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META-ANALYSIS: ASSOCIATION OF OBESITY WITH INCIDENCE OF POLYCYSTIC OVARIAN SYNDROME (PCOS)

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ABSTRACT

Polycystic Ovary Syndrome (PCOS) is one of the disorders that often attacks women that cause difficulty obtaining pregnancy. PCOS causes 5-10% of women of reproductive age to become infertile. In Indonesia itself, the exact incidence of PCOS is unknown. Most people with Polycystic Ovary Syndrome (PCOS) do not know that they have the syndrome. This cannot be separated from precipitating factors, one of which is obesity or high body mass index. The purpose of this meta-analysis was to estimate the strength of the effect of obesity on the incidence of PCOS. This study is a systematic review and meta-analysis. Primary data is retrieved through the electronic databases PubMed, Science Direct, Web of Science, Springer Link and Cochrane Database. By using the search keywords "obesity AND risk factor AND PCOS", "body mass index" AND "polycystic ovary syndrome". Articles taken between 2013-2023. Statistical analysis was performed using the RevMan 5.3 application. 6 articles qualified quantitatively for analysis. Increased body mass index or obesity, especially the abdomen, will increase the risk of PCOS 1.99-fold compared to women who have a normal body mass index and are statistically significant (OR 1.99; 95% CI: 1.79 – 2.20; p value < 0.001). Body mass index or obesity, especially the abdomen, will increase the risk of PCOS 1.99 times compared to women who have a normal body mass index.

Keywords: meta analysis; polycystic ovary syndrome (pcos); obesity

INTRODUCTION

The World Health Organization (WHO) in 2019 said that new infertile couples every year continue to increase, estimated infertility cases by 10%. The global picture of the infertility population is around 50-80 million couples or occurs in 1 in 7 couples. Infertility in developing countries is higher at around 30% compared to developed countries at only 5–8%. In a study in Ghana in 2013 mentioned the percentage of infertility 26.9% of women and 21.1% of men. Latin America and the Caribbean have about a 1.5% primary infertility rate. Infertility in Asia is highest in Turkmenistan at 43.7% and 21.3% in Indonesia (Puspitasari, 2018 ; Rodiani, 2019).

Polycystic Ovary Syndrome (PCOS) is one disorder that often attacks women who cause difficulty obtaining pregnancy. PCOS causes 5-10% of women of reproductive age to become infertile. In Indonesia itself, the exact incidence of PCOS is unknown. According to Wahyuni's research in 2015, 67 out of 93 PCOS patients (72.04%) experienced infertility. In 2015 as many as 5.8% of Polycystic Ovary Syndrome (PCOS) sufferers experienced infertility (Ibraheem, 2020; Chen, 2021).

Most people with Polycystic Ovary Syndrome (PCOS) do not know that they have the syndrome. This cannot be separated from the driving or triggering factors. There was a significant association between body mass index (p = 0.047 OR = 1.943), hirsutism (p = 0.003 OR = 8.361) and polycystic ovary syndrome. Body Mass Index (BMI) is divided into several categories, overweight 25-29.9 kg/m2, and obesity >30 kg/m2. Women with PCOS have a higher body mass index than women who are not diagnosed with PCOS (Kazemi, 2021).

Research in the United States found that more than half of patients with PCOS are overweight or obese. PCO patients with obesity are 2.7 times more at risk of impaired ovarian follicle maturation process than PCO patients who are not obese (p = 0.006; OR=2.7) (CI,95%:1.329–5.34) (Ma, 2021). 19 Research also states that obesity is not significantly associated with infertility, but being overweight is something to consider because ethnic variations that cause overweight can increase the risk (Yang, 2021) .

METHOD

The research design is a meta-analysis conducted based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher, 2015) The database search is conducted from April 2023. The database includes PubMed and google scholar, Keywords for this review include: "*obesity AND risk factor AND PCOS", "body mass index" AND "polycystic ovary syndrome"*. A critical assessment of the article is carried out by the authors of the entire author, disagreements are resolved through discussion. Articles that do not fall into qualitative criteria, most of them will be discussed in this article and used as a source of literature. all articles will be quantitatively analyzed using Review Manager (RevMan) 5.3. Full paper published in English or Indonesian. Report complete analysis results including *adjusted risk ratio, confident interval*, and *p-value.* The article was analyzed by multivariate analysis reported in the closeness of the odds ratio relationship. Cross-sectional *articles,* experiments (RCTs), experimental quasy, or reviews. Full paper in Chinese, Spanish, Arabic, Russian, and French. The article was analyzed by bivariate analysis.

RESULTS

Table 1.
Article analysis

Author	Subject and location	Result
(Ryu, 2023) Maternal Polycystic Ovary Syndrome and the Risk of Early Childhood Obesity in Female Offspring: A Nationwide Population-Based Study	1,213 women had a history of PCOS and 130,592 women did not. Korean	Female offspring aged 66–80 months born to women with PCOS had significantly higher BMI than those born to women without PCOS; there was no significant difference in that of male offspring regardless of maternal PCOS. In the generalized estimating equation and multivariable logistic regression analyses, the female offspring born to women with PCOS had a significantly higher risk of obesity during the age of 42–54 and 66–80 months (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.09–2.21 and OR, 1.5; 95% CI, 1.05–2.15, respectively), than those born to women without PCOS, after adjusting for several confounding factors.
(Liu, 2022) Assessment of neutrophil to lymphocyte ratio, C-reactive protein,	A total of 112 patients between 16 and 40 years of age (mean 26.06 ± 4.84 years) who presented to the clinic of Gynecological	The odds ratios and 95% confidence intervals of those variables (NLR, hs-CRP, MPV) were found significant (P < .05). NLR, hs-CRP, and MPV variables were found statistically significant in the

Author	Subject and location	Result
mean platelet volume in obese, and nonobese patients with polycystic ovary syndrome	Endocrinology in Hangzhou Women's Hospital	analysis of receiver operating characteristics.
(Saad, 2020) Common Variant rs9939609 in Gene FTO Confers Risk to Polycystic Ovary Syndrome	The first set comprise of 741 PCOS and 704 control subjects. The second phase of replication study was performed among another independent group of 2858 PCOS and 2358 control subjects using TaqMan-MGB probe assay. All subjects are from Han Chinese.	To further elucidate whether this association is resulted from obesity or PCOS per se, the samples were divided into two groups–obese and non-obese PCOS, and the results were still positive in obese group (P obese = 5.81E-05, OR = 1.55), as well as in non-obese PCOS group (P non-obese = 7.06E-04, OR = 1.28)
(Bedrick, 2020) Self-administered questionnaire to screen for polycystic ovarian syndrome	women ages 18–50 with and without PCOS as defined by modified Rotterdam criteria to complete a self-administered survey of common PCOS signs and symptoms in Washington City	In multivariate logistic regression, women who used depilatory techniques had an adjusted odds ratio (aOR) of PCOS of 6.6 (95% confidence interval [CI] 2.5–17.3, p = 0.0002). Those with obesity had similar aOR of PCOS (aOR 6.7, 95% CI 2.5–17.9, p = 0.0001).
(Greenwood, 2020) Obesity and depression are risk factors for future eating disorder-related attitudes and behaviors in women with polycystic ovary syndrome	One hundred sixty-four women with PCOS by the Rotterdam criteria. California, United Stated	Obesity at baseline conferred a 6.9-fold increase in the odds of elevated EDE-Q score (adjusted odds ratio 1⁄4 6.89; 95% confidence interval, 2.70, 17.62), while a positive depression screen conferred 3.6-fold increased odds (adjusted odds ratio 1⁄4 3.58; 95% confidence interval, 1.74-7.35). Compared with white women, nonwhite women were at risk of higher EDE-Q scores.
(Venkatesh, 2022) Obesity and risk of female reproductive conditions: A Mendelian randomisation study	We included 257,193 individuals self-identifying as females of white ancestry in UKBB in our analyses. Baseline measurements of BMI (total body weight [kg]/standing height squared [m2]) and waist-to-hip ratio (WHR) (waist circumference [WC] [cm]/hip circumference [HC] [cm]), and WHR adjusted for BMI (WHRadjBMI) were used to estimate general obesity (BMI) and central obesity (WHR and WHRadjBMI. United Kingdom.	Genetically pre-dicted visceral adipose tissue (VAT) mass was associated with the development of HMB (OR [95% CI] per 1-kg increase in predicted VAT mass = 1.32 [1.06–1.64], P = 0.0130), PCOS (OR [95% CI] = 1.15 [1.08–1.23], P = 3.24 × 10−05), and pre-eclampsia (OR [95% CI] = 3.08 [1.98–4.79], P = 6.65 × 10−07). Increased waist circumference posed a higher genetic risk (ORs = 1.16–1.93) for the development of these disorders and UF than did increased hip circumference (ORs = 1.06–1.10). Leptin, fasting insulin, and insulin resistance each mediated between 20% and 50% of the total genetically predicted association of obesity with pre-eclampsia.

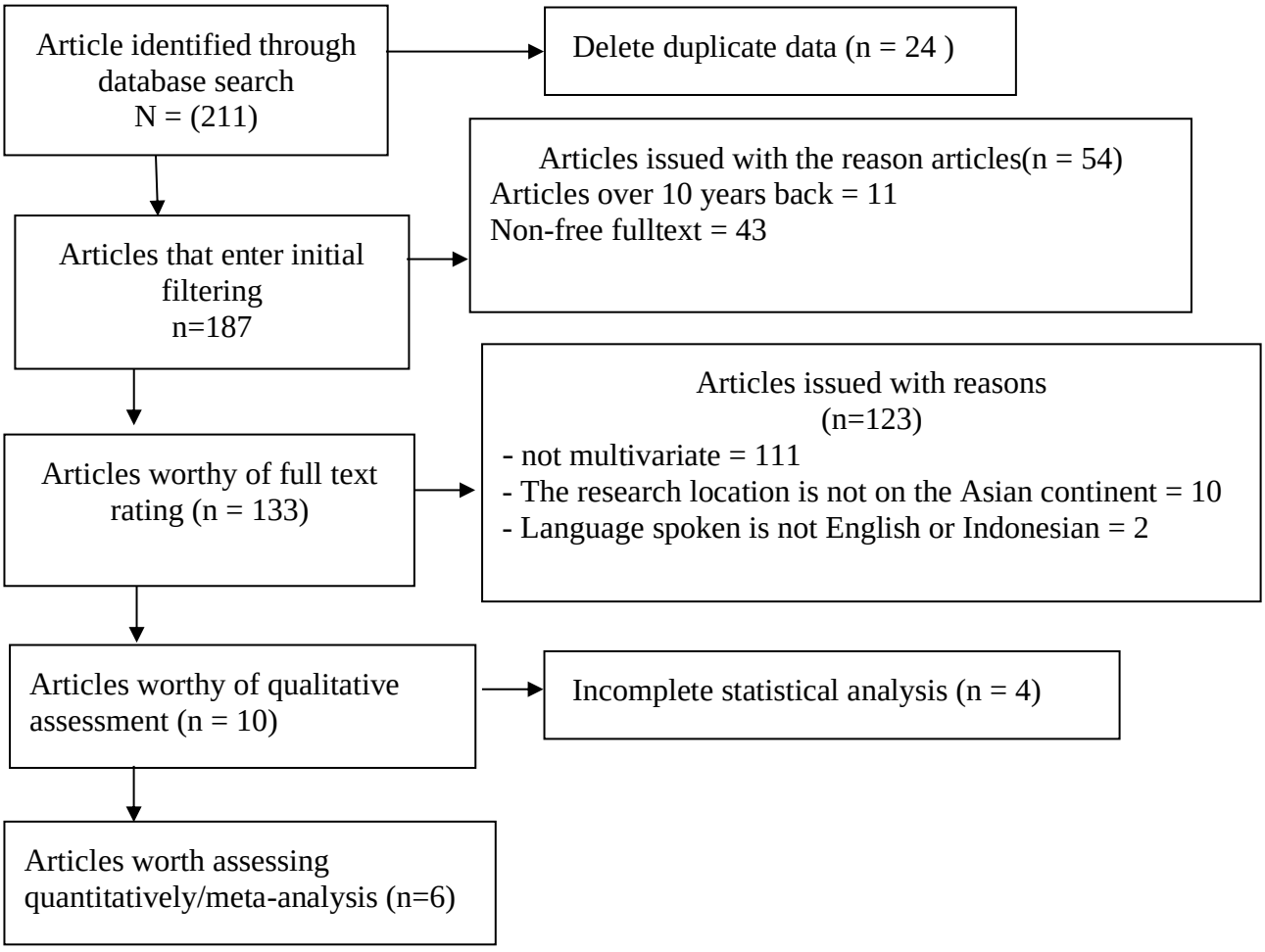

Figure 1. Research and data search flow based on PRISMA guidelines

Forest Plot Analysis

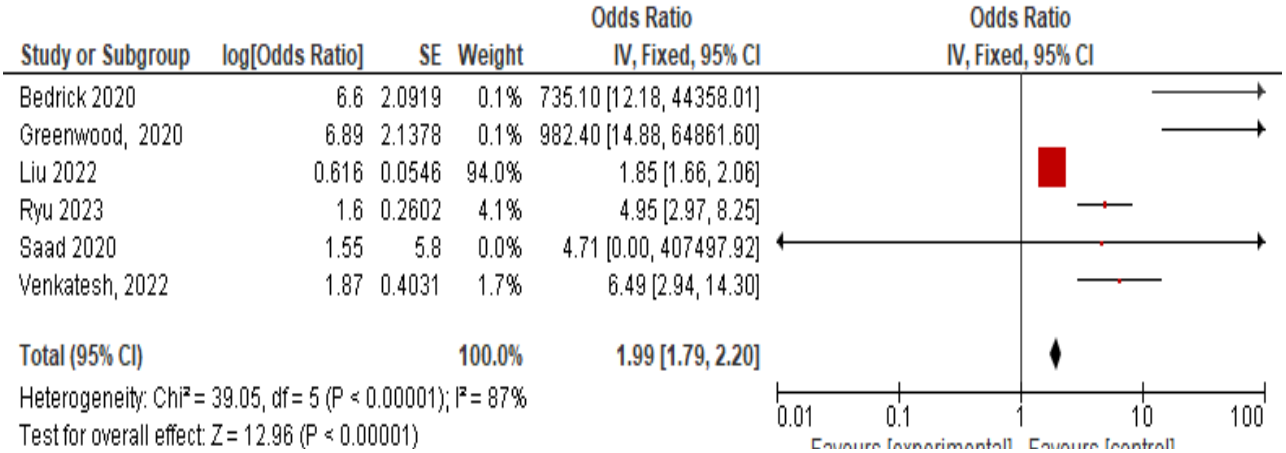

Figure 2. Forest plot meta-analysis of the relationship of obesity with PCOS incidence

Based on the results of the forest plot analysis above, it can be seen that women who suffer from obesity or obesity have a risk of suffering from PCOS 1.99 times or almost 2 times compared to women who have normal weight, and statistically significant Odds Ratio (OR 1.99; 95% CI: 1.79 – 2.20; p value < 0.001).

DISCUSSION

Obesity, especially abdominal obesity, is a common manifestation of PCOS prevalence depending on geographic location and ethnicity. Studies have shown that abdominal obesity can be associated with various clinical features of PCOS. For example, due to adipose tissue dysfunction, adipocytes secrete non-physiological levels of adipokines, including IL6, IL8, TNF-α, *leptin, adiponectin, resistin, lipocalin 2, chemoattractant protein monocytes-1* (MCP1), retinol-4 binding protein (RBP4), and *CXC-chemokine ligand* 5 (CXCL5), which may be involved in insulin resistance (IR) (Kazemi et al. 2021).

In addition, a recent study has shown that obesity may serve as a better predictor of skeletal muscle mass in female PCOS than hyperandrogenism and IR, which may worsen PCOS complications. Interestingly, adipose tissue dysfunction can affect follicle development. IL-10 secreted by adipocytes impairs VEGF-induced angiogenesis and further interferes with folliculogenesis (Yang et al. 2021).

Moreover, molecular mechanisms regarding androgens and adipose function in PCOS mentioned recently, excess androgens can inhibit adipogenesis, weaken activation of thermogenesis and reduce mitochondrial respiration in adipose tissue. Bioinformatics analysis to identify CHRDL1 genes that may be responsible for PCOS obesity by inhibiting bone morphogenetic protein 4 signaling or regulating IGF-1 (Chen, 2021).

The results of this study are also in accordance with research conducted by (Rodiani, 2019) entitled "Policystic Ovary Syndrome: Risk of Infertility that can be Prevented through Weight Loss in Obese Women" reported that lifestyle modifications, one of which is reducing weight and belly fat by reducing calorie intake. This is proven to reduce androgen levels, reduce insulin resistance so that it is expected to restore the frequency and amplitude of LH in normal amounts so that the menstrual cycle can run normally so that it is expected to reduce the risk of infertility in polycystic ovarian syndrome (PCOS).

CONCLUSION

Body mass index or obesity, especially the abdomen, will increase the risk of PCOS 1.99 times compared to women who have a normal body mass index.

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