Journal of Advances and Scholarly Researches in Allied Education
Vol. 18, Issue No. 4, July-2021, ISSN 2230-7540

Metformin and Lifestyle Modification in Polycystic Ovary Syndrome: Systematic Review

Ranjeet Kumar[1]* Ammar Ahmad Khan[2] Somesh Yadav[3] Nagar Krunal Natvarlal[4] Mosim[5] Love Kumar[6]

Abstract – Polycystic ovarian syndrome (PCOS), a prevalent endocrine disease with reproductive and metabolic implications, causes anovulation, infertility, and a higher incidence of diabetes mellitus. Its aetiology is strongly linked to obesity, particularly central obesity, and insulin resistance. The primary treatment strategy is dietary weight loss; however, effective methods for achieving and maintaining weight loss, as well as reproductive and metabolic improvements, are unknown. Lifestyle modification programs focused on behavioral management and nutritional and exercise treatments have decreased the incidence of diabetes and metabolic syndrome in the general population, and have shown some early effectiveness in improving reproductive outcomes in polycystic ovarian syndrome patients. However, since there is a scarcity of research on successful food and exercise programs for polycystic ovarian syndrome, organized recommendations for adopting components of lifestyle modification programs in this group should be assessed.

Keywords – PCOS, Metformin, Lifestyle Modification, Systematic Review

----------X----------

INTRODUCTION

PCOS symptoms include insulin resistance, poor glucose tolerance, dyslipidemia, elevated androgen levels, ovulation failure, and infertility. Because PCOS is associated with insulin resistance, most women with the disease are at a greater risk of acquiring type 2 diabetes.

The Rotterdam criteria are globally recognized and utilized in the diagnosis of PCOS, which requires two of the three symptoms: excess androgens, ovulatory dysfunction, and polycystic ovarian morphology (created by the Australian PCOS Alliance and the US National Institutes of Health [NIH]). Insulin resistance, dyslipidemia, and type 2 diabetes are all important symptoms of metabolic disorders.

Metformin reduces insulin resistance in PCOS, therefore it's conceivable that it may aid in PCOS treatment when used in conjunction with lifestyle modifications.

Although the cause of PCOS is unknown, it is clear that it is a multifactorial disorder linked to biochemical abnormalities and a pro-inflammatory metabolic imbalance. Obesity and PCOS are linked, according to recent research, with obesity increasing the prevalence of PCOS and PCOS leading to weight gain and obesity. Weight loss improves menstrual function, fertility, pregnancy outcomes, and endocrine parameters, all of which are clinically beneficial. The effectiveness of LSM for PCOS, on the other hand, varies depending on the type of lifestyle management used and the characteristics of PCOS. Women with PCOS who are overweight or obese should benefit from LSM because it causes adiposity reduction and ovulation; however, it is unclear whether LSM is also effective in women with PCOS who are of normal weight.

To assess the effects of therapies in the management of PCOS, a systematic review is required. Efficacy of LSM and metformin for PCOS has been confirmed in several systematic reviews, with improvements in body weight, insulin resistance, hyperandrogenism, and ovulation. Although a previous systematic review compared the effects of LSM+metformin and LSM+placebo on PCOS, there were some errors, such as using baseline data instead of final result data18, resulting in a significant effect of metformin. The goal of this study was to evaluate the effects of LSM on PCOS, compare them to those of metformin, and see if the combination of LSM and metformin is more effective against PCOS than either of them alone.

METHODS:

This systematic Review looked at the effectiveness of lifestyle + metformin vs. lifestyle+placebo and metformin alone With the lifestyle+placebo in improving anthropometric, reproductive, metabolic, cardiovascular, and psychological outcomes in

women with PCOS. A diverse clinical research team, including an expert in evidence synthesis, finished it (M.L.M.).

- **Selection criteria**

Using the PICO (population, intervention, comparison, outcome) paradigm, all RCTs comparing lifestyle + metformin against lifestyle placebo, metformin alone versus lifestyle placebo for women of any age with PCOS were included.

The research covered PCOS diagnoses based on Rotterdam criteria (including NIH criteria) in women of any age, including adolescents, pre- and postmenopausal women, and with any BMI. Hypothyroidism, congenital adrenal hyperplasia, and Cushing's syndrome were eliminated, as were concurrent medication usage (e.g. OCPs, orlistat, clomiphene citrate, etc.), even though they were the identical across groups. Prescription multivitamins and folic acid supplements were approved throughout pregnancy. The interventions of interest were lifestyle plus metformin (at any dosage and for any period of time) or metformin alone.

Lifestyle modification was described as any time of nutrition, behavioral change (via education, counseling, cognitive therapy, or stress management), exercise, or a combination of these. My curiosity was aroused by the lifestyle vs. placebo comparison.

- **Search method**

The literature was searched up until August 2014, and only articles written in English were included.

- **Data sources**

To find relevant literature, researchers used the Ovid MEDLINE (since 1946), EMBASE (since 1980), Pubmed, Scopus, Cochrane, PsycINFO, CINAHL, NHMRC (clinical practice guidelines clearinghouse), Clinical Trials registry, and ANZCTR databases. Additional studies were found by searching bibliographies of relevant studies identified by the search strategy, as well as relevant reviews.

- **Study selection**

If the information provided suggested that the study met the inclusion criteria, full articles were retrieved for further review. The study was reviewed and discussed with other reviewers if there was any doubt about its inclusion (L.J.M. and H.J.T).

RESULTS:

Study selection

Study flow chart describe in Figure 1. 11 articles were identified as relevant for this study after a full-text review. By manually scanning relevant bibliographies, two additional papers were discovered, bringing the total number of publications included in the meta-analysis to thirteen.

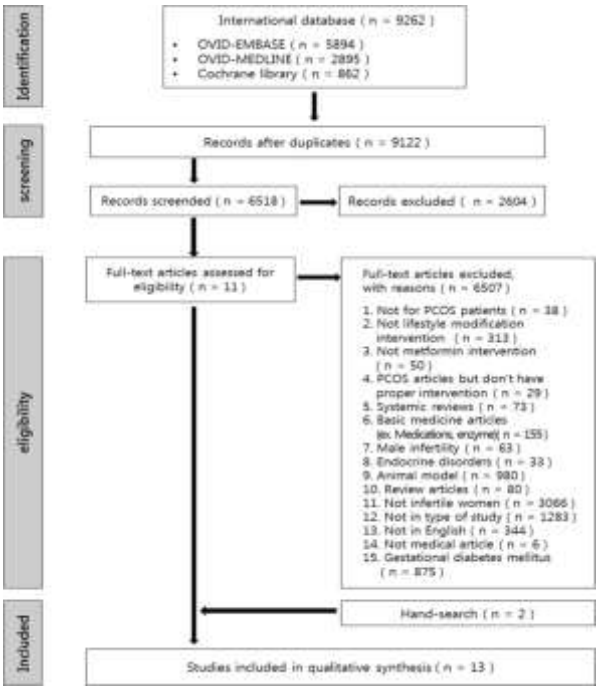
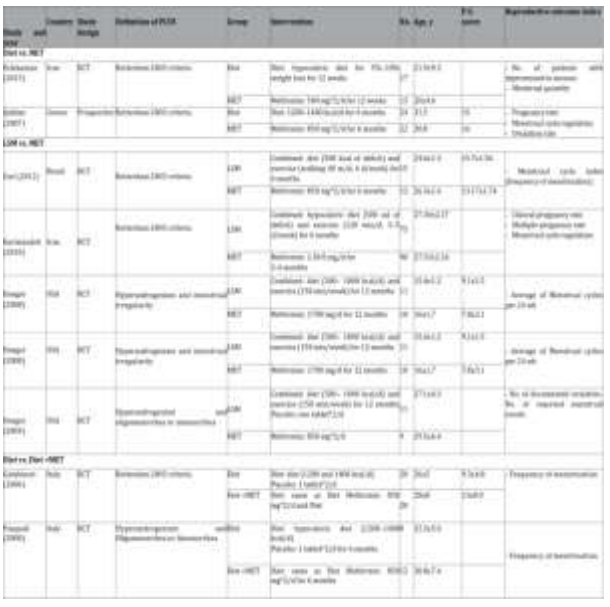


Figure 1: Study flow chart

The 13 studies, which included 11 randomized controlled trials (RCTs), one clinical trial, and one prospective study, are summarized in Table 1. Four studies from Europe, four studies from North America, two studies from South America, two studies from the Middle East, and one study from Africa were published between 2000 and 2018. Six studies compared LSM to metformin alone, eight studies compared LSM+metformin to LSM, and one study was included in both categories.

Table 1: Characteristics of the studies that was included



Here: BMI: body mass index, CO: control, Ex: exercise, F-G score: Ferriman-Gallwey score, LSM: lifestyle modifcation (diet+exercise), MET: metformin, No.: number of patients, OC: oral contraceptive pills, PCOS: polycystic ovary syndrome, RCT: randomized controlled trial, WHR: waist-hip ratio.

CONCLUSION:

Metformin is an important part of the treatment for PCOS. Metformin's effectiveness in overweight women with PCOS has yet to be determined. It is concluded that except in terms of serum testosterone levels, LSM has more benefits than metformin alone. When compared to LSM, the efficacy of LSM + metformin is limited to fasting serum insulin levels and menstrual cycles, and adding metformin to LSM had no significant benefits in lowering BMI. Based on these findings, we recommend carefully selecting the appropriate treatment while taking into account metformin's side effects. Before prescribing metformin to women with PCOS, LSM should be the primary recommendation if metformin is not indicated. To confirm the currently controversial benefits of LSM+ metformin and to clarify the therapeutic role of this combination against PCOS, a large-scale multicenter study is needed.

REFERENCES:

A. Gambineri, C. Pelusi, S. Genghini et. al. (2004). "Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome," *Clinical Endocrinology*, vol. 60, no. 2, pp. 241–249.

A. Gambineri, L. Patton, A. Vaccina et. al. (2006), "Treatment with flutamide, metformin, and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12-month, placebo-controlled study," *The Journal of Clinical Endocrinology & Metabolism*, vol. 91, no. 10, pp. 3970–3980.

Almenning I, Rieber-Mohn A, Lundgren KM, Shetelig Løvvik T, Garnæs KK, Moholdt T. (2015). Effects of high intensity interval training and strength training on metabolic, cardiovascular and hormonal outcomes in women with polycystic ovary syndrome: a pilot study. *PloS One*; 10(9): pp. e0138793.

Apovian CM, Aronne LJ, Bessesen DH, McDonnell ME, Murad MH, Pagotto U, Ryan DH, Still CD (2015). Pharmacological management of obesity: an endocrine society clinical practice guideline. J Clin Endocrinol Metab; 100: pp. 342– 362

Bailey CJ, Turner RC (1996). Metformin. N. Engl. J. Med.; 334: pp. 574– 579.

Batra A, Saxena P, Salhan S, Mittal P, Sharma M. (2009). Role of Metformin in the treatment of polycystic ovarian disease. Int J Gynecol Obstet; 107: pp. S121.

Brown AJ, Setji TL, Sanders LL, Lowry KP, Otvos JD, Kraus WE, et. al. (2009). Effects of exercise on lipoprotein particles in women with polycystic ovary syndrome. *Medicine and Sciences in Sports and Exercise*; 41(3): pp. 497-504.

Guzick DS, Wing R, Smith D, Berga SL, Winters SJ (1994). Endocrine consequences of weight loss in obese, hyperandrogenic, anovulatory women. *Fertility and Sterility*; 61(4): pp. 598-604.

Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS (2004). A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertility and Sterility*; 82(2): pp. 421-9.

Jedel E, Labrie F, Oden A, Holm G, Nilsson L, Janson PO, et. al. (2011). Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: a randomised controlled trial. *American Journal of Physiology-Endocrinology and Metabolism*; 300(1): pp. E37-45.

K. M. Hoeger, L. Kochman, N. Wixom, K. Craig, R. K. Miller, and D. S. Guzick (2004). "A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study," *Fertility and Sterility*, vol. 82, no. 2, pp. 421–429.

Ladson G, Dodson WC, Sweet SD, Archibong AE, Kunselman AR, Demers LM, Lee PA, Williams NI, Coney P, Legro RS (2011a). Effects of metformin in adolescents with polycystic ovary syndrome undertaking lifestyle therapy: a pilot randomized double-

blind study. Fertil Steril; 95: pp. 2595 – 2598.e2596.

M. A. Karimzadeh and M. Javedani (2010). "An assessment of lifestyle modification versus medical treatment with clomiphene citrate, metformin, and clomiphene citrate-metformin in patients with polycystic ovary syndrome," *Fertility and Sterility*, vol. 94, no. 1, pp. 216–220.

Mani H, Chudasama Y, Hadjiconstantinou M, Bodicoat DH, Edwardson C, Levy MJ, et. al. (2018). Structured education programme for women with polycystic ovary syndrome: a randomised controlled trial. *Endocrine Connections*; 7(1): pp. 26-35.

Moghetti P, Castello R, Negri C, Tosi F, Perrone F, Caputo M, Zanolin E, Muggeo M (2000). Metformin effects on clinical features, endocrine and metabolic profiles, and insulin sensitivity in polycystic ovary syndrome: a randomized, double-blind, placebo-controlled 6-month trial, followed by open, long-term clinical evaluation. J Clin Endocrinol Metab; 85: pp. 139– 146.

Pasquali R, Gambineri A, Biscotti D, Vicennati V, Gagliardi L, Colitta D, Fiorini S, Cognigni GE, Filicori M, Morselli-Labate AM (2000). Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in abdominally obese women with and without the polycystic ovary syndrome. J Clin Endocrinol Metab; 85: pp. 2767 –2774.

Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V (2006). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia; 49: pp. 289– 297.

S. Bonakdaran, Z. Mazloom Khorasani, B. Davachi, and J. Mazloom Khorasani (2012). "The effects of calcitriol on improvement of insulin resistance, ovulation and comparison with metformin therapy in PCOS patients: a randomized placebo- controlled clinical trial," *Iranian Journal of Reproductive Medicine*, vol. 10, no. 5, pp. 465–472.

Saremi A, Nader, Karmali M, Kazemi M (2013). Serum level of anti-mullerian hormone after exercise training in women with polycystic ovary syndrome: a randomised controlled trial. *Iranian Journal of Obstetrics, Gynecology and Infertility*; 16(64): pp. 10.

Turan V, Mutlu EK, Solmaz U, Ekin A, Tosun O, Tosun G, et. al. (2015). Benefits of short-term structured exercise in non-overweight women with polycystic ovary syndrome: a prospective randomised controlled study. *Journal of Physical Therapy Science*; 27(7): pp. 2293-7.

Vigorito C, Giallauria F, Palomba S, Cascella T, Manguso F, Lucci R, et. al. (2007). Beneficial effects of a three-month structured exercise training program on cardiopulmonary functional capacity in young women with polycystic ovary syndrome. *Journal of Clinical Endocrinology and Metabolism*; 92(4): pp. 1379-84.

Corresponding Author

Ranjeet Kumar*

ranjeetkumar2784@gmail.com