

# Comparative risk reduction of complications pertaining to polycystic ovarian syndrome by multiple treatment options

Darakhshan Masroor<sup>1</sup>, Sheikh Abdul Khaliq<sup>2\*</sup>, Syed Muzzammil Ahmad<sup>3</sup> and Nudrat Fatima<sup>4</sup>

<sup>1</sup>Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi, Pakistan

<sup>2</sup>Department of Pharmacy Practice & Pharmaceutics, Faculty of Pharmacy, Hamdard University, Karachi, Pakistan

<sup>3</sup>College of Pharmacy, Western University of Health Sciences, Pomona, California, USA

<sup>4</sup>Department of Pharmacognosy, Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan

**Abstract:** The aim of study was to find effective treatment option which reduces the risk of complications among patients of polycystic-ovarian-syndrome. A cross-sectional study was conducted from January-2019 to December-2019. Data was collected from 200 patients that have visited hospitals and clinics located in Karachi. A questionnaire was used in the survey. Collected data was analyzed with SPSS-22. Hormonal-imbalance ( $p=0.0001$ ), polycystic-ovaries ( $p=0.008$ ), irregular-menstruation ( $p=0.0001$ ), obesity ( $p=0.0001$ ), diabetes ( $p=0.0001$ ) and infertility ( $p=0.014$ ) significantly treated by allopathic-medications. Hormonal-imbalance ( $p=0.025$ ), polycystic-ovaries ( $p=0.0001$ ), irregular-menstruation ( $p=0.0001$ ), obesity ( $p=0.046$ ), diabetes ( $p=0.001$ ), acne ( $p=0.046$ ), anxiety ( $p=0.014$ ), depression ( $p=0.014$ ) and eating disorder ( $p=0.046$ ) significantly treated by homeopathic-medications. Polycystic-ovaries ( $p=0.0001$ ), irregular-menstruation ( $p=0.0001$ ), obesity ( $p=0.014$ ), diabetes ( $p=0.0001$ ) and acne ( $p=0.014$ ) significantly treated by herbal-medications. Allopathic treatment was found effective in reducing risk of complication associated with PCOS; hormonal-imbalance (59%), hirsutism (42%), obesity (89%), diabetes (90%), hypertension (17%), infertility (60%) and anxiety (75%). Risk reduction of complications by Homeopathic treatment; polycystic-ovaries (54%), irregular menstruation (91%) and depression (43%). Combination treatment was found effective in reducing the risk of acne (43%) and eating disorder (100%). Allopathic treatment is effective in reducing the majority of risks of complications and the complications of polycystic-ovaries-syndrome can be significantly controlled with the homeopathic mode of treatment.

**Keywords:** Polycystic ovaries, syndrome, complications, hormonal imbalance, risk reduction, treatment options.

## INTRODUCTION

The Polycystic Ovarian Syndrome (PCOS) is a female disorder that is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphologic features (Teede *et al.*, 2010). Women with PCOS may present one or more of the reproductive, metabolic or psychological complications (Gilbert *et al.*, 2018), such as hyperandrogenism, irregular menstruation, ovarian cysts, hirsutism, acne, diabetes, obesity, hypertension, depression and infertility (Sidra *et al.*, 2019). These complications can undoubtedly stigmatizing women, lower their quality of life and further increase the healthcare burden (Rodriguez-Paris *et al.*, 2019; Brutocao *et al.*, 2018). Studies have shown that 85% of PCOS patients have poor quality of life (Sidra *et al.*, 2019). Therefore, treatment should be symptom oriented with adequate follow up as well as can be adapted to the patient's changing circumstances, needs and expectations (Escobar-Morreale, 2018).

Advance research studies are now focusing on Complementary and Alternative Medicine (CAM) system of treatment and it is estimated that globally a large group

of population rely on CAM for the treatment of minor and major health disorders (Ernst, 2000). According to study, CAM is attaining the popularity in Pakistan and approximately half of the population prefers to use CAM for treating different ailments, where homeopathy, herbal and combination therapies are the most commonly chosen modes of intervention (Shaikh *et al.*, 2009). Traditionally, in Pakistan medicinal plants are splendidly used for the treatment of common ailments (Masroor *et al.*, 2020). It is reported that the dissatisfaction with conventional medicine increases the use of CAM (Sidra *et al.*, 2019). Similarly, for the management or treatment of polycystic ovarian syndrome, many women prefer complementary and alternative systems of treatment (Masroor *et al.*, 2020).

Till to date, any satisfactory study has not been conducted comparing the effectiveness of different systems of treatment for the management of PCOS and its complications (Masroor *et al.*, 2020). Therefore, the purpose of this study is to investigate the efficacy and determination of risk reduction of complications by various systems of medicine (allopathic, homeopathic, herbal and combination) that are commonly chosen by a large population of Pakistan for treatment of polycystic ovarian syndrome.

\*Corresponding author: e-mail: sheikh1974@gmail.com

## MATERIALS AND METHODS

This observational cross-sectional study was conducted in Karachi, Pakistan from January 2019 to December 2019. Precision analytical technique (Aparasu, 2011) was used to calculate the number of participants in the study. Minimum sample size of study was 198 patients. Patients with PCOS were recruited through outpatient clinics at multiple centers, hospitals, Private Homeopathic Clinic and Matabs of Herbal medicine practitioners (Hakeems). Women with PCOS (n = 200) were interviewed. For this purpose, a specially designed, validated and structured questionnaire entitled “Comparative Effectiveness of Treatments for PCOS” (CET-PCOS) was used to collect the data (Masroor *et al.*, 2020). The questionnaire was filled by communicating with the patients at out-patient clinics, Matabs or through social media forums.

### Inclusion criteria

Women that have been diagnosed with PCOS, in the age group of 18-45. Participants must meet the Rotterdam diagnostic criteria of PCOS (Escobar-Morreale, 2018), which defines PCOS by the presence of any two or all the three clinical features i.e. oligo/amenorrhea, hyperandrogenism and polycystic ovaries on ultrasound.

### Exclusion criteria

Females were excluded if they were not found to meet the above-mentioned criteria, suspects of PCOS, PCOS patients who were pregnant or breastfeeding, taking weight-loss medication.

The Institutional Bio-Ethical Committee (IBC) of University of Karachi approved the study design and method (Reference Number: IBC-KU 50). Prior to initiating the survey, an informed consent was obtained from each patient after explaining the research and its objectives. Patients were included only after they signed the informed consent. All researchers ensured patient data confidentiality and compliance with the Declaration of Helsinki (Shrestha & Dunn, 2020).

### Comparative effectiveness of treatments for PCOS questionnaire

A 40-items questionnaire entitled “Comparative Effectiveness of Treatments for PCOS” (CET-PCOS) was developed in which conventional and alternative therapies were compared in terms of patient’s satisfaction to calculate the ultimate outcomes of all therapies. The first section consisted of patient’s demographics. The second portion comprised of information regarding the patient’s PCOS diagnostic symptoms like hyperandrogenism, polycystic ovaries, irregular menstrual cycle and the associated complications or comorbidities of PCOS. Finally, the last portion was based on patient’s chosen system of treatment and outcome measures of these respective treatments.

### Limitations of study

Current study focused on different systems of medicines rather different drugs for the treatment and management of PCOS. Microanalysis of different drugs available in each treatment (Allopathic, homeopathic and herbal) requires additional studies. Complications reduction was the main endpoint of current study rather than efficacy parameters, which requires additional studies. There is a need to develop strong scientific evidence by carrying out clinical trials for homeopathic medicines to validate the findings of current study.

## STATISTICAL ANALYSIS

The data was processed on Statistical Package for Social Sciences (SPSS version 22) for statistical analysis. All data collected by surveying CET-PCOS questionnaire were recorded in a SPSS spreadsheet after coding and defining all the variables. Descriptive and inferential statistics were used to determine the association among PCOS complications- and therapy-related non-parametric variables and clinical outcomes using Wilcoxon Signed Rank test, a p-value of <0.05 indicates statistical significance.

## RESULTS

In total, 200 patients; 96 (48%) preferred allopathic, 42 (21%) preferred homeopathic, 51 (25.5%) preferred herbal and 11 (5.5%) preferred combination mode of intervention (fig. 1).

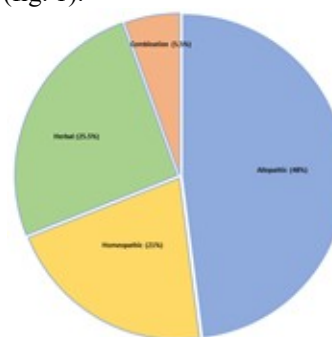


Fig. 1: Pie chart showing PCOS patient’s choice for treatment modes.

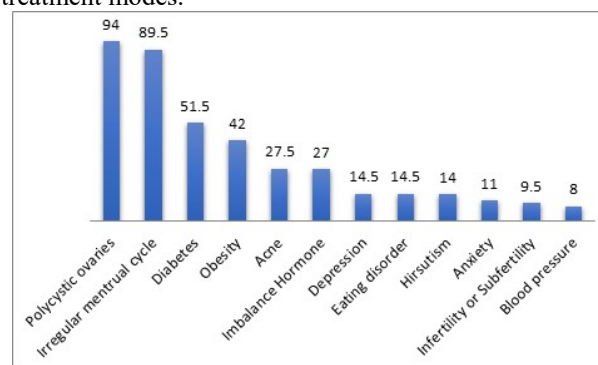


Fig. 2: Bar graph showing the percentage of complications among PCOS patients.

**Table 1:** Diagnostic characteristics of patients on basis of Rotterdam criteria

Category	Sign and symptoms	Frequency n (%)	
1	Elevated level of hormone 'androgen' or 'testosterone' & Polycystic Ovaries on ultrasound	Yes	26 (13)
		No	174 (87)
2	Elevated level of hormone 'androgen' or 'testosterone' & Infrequent menstruation	Yes	12 (6)
		No	188 (94)
3	Polycystic Ovaries on ultrasound & Infrequent menstruation	Yes	146 (73)
		No	54 (27)
4	Elevated level of hormone 'androgen' or 'testosterone' & Polycystic Ovaries on ultrasound & Infrequent menstruation	Yes	16 (8)
		No	184 (92)

**Table 2:** Represents the improvement in different symptoms and complications of PCOS by different modes of intervention.

PCOS symptoms & complications	Mode of Intervention			
	Allopathic	Homeopathic	Herbal	Combination
Imbalance hormone	0.0001*	0.025*	0.083	0.317
Polycystic ovaries	0.008*	0.0001*	0.0001*	0.025*
Irregular menstrual cycle	0.0001*	0.0001*	0.0001*	0.008*
Hirsutism	0.083	0.083	0.157	-
Obesity	0.0001*	0.046*	0.014*	0.157
Diabetes	0.0001*	0.001*	0.0001*	0.083
Hypertension	0.157	1.00	-	-
Acne	0.157	0.046*	0.014*	0.083
Infertility or subfertility	0.014*	0.083	0.317	1.00
Anxiety	0.083	0.014*	0.083	-
Depression	1.00	0.014*	1.00	-
Eating disorder	0.083	0.046*	0.157	-

Wilcoxon Signed Ranks Test, \*Significant ( $p < 0.05$ ), Insignificant ( $p \geq 0.05$ )

In the collected data of 200 patients, more than half i.e. 146 patients were diagnosed with the presence of polycystic ovaries & irregular menstruation, 26 patients with imbalance of hormone and polycystic ovaries, 16 patients with all the three conditions and 12 patients with imbalance of hormone and irregular menstruation (table 1). These symptoms further cause various complications such as hirsutism were found in 14% of patients and acne in 27.5% of patients, the endocrinological disorders; obesity in 42% diabetes in 51.5% and hypertension in 8% of patients, the reproductive disorder; infertility or subfertility are reported by 9.5% of women. The psychological complications 11% reported anxiety while depression and eating disorder were reported by 14.5% of patients (fig. 2). Most of complications and symptoms pertaining to PCOS were significantly ( $p < 0.05$ ) improved by Homeopathic treatment, which is then followed by Allopathic, Herbal and Combination treatments (table 2).

## DISCUSSION

A polycystic ovary syndrome (PCOS) patient presents with various serious complications and if left untreated may exacerbate the syndrome. Moreover, in long term, they reduce the quality of life of the patient (Sidra *et al.*, 2019). The biochemical hyperandrogenism is one of

major factor behind PCOS which is characterized by the imbalance of hormone or elevated level of hormones; the androgen or the testosterone (Rosenfield & Ehrmann, 2016). Hyperandrogenism is one of the prevalent cardinal symptoms of PCOS (table 1). Current study reveals that allopathic ( $p = 0.0001$ ) and homeopathic ( $p = 0.025$ ) treatments are found to be effective in significantly improving the condition of hormonal imbalance. In addition to this, herbal ( $p = 0.083$ ) and combination ( $p = 0.317$ ) treatments were found insignificant in balancing the hormonal disturbance (table 2). The results of allopathic mode of treatment on imbalance of hormone are supported by a number of studies.

These studies demonstrated the use of combined oral contraceptives as well as metformin for the noticeable decline in the androgenic parameters ( $p < 0.001$ - $p < 0.01$ ) (Zahra *et al.*, 2016) (Moggetti, 2000) (Amiri *et al.*, 2020). Similarly, in homeopathy, Thujaoccidentalis has been used to rectify the hormonal aggravation (Sawant *et al.*, 2017). It is a common believe that homeopathic mode of treatment cure the condition without the any potential danger of adverse effects (Malvekar *et al.*, 2020), however, enough scientific evidences are not available to support this phenomenon. Since PCOS majorly depend on hormonal level of a patient (Rosenfield & Ehrmann,

Table 3: represents the risk reduction of complications with each treatment options.

Complications Associated with PCOS	Allopathic			Homeopathic			Herbal			Combination		
	Before Treatment (%)	After Treatment (%)	Risk Reduction (%)	Before Treatment (%)	After Treatment (%)	Risk Reduction (%)	Before Treatment (%)	After Treatment (%)	Risk Reduction (%)	Before Treatment (%)	After Treatment (%)	Risk Reduction (%)
Imbalance hormone	28	11.5	59%	35.7	23.8	33%	19.6	13.7	30%	18.2	9.1	50%
Polycystic ovaries	92.7	85.4	08%	92.9	42.8	54%	96.1	49.0	49%	100	54.5	46%
Irregular menstrual cycle	93.8	41.7	56%	81	7.1	91%	90.1	17.6	80%	81.2	18.2	78%
Hirsutism	7.3	4.2	42%	21.4	14.2	34%	21.6	17.6	19%	9.1	9.1	00%
Obesity	27.1	3.1	89%	52.4	42.9	18%	58.8	47.1	20%	54.5	36.4	33%
Diabetes	51	5.2	90%	59.5	40	33%	43.1	17.6	59%	63.6	36.4	43%
Hypertension	12.5	10.4	17%	4.8	4.8	00%	-	-	-	9.1	9.1	00%
Acne	24	21.9	9%	33.3	23.8	29%	27.5	15.7	43%	36.4	9.1	75%
Infertility or subfertility	10.4	4.2	60%	9.5	7.14	25%	5.9	3.9	34%	81.2	81.2	00%
Anxiety	4.2	1.04	75%	31	16.7	46%	9.8	3.9	60%	-	-	-
Depression	11.5	11.5	00%	33.3	19.1	43%	5.9	5.9	00%	9.1	9.1	00%
Eating disorder	12.5	9.4	25%	23.8	14.3	40%	11.8	7.8	34%	9.1	00	100%

2016), allopathic and homeopathic treatment can be considered as best option for treatment of PCOS.

However, here allopathic treatment proved best mode of treatment among all treatments by reducing the risk of hormonal imbalance up to 59%, followed by combination 50%, homeopathic 33% and herbal 30%. Combination treatment results are not considerable due to its very small sample size (table 3).

Concerning the hirsutism, it has been found that it is the only PCOS complication i.e. very difficult to treat with all the four types of interventions; allopathic (p=0.083), homeopathic (p=0.083) and herbal (p=0.157) treatments showed non-significant improvement in the condition of hirsutism (table 2). Present study showed that the allopathic and homeopathic treatments are ineffective in improving the condition of hirsutism despite significantly rectifying the condition of biochemical hyperandrogenism. The root cause of this discrepancy is unclear but we cannot ignore the fact that in hirsutism, a long-term treatment is necessary (Szilagyi *et al.*, 2000). A meta-analysis of 35 clinical trials states, treatment period of at least 6 to 12 months has a therapeutic influence on hirsutism (Amiri *et al.*, 2018). Interestingly, it is noticed in current study that risk of development of hirsutism was found markedly reduced by 42% with allopathic treatment, followed by the homeopathic 34% and herbal 19% treatments (table 3).

Another complication pertaining to PCOS is acne, homeopathic (p=0.046) and herbal (p=0.014) therapies were found significantly effective modes of treatment for acne. [table 2] Another clinical study of homeopathic medicine in PCOS patients also reported a significant improvement in complaints of acne (Malvekar *et al.*, 2020). Similarly, several randomized control trial on topical herbal medicines also found an effective mode of treatment (p < 0.05) (Sung *et al.*, 2020). Although, studies have reported efficacy of several topical and systemic anti-acne agents in allopathic system of medicines e.g., Benzoyl peroxide, combined oral contraceptives such as norgestimate, drospirenone (Oge *et al.*, 2019), but, in current study allopathic and combination treatments results were not found significant. Though the combination treatment reduced the risk of acne to 75% but due to small sample size results are inconclusive, so only herbal and homeopathic treatments with risk reduction values of 43% and 19% respectively are considered as effective treatments in acne (table 3)

The polycystic ovaries and the irregular menstruation have been found as the most prevalent complication in PCOS women (fig. 2). Clinical importance of these complications are very high, as they are considered as the major symptom in diagnosis of PCOS (table 1). It is found that irregular menstrual cycle significantly

controlled by all types of interventions; allopathic ( $p=0.0001$ ), homeopathic ( $p=0.0001$ ), herbal ( $p=0.0001$ ) and combination ( $p=0.008$ ) (table 2). In this condition, prescribing combined oral contraceptives is a common practice in allopathic treatment, however its use is attributed to the major risk of thromboembolism (Witchel *et al.*, 2019). Findings of current study regarding homeopathic and herbal therapy in restoring menses normalcy are supported by several previous studies, literatures have reported efficacy of homeopathic medicines e.g. Sepia, Pulsatilla, Calcarea carb, Natrum mur and Thujaoccidentalis and herbs e.g. Cinnamon species, Vitex agnus- castus, Foeniculum vulgare Mill., and Linum usitatissimum L. with fewer or no adverse effects (Sawant *et al.*, 2015), (Jazani *et al.*, 2019). As far as concerned with the risk reduction of irregular menstrual cycle in each treatment option, 91% reduction in risk was noted with homeopathic treatment, while other treatments also reduce the risk by 80% and 76% in herbal and combination treatments respectively. Lowest risk reduction was observed in allopathic treatment i.e. 56% (table 3).

In allopathy, combined oral contraceptives and an insulin sensitizer metformin are commonly prescribed for successful management of polycystic ovaries (Witchel *et al.*, 2019). This might be the reason of significant reduction of polycystic ovaries by allopathic ( $p=0.008$ ) treatment, although results are statistically significant, however, clinically insignificant. Zahra *et al.*, and Moghetti *et al.*, reported the similar discrepancy in clinical and statistical outcomes of metformin on PCOS. Other therapies; homeopathic ( $p=0.0001$ ), herbal ( $p=0.0001$ ) and combination ( $p=0.025$ ) showed significant results. In a recent observational study of Gupta *et al.*, it is also reported significant improvement in condition of cystic ovaries ( $p<0.001$ ) by homeopathic medicines. In homeopathic system of medicines; Thujaoccidentalis, Oophorinum and Sepia are commonly used for cystic ovaries (Bhadoriya & Jain, 2020). Similarly, herbal medicines; Foeniculum vulgare Mill., Linum usitatissimum L., Matricaria chamomilla L. and Trigonella foenumgraecum L. are reported as helpful in treating ovarian cysts (Hosseinkhani *et al.*, 2018). Although combination treatment showed significant results in treating the complications like polycystic ovaries ( $p=0.025$ ) and irregular menstrual cycle ( $p=0.008$ ) but because of its small sample size, it does not clinically signify the findings. Considering the risk reduction values, again the homeopathic (54%) treatment found as the most effective therapy in comparison to herbal (49%), combination (46%) and allopathic (8%) (table 3).

Women with PCOS are at an increased risk of type 2 diabetes. The incidence of type 2 diabetes increases substantially with increasing obesity (Kakoly *et al.*, 2018). The results of current study are significant to

correct the complication of diabetes and obesity in PCOS patients. It is observed that allopathic ( $p=0.0001$ ), homeopathic ( $p=0.001$ ) and herbal ( $p=0.0001$ ) mode of treatment significantly improved the glycemic control, while obesity is also significantly reduced by allopathic ( $p=0.0001$ ), homeopathy ( $p=0.046$ ), herbal ( $p=0.014$ ) treatments (table 2). Although in the present study homeopathic medicines for PCOS have been found effective in managing blood glucose level as well as obesity, but unfortunately, to endorse these results very limited scientific evidences are available. However, in herbal mode of treatment several herbs alone or in combination are reported to have anti-hyperglycemic effects while some have laboratory and clinical evidences in reducing body weight as well (Hosseinkhani *et al.*, 2018). However, whatever the literature is mentioning, it is noted in current study that risk reduction obesity and diabetes are significant by allopathic treatment i.e. 89% and 90% respectively (table 3).

It is observed that complication of hypertension has been untreated with all the mode of treatments. Risk reduction of hypertension by allopathic treatment was only 17%. We cannot overlook this fact that hypertension in women with PCOS may contribute to the increased risk of cardiovascular disease. Treatment of the risk factors inherent to PCOS, such as hyperandrogenism, insulin resistance, and obesity may minimize the risk of the development of hypertension (Bentley-Lewis *et al.*, 2011).

Infertility is another major complication of PCOS, the only treatment which significantly reduced this complication is allopathic ( $p=0.014$ ) with risk reduction by 60%. [table 2, table 3]. Several evidences emphasized life style modification to increased pregnancy rate or with the use of medications like clomiphene citrate, letrozole and dexamethasone alone or in combinations to improve live birth rates in different types of infertility associated with PCOS (Ecklund & Usadi, 2015). It is noticeable that in this study homeopathy is clinically effectively in treating most of the complications of PCOS but failed to give statistical significance in treating infertility ( $p=0.083$ ), while in some studies, positive and satisfactory results are noted in reducing the complication of infertility (Rath, 2020) (Rath & Gautam, 2021). Herbal treatment reduces the risk of infertility by 34% and homeopathic by 25% in current study (table 3).

A large amount of literature have shown that women with PCOS experience a decreased health-related quality of life and have shown higher rates of anxiety and depression (Brutocao *et al.*, 2018). Similarly, women with PCOS have been reported to have a higher prevalence of eating disorders compared to women without PCOS (Pirota *et al.*, 2019). Interestingly, depression ( $p=0.014$ ) and anxiety ( $p=0.014$ ) have been

better managed only by homeopathic treatment (table 2). This might be due to the fewer or mild adverse events associated with the homeopathic mode of therapy. Allopathic treatment results in treating the anxiety were not significant but it has markedly reduced the risk of anxiety by 75% followed by herbal treatment 60%. It is interesting that despite significant reduction of depression by homeopathic treatment, risk reduction was lowest i.e. 43% compare to allopathic and herbal treatment (table 3).

Homeopathic therapy was also found to have significant effect on improving eating disorder or eating behavior ( $p=0.046$ ) in PCOS women (table 2). The betterment in this complication is also noted in another study in which 34 patients were treated with the homeopathic medicine Antimonium crudum and showed similar effects, effects are also similar with commonly prescribed PCOS medicine Pulsatilla, Sepia or Natrum muriaticum (Sarembaud, 2018). However, in the evaluation of data of risk reduction of eating disorder, it is observed that combination treatment was most effective in reducing risk of eating disorder by 100%, however, due to its insufficient sample size, it is not conclusive that combination treatment is best. Therefore, homeopathic (40%) and herbal (34%) treatments should be considered most effective system of treatments in reducing risks of eating disorder (table 3).

## CONCLUSION

In this cross-sectional observational study, the alternative mode of treatments i.e., homeopathic and herbal therapy has been preferred by majority of PCOS women. It seems that homeopathic treatment is best among all by significantly controlling the most of the complications associated with PCOS, however, risk of majority of complications are reduced by allopathic treatment. There is a need to develop strong scientific evidence by carrying out clinical trials for homeopathic medicines to validate the findings of current study.

## REFERENCES

- Amiri M, Kabir A, Nahidi F, Shekofteh M and Tehrani FR (2018). Effects of combined oral contraceptives on the clinical and biochemical parameters of hyperandrogenism in patients with polycystic ovary syndrome: A systematic review and meta-analysis. *Eur. J. Contracept. Reprod. Health Care*, **23**(1): 64-77.
- Amiri M, Nahidi F, Bidhendi-Yarandi R, Khalili D, Tohidi M and Tehrani FR (2020). A comparison of the effects of oral contraceptives on the clinical and biochemical manifestations of polycystic ovary syndrome: A crossover randomized controlled trial. *Hum. Reprod*, **35**(1): 175-186.
- Aparasu RR (2011). Sampling methods; Chapter 107. In Research methods for pharmaceutical practice and policy. London: Pharmaceutical Press, pp.107-124.
- Bentley-Lewis R, Seely E and Dunaif A (2011). Ovarian hypertension: Polycystic ovary syndrome. *Endocrinol. Metab. Clin. North Am.*, **40**(2): 433-449.
- Bhadoriya Y and Jain A (2020). Polycystic ovarian syndrome and management through alternative approaches W.S.R. to Homeopathy. *Eur. J. Biomed. Pharm. Sci.*, **7**(6): 321-324.
- Brutocao C, Zaiem F, Alsawas M, Morrow AS, Murad MH and Javed A (2018). Psychiatric disorders in women with polycystic ovary syndrome: A systematic review and meta-analysis. *Endocr.*, **62**(2): 318-325.
- Ecklund LC and Usadi RS (2015). Endocrine and reproductive effects of polycystic ovarian syndrome. *Obstet. Gynecol. Clin.*, **42**(1): 55-65.
- Ernst E (2000). The role of Complementary and Alternative Medicine. *BMJ*, **321**(7269): 1133-1135.
- Escobar-Morreale HF (2018). Polycystic ovary syndrome: Definition, aetiology, diagnosis and treatment. *Nat. Rev. Endocrinol.*, **14**(5): 270-284.
- Gilbert EW, Tay CT, Hiam DS, Teede HJ and Moran LJ (2018). Comorbidities and complications of polycystic ovary syndrome: An overview of systematic reviews. *Clin. Endocrinol.*, **89**(6): 683-699.
- Gupta G, Gupta N, Singh S, Roja V and Dewan D (2021). Homoeopathic treatment of women with polycystic ovarian syndrome: A prospective observational study. *Indian J. Res. Homoeopathy*, **15**(1):12.
- Hosseinkhani A, Asadi N, Pasalar M and Zarshenas MM (2018). Traditional Persian medicine and management of metabolic dysfunction in polycystic ovary syndrome. *J. Tradit. Complement. Med.*, **8**(1): 17-23.
- Jazani AM, Azgomi HND, Azgomi AND and Azgomi RND (2019). A comprehensive review of clinical studies with herbal medicine on polycystic ovary syndrome (PCOS). *Daru, J. Pharm. Sci.*, **27**(2): 863-877.
- Kakoly NS, Earnest A, Teede HJ, Moran LJ and Joham AE (2018). The impact of obesity on incidence of type 2 diabetes mellitus (T2DM) among women with polycystic ovary syndrome (PCOS). *Diabetes Care*, **42**(4): 560-567.
- Malvekar PA, Nadgauda SS and Jadhav AB (2020). A clinical study to see the effect of homoeopathic medicines in polycystic ovarian syndrome of reproductive age group between 12-45 years. *Int. J. Health Sci.*, **10**(3): 43-47.
- Masroor D, Khaliq SA, Azhar I and Ahmad SM (2020). Development and validation of questionnaire to compare treatment options of polycystic ovarian syndrome. *J. Int. Res. Med. Pharm. Sci.*, **15**(1): 1-3.
- Moggetti P (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**(1): 139-146.

- Oge LK, Broussard A and Marshall M (2019). Physician Health & Well-being Conference. *In: Naples, FL: American Family Physician*, pp.475-484.
- Pirotta S, Barillaro M, Brennan L, Grassi A, Jeanes YM, Joham AE, Kulkarni J, Couch LM, Lim SS and Moran LJ (2019). Disordered eating behaviours and eating disorders in women in Australia with and without polycystic ovary syndrome: A cross-sectional study. *J. Clin. Med.*, **8**(10): 1682.
- Rath P and Gautam S (2021). Homoeopathic Management in a Case of Infertility with PCOS. *Homæo. Links.*, **34**(2): 148-152.
- Rath P (2020). A case of infertility with to PCOS treated successfully with homoeopathy. *Int. J. Hom. Sci.*, **4**(2): 249-260.
- Rodriguez-Paris D, Remlinger-Molenda A, Kurzawa R, Głowska A, Spaczyński R, Rybakowski F, Pawełczyk L and Banaszewska B (2019). The occurrence of psychiatric disorders in women with polycystic ovary syndrome. *Psychiatr Pol.*, **53**(4): 955-966.
- Rosenfield RL and Ehrmann DA (2016). The pathogenesis of polycystic ovary syndrome (PCOS): The hypothesis of PCOS as functional ovarian hyperandrogenism revisited. *Endocr. Rev.*, **37**(5): 467-520.
- Sarembaud A (2018). Is the homeopathic medicine Antimonium Crudum a suitable answer to bulimia? *Rev. Homeopath.*, **9**(3): 31-33.
- Sawant A, Patil S and Shah S (2017). Review on PCOD/PCOS & its treatment in different medicinal systems allopathy, ayurveda, homeopathy. *Sci. Jurno*, **1**(1): 1-16.
- Shaikh SH, Malik F, James H and Abdul H (2009). Trends in the use of complementary and alternative medicine in Pakistan: A population-based survey. *J. Altern. Complement. Med.*, **15**(5): 545-550.
- Shrestha B and Dunn L (2020). The declaration of helsinki on medical research involving human subjects: A review of seventh revision. *J. Nepal Health Res. Counc.*, **17**(4): 548-552.
- Sidra S, Tariq MH, Farrukh MJ and Mohsin M (2019). Evaluation of clinical manifestations, health risks and quality of life among women with polycystic ovary syndrome. *PlosOne.*, **14**(10): 1-17.
- Sung SH, Choi GH, Lee NW and Shin BC (2020). External application of herbal medicines for acne vulgaris: A systematic review and meta-analysis. *J. Pharmacopunct.*, **23**(1): 8-17.
- Szilagyi A, Homoki J, Bellyei S and Szabo I (2000). Hormonal and clinical effects of chronic gonadotropin-releasing hormone agonist treatment in polycystic ovary syndrome. *Gynecol. Endocrinol.*, **14**(5): 337-341.
- Teede H, Deeks A and Moran L (2010). Polycystic ovary syndrome: A complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. *BMC Med.*, **8**(1): 1-10.
- Witchel SF, Oberfield SE and Pena AS (2019). Polycystic ovary syndrome: Pathophysiology, presentation and treatment with emphasis on adolescent girls. *J. Endocr. Soc.*, **3**(8): 1545-1573.
- Zahra M, Shah M, Ali A and Rahim R (2016). Effects of metformin on endocrine and metabolic parameters in patients with polycystic ovary syndrome. *Horm. Metab. Res.*, **49**(02): 103-108.