

## **Prevalence of metabolic syndrome among Iranian Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-analysis**

**Introduction:** Polycystic ovary syndrome (PCOS) is a common endocrine disorder that is associated with an increased the risk of metabolic syndrome (MetS) and hence increased cardiovascular diseases in women. This systematic review and meta-analysis aimed at examining the prevalence of MetS in Iranian women with PCOS.

**Methods:** This was a systematic review and meta-analysis of English and Persian studies, using the following keywords: Polycystic Ovary Syndrome, Hyperandrogenism, Metabolic Syndrome, "MetSyn," X Syndrome, and Iran in several national and international databases (Scientific Information Database (SID), Magiran, Web of Science, Google Scholar, PubMed, and Scopus from inception to February 2019. Heterogeneity among the studies was assessed using the Cochran's Q test. The random affects model was then used to estimate the overall prevalence of MetS. ALL the analyses were performed using STATA, version 12.

**Results:** Overall, 10 studies were included in the study. The overall prevalence of MetS among Iranian women with PCOS was 26.6% (95% CI: 16.60-31.70). In addition, the mean body mass index (BMI) was 27.47 (95% CI: 25.46-29.48) and the mean waist circumference was 87.94 (95% CI: 84.28-91.60). According the meta-regression results, there were no significant associations between the prevalence of MetS and sample size, year of publication, waist circumference, BMI, and age.

**Conclusion:** One-fourth of Iranian women with PCOS have MetS. Given the overlap between anthropometric and metabolic abnormalities in PCOS and the features of MetS, accurate identification of patients with MetS is important to ensure early diagnosis and subsequent interventions to effectively manage the condition. **Keywords:** Polycystic ovary syndrome, Metabolic syndrome, Prevalence, Systematic review, Meta-analysis, Iran

## **Introduction**

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in women of reproductive age that is characterized by chronic non ovulation and hyperandrogenism (1). In addition to infertility, PCOS is accompanied by psychological problems (e.g. increased anxiety and depression, reduced quality of life) and metabolic disorders (impaired glucose tolerance (IGT), diabetes (2). Although the etiology of PCOS remains unknown, certain genetic and environmental factors make certain women vulnerable to this syndrome (3). Patients with PCOS are always at risk of dyslipidemia, obesity, and hypertension and hence higher risk of cardiovascular diseases (4, 5). Insulin resistance and compensatory hyperinsulinemia are among the main factors involved in PCOS (6). One-third of patients with PCOS have IGT, and 7.5% have diabetes (7).

Wild et al. (2000) showed that women with PCOS were 2.2, 1.4, and 2.8 times more likely than those without this syndrome to have diabetes, hypertension, and cardiovascular disease, respectively (8). There is a considerable overlap between many of anthropometric and metabolic abnormalities in PCOS and the features of metabolic syndrome (MetS) that is a collection of cardiovascular risk factors including high blood pressure, central obesity, elevated fasting plasma glucose concentrations, and low levels of high-density lipoprotein (HDL) cholesterol (5)(9). It is predicted that this pandemic will affect half of the world' population in the next 20 years (10). The risk of myocardial infarction and stroke is twice as high in patents with MetS as those without it (11).

Previous studies focused on the prevalence of MetS in Iranian women with PCOS have reported different results, with prevalence rates ranged from 7.1% to 46.4% (12, 13). Given the negative consequences of MetS (e.g. cardiovascular disease, diabetes) for those with PCOS, determining its overall prevalence in the Iranian population can help policymakers and healthcare providers design interventions aimed at effective and early prevention, control, and management of MetS in Iranian women with PCOS.

## **Methods**

### **Search strategy**

In this study, the prevalence of MetS in Iranian women with PCOS was analyzed based on articles published in national and international journals without time limitation and based on the PRISMA statement (14). The search was conducted in national databases of Scientific

Information Database (SID) and Magiran and international databases of Web of Science, Google Scholar, PubMed, and Scopus, using the following keywords: Polycystic Ovary Syndrome, Hyperandrogenism, Metabolic syndrome, "MetSyn," and X syndrome and their possible combinations. In the Iranian databases, the Persian equivalents of the keywords were utilized. The references of the articles were also examined to access more relevant articles.

### **Study selection and data extraction**

All the studies in Persian or English, reporting the prevalence of MetS in Iranian women with PCOS were included in the analysis. The exclusion criteria were review studies, interventional studies, letters to the editor, repeated studies, and full text not available. Two researchers independently reviewed the titles and abstracts, and extracted the full texts of relevant studies. Disagreements between the two researchers would be resolved by the correspondent author who was experienced in meta-analysis. The selected articles' characteristics, including name of the first author, year of publication, city of study, methodical quality, total sample size, number of women with PCOS and MetS included in the study, and mean age, mean body mass index (BMI), and mean waist circumference of the samples, were recorded on a spreadsheet.

### **Statistical analysis**

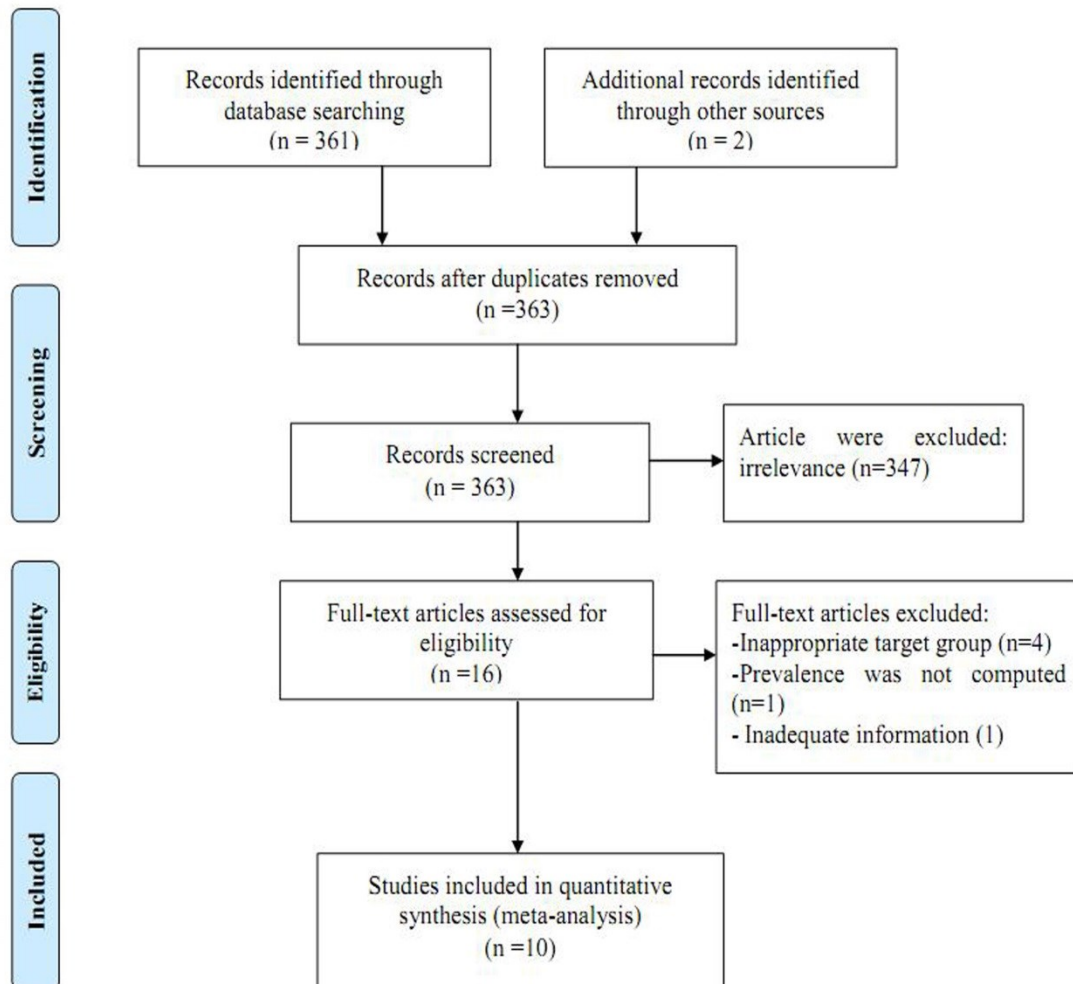
The variance was calculated using a binomial distribution, and the weighted mean was used to combine prevalence rates in different studies. Heterogeneity among the selected studies was assessed using the Cochran's Q Test and the  $I^2$  statistic, and was classified into three categories: below 25% (low heterogeneity), 25-75% (moderate heterogeneity), and above 75% (high heterogeneity). Sensitivity analysis was used to examine the role of each study in the pooled prevalence. Subgroups analysis was used to examine the prevalence of MetS based on methodological quality and the diagnostic criteria of MetS, and a Funnel plot based on the Egger's test was used to examine publication bias. The univariate meta-regression analysis was utilized to assess the association between the prevalence of MetS in women with PCOS with year of study, sample size, and samples' mean age, mean BMI, and mean waist circumference. All the analyses were performed using Stata, version 12.

## **Results**

### **Characteristics of the included studies**

Among the 363 articles identified from the national and international databases, a total of 347 articles were excluded from the analysis. Among the 16 remaining articles, another 6 studies

were excluded (4 articles were focused on a different target population, one article had not reported the prevalence of MetS, and one article had incomplete data. Finally, a total of 10 articles were analyzed based on the PRISMA statement.



**Figure 1.** Process of selecting and screening the studies based on the PRISMA statement.

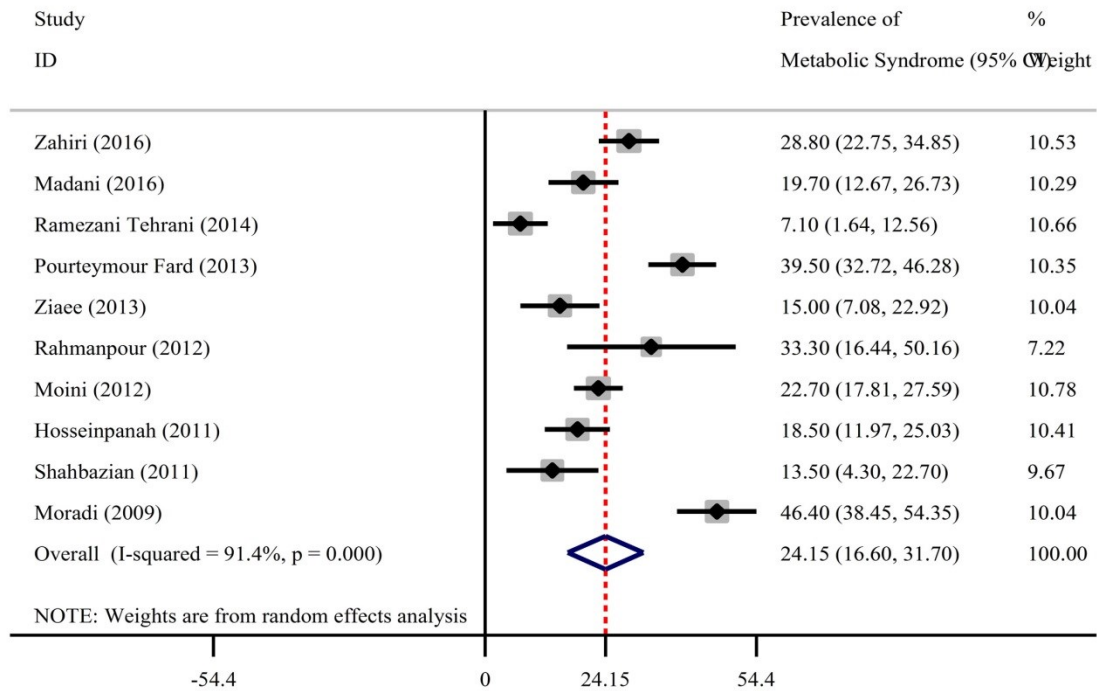
The total sample size was 1353 (135 participants per study on average). Sample size ranged from 30 to 282 patients. In terms of methodological quality, four articles had a good quality and seven articles had a moderate quality. In terms of diagnostic criteria for MetS, seven articles had used the ATP III, two articles had used the JIS, and one article had used the IDF.

**Table 1.** Characteristics of the selected articles.

First Author	Year of Publication	Sample size	Place	BMI	Scale	Prevalence
Zahiri (15)	2016	215	Rasht	28.98±11.19	ATP III	28.8
Madani (16)	2016	123	Tehran	29.80±3.40	ATP III	19.7
Ramezani Tehrani (12)	2014	85	Khouzestan	-	JIS	7.10
Pourteymourfard Tabrizi (17)	2013	200	Tabriz	27.12±2.34	ATP III	39.50
Ziaee (18)	2013	78	Qazvin	23.90±0.20	ATP III	15
Rahmanpour (19)	2012	30	Zanjan	23.40±3.09	DIF	33.3
Moeini (20)	2012	282	Tehran	-	ATP III	22.7
Hosseinpanah (21)	2011	136	Tehran	26.4±5.8	JIS	18.5
Shahbazian (22)	2011	53	Ahvaz	31.4±5.2	ATP III	13.5
Moradi (13)	2009	151	Tehran	29±7	ATP III	46.4

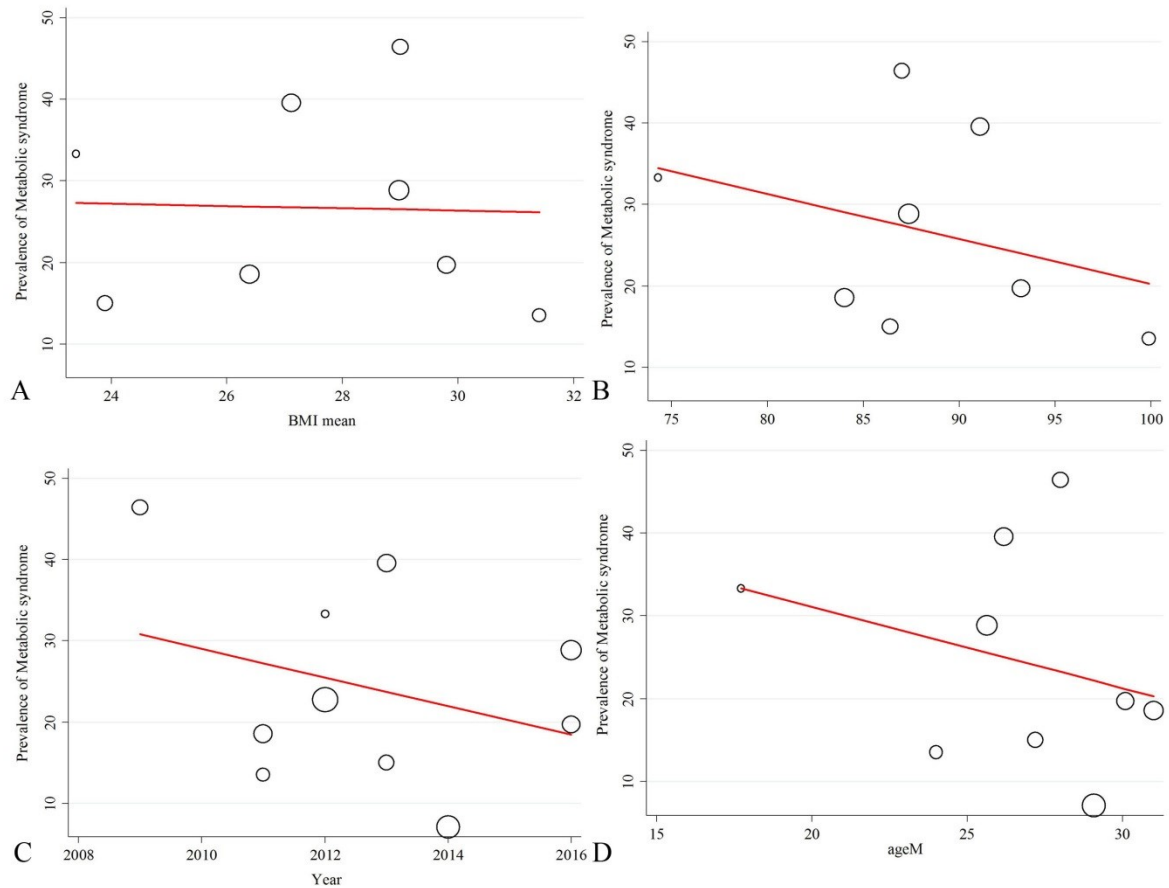
### Meta-analysis

The overall prevalence of MetS in women with PCOS was 24.1% (95% CI: 16.60-31.70). In addition, the prevalence of MetS in women with PCOS based on the ATP III and the JIS criteria was 26.60% (95% CI: 18.37-34.83) and 12.65% (95% CI: 1.49-23.82), respectively. Moreover, the findings showed that the prevalence of MetS was higher in the articles with a higher methodological quality (29.98%; 95% CI: 20.74-39.22) than those with a moderate quality (20.45%; 95% CI: 10.40-30.51).



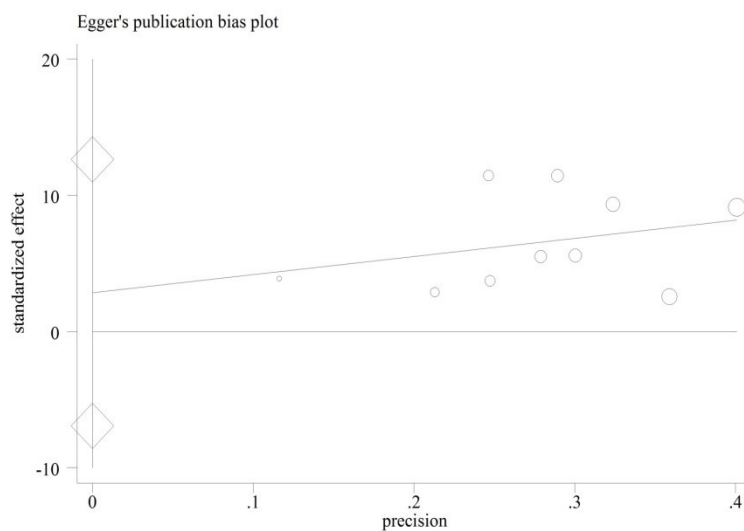
**Figure 2:** Forest plot of the prevalence of MetS in women with PCOS. The 95% confidence interval for each study is shown in the form of horizontal lines around the central mean, the midpoint of the dotted line represents the mean overall score, and the lozenge shape shows the confidence interval of the prevalence rate.

The mean age of the samples was 26.53 years. In addition, the mean BMI and mean waist circumference in the participants were 27.47 (95% CI: 25.46-29.48) and 87.94 (95% CI: 84.28-91.60), respectively. The results of meta-regression analysis indicated no significant relationship between the prevalence of MetS in women with PCOS and year of publication (P=0.375), sample size (P=0.299), mean age (P=0.473), mean BMI (P=0.941), and mean waist circumference (P=0.451).



**Figure 3:** Meta-regression of the prevalence of MetS in women with PCOS. The prevalence of MetS based on BMI (A), Waist circumference (B), Year of publication (C), and mean age of samples (D). Circles indicate the weight of the studies.

According to the results of sensitivity analysis, the removal of each study did not lead to a significant change in the pooled prevalence of MetS. In addition, the publication error was not significant ( $P=0.521$ ).



**Figure 4:** Publication bias

## Discussion

The aim of the present systematic review and meta-analysis was to examine the overall prevalence of MetS in Iranian women with PCOS. According to the results, the prevalence of MetS in Iranian women with PCOS was 24.15%, with large variation depending on the MetS diagnostic tool used in the study. In other words, about one-fourth of Iranian women with PCOS also suffer from MetS; this is consistent with the prevalence rate reported in Brazil (23). The high prevalence of MetS in patients with PCOS is not surprising, given that there are common features between PCOS and MetS, and that both conditions are related to insulin resistance. In Asia, prevalence rates of 37.5% (India) and 35.3% (Thailand) have been reported for MetS in women with PCOS (24, 25).

Two other studies have reported prevalence rates of 46% and 43% for MetS among American women with PCOS (6, 26). In a study conducted in Italy, the prevalence of MetS in women with PCOS based on the ATP III and WHO criteria was found to be 8.2% and 16%, respectively (27). Different prevalence rates in the studies could be due to different genetic factors, dietary habits, physical activity levels, and lifestyles. One reason for the variations in prevalence of MetS in Iranian women is that there are multiple definitions for this syndrome. For example, given the small physique of the Asian population compared to the Europeans, some studies in Asia have used a modified criteria to diagnose MetS, according to which a waist circumference greater than 80 cm is a common feature of those with MetS (9, 28). The studies analyzed in the present meta-analysis had not used modified criteria of MetS; this can partly explain the relatively lower prevalence of MetS among Iranian women with PCOS.

A meta-analysis by Fazleen et al. showed that women with PCOS were 2.7 times more likely than those without PCOS to develop MetS (3). Contrary to the results of the aforementioned studies, Vibrikova et al. found no significant difference between women with PCOS and healthy women in the prevalence of PCOS (29). In a study by Glueck et al. among 138 women with PCOS, a prevalence rate of 46% was found for MetS (26). Apridonidze et al. also reported a prevalence of 43% for MetS in women with PCOS (6).

In the present study, no significant relationship was found between prevalence of MetS and age, BMI, waist circumference, and year of publication. A study by Soares showed that the prevalence of MetS increased with BMI, so that it was 3.2%, 19.2%, and 52.3% in normal, overweight, and obese women, respectively (23). In addition, insulin resistance is intensified in the presence of obesity; more than 40% of patients with PCOS suffer from obesity (30).



Lergo also believes that 70% of these women have impaired lipid levels (31). A study in Italy showed that the prevalence of MetS in women with PCOS increased with age, so that it was 12.1% in women aged 20-24 years, 31.7% in women aged 25-29 years, and 42.9% in women aged 30-34 years (27).

One of the strengths of the present study was that it was the first meta-analysis in Iran focused on examining and reporting the overall prevalence of MetS in women with PCOS. The study results can be useful in making health decisions and also in conducting future studies on this issue. On the other hand, some of the necessary information were missing in a number of the analyzed studies; this can be regarded as a limitation of the present study.. Given the increased risk of morbidity associated with MetS, it seems necessary to identify those women with PCOS who are at risk of developing MetS, and provide them with effective interventions aimed at controlling and treating their symptoms.

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