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Review

The prevalence of metabolic syndrome in patients with polycystic ovary syndrome: A systematic review and meta-analysis

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is an endocrinopathy with unknown pathophysiology among women of reproductive age. Several studies have been conducted to determine the prevalence of metabolic syndrome (MetS) among PCOS patients. However, the results were contradictory. The present study was conducted to evaluate the prevalence of MetS in PCOS patients using the related published data.

Method: The present systematic review was perfumed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search was done using MeSH keywords in databases of PubMed, Scopus, Embase, CINAHL, Web of Science, Cochrane Library, EBSCO, and Google scholar search engine as well as the reference list of the retrieved papers without time limit until October 2018. We used Cochran's Q test and I^2 Index to evaluate the heterogeneity among the studies and the random effects model was used to combine the results. Data analysis was performed using Stata ver. 11.1.

Results: Forty six studies including 8946 patients with PCOS were included in the final analysis. Total heterogeneity was high (I^2: 91.43%, $P < 0.001$). The prevalence of MetS in PCOS patients was estimated to be 30% (95%CI: 27–33). Subgroup analysis based on MetS diagnostic criteria showed an estimated prevalence of 0.27% (95%CI: 0.18–0.37), 0.30% (95%CI: 0.27–0.34), 0.32 (95%CI: 0.25–0.39), 0.32 (95%CI: 0.27–0.37) and 0.24 (95%CI: 0.14–0.34) for IDF, NECP-ATPIII, AHA NHLBI, CDS, and unknown criteria, respectively.

Conclusion: Considering the prevalence of MetS in PCOS patients, diagnosis of MetS in PCOS patients is necessary to reduce the mortality and morbidity rates.

1. Introduction

Polycystic ovary syndrome (PCOS) is an endocrinopathy with 7–15% prevalence that affects women of reproductive age [1,2]. The pathophysiology of this disorder is unknown, yet genetic and environmental factors may be at work [3,4]. This disorder is characterized by hyperandrogenism, polycystic ovary morphology and chronic anovulation [5]. PCOS women are at increased risk of metabolic and endocrine disorders [6]. Different studies have shown higher risk of metabolic syndrome (MeTS) in PCOS women [7–9]. There have been several diagnostic criteria for MetS including World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), International Diabetes Federation (IDF), Chinese Diabetes Society (CDS), American Heart Association and the National Heart, Lung and Blood Institute (NHLBI/AHA), joint scientific statement (JSS), and American College of Endocrinology (ACE) [10–16]. Patients with MetS are at increased risk of type 2 diabetes mellitus (T2DM), cardiovascular disorders, coronary heart disease (CHD), stroke and mortality [17]. A meta-analysis is a method for pooled the results of numerous scientific research. The purpose of using this approach is to find a reliable estimate [18–19]. Several studies have been conducted on the prevalence of MetS in PCOS patients, demonstrating contradictory results [20–23]. This systematic review and meta-analysis was conducted to evaluate the prevalence of MetS in PCOS patients using the related published data.

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2. Method

2.1. Study protocol

To estimate the prevalence of MetS in PCOS patients, the present study was performed using preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines [24]. Two authors independently performed all procedures of the study and a third author resolved any disagreement between researchers.

2.2. Search strategy

Using the keywords "Metabolic Syndrome"[Mesh], "Epidemiology"[Mesh], "Prevalence"[Mesh], "Polycystic Ovary Syndrome"[Mesh] and "Hyperandrogenism"[Mesh], the search was conducted on databases PubMed, Scopus, Science Direct, Embase, CINAHL, Web of Science, Cochrane Library, EBSCO and Google scholar search engine as well as the reference list of the retrieved papers without time limit until October 2018.

2.3. Inclusion and exclusion criteria

The studies evaluated the prevalence of MetS in PCOS patients with at least an English abstract included the study. Exclusion criteria were: 1. Non-random sample; 2. Irrelevant studies; 3. Sample size other than PCOS patients; 4. Duplicates studies; 5. Patients treated with steroids; 6. Review articles, congress papers, case reports, comments, letters to editor; and 6. Low-quality studies.

2.4. Quality assessment

The selected articles were reviewed using modified Scale of Newcastle Ottawa (NOS), and the studies that gained a score of four were included in the study [25].

2.5. Data extraction

In the next step, the included studies were reviewed and the following data were extracted: author(s) name, country of study, study design, name of journal, samples characteristics (e.g. mean age and SD [standard deviation] and BMI [body mass index]), diagnostic criteria for MetS, prevalence of MetS.

2.6. Statistical analysis

Considering the Cochrane handbook, heterogeneity among studies was evaluated using Q Cochran test and I^2 index. In this regard, the interpretation is as follows: 0–24% may not be noteworthy, 25–49% may indicate a moderate heterogeneity, 50–75%

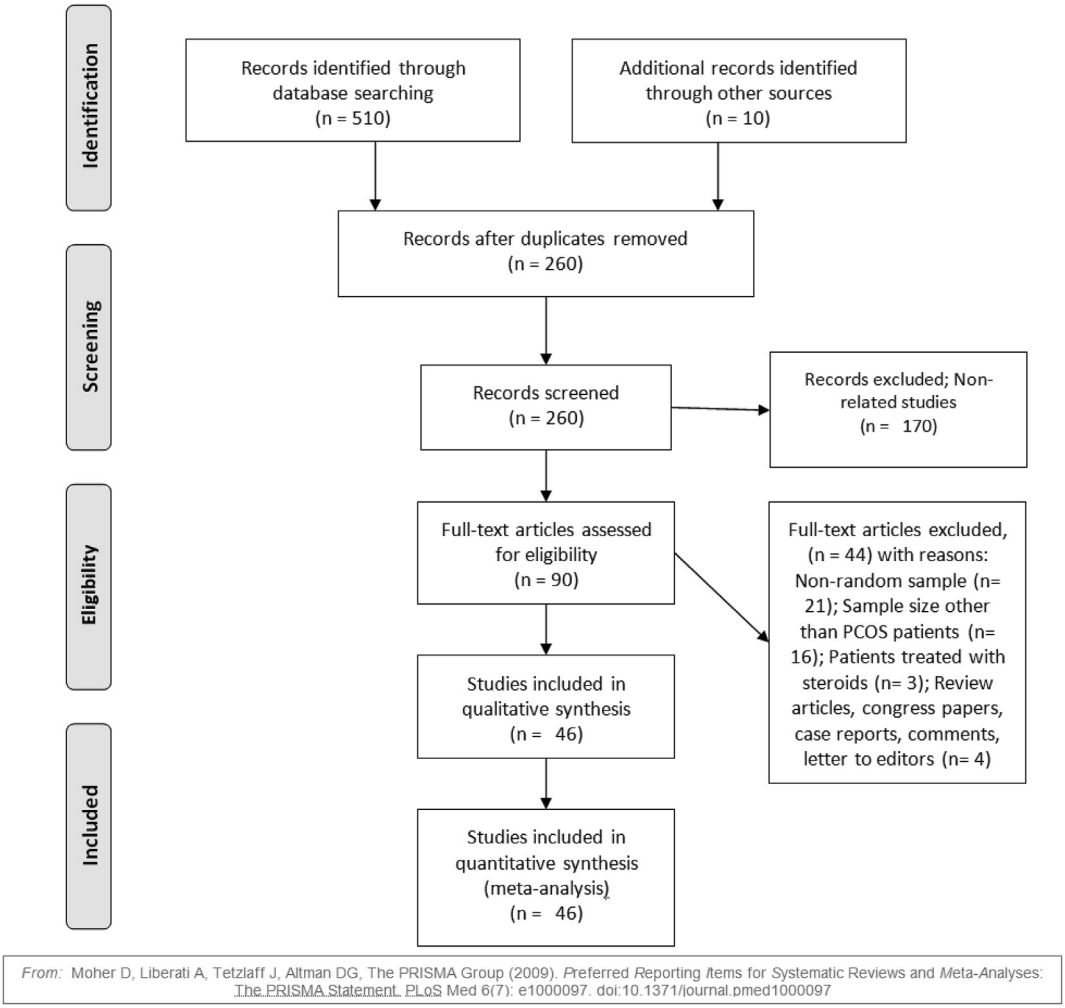

Fig. 1. PRISMA flowchart.

indicates substantial heterogeneity, and over 75% indicates considerable heterogeneity [26]. Additionally, subgroup analysis and meta-regression were performed to find the cause of heterogeneity. The sensitivity analysis was performed through the omission of one study at a time for the reliability of the results. Random effects model was used for combining the result of different studies. Publication bias was evaluated using Egger's test. Data analysis was performed using Stata ver. 11.1. Data were presented through flowcharts, summary tables, and funnel plots, and $p < 0.05$ was considered significant.

3. Results

3.1. Overview of search and characteristics of the included studies

After searching in target databases in this meta-analysis, 520 articles were collected, among which 260 duplicate articles were excluded. Then title and abstract of studies were reviewed and 170 irrelevant studies were excluded (Fig. 1). In the final step, 46 studies including 8946 PCOS patients were included the final analysis (Table 1).

3.2. Prevalence of MetS in PCOS patients

Total heterogeneity in the present study was high (I^2: 91.43%, $P < 0.001$). The Prevalence of MetS in PCOS patients in 46 eligible studies was estimated to be 30% (95% CI: 27–33) (Fig. 2).

3.3. Subgroup analysis

Subgroup analysis based on MetS diagnostic criteria showed an estimated prevalence of 0.27% (95% CI: 0.18–0.37), 0.30% (95% CI: 0.27–0.34), 0.32 (95% CI: 0.25–0.39), 0.32 (95% CI: 0.27–0.37) and 0.24 (95% CI: 0.14–0.34) for IDF, NECP-ATPIII, AHA NHLBI, CDS, and unknown criteria, respectively (Fig. 3).

Table 1
Data Obtained from Reviewed Studies on Prevalence of MetS in PCOS patients.

Author [refrense]	year	MetS-Criteria	Sample size	Mean age (SD)	Mean BMI (SD)	MetS-Positive
Xiang [20]	2013	IDF	105			45
Jee [21]	2010	Unknown	160			31
Ehrmann [22]	2006	Unknown	368			123
Xu [23]	2016	CDS	99			31
Ersan [27]	2012	ATPIII	91			15
Bil [28]	2016	ATPIII	100			22
Yin [29]	2013	IDF	160			8
Bhattacharya [30]	2008	IDF	117			54
Ebrahimi [31]	2015	ATPIII	63	26.9(5.7)	31.4(3.8)	18
Sam [32]	2005	ATPIII	51	28(7)	32.9(7)	29
Apridonidze [33]	2005	ATPIII	106			46
Chan [34]	2017	AHA/NHLBI	1089	28		389
Wongwananuruk [35]	2009	IDF	100			26
Wongwananuruk [35]	2009	ATPIII	100			25
El-Mazny [36]	2010	ATPIII	50			20
Abdelazim [37]	2015	ATPIII	220			67
Madani [38]	2016	ATPIII	624	28.6(4.3)	26.7(3.7)	123
Mehrabian [39]	2011	ATPIII	539			134
Ni [40]	2009	IDF	578	27	21.9	97
Xiaoyan [41]	2012	Unknown	336			63
Marcondes [42]	2007	ATPIII	73	25(6)	30.4(7.8)	28
Shabir [43]	2014	IDF	37	23(3.6)	25.4(3.9)	10
Shabir [43]	2014	ATPIII	37	23(3.6)	25.4(3.9)	8
Pourteymour [44]	2013	ATPIII	200	26.18(4.27)	27.12(2.34)	79
Zahiri [45]	2016	ATPIII	215	25.63(5.17)	28.98(11.19)	62
Siklar [46]	2015	IDF	53	15.3(1.3)	25.32(5.6)	5
Moran [47]	2013	JSS	178	(6.3)33.2	(6.4)35.2	55
Bhattacharya [48]	2010	IDF	198			94
Bhattacharya [48]	2010	ATPIII	198			75
Cussons [49]	2008	WHO	168	34.3(6.3)	32.3(8.1)	55
Kong [50]	2011	ATPIII	89	32	24	19
Mandrelle [51]	2012	ATPIII	120	26.15(4.25)	25.95(4.63)	45
Varghese [52]	2015	ATPIII	45	26.6(4.6)	26.19	24
Hu [53]	2010	CDS	232			74
Gómez [54]	2012	ATPIII	196			42
Vrbíková [55]	2010	ATPIII	179			51
Indhavivadhana [56]	2010	IDF	250	25.4(5.8)	26.2(7.6)	53
Indhavivadhana [56]	2010	ATPIII	250	25.4(5.8)	26.2(7.6)	45
Indhavivadhana [56]	2010	AHA/NHLBI	250	25.4(5.8)	26.2(7.6)	53
Pekhlivanov [57]	2007	ATPIII	65			29
Weerakiet [58]	2007	IDF	170	28.8(5.9)	27.1(7)	60
Acevedo [59]	2005	ACE	39	29.4(8.6)	36	17
Pantasri [60]	2010	IDF- AHA/NHLBI	70	25.6(5.7)	24.8(6.3)	17
Soares [61]	2008	NECP-ATPIII	102	26.4(5.3)	29.4(6.7)	29
Das BP [62]	2018	AHA/NHLBI(ATP III 2005)	66			24
Kar [63]	2013	ModifiedAHA/NHLBI ATP III (2005)	410			144

MetS: Metabolic syndrome; SD: Standard deviation; BMI: Body mass index; IDF: International diabetes foundation; JSS: Joint scientific statement; NCEP ATPIII: The national cholesterol education program adult treatment panel; AHA/NHLB: American heart association and the national heart, lung and blood institute; WHO: World health organization; JIS: Joint interim statement.

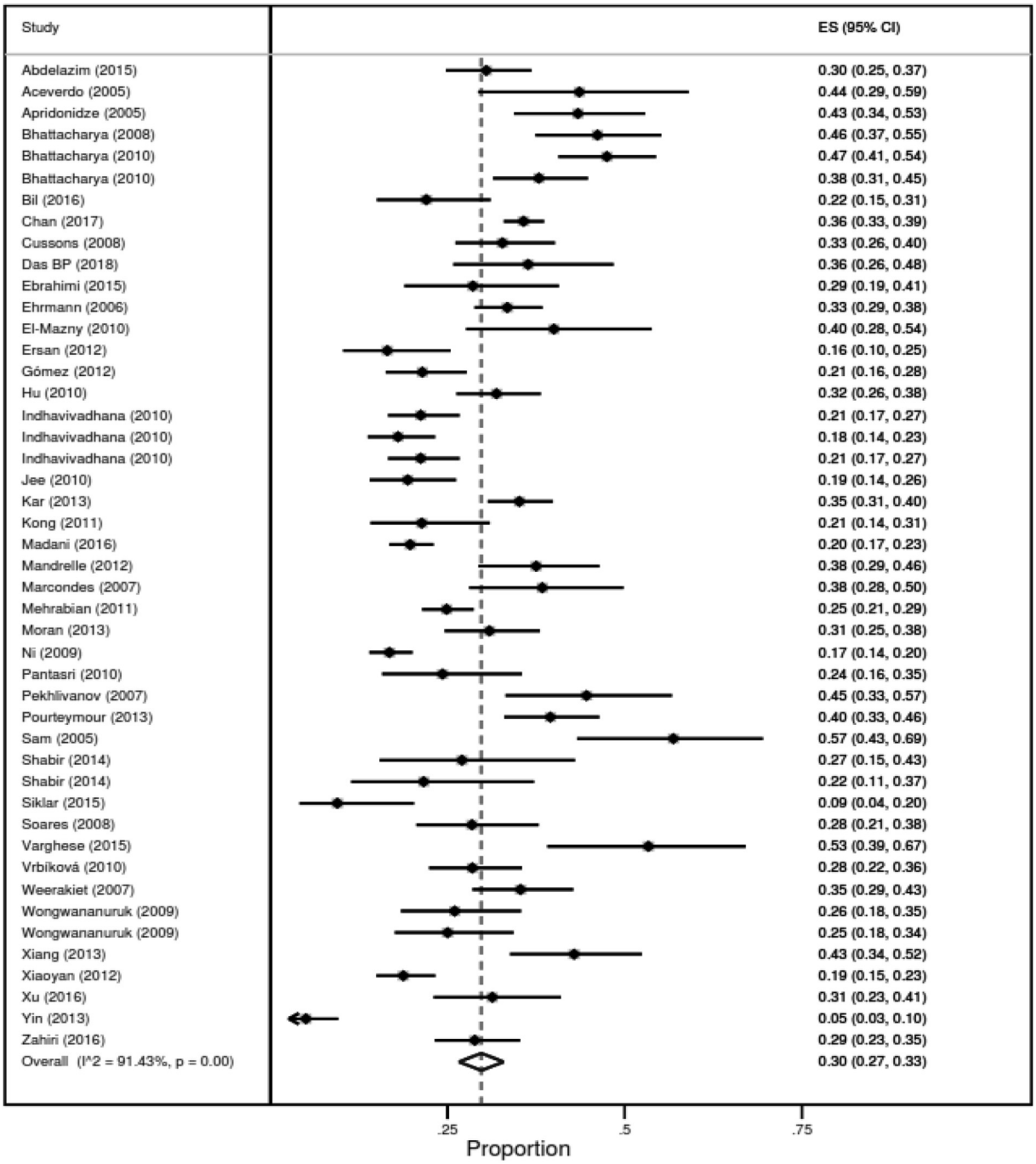

Fig. 2. Meta-Analysis of studies regarding the prevalence of MetS in PCOS patients (mean point of each segment shows the prevalence, and the length of each segment shows 95% CI in each study; the diamond mark shows the pooled prevalence).

3.4. Publication bias and sensitivity analysis

P-value for publication bias in Egger's test was 0.002 (Fig. 4). Sensitivity analysis indicated that the pooled result through omission of one study is strong.

4. Discussion

After analysis of 46 studies in the present study, the pooled prevalence of MetS in PCOS patients was estimated to be 30%, Indicate high prevalence of MetS in PCOS patients.

Studies show that the prevalence of MetS is associated with weight and it increases with weight [64]. Oxidative stress in accumulated fat underlies the development of MeTS and a potential therapeutic target for obesity-associated MeTS is the redox state in adipose tissue [65]. Lipid accumulation product (LAP) is related to MetS and has a diagnostic accuracy for MS in PCOS women [20].

A meta-analysis by Moran et al. using 16 studies showed an increase in the prevalence of impaired glucose tolerance (IGT), type 2 diabetes mellitus (DM2), and MetS in patients with PCOS, and the

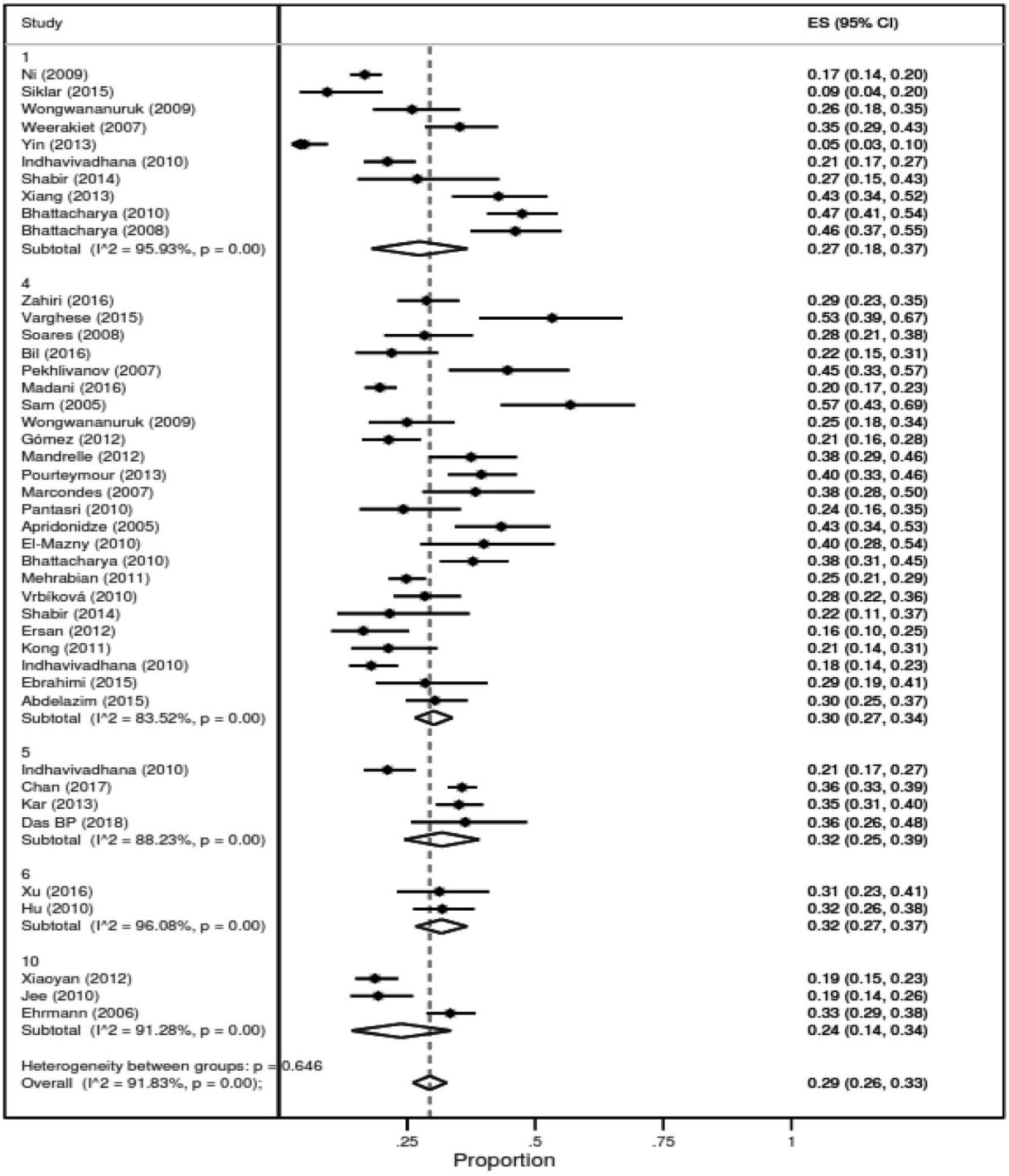

Fig. 3. Subgroup analysis based on MetS diagnostic criteria in meta-analysis of the prevalence of MetS in PCOS patients (mean point of each segment shows the prevalence, and the length of each segment shows 95% CI in each study; the diamond mark shows the pooled prevalence).1 = IDF, 4 = NECP-ATPIII, 5 = AHA NHLBI, 6 = CDS, 10 = unknown.

OR for the prevalence of MetS was 2.88 (95% CI: 2.40–3.45; $p < 0.001$) in this study [66].

A meta-analysis by Otaghi et al. using case-control studies to evaluate the association between PCOS and MetS demonstrated an increased risk of MetS in PCOS patients, and the OR for association between PCOS and MetS was 2.57 (95% CI: 2.18–3.02; $P < 0.001$) in this study [67].

The study by Meyer et al. showed that women with PCOS had a higher carotid intima-media thickness (CIMT) compared with non-PCOS control group, indicating the increase in the risk of atherosclerosis in women with PCOS [68]. Another meta-analysis by Zhao suggested that PCOS is associated with CHD risk, but is not associated with MI and the OR for association between PCOS and CHD was 1.44 (95% CI: 1.13–1.84; $P = 0.004$) [69].

One of limitation of this study was different definitions used for MetS in the included studies. Another limitation is that the risk of MetS may increase in some phenotypes of PCOS, which was not assessed in this study.

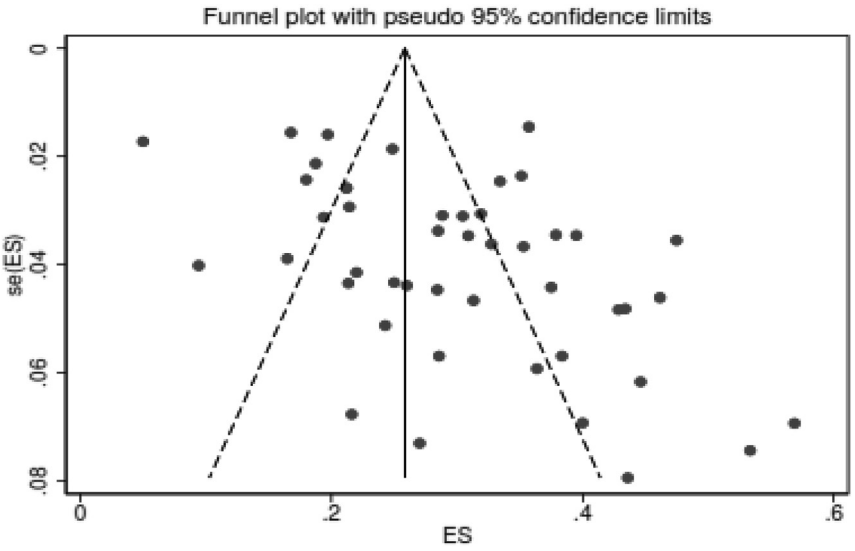

Fig. 4. Publication bias in meta-analysis of studies regarding the prevalence of MetS in PCOS patients.

5. Conclusion

In the present study, considering the prevalence of MetS in PCOS patients, diagnosis of MetS in PCOS patients is necessary to reduce the mortality and morbidity rates. Healthcare programs, diet and exercise programs in combination with pharmaceutical therapeutics must be considered. Further investigation is required for evaluating the pathophysiology mechanism and therapeutic interventions.

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Conflicts of interest

There is no conflict of interest at all.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.06.008.

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