Zygote

cambridge.org/zyg

Research Article

Cite this article: Kamardi S *et al*. (2021) Impact of body mass index on intracytoplasmic sperm injection in women with polycystic ovary syndrome. *Zygote*. **29**: 229–233. doi: 10.1017/S0967199420000830

Received: 12 September 2020
Revised: 15 November 2020
Accepted: 5 December 2020
First published online: 18 January 2021

Keywords:
BMI; Embryo quality; Oocyte quality; Ovarian response; Polycystic ovary syndrome (PCOS); Success rates

Author for correspondence:
Jaqueline Sudiman. Bali Royal Hospital, Royal IVF Clinic, Denpasar-Bali, Indonesia.
E-mail: j_sudiman@yahoo.com; jaqueline@unud.ac.id

Impact of body mass index on intracytoplasmic sperm injection in women with polycystic ovary syndrome

Stanly Kamardi[1], IGN Harry Wijaya Surya[1], I Nyoman Bayu Mahendra[1], IB Putra Adnyana[1,2], Anom Suardika[1,2], Nono Tondohusodo[1,2] and Jaqueline Sudiman[2,3]

[1]Obstetrics and Gynaecology Department, Faculty of Medicine, Udayana University, Denpasar-Bali, Indonesia; [2]Bali Royal Hospital, Royal IVF Clinic, Denpasar-Bali, Indonesia and [3]Anatomy Department, Faculty of Medicine, Udayana University, Denpasar-Bali, Indonesia

Summary

Polycystic ovary syndrome (PCOS) is a condition that affects fertility. There are two types of PCOS; the normal/lean type and overweight/obese type. The aim of this study was to assess baseline characteristics, ovarian response, quality of oocytes, embryos, pregnancy, implantation and live birth rates in normal/lean and overweight/obese patients with PCOS undergoing ICSI compared with patients without PCOS. This retrospective case–control analytical study included 38 normal/lean and 17 overweight/obese patients with PCOS, and 98 normal/lean and 17 overweight/obese patients without PCOS. Parameters were observed based on baseline characteristics, ovarian response to dosage and duration of gonadotropin administered, number of oocytes, matured oocytes, fertilization rate, embryo quality and development, pregnancy, implantation and live birth rates. Basal serum luteinizing hormone in normal/lean PCOS was significantly higher compared with non-PCOS groups. Total dosage of gonadotropin used was significantly lower in normal/lean PCOS compared with other groups. End estradiol levels in normal/lean PCOS was significantly higher compared with the non-PCOS groups. Number of follicles, retrieved oocytes and matured oocytes were significantly higher in PCOS groups compared with the non-PCOS groups. However, there were no differences in fertilized oocytes, cleavage, number of top-quality embryos, pregnancy, implantation, and live birth rates among groups. This present study suggests that normal/lean PCOS requires lower gonadotropin dosages and that patients with PCOS have more follicles and oocytes compared with patients without PCOS, however the number of fertilized oocytes and embryos from patients with PCOS were the same as those from patients without PCOS and suggested that the quality of retrieved oocytes in PCOS might be compromised.

Introduction

Polycystic ovary syndrome (PCOS) is a condition that affects fertility in women. It is an endocrine and metabolic disorder that is defined based on the Rotterdam criteria and includes two out of the following three signs; oligo- and/or anovulation, clinical and/or biochemical indications of hyperandrogenism, and polycystic ovaries. PCOS occurs in 6–10% of reproductive women and accounts for nearly 70% of infertility cases (Barbosa *et al*., 2016).

The pathophysiology of PCOS can be explained based on the condition of gonadotropin hormone, insulin resistance, and sex-hormone binding globulin (SHBG). Based on the condition of the gonadotropin hormone, Patients with PCOS experience impaired secretion of gonadotropin-releasing hormone (GnRH). This results in an increase in the ratio of the serum concentration of luteinizing hormone (LH) compared with follicle stimulating hormone (FSH), which triggers oligo-ovulation/anovulation. LH plays a role in androgen production in ovarian theca cells, whereas FSH plays a role in the aromatization of androgens to estradiol in granulosa cells. In patients with PCOS, high LH levels cause an increase in intra-follicular androgen levels and trigger follicular atresia, resulting in anovulatory conditions. In addition, there can be increased levels of free androgens in the blood causing symptoms of acne and hirsutism. The condition of insulin resistance in POCS triggers an increase in androgen production due to stimulation of LH in the ovary, it inhibits SHBG secretion in the liver, increases production of androgens in the adrenal glands, and triggers obesity (Wilson, 2008). Approximately half of the patients with PCOS are also obese or overweight (Fauser *et al*., 2012). Obesity worsens the cardiometabolic condition in PCOS and triggers ovulation dysfunction, decreases implantation and pregnancy rates, increases miscarriage rates, and increases maternal and fetal complications (Wilson, 2008; Kini, 2012; McCartney and Marshall, 2016). Moreover, it has been reported that obesity also decreases the quality of oocytes, embryos, and pregnancy rates, in patients with PCOS and women who did not have PCOS (Dokras *et al.*, 2006; Bu *et al.*, 2013; Bailey *et al.*, 2014; Huang *et al.*, 2014; Kalem *et al.*, 2016; Wang *et al.*, 2016; Rehman *et al.*, 2018).

First-line infertility therapy for PCOS is lifestyle intervention or ovulation induction therapy with drugs such as clomiphene citrate and/or metformin. Laparoscopic ovarian drilling or gonadotropin stimulation are the second-line therapies, and *in vitro* fertilization (IVF) is a third line therapy when there is no response to medical treatment (Bergh *et al.*, 2016; Teede *et al.*, 2018). It has been reported that obese women with PCOS require higher FSH dosages, have an increased likelihood of cycle cancellation, lower numbers of retrieved and matured oocytes, and decreased pregnancy rates compared with normal/lean patients with PCOS (Fedorcsak *et al.*, 2001; Mulders *et al.*, 2003). However, some studies have also shown there was no statistical difference regarding clinical pregnancy between normal/lean and obese type of PCOS (McCormick *et al.*, 2008; Kalem *et al.*, 2016). There is still debate about whether PCOS compromises the quality of oocytes, and due to the contradictions among researchers about how weight affects patients with PCOS differently in oocyte and embryo qualities, and the success rate of IVF, we need to explore this field deeper.

Indicators of IVF success can be observed by the number of retrieved oocytes, quality of matured oocytes and embryos, pregnancy rates, miscarriage status, and live birth rates (American College of Obstetricians and Gynecologists, 1998; Beydoun *et al.*, 2009). The aim of this study was to compare the effect of normal/lean weight women with PCOS with overweight/obese women with PCOS on an ICSI performance. We also aimed to gain further insights into how body mass index (BMI) in PCOS affected the dose and length of hormonal stimulation in IVF.

Materials and methods

We conducted this retrospective case–control study at the Royal IVF Clinic, Bali Royal Hospital, Indonesia. We used secondary data from medical records of all patients who matched our criteria and had undergone intracytoplasmic sperm injection (ICSI) treatment between 2015 and 2018. This research was approved by the local ethics committee of Udayana University (156/UN14.2.2. VII.14/LP/2019).

Data from 170 patients under the age of 38 years old and who had undergone ICSI were collected. The inclusion criteria were patients who had been diagnosed with PCOS in accordance with the diagnostic criteria of the Rotterdam consensus. Based on these criteria, patients with PCOS were selected who had two out of the three following criteria; anovulation (absence of vaginal bleeding for at least 6 months) or oligomenorrhea (interval menstrual period between ≥35 days and < 6 months), hyperandrogenism such as acne and hirsutism, and polycystic ovaries identified by ultrasound examination. Patients who had tubal occlusion based on hysterosalpingographic or laparoscopic examination, or infertile due to male infertility, were included in this study as control groups. Patients with endometriosis, poor hormonal responses, with any other causes of infertility, or aged above 38 years old were excluded from this study. We used ICSI in all groups to eliminate any bias of male infertility, we controlled selection bias using the inclusion and exclusion criteria. Confounding bias was controlled by design, matching the case and control groups in age, number of cycles, and type and duration of infertility. In total, 55 patients with PCOS and 115 patients without PCOS were selected for this study and these were then divided into two groups, each based on their BMI. BMI was calculated using the formula: weight (kg)/height (m^2). Patients were classified as normal/lean with a BMI value between 18.5 and 24.9 kg/m^2, and overweight/obese with a BMI value ≥25 kg/m^2 (Purnell, 2008).

The resulting four groups consisted of 38 normal/lean patients with PCOS (group A), 17 overweight/obese patients with PCOS (group B), 98 normal/lean patients without PCOS (group C), and 17 overweight/obese patients without PCOS (group D).

In all patients, controlled ovarian hyperstimulation was performed using short antagonist protocols. Briefly, patients were administrated recombinant FSH (rFSH, Gonal F, Serono) based on age and follicle size. Ovulation stimulation was triggered using human chorionic gonadotropin (hCG, Pregnyl; Organon, Brussels, Belgium). At 2 h after oocyte retrieval, oocytes were denuded and all matured oocytes were inseminated by ICSI. All fertilized oocytes were cultured for 3 days in culture medium (G1, VitroLife). Two or three embryos were transferred on day 3 of culture.

The first parameters that we evaluated in this study were baseline characteristics (FSH, LH, prolactin and estradiol hormone levels), total rFSH dosage was used, the length of ovulation induction, endometrial thickness on the day of hCG administration, level of estradiol on last evaluation, number of follicles, number of oocytes retrieved, number of matured oocytes, number of oocytes fertilized, number of embryos developed, and the numbers of grades 1, 2 and 3 embryos.

Embryos were classified based on the modified grading by Dong *et al.* (2013). Grade 1 embryos were defined as 4–6 cells on day 2, eight or more cells on day 3, equal, fragmentation <10%, and no multinucleated blastomeres; Grade 2 embryos were defined as 2–3 cells on day 2, 6–7 cells on day 3, equal or less equal, 10–20% fragmentation, and no multinucleated blastomeres; Grade 3 embryos were defined as 0–2 cells on day 2, 1–5 cells on day 3, unequal, fragmentation >25%, with or without multinucleated blastomeres. Grades 1 and 2 embryos were considered top-quality embryos.

The second outcomes measured were the instances of chemical pregnancy (level of hCG ≥50 mIU/ml), clinical pregnancy (gestational sac seen on USG), the implantation rate (the ratio of gestational sac/number of embryos transferred), and live birth rate (number of baby delivery/number of gestational sac).

Statistical analysis

Data were expressed as mean ± standard deviation (SD) or number (percentage) and analyzed using SPSS v.17.0. Means were analyzed using ANOVA for parametric data followed by Bonferroni correction if the data were normally distributed, or Games–Howell test if the data were not normally distributed; and Kruskal–Wallis test for non-parametric data. Proportions were compared using the chi-squared test. Odd ratio (95% CI) was used only for proportion data (chemical pregnancy, clinical pregnancy, implantation and delivery rates). All statistical significance was set as $P < 0.05$.

Results

Baseline characteristics

Baseline characteristics of PCOS and patients without PCOS are shown in Table 1. No differences were found in age, infertility type, number of ICSI cycles, type of infertility, and duration of infertility.

https://doi.org/10.1017/S0967199420000830 Published online by Cambridge University Press

Table 1. Baseline characteristics of normal/lean and overweight/obese patients with or without PCOS

Characteristics	With PCOS (mean ± SD)		Without PCOS (mean ± SD)	
	Normal/lean (A)	Overweight/obese (B)	Normal/lean (C)	Overweight/obese (D)
Number of sample (*n*)	38	17	98	17
Age (years)	30.1 ± 4.0	30.4 ± 4.3	31.4 ± 4.2	31.8 ± 4.0
BMI (kg/m^2)	22.5 ± 1.3[a]	29.4 ± 3.4[b]	22.6 ± 1.6[a]	26.5 ± 1.4[b]
Number of cycle (*n* (%))				
1	30 (78.9%)	15 (88.2%)	74 (75.5%)	14 (82.4%)
>1	8 (21.1%)	2 (11.8%)	24 (24.5%)	3 (17.6%)
Type of infertility (*n* (%))				
Primary	30 (78.9%)	14 (82.4%)	75 (76.5%)	11 (64.7%)
Secondary	8 (21.1%)	3 (17.6%)	23 (23.5%)	6 (35.3%)
Duration of infertility (years)	4.3 ± 2.7	4.9 ± 4.8	5.3 ± 3.3	5.6 ± 2.4
Basal hormone				
FSH (mIU/ml)	5.27 ± 1.40	5.02 ± 1.52	5.67 ± 1.83	5.61 ± 1.85
LH (mIU/ml)	3.84 ± 1.34[a]	3.19 ± 1.04[a, b]	3.02 ± 1.32[b]	2.82 ± 1.00[b]
Prolactin (ng/ml)	23.00 ± 11.10	23.32 ± 15.27	24.09 ± 12.65	18.21 ± 6.87
Estradiol (pg/ml)	36.35 ± 11.42	40.34 ± 11.11	35.84 ± 9.94	32.89 ± 6.75

[a,b] Different superscripts denote statistical difference ($P < 0.01$).

There were significantly higher basal LH levels in group A compared with groups C and D ($P < 0.01$).

Ovarian stimulation parameters and IVF outcomes

Total dosage of rFSH required was significantly lower in group A compared with groups B, C and D ($P < 0.01$) with end estradiol levels significantly higher in group A compared with groups C and D ($P < 0.001$; Table 2). There was no difference in duration of stimulation (days) among groups. There were, however, significantly higher numbers of follicles, retrieved oocytes, and matured oocytes in PCOS groups compared with the non-PCOS groups ($P < 0.001$), the number of fertilized oocytes did not differ significantly (Table 2). Moreover, there were no significant differences in the number of high-quality embryos on day 2 and day 3 among groups (Table 2). There was a slightly lower implantation rate in the overweight/obese non-PCOS group, however it was not significant compared with any other groups (Table 3). There was no significant difference in live birth rate among groups.

Discussion

ICSI, which is part of the IVF treatment, could be an option for patients with PCOS to achieve pregnancy. The success of ICSI is not only influenced by uterus receptivity, but also by the quality of oocytes and development of embryos. Several studies have reported that obesity affects the quality of oocytes, embryos, and pregnancy rates in patients with or without PCOS (Dokras *et al.*, 2006; Bu *et al.*, 2013; Bailey *et al.*, 2014; Huang *et al.*, 2014; Kalem *et al.*, 2016; Wang *et al.*, 2016; Rehman *et al.*, 2018). In this study, we compared the success rate of ICSI in patients with PCOS and further classified whether obesity status would be exaggerated by the presence of PCOS, which compromises ovarian stimulation response and ICSI outcomes, such as embryo development, pregnancy, and live birth rates. We also examined these outcomes in overweight/obese patients without PCOS as controls to observe the effect of overweight/obesity itself.

In this present study, we observed that the normal/lean type patients with PCOS had higher basal LH levels compared with the non-PCOS groups. These results are similar to findings in previous studies that reported a significantly higher basal LH level in PCOS groups compared with non-PCOS groups (Beydoun *et al.*, 2009; Wang *et al.*, 2016). Differences in basal LH obtained in this study, and in some previous studies, were consistent with the theory that LH levels in PCOS increased due to the disrupted production of GnRH (Kini, 2012).

In this study the total dosage of rFSH given was significantly lower in normal/lean patients with PCOS compared with other groups. These results were consistent with previous studies that reported that the dosage of gonadotropin given in the normal/lean PCOS group tended to decrease compared with the levels in patients from the overweight/obese PCOS group to avoid the risk of ovarian hyperstimulation syndrome (OHSS) (Fedorcsak *et al.*, 2000). Obesity in patients with PCOS also affected ovarian stimulation during IVF and may be due to high intra-follicular concentrations of leptin produced by adipose tissue that cause relative gonadotropin resistance (Fedorcsak *et al.*, 2000; O'Neill *et al.*, 2015).

Based on the number of follicles, there was a significantly higher follicle number in PCOS groups than in non-PCOS groups. In PCOS, high LH levels trigger the formation of androgen hormones, which in turn cause follicular atresia. This causes anovulation, and triggers an increase in the number of small follicles. In addition, it is thought that increasing levels of anti-Müllerian hormone (AMH) play a role in the cessation of follicular development (Wilson, 2008; Rehman *et al.*, 2018; Kriedt *et al.*, 2019).

Even though the numbers of follicles, retrieved oocytes, and matured oocytes were higher in the PCOS groups, the numbers

Table 2. Ovarian response and embryo development of normal/lean and overweight/obese patients with or without PCOS

Characteristics	With PCOS (mean ± SD)		Without PCOS (mean ± SD)	
	Normal/lean (A)	Overweight/obese (B)	Normal/lean (C)	Overweight/obese (D)
Total dosage of rFSH (IU)	1665.00 ± 426.52[a]	1921.67 ± 436.08[b]	1825.44 ± 411.85[b]	2006.25 ± 387.78[b]
Duration of stimulation (days)	7.6 ± 1.0	8.1 ± 1.0	7.8 ± 0.9	8.1 ± 1.1
End estradiol levels (pg/ml)	2893.23 ± 1397.87[a]	2401.09 ± 584.27[a,b]	2187.07 ± 752.32[b]	2062.72 ± 779.68[b]
Number of follicle	24.50 ± 10.17[a]	24.76 ± 11.88[a]	15.72 ± 6.60[b]	13.29 ± 5.58[b]
Number of retrieved oocyte	12.63 ± 6.18[a]	12.53 ± 5.52[a]	8.81 ± 3.53[b]	8.29 ± 4.22[b]
Number of matured oocyte	9.45 ± 4.60[a]	9.41 ± 5.08[a]	6.98 ± 3.13[b]	6.53 ± 3.86[b]
Number of fertilized oocyte (%)	7.03 ± 3.77 (74.37%)	7.12 ± 4.15 (75.63%)	5.52 ± 2.51 (79.09%)	5.65 ± 3.06 (86.49%)
Total number of embryo day 2	6.89 ± 3.70	7.00 ± 4.00	5.50 ± 2.52	5.59 ± 3.00
Grade 1	4.03 ± 3.22	4.41 ± 3.71	3.01 ± 2.35	2.53 ± 2.70
Grade 2	2.55 ± 2.05	2.18 ± 2.65	2.22 ± 2.32	2.41 ± 2.35
Grade 3	0.32 ± 0.81	0.41 ± 1.46	0.27 ± 0.65	0.65 ± 1.12
Total number of embryo day 3	6.74 ± 3.78	7.00 ± 3.86	5.42 ± 2.51	5.41 ± 2.98
Grade 1	3.05 ± 2.54	3.24 ± 2.33	2.38 ± 1.85	1.94 ± 1.85
Grade 2	2.95 ± 2.81	3.00 ± 2.76	2.41 ± 2.06	2.47 ± 2.24
Grade 3	0.74 ± 1.25	0.76 ± 1.95	0.63 ± 1.01	1.00 ± 1.50
Number of transferred embryo	2.45 ± 0.65	2.65 ± 0.70	2.49 ± 0.65	2.38 ± 0.72
Endometrial thickness (mm)	10.7 ± 1.8	10.6 ± 1.9	10.7 ± 1.7	10.9 ± 1.6

[a,b] Different superscripts denote statistical difference ($P < 0.01$).

Table 3. ICSI Outcomes of normal/lean and overweight/obese patients with or without PCOS

Characteristics	With PCOS		Without PCOS	
	Normal/lean (A)	Overweight/obese (B)	Normal/lean (C)	Overweight/obese (D)
Chemical pregnancy rate	16 (42.1%)	10 (58.8%)	50 (51.0%)	9 (52.9%)
Clinical pregnancy rate	15 (39.5%)	10 (58.8%)	48 (49.0%)	9 (52.9%)
Implantation rate	23 (24.7%)	14 (31.1%)	53 (21.7%)	7 (18.4%)
Live birth rate	21 (91.3%)	12 (85.7%)	52 (98.1%)	6 (85.7%)

of fertilized oocytes and high-quality embryos were the same between the PCOS groups and non-PCOS groups; this meant that more oocytes in patients with PCOS are not useable. This may happen because the quality of retrieved oocytes in patients with PCOS is compromised compared with patients without PCOS, such as decreasing the mitochondrial deoxyribonucleic acid (mtDNA) and disruption of mitochondrial structure in oocytes (Jia *et al.*, 2016).

Looking at pregnancy, implantation, and live birth rates, there were no differences among groups. These results are similar to previous studies that showed that there were no differences in success rates of IVF/ICSI between patients with or without PCOS (Beydoun *et al.*, 2009; Jia *et al.*, 2016; Kriedt *et al.*, 2019). In this present study, obesity also does not affect the success rate of ICSI in PCOS groups and non-PCOS groups, however obesity was related to an increased gonadotropin requirement. A previous study from Kalem *et al.* (2016) showed there were a significant reduction in retrieved oocytes and matured oocytes in obesity PCOS compared with lean PCOS. Moreover, Bailey *et al.* (2014) showed obese patients with PCOS had decreased clinical pregnancies and live birth rates compared with lean patients with PCOS. In our study, the obesity effect could not be obvious because we had a very small sample size of obese patients (BMI ≥30 kg/m) in the PCOS group ($n = 4$) and control group ($n = 5$), and so combined the overweight and obese patients for each of these two groups. We found a decrease in the clinical pregnancy rate in overweight/obese patients without PCOS compared with normal/lean patients without PCOS, but this was not statistically significant. A study from Dokras *et al.* (2006) showed that morbidly obese patients without PCOS (BMI ≥40 kg/m^2) had a higher cycle cancellation rate compared with normal/lean patients without PCOS, but they also showed no significant differences in live birth rates.

On IVF procedure, ovarian induction by a gonadotropin (rFSH) analogue resulted in a large number of retrieved oocytes, but could cause OHSS, therefore reducing the dosage could overcome this risk. Obese patients with PCOS required a higher dosage of gonadotropin compared with normal/lean patients with PCOS. We suggest that BMI status needs to be considered in patients with PCOS who undergo IVF treatment to achieve optimal outcomes.

https://doi.org/10.1017/S0967199420000830 Published online by Cambridge University Press

Even though the success rates of ICSI in PCOS did not differ significantly compared with the non-PCOS groups, prospective cohort studies with primary data are needed to show the causal factor that impacts the similarly high-quality embryo and pregnancy rates between PCOS and non-PCOS groups. The limitation of this study was the small sample size.

To conclude, normal/lean patients with PCOS require lower gonadotropin dosages. Obesity did not affect the success rate of ICSI, however it tended to increase the gonadotropin dosage needed in PCOS groups. Oocyte quality in patients with PCOS may be compromised compared with patients without PCOS, however no differences in pregnancy, implantation, and live birth rates were observed among groups. Future studies with bigger data samples are required to examine the effects of PCOS and obesity on long term health.

Acknowledgements. The authors would like to thank the Bali Royal Hospital (BROS) for provide the data and G.K. Heinemann for checking the manuscript for grammatical errors.

Financial support. None.

Conflicts of interest. None

Ethical standards. The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. This research was approved by the local ethics committee of Udayana University (156/UN14.2.2.VII.14/LP/2019).

References

American College of Obstetricians and Gynecologists (1998). *Precis, Reproductive Endocrinology: An Update in Obstetrics and Gynecology*. Danvers: Copyright Clearance Center, pp. 92–103.

Bailey AP, Hawkins LK, Missmer SA, Correia KF and Yanushpolsky EH (2014). Effect of body mass index on *in vitro* fertilization outcomes in women with polycystic ovary syndrome. *Am J Obstet Gynecol* **211**, 163e161–6.

Barbosa G, de Sá LBPC, Rocha DRTW and Arbex AK (2016). Polycystic ovary syndrome (PCOS) and fertility. *OJEMD* **6**, 58–66.

Bergh CM, Moore M and Gundell C (2016). Evidence-Based management of infertility in women with polycystic ovary syndrome. *J Obstet Gynecol Neonatal Nurs* **45**, 111–22.

Beydoun HA, Stadtmauer L, Zhao Y, Russell H, Matson DO and Oehninger S (2009). Impact of polycystic ovary syndrome on selected indicators of *in vitro* fertilization and intracytoplasmic sperm injection treatment success. *J Womens Health (Larchmt)* **18**, 717–23.

Bu Z, Dai W, Guo Y, Su Y, Zhai J and Sun Y (2013). Overweight and obesity adversely affect outcomes of assisted reproductive technologies in polycystic ovary syndrome patients. *Int J Clin Exp Med* **6**, 991–5.

Dokras A, Baredziak L, Blaine J, Syrop C, Van Voorhis BJ and Sparks A (2006). Obstetric outcomes after *in vitro* fertilization in obese and morbidly obese women. *Obstet Gynecol* **108**, 61–9.

Dong X, Liao X, Wang R and Zhang H (2013). The impact of endometriosis on IVF/ICSI outcomes. *Int J Clin Exp Pathol* **6**, 1911–8.

Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, Carmina E, Chang J, Yildiz BO, Laven JS, Boivin J, Petraglia F, Wijeyeratne CN, Norman RJ, Dunaif A, Franks S, Wild RA, Dumesic D and Barnhart K (2012). Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril* **97**, 28–38.

Fedorcsak P, Storeng R, Dale PO, Tanbo T, Torjesen P, Urbancsek J and Abyholm T (2000). Leptin and leptin binding activity in the preovulatory follicle of polycystic ovary syndrome patients. *Scand J Clin Lab Invest* **60**, 649–55.

Fedorcsak P, Dale PO, Storeng R, Tanbo T and Abyholm T (2001). The impact of obesity and insulin resistance on the outcome of IVF or ICSI in women with polycystic ovarian syndrome. *Hum Reprod* **16**, 1086–91.

Huang K, Liao X, Dong X and Zhang H (2014). Effect of overweight/obesity on IVF-ET outcomes in chinese patients with polycystic ovary syndrome. *Int J Clin Exp Med* **7**, 5872–6.

Jia L, Li J, He B, Jia Y, Niu Y, Wang C and Zhao R (2016). Abnormally activated one-carbon metabolic pathway is associated with mtDNA hypermethylation and mitochondrial malfunction in the oocytes of polycystic gilt ovaries. *Sci Rep* **6**, 19436.

Kalem MN, Kalem Z, Sari T, Ates C and Gurgan T (2016). Effect of body mass index and age on *in vitro* fertilization in polycystic ovary syndrome. *J Turk Ger Gynecol Assoc* **17**, 83–90.

Kini S (2012). Polycystic ovary syndrome: diagnosis and management of related infertility. *Obstet Gynaecol Reprod Med* **22**, 347–53.

Kriedt KJ, Alchami A and Davies MC (2019). PCOS: diagnosis and management of related infertility. *Obstet Gynaecol Reprod Med* **19**, 1–5.

McCartney ChR and Marshall JC (2016). Polycystic ovary syndrome. *N Engl J Med* **375**, 1398–9.

McCormick B, Thomas M, Maxwell R, Williams D and Aubuchon M (2008). Effects of polycystic ovarian syndrome on *in vitro* fertilization-embryo transfer outcomes are influenced by body mass index. *Fertil Steril* **90**, 2304–9.

Mulders AG, Laven JS, Imani B, Eijkemans MJ and Fauser BC (2003). IVF outcome in anovulatory infertility (WHO group 2)—including polycystic ovary syndrome—following previous unsuccessful ovulation induction. *Reprod Biomed Online* **7**, 50–8.

O'Neill KE, Senapati S and Dokras A (2015). Use of gonadotropin-releasing hormone agonist trigger during *in vitro* fertilization is associated with similar endocrine profiles and oocyte measures in women with and without polycystic ovary syndrome. *Fertil Steril* **103**, 264–9.

Purnell JQ (2018). Definitions, Classification, and Epidemiology of Obesity. 2018 Apr 12. In: Feingold KR, Anawalt B, Boyce A, Chrousos G, de Herder WW, Dungan K, Grossman A, Hershman JM, Hofland HJ, Kaltsas G, Koch C, Kopp P, Korbonits M, McLachlan R, Morley JE, New M, Purnell J, Singer F, Stratakis CA, Trence DL and Wilson DP (eds). Endotext [Internet]. South Dartmouth (MA): MDText.com.

Rehman R, Mehmood M, Ali R, Shaharyar S and Alam F (2018). Influence of body mass index and polycystic ovarian syndrome on ICSI/IVF treatment outcomes: A study conducted in Pakistani women. *Int J Reprod Biomed (Yazd)* **16**, 529–34.

Teede H, Misso M, Costello M, Dokras A, Laven J, Moran L, Piltonen T and Norman R on behalf of the International PCOS Network (2018). *International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome*. Melbourne: Monash University; Australian Government National Health and Medical Research Council.

Wang F, Dai W, Yang XH, Guo YH and Sun YP (2016). Analyses of optimal body mass index for infertile patients with either polycystic or non-polycystic ovary syndrome during assisted reproductive treatment in China. *Sci Rep* **6**, 34538.

Wilson EE (2008). *Polycystic Ovarian Syndrome and Hyperandrogenism*. McGraw-Hill, New York.