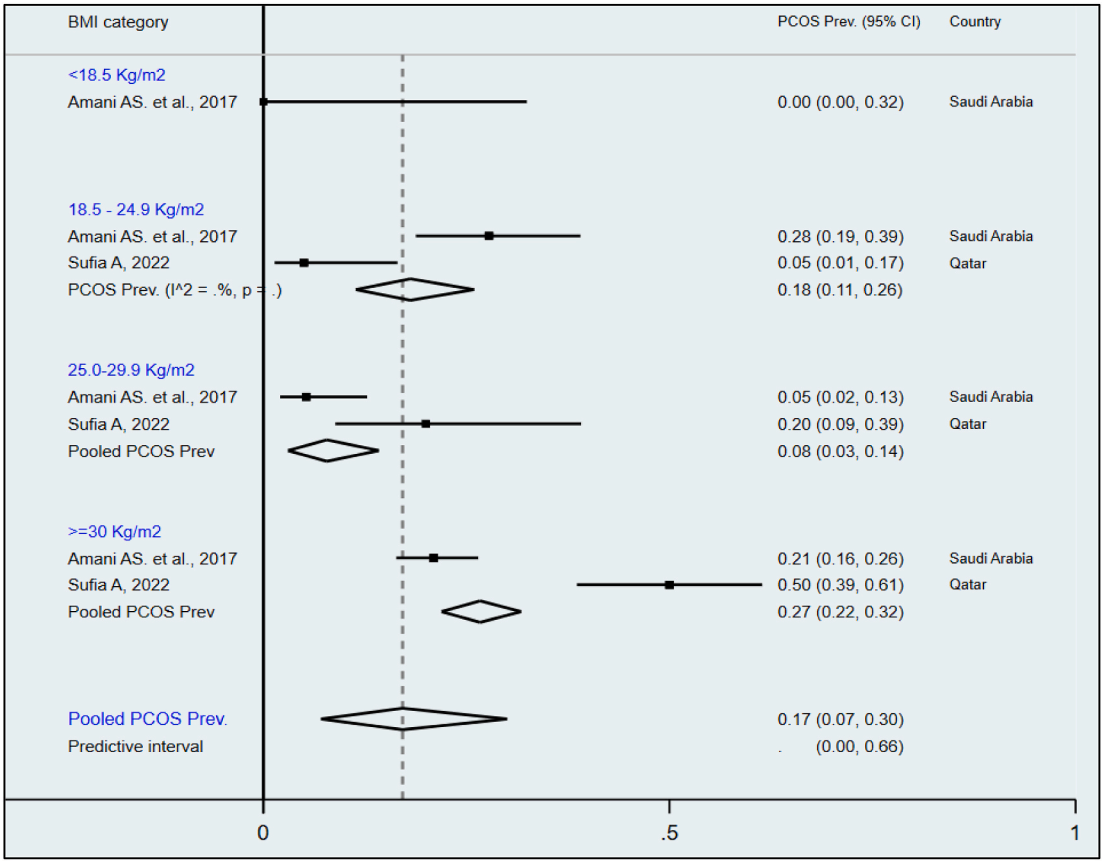

Fig. 3. Forest plot for the weighted pooled prevalence of PCOS among infertile women by body mass index (BMI) category. Overall heterogeneity I^2 = 89.48 %, p = 0.00). Heterogeneity between groups: p = 0.000. Inestimable predictive distribution with <3 studies.

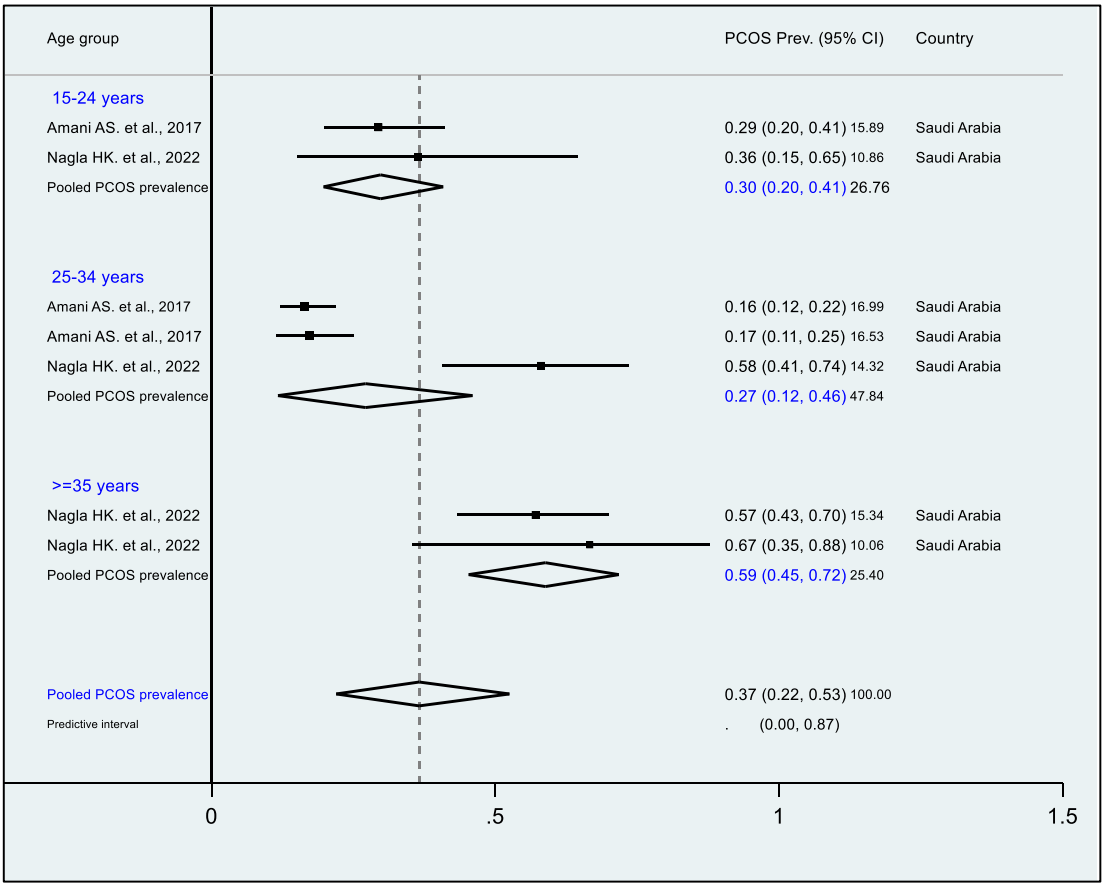

Fig. 4. Forest plot for the weighted pooled prevalence of PCOS among infertile women by three age groups. Heterogeneity: $I^2 = 89.69$ %, p = 0.00, Random-effects model. Inestimable predictive distribution with <3 studies. Heterogeneity between groups: p = 0.002.

female populations in the GCC countries and presents a synthesis of evidence regarding its prevalence. The findings indicate that nearly one-third (30.0 %) of infertile female populations in the GCC countries were diagnosed with PCOS. Notably, women with primary infertility, those aged 35 years and above, and those with an obese BMI range exhibited a higher burden of PCOS prevalence compared to their counterparts.

It's evident from the limited number of studies included in this review that research conducted within the GCC countries on the topic is scarce. More than half of the records originated from Saudi Arabia, with just one study each from the other three countries. It's noteworthy that no studies providing evidence of PCOS among infertile women were found within the UAE and Bahrain. Despite the availability of research on PCOS prevalence in various other population subgroups within these countries [32–35] there remains a need for further investigation into its prevalence among women diagnosed with infertility. The limited number of studies also raises concerns about the reliability of the subgroup analysis results, necessitating cautious interpretation [36].

The overall pooled prevalence of PCOS estimated in this review underscores that a substantial number of women diagnosed with infertility in the GCC region are affected by PCOS. Given the well-established relationship between PCOS and infertility in the literature, this finding suggests that PCOS plays a significant role in the growing burden of infertility in these countries. Subgroup analysis suggests that infertile women with obese BMI (30 kg/m^2 and above) had higher prevalence of PCOS. Although only two studies were included in the analysis, literature indicates significant association of higher BMI with PCOS [37]. Obesity and weight gain have been shown to have adverse effects on pregnancy outcomes, underscoring the importance of personalized weight management plans as a key component of any treatment option offered to patients [38,39]. Additionally, the results from the subgroup analysis suggest that PCOS prevalence is higher among infertile women aged 35 years and above compared to younger women. Research on the association between age, PCOS, and infertility is limited, with some trials indicating a potentially negative effect of age on the prognosis for ovulation induction among older women with PCOS [40,41] while others have reported the opposite, showing a positive effect of advancing age among women [41]. Similarly, in terms of the type of infertility, PCOS was found to be more prevalent in women diagnosed with primary infertility. Research on whether PCOS primarily causes primary or secondary infertility is also scarce, as it is considered to be associated with both types. Therefore, it is advisable to consider screening for PCOS among women at risk (e.g., aged 35 years and older and obese women) of developing infertility and those already diagnosed with infertility and sub-fertility. This personalized approach can be crucial in improving the overall management and health outcomes for these individuals.

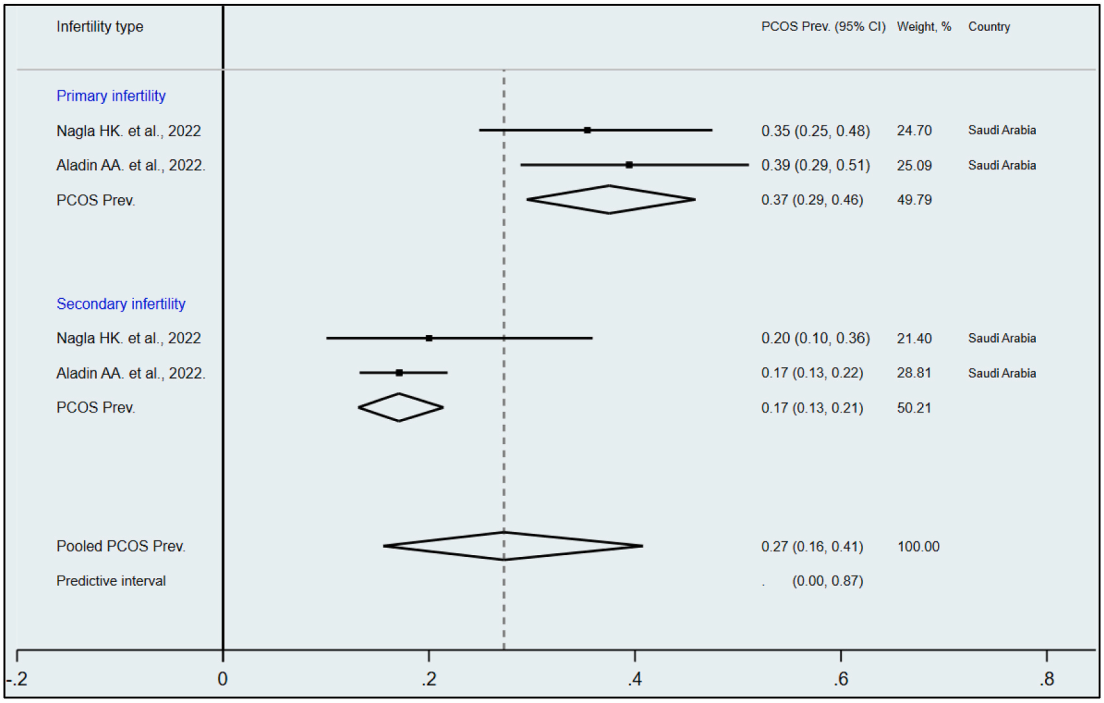

Fig. 5. Forest plot for the weighted prevalence of PCOS among infertile women with primary and secondary infertility. Heterogeneity: $I^2 = 85.50$ %, p = 0.00. Inestimable predictive distribution with <3 studies. Heterogeneity between groups: p = 0.002.

Several mechanisms may contribute to the role of PCOS in developing infertility, including endocrine disruptions characterized by elevated levels of androgens, insulin, and LH, which can lead to ovulatory dysfunction with implications for egg quality, embryonic development, and implantation [42]. Research has explored various interventions aimed at improving fertility among women with PCOS. These interventions encompass non-pharmacological approaches such as lifestyle modifications (e.g., weight reduction, dietary changes, and exercise) [43,44] drug-induced ovulation induction using medications like clomiphene citrate and letrozole, the improve in insulin resistance with metformin, assisted conception techniques like in-vitro fertilization and embryo transfer, and surgical treatments like ovary drilling [45]. However, the effectiveness of these treatment modalities hinges on timely diagnosis and access to appropriate care [9] which could be a challenge in GCC countries. Research suggests that there is limited awareness among women on this topic in some countries, such as the UAE [46].

The review has shed light on several limitations inherent in the included studies. A consistent limitation was the lack of recorded specific criteria used to diagnose PCOS, making comparisons across studies challenging. It is imperative for future studies conducted across healthcare facilities to adopt uniform and standardized criteria for PCOS diagnosis to facilitate meaningful comparisons between results. The number of retrieved studies was also limited, underscoring the need for more evidence to comprehensively understand the PCOS scenario in each GCC country. While the basic sociocultural aspects of the population in the region may be similar, variations in healthcare systems and fertility management programs exist across these countries. Another limitation was that the majority of studies were conducted in a single geographical location (Saudi Arabia), which limits the generalizability of the results to the entire GCC region. Moreover, in the light of high heterogeneity (I-squared: 91.98 %) observed for the pooled prevalence, the results need to be interpreted with caution. As all the studies included were of observational design, this meta-analysis has an inherent limitation, preventing causal inference. The data quality of individual study varied based on eligibility criteria for participants and data collection method used, thus leading to bias in the pooled results.

However, our study has several strengths. It is the first review to address PCOS among infertile female populations in the GCC countries, to the best of our knowledge. Furthermore, the rigorous and transparent methodology employed throughout the review process, involving more than two reviewers at each stage, ensured that all relevant publications were included in the analysis.

5. Conclusion

Three out of every 10 infertile women in four out of six GCC countries were diagnosed with PCOS. This review offers compelling evidence that PCOS significantly affects a substantial portion of infertile women, emphasizing its pivotal role in the escalating burden of infertility in these nations. There is an urgent need for increased awareness on this subject, which should inform healthcare policies, guidelines, and public education initiatives. Moreover, the call for further research on this topic within the region cannot be overemphasized.

CRediT authorship contribution statement

Zufishan Alam: Writing – review & editing, Writing – original draft, Data curation. **Saleh Alseari:** Investigation. **Mahra Alameemi:** Investigation. **Mayytha Alzaabi:** Investigation. **Reem Alkhoori:** Investigation. **Linda Östlundh:** Investigation. **Omar Melhem:** Writing – review & editing. **Mohammed Altigani Abdalla:** Writing – review & editing. **Rami H. Al-Rifai:** Writing – review & editing, Supervision, Conceptualization.

Ethics approval

Not Applicable.

Data and code availability statement

Data will be made available on justified request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e40603.

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