

META-ANALYSIS OF DETERMINANTS OF THE INCIDENCE OF *POLYCYSTIC OVARIAN SYNDROME (PCOS)* IN INDONESIA

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ABSTRACT

In 2013 the infertility rate in Indonesia has increased to 15-25% of all married couples or 4 to 6 million couples require infertility treatment to get offspring. Infertility in women is generally caused by ovulation disorders, one of the causes of ovulation disorders is Polycystic Ovary Syndrome (PCOS). PCOS is caused by various factors or determinants. The purpose of this study was to analyze the influence of determinants of obesity, stress and employment status factors on the incidence of PCOS in women in Indonesia. This study was conducted with *systematic review* and meta-analysis. Research data is searched from: PubMed and google scholar. By using the search keywords "determinant AND PCOS", " risk factor AND PCOS", " Factor associated AND PCOS AND adjusted odds ratio", and "Risk Factors AND PCOS AND adjusted odds ratio", "obesity AND PCOS", "stress AND PCOS", "Occupation AND PCOS". Indonesian women who are obese will increase the risk of PCOS incidence by 34 times and statistically significant Odds Ratio (OR 34.32; 95% CI: 10.45 – 112.67; p value < 0.001). Severe stress increases the risk of PCOS by 75 times (OR 75.84; 95% CI: 6.91 – 832.00; p value = 0.0004). and women who have jobs will increase the risk of PCOS events up to 35 times (OR 35.41; 95% CI: 2.81 – 446.69; p value = 0.006). In Indonesian women factors Obesity, stress and employment status can increase the risk of PCOS.

Keywords: determinant; obesity; occupation; PCOS; stress

INTRODUCTION

The ovaries are female reproductive organs with two functions, namely producing and releasing oocytes, and producing and secreting hormones such as progesterone and estrogen that function to contribute to the menstrual cycle including during pregnancy and breast growth and development. But not all women have ovaries that function normally as they should, many factors can make a woman's ovaries physiologically disturbed. (Yanti, 2016) A disease that can interfere with the function of the ovaries and cause clinical symptoms is Polycystic Ovary Syndrome (SOPK). Polycystic ovaries are conditions where the ovaries are 2-5 times larger than normal size, the surface appears white, and the cortex thickens with multiple cysts (Santoso, 2014). In women of reproductive age, Polycystic Ovary Syndrome (SOPK) is one of the most common gynecological problems. According to the European Society of Human Reproduction and Embryology / American Society of Reproductive Medicine, the prevalence of SOPK was found to be 15-20%. The diagnosis of this syndrome is based on two of three criteria: anovulation or chronic anovulation, 2 hyperandrogenemia, and clinical and/or biochemical signs characteristic of polycystic ovaries (Fitria, 2016)

In 2013 the infertility rate in Indonesia has increased to 15-25% of all married couples. Of the 39.8 million couples of childbearing age, 10–15% are declared infertile and 4–6 million couples require infertility treatment to conceive. Infertility in women is generally caused by ovulation disorders, one of the causes of ovulation disorders is Polycystic Ovary Syndrome (PCOS). Polycystic Ovary Syndrome (PCOS) is still a problem in the field of reproductive health globally. Based on this

background, researchers are interested in conducting a meta-analysis of the determinants of risk factors for PCOS events, including: obesity, severe stress and employment status.(Ajmal, 2019)

METHOD

This research was conducted with *Systematic Review* and meta-analyses that use secondary data from previous research results. *Systematic review* The method used in synthesizing primary research data with the exploitation of reported data through a systematic- explicit search process integrates the entered data *Reviews*. Meta-analysis is an epidemiological study that combines statistical data against the results of primary research in previous studies on the same hypothesis to obtain quantitative summary results.(Moher, 2015) Research data is sought from several indexings including: PubMed and Google Scholar. By using the search keywords "determinant AND PCOS", " risk factor AND PCOS", " Factor associated AND PCOS AND adjusted odds ratio", and "Risk Factors AND PCOS AND adjusted odds ratio", "obesity AND PCOS", "stress AND PCOS", "Occupation AND PCOS". Full paper article with observational study design. Articles published in English and/or Indonesian. Include the results of research in the form of *adjusted odds ratio* as an indication of the most ideal analysis for multivariate research. *Outcome* is a PCOS event. The location and subjects of the study were conducted in Indonesia. Researchers use adjusted odds ratio to get the same final result in the study analyzed, then calculate the overall relationship of combining data. Data analysis performed using Review Manager (RevMan) 5.4 was used to calculate the overall mean difference, describing a 95% confident interval (CI) using an effect model, I2, or heterogeneity of data.

RESULTS AND DISCUSSION

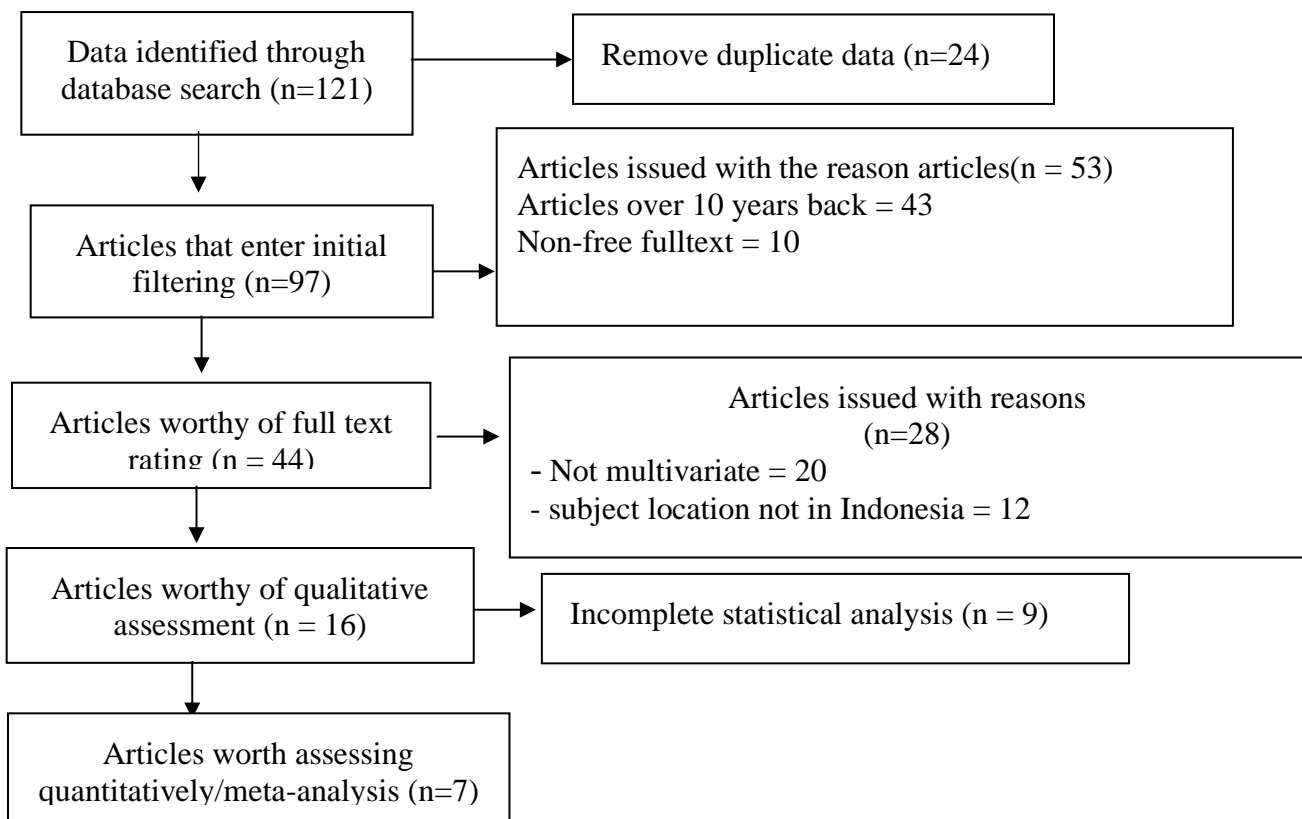


Figure 1. Research and data search flow based on PRISMA guidelines

Table 1.
Summary of data search results

Researchers	Subjects and methods	Result
(DESRINA, 2013) Risk Of Obesity Against Polycystic Ovary Syndrome Rsia Widiyanti Palembang IN 2009- 2011	The data collected were primary and secondary data from medical records of patients with polycystic ovarian syndrome at the Widiyanti Mother and Child Hospital in Palembang for the period 2009-2011. The study population was all patients treated at the Widiyanti mother and child hospital for the period 2009-2011, while the study case sample was all patients with polycystic ovary syndrome and the study control sample was not polycystic ovary syndrome patients.	From the results of the study, the number of samples was 16 patients, the largest group of cases was found in obesity, namely 24 people (63.16%) and non-obesity, namely 14 people (36.84%). The most control groups were found in non-obese people (31.58%) and obese 7 people (18.42%) (95% Confidence Interval (CI) 2.651-21.743, Odds Ratio (OR) 7.592). It can be concluded that there is a relationship between obesity and polycystic ovary syndrome ($P < 0.05$).
(DESSY A NINGSI, 2019) Factors Related To The Incidence Of Infertility In Poly Obgyn Rsud Dr. Soetomo Surabaya.	This study is an observational analytical study with a hospital-based case control design at the Obgyn Poly of RSUD dr. Soetomo Surabaya which was conducted from March to April 2019. The samples used in this study were from 42 infertile women and 42 fertile women taken by Purposive Sampling method.	The results of statistical tests showed no significant relationship between the incidence of infertility with maternal age (p 0.595), menstrual cycle (p 0.202), stress level (p 0.906), caffeine consumption habits (p 1), previous surgery history (p 0.659), husband's smoking habits (p 0.578) and quality of sexual intercourse (p 0.507). The factor that has a significant relationship with the incidence of infertility is BMI (p 0.039) and is the most influential factor on the incidence of infertility with a value of $OR = 2.463$ (95% CI 1.038 – 6.731)
(Putri, 2019) The relationship between sedentary lifestyle and overweight on the risk of polycystic ovarian syndrome in students of SMAN 5 Surabaya	This research used observational analytic method and cross-sectional design. The sample of this research is chosen by random sampling on all female students	Women with sedentary lifestyle has 6,373 folds higher risk of PCOS than normal people and people with overweight has 16,260 folds higher risk of PCOS than normal people. In conclusion, sedentary lifestyle and overweight have the role of increasing the risk of PCOS in adolescents.

<p>(FADILAH, 2019) The Relationship Between Body Fat Composition And The Risk Of Polycystic Ovary Syndrome In Adolescent Girls Aged 15-19 Years In Palembang City</p>	<p>This research is an observational analytical study with a cross sectional design. The research sample was Sriwijaya University Students and SMAN 1 Palembang Students totaling 139 respondents</p>	<p>The results of statistical tests showed a significant relationship between body fat composition and the risk of polycystic ovary syndrome (p value = 0.001) and r value = 5.44.</p>
<p>(Indarwati, 2017) Analysis of factors influencing female infertility</p>	<p>The study was conducted at Sekar Clinic Dr. Moewardi Hospital, Surakarta from February to March, 2017. A sample of 105 fertile women, consisting of 35 infertile women and 70 fertile women</p>	<p>Female infertility was affected by aged ≥ 35 years old (OR= 4.45; CI 95%= 1.27 to 15.54; p=0.019), career women (OR=3.91; CI 95%= 1.14 to 13.38; p=0.043), high level of stress (OR=3.89; CI 95%=1.04 to 14.46; p=0.046), body mass index (OR=4.37; CI 95%= 1.03 to 18.61; p<0.001), abnormal reproductive organs (OR=11.67; CI 95%= 2.80 to 48.54; p=0.030).</p>
<p>(Yuliarfani, 2022) Effects of Work, Stress, Obesity, and Menstrual Cycle with the Incidence of Infertility in Women</p>	<p>This research was conducted at the Indonesian Boy Clinic, Awal Bros Hospital, Tangerang City. This research process was carried out in July 2019 - January 2020. The population in this study was all women couples of childbearing age who visited the Indonesian Boy Clinic Awal Bros Hospital in Tangerang City and the sample used was 104 respondents.</p>	<p>The results of the chi square hypothesis test obtained a pvalue of 0.002 can be concluded that there is a relationship between stress and the incidence of infertility. In addition, an Odds Ratio (OR) value of 3.958 was obtained, meaning that respondents who experienced stress had a 3.958 times chance of experiencing ovarian disorders. In addition, an Odds Ratio (OR) value of 3.427 was obtained, meaning that respondents who were obese had a 3.427 times chance of experiencing primary infertility compared to respondents who were not obese.</p>
<p>(Mulyani, 2021) Factors related to primary infertility in couples of childbearing age in the work area of Uptd Puskemas Lembak Kab. Muara Enim in 2021</p>	<p>This research is an analytical survey with a cross sectional approach. The population is 175 EFAs with infertility. The size of the study sample was calculated random sampling with lottery techniques.</p>	<p>p value=0.061 $< \alpha = 0.05$ means there is no relationship between age and primary infertility, p value=0.026 $< \alpha 0.05$ means there is a relationship between nutritional status and primary infertility and p value 0.617 $> \alpha = 0.05$; OR:1.74 means there is no occupational relationship with primary infertility</p>

Forest Plot Analysis

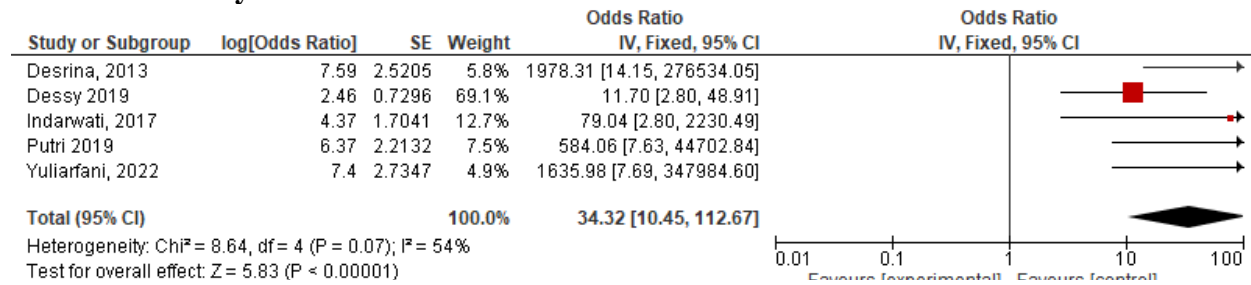


Figure 2. Forest Plots Association between Obesity and PCOS Incidence

Based on the results of the forest plot analysis in figure 2 above, it can be seen that in Indonesian women who are obese or increased body mass index will increase the risk of PCOS events up to 34 times compared to women who do not experience severe stress and statistically significant Odds Ratio (OR 34.32; 95% CI: 10.45 – 112.67; p value < 0.001).

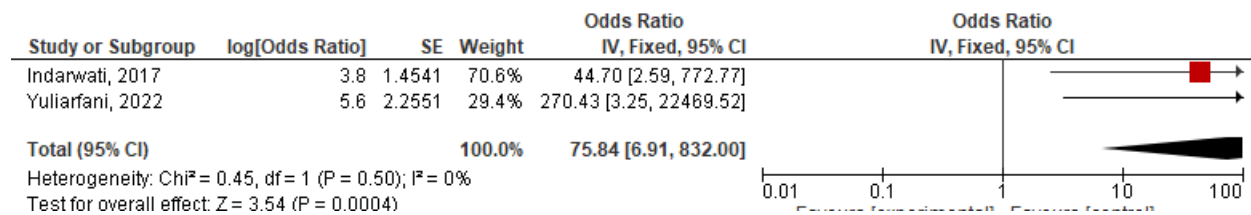


Figure 3. Forest Plot of Relationship between Stress and PCOS Incidence

Based on the results of the forest plot analysis in figure 3 above, it can be seen that women who experience severe stress will increase the risk of PCOS events up to 75 times compared to women who do not experience stress and statistically significant Odds Ratio (OR 75.84; 95% CI: 6.91 – 832.00; p value = 0.0004).

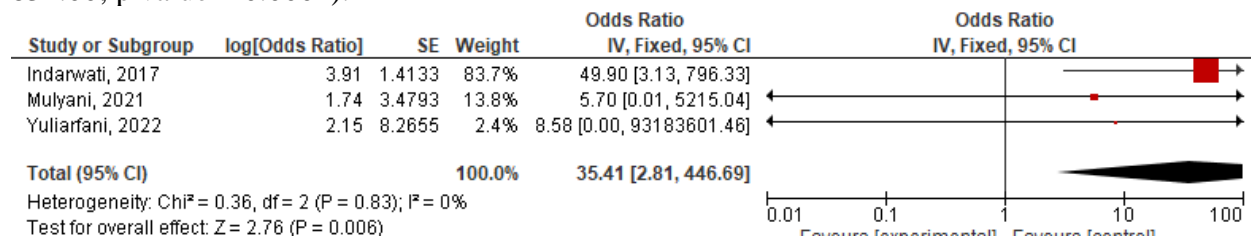


Figure 4. Forest Plot Relationship between Working Women's Status and PCOS Incidence

Based on the results of the forest plot analysis in figure 4 above, it can be seen that women who have jobs will increase the risk of PCOS events up to 35 times compared to women who do not work outside the home and statistically significant Odds Ratio (OR 35.41; 95% CI: 2.81 – 446.69; p value = 0.006). Obesity being the easiest determinant and often occurs, 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, 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. (Artimani, 2018) 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 *CHRD1* genes that may be responsible for PCOS obesity by inhibiting bone morphogenetic protein 4 signaling or regulating IGF-1. (Chen, 2021)

Stress and work are strongly associated with the incidence of PCOS. Even stress has a two-way relationship, which can cause PCOS and PCOS conditions can be a trigger for stress. Other studies also state that stress can cause sleep disorders, phobias, and biochemical reactions that can trigger the occurrence of PCOS characterized by physiological parameters such as hyperandrogenemia, such as free androgen index (FAI), dehydroepiandrosterone sulfate (DHEA-S) and 17-OH progesterone have been associated with PCOS symptoms, homeostatic model assessment (HOMA-IR) and blood lipid profiles. However, there is still a long way to go until we establish a definitive causative relationship between the physiological and psychological phenomena that occur in PCOS. (Palioura, 2014; Papalou, 2017)

CONCLUSION

In Indonesian women factors Obesity, stress and employment status can increase the risk of PCOS.

REFERENCES

- Ajmal, N. K. S. Z. & S. R., 2019. Polycystic ovary syndrome (PCOS) and genetic predisposition: A review article. *European journal of obstetrics & gynecology and reproductive biology*, X(3), p. 100060.
- DESRINA, D. E. K. Y. & A. H., 2013. Risiko Obesitas Terhadap Sindrom Ovarium Polikistik Rsia Widiyanti Palembang Tahun 2009-2011. (*Doctoral dissertation, Sriwijaya University*).
- DESSY A NINGSI, N., 2019. Faktor Yang Berhubungan Dengan Kejadian Infertilitas Di Poli Obgyn RSUD Dr. Soetomo Surabaya. (*Doctoral dissertation, Universitas Airlangga*).
- Yanti, D. A. & S. A., 2016. Faktor Determinant terjadinya Kanker Ovarium di Rumah Sakit Umum Daerah Abdoel Moelok Provinsi Lampung 2015. *E Journal UMM*.
- Fitria, S., 2016. Pengaruh sindrom polikistik ovarium terhadap peningkatan faktor risiko infertilitas. *Medical Journal of Lampung University*, 5(2).
- Putri, S. N., 2019. Hubungan Sedentary Lifestyle Dan Overweight Terhadap Risiko Sindroma Ovarium Polikistik Pada Siswa SMAN 5 Surabaya. (*Doctoral dissertation, UNIVERSITAS AIRLANGGA*).

- FADILAH, M. Z. E. F. & A. S., 2019. Hubungan Antara Komposisi Lemak Tubuh Dengan Risiko Kejadian Sindrom Ovarium Polikistik Pada Remaja Perempuan Usia 15-19 Tahun Di Kota Palembang. (*Doctoral dissertation, Sriwijaya University*).
- Indarwati, I. H. U. R. B. & D. Y. L. R., 2017. Analysis of factors influencing female infertility. *Journal of Maternal and Child Health*, 2(2), pp. 150-161.
- Yuliarfani, N. & N. N., 2022. Pengaruh Pekerjaan, Stres, Obesitas, dan Siklus Menstruasi dengan Kejadian Infertilitas pada Wanita. *JUMANTIK (Jurnal Ilmiah Penelitian Kesehatan)*, 7(1), pp. 21-31.
- Mulyani, U. S. D. & S. E. P., 2021. Faktor-Faktor Yang Berhubungan Dengan Infertilitas Primer Pada Pasangan Usia Subur Di Wilayah Kerja Uptd Puskesmas Lembak Kab. Muara Enim Tahun 2021. *NUSANTARA: Jurnal Ilmu Pengetahuan Sosial*, 8(8), pp. 2698-2710.
- Kazemi, M. H. A. P. R. A. L. M. E. Z. G. A. & C. P. D., 2021. Effects of dietary glycemic index and glycemic load on cardiometabolic and reproductive profiles in women with polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials. *Advances in Nutrition*, 12(1), pp. 161-178.
- Artimani, T. K. J. M. M. Y. M. K. E. G. M. .. & K. N., 2018. Evaluation of pro-oxidant-antioxidant balance (PAB) and its association with inflammatory cytokines in polycystic ovary syndrome (PCOS). *Gynecological endocrinology*, 34(2), pp. 148-152..
- Chen, W. & P. Y., 2021. Metabolic syndrome and PCOS: Pathogenesis and the role of metabolites. *Metabolites*, 11(2), p. 869.
- Palioura, E. K. E. & D.-K. E., 2014. Endocrine disruptors and polycystic ovary syndrome: a focus on Bisphenol A and its potential pathophysiological aspects. *Hormone Molecular Biology and Clinical Investigation*, 17(3), pp. 137-144.
- Papalou, O. & D.-K. E., 2017. The role of stress in PCOS. *Expert Review of Endocrinology & Metabolism*, 12(1), pp. 87-95.
- Moher, D. e. a., 2015. Preferred reporting items for systematic review and meta-analysis protocols. (*PRISMA-P*) 2015 statement, pp. 1-9.

