## Original article

# Gestational Diabetes Mellitus in Women with Polycystic Ovary Syndrome Undergoing Assisted Reproduction

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**Abstract:** Polycystic ovary syndrome (PCOS) is a common endocrine metabolic disorder in women of reproductive age. PCOS is often associated with insulin resistance and carries an increased risk of gestational diabetes mellitus (GDM). The aim of this study was to evaluate the risk of GDM in women with a history of PCOS. This was a retrospective cohort study conducted at a single center in Vietnam between January 2014 and December 2017. A total of 400 women who conceived through assisted reproductive technology (ART) were included, 200 who had been diagnosed with PCOS, and 200 without a PCOS diagnosis as controls. Multivariable logistic regression models were used to examine the association between risk of GDM and PCOS after adjusting for confounders. GDM was present in 37% of those with PCOS, compared with 26.5% in those without PCOS (RR 1.4, 95% CI 1.04–1.87, p=0.02). The prevalence of GDM did not differ significantly between PCOS phenotype groups (p=0.28). Women with PCOS undergoing ART had a higher risk of GDM after adjusting for differences in age, pre-pregnancy body mass index, type of infertility, ART indications, and type of ART (adjusted OR 2.04, 95% CI 1.06–3.92). First-trimester fasting plasma glucose (FPG) was also an independent predictor for GDM (adjusted OR 1.54, 95% CI 1.01–2.34). This study suggests that PCOS and first-trimester FPG are independent risk factors for the development of GDM.

**Keywords:** polycystic ovary syndrome, gestational diabetes mellitus, assisted reproductive technology.

## 1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. The prevalence of PCOS is estimated to be between 4% and 15% of women of reproductive age, depending on the diagnostic criteria used [1-3]. PCOS usually includes signs and symptoms such as hyperandrogenism, ovarian dysfunction and polycystic ovary morphology [4]. However, the pathogenesis of this syndrome is relatively complex and remains controversial. Approximately 50% of women with PCOS have accompanying metabolic syndrome [5]. Women with PCOS often have insulin resistance and may therefore be at increased risk of developing gestational diabetes mellitus (GDM) and type 2 diabetes mellitus [6].

A number of studies show an increased risk of GDM in women with PCOS [7-9], but few have studied this association

in Vietnamese women. The prevalence of GDM in women with PCOS ranges from 18.2% to 54.9%, depending on age, race, GDM diagnostic criteria used and dominant PCOS phenotype [1, 3, 7, 8]. The Rotterdam criteria recognize four PCOS phenotypes: phenotype A - Frank PCOS: oligo-ovulation (OA), hyperandrogenism (HA), and polycystic ovaries (PCO), phenotype B - Non-PCO PCOS: OA, HA, and normal ovaries, phenotype C - Ovulatory PCOS: HA, PCO, and regular menstrual cycles, and phenotype D - Mild or Normo-androgenic PCOS: OA, PCO, and normal androgens [4]. The long-term disease outcomes in different PCOS phenotypes are being studied. There is evidence that women with hyperandrogenic PCOS phenotype increase risks of endocrine and metabolic abnormalities [10-12].

Current evidence suggests that Asian women have lower body mass index (BMI), fewer symptoms of

hyperandrogenism and different dominant PCOS phenotype than European women [10, 13, 14], but metabolic disorders are more prevalent among Asian women than women of other ethnicities [15]. Therefore, there is a need for a separate study in Vietnamese women in order to determine the risk of GDM in women with PCOS in this specific population.

## 2. MATERIALS AND METHOD

### 2.1. Study design

This retrospective cohort study was performed at My Duc Hospital, Ho Chi Minh City, Vietnam, between January 1, 2014 and December 31, 2017.

### *2.1.1 Inclusion and exclusion criteria*

Included women were those aged 18-38 years who conceived through assisted reproductive technology (ART) and underwent a routine 75g oral glucose tolerance test (OGTT) between 24 and 28 weeks' gestation. Exclusion criteria were a history of pre-existing diabetes or previous GDM, hypertension, coronary artery disease, congestive heart failure, dyslipidemia, or hypothyroidism.

Information on the following pre-pregnancy and early pregnancy variables was collected for each enrolled woman: age, presence or absence of PCOS, PCOS phenotype, pre-pregnancy BMI, type of infertility, duration of infertility, ART indications, type of ART, antral follicle count (AFC), anti-mullerian hormone (AMH), first-trimester fasting plasma glucose (FPG), and whether there was a singleton or multiple pregnancy.

### *2.1.2 Outcome variable: gestational diabetes mellitus*

A diagnosis of PCOS was made using the Rotterdam 2003 criteria [4] when at least two of the following three criteria were met: polycystic ovaries, oligo-ovulation, and hyperandrogenism. Polycystic ovaries (PCO) were defined as the presence of 12 or more follicles in each ovary measuring 2–9 mm in diameter, and/or increased ovarian volume >10 ml. Oligo-ovulation (OA) was defined as a menstrual cycle length of >35 days. Hyperandrogenism (HA) was defined based on biochemical hyperandrogenism: a free testosterone index (FTI) >6 nmol/L. FTI was calculated from the measurement of sex hormone binding globulin (SHBG) and total testosterone. FTI = Total testosterone (nmol/L) x 100/ SHBG (nmol/L).

Four PCOS phenotypes were identified based on the Rotterdam 2003 criteria: A (HA+OA+PCO), B (HA+OA), C (HA+PCO), and D (OA+PCO).

GDM was diagnosed according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria [16] with patients required to meet at least one of the following criteria: fasting plasma glucose level ≥5.1 mmol/L, 1-hour plasma glucose level ≥10.0 mmol/L, and 2-hour plasma glucose level ≥8.5 mmol/L (16).

### 2.2. Ethical Statement

This study was approved by the Institutional Review Board of the University of Medicine and Pharmacy at Ho Chi Minh City and My Duc Hospital. Patient information was kept confidential. Informed consent was not required for this study.

### 2.3. Statistical Analysis

Data were analyzed using Stata statistics version 13.0 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP). Women with PCOS and those without PCOS were compared using the chi-squared test for categorical variables and the *t*-test for continuous variables. Multivariable logistic regression models were used to examine the association of GDM and risk factors (PCOS and first-trimester FPG) after adjusting for the following confounders: age, pre-pregnancy BMI, type of infertility, ART indications, and type of ART.

The significant difference was set at p value <0.05.

## 3. RESULTS

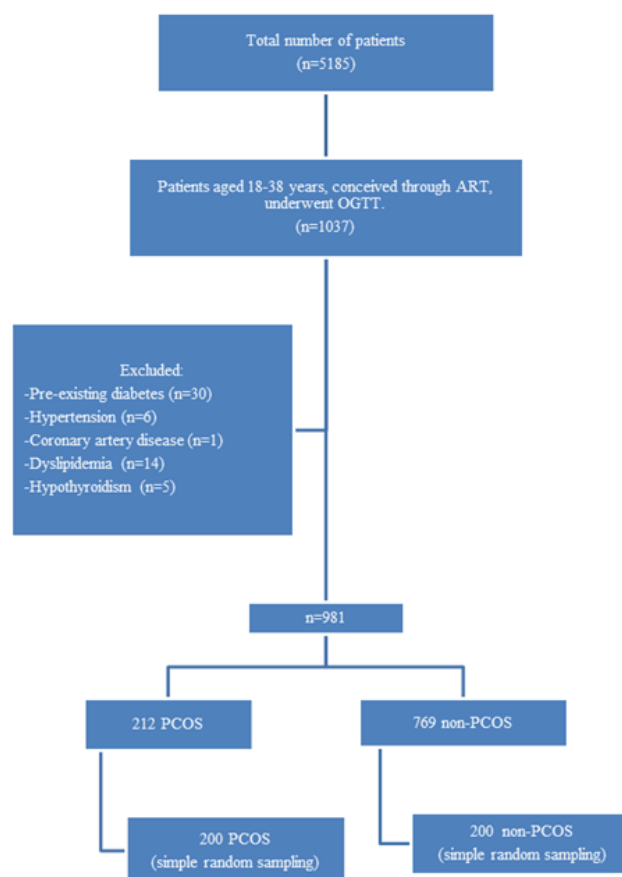### 3.1. Study participants



**Figure 1.** Flow chart of case selection and exclusion.

From January 2014 to December 2017, a total of 5185 patients presented to My Duc Hospital, of whom 1037 patients were aged 18-38 years, had conceived through ART and had undergone a routine 75g OGTT. After excluding 30 cases of pre-existing diabetes or previous GDM, six cases of

hypertension, one case of coronary artery disease, 14 cases of dyslipidemia, and five cases of hypothyroidism, there were 981 eligible patients. This included 212 patients diagnosed with PCOS according to the Rotterdam 2003 criteria, and 769 without PCOS. From each of these two groups, 200 cases were randomly selected. Figure 1 shows the flow chart of case selection and exclusion.

**Table 1.** Characteristics of women with and without a history of PCOS

| Characteristics | PCOS (n=200) | No PCOS (n=200) | p value |
|---|---|---|---|
| Age – years (mean ± SD) | 30.96 ± 3.72 | 32.55 ± 3.74 | <0.01 |
| Age group – years (%) | | | |
| <25 | 8 (4) | 4 (2) | |
| 25-29 | 73 (36.5) | 44 (22) | <0.01 |
| 30-34 | 81 (40.5) | 81 (40.5) | |
| > 35 | 38 (19) | 71 (35.5) | |
| Pre-pregnancy BMI - kg/m2 (mean ± SD) | 21.40 ± 3.20 | 20.93 ± 2.28 | 0.08 |
| Pre-pregnancy BMI group - kg/m2 (%) | | | |
| ≤18.4 | 15 (7.5) | 24 (12) | |
| 18.5-24.9 | 160 (80) | 164 (82) | 0.08 |
| 25-29.9 | 23 (11.5) | 11 (5.5) | |
| 30 | 2 (1) | 1 (0.5) | |
| Type of infertility - n (%) | | | |
| Primary | 145 (72.5) | 132 (66) | 0.16 |
| Secondary | 55 (27.5) | 68 (34) | |
| Duration of infertility–years (mean ± SD) | 3.43 ± 2.33 | 3.76 ± 2.58 | 0.18 |
| ART indications – n (%) | | | |
| Male factor | 83 (41.5) | 18 (9) | |
| Tubal factor | 14 (7) | 74 (37) | |
| Endometriosis | 0 (0) | 14 (7) | |
| Ovulatory disorders | 99 (49.5) | 43 (21.5) | <0.01 |
| Unexplained | 0 (0) | 51 (25.5) | |
| Others | 4 (2) | 0 (0) | |
| Type of ART – n (%) | | | |
| ICSI – fresh ET | 12 (6) | 13 (6.5) | |
| ICSI – frozen ET | 103 (51.5) | 173 (86.5) | |
| IVM – fresh ET | 21 (10.5) | 11 (5.5) | <0.01 |
| IVM – frozen ET | 64 (32) | 3 (1.5) | |
| AFC – n (mean ± SD) | 26.15 ± 10.60 | 12.2 ± 6.03 | <0.01 |
| AMH – ng/ml (mean ± SD) | 10.74 ± 3.92 | 4.85 ± 2.91 | <0.01 |
| Singleton/multiple pregnancy – n (%) | | | |
| Singleton | 168 (84) | 178 (89) | 0.14 |
| Multiple | 32 (16) | 22 (11) | |
| First-trimester FPG-mmol/l (mean ± SD) | 4.43 ± 0.50 | 4.46 ± 0.54 | 0.53 |

*AFC, antral follicle count; ART, assisted reproductive technology; BMI, body mass index; ET, embryo transfer; FPG, fasting plasma glucose; ICSI, intracytoplasmic sperm injection; IVM, in-vitro maturation of oocytes; PCOS, polycystic ovary syndrome; SD, standard deviation.*

**Table 2.** Prevalence of GDM in women with and without PCOS

| GDM | PCOS (n=200) | No PCOS (n=200) | Risk difference (95% CI) | Risk ratio (95% CI) | p-value |
|---|---|---|---|---|---|
| GDM | 74 (37%) | 53 (26.5%) | 0.105 | 1.40 | 0.02 |
| No GDM | 126 (63%) | 147 (73.5%) | (0.01-0.20) | (1.04-1.87) | |

*CI, confidence interval; GDM, gestational diabetes mellitus; PCOS, polycystic ovary syndrome*

**Table 3.** Comparison of GDM between PCOS phenotype groups

| PCOS phenotype | n (%) | GDM | No GDM | p value |
|---|---|---|---|---|
| A | 65 (32.5) | 24 (36.92%) | 41 (63.08%) | |
| B | 8 (4.0) | 3 (37.5%) | 5 (62.5%) | 0.28 |
| C | 15 (7.5) | 9 (60%) | 6 (40%) | |
| D | 112 (56.0) | 38 (33.93%) | 74 (66.07%) | |

*A = hyperandrogenism + oligo-ovulation + polycystic ovaries*

*B = hyperandrogenism + oligo-ovulation*

*C = hyperandrogenism + polycystic ovaries*

*D = oligo-ovulation + polycystic ovaries*

*GDM, gestational diabetes mellitus; PCOS, polycystic ovary syndrome*

General characteristics of patients according to PCOS status are presented in Table 1. Women with PCOS were significantly younger than those without PCOS. The most common ART indication for women with PCOS was ovulatory disorders, with unexplained infertility the most common for women without PCOS. Women with PCOS had higher AFC and AMH than those without PCOS. There were no significant between group differences in BMI, type of infertility, duration of infertility, type of ART, singleton or multiple pregnancy, or first-trimester FPG.

**3.2. Gestational diabetes**

GDM was present in 37% of women in the PCOS group, compared with 26.5% in the group of women without PCOS (risk ratio [RR] 1.4, 95% confidence interval [CI] 1.04 – 1.87, p=0.02) (Table 2). Women with a diagnosis of PCOS had a higher risk of GDM than women with no such diagnosis.

The most common PCOS phenotype in this study was phenotype D (OA+PCO; 56%), followed by phenotype A (HA+OA+PCO; 32.5%), phenotype C (HA+PCO; 7.5%) and phenotype B (HA+OA; 4%). Women with phenotype C had the highest prevalence of GDM (60%), but the differences in prevalence of GDM did not differ significantly between phenotype groups (p=0.28; Table 3).

In the crude analysis, factors that affected the risk of GDM were pre-pregnancy BMI, PCOS and first-trimester FPG. To assess whether the increased risk for GDM remained after adjusting for potential confounders, multiple logistic regression analysis was conducted (Table 4). Pre-pregnancy BMI was no longer a significant risk factor for GDM after adjusting for potential confounders.

Women with PCOS undergoing ART had a higher risk of GDM after adjusting for differences in age, pre-pregnancy BMI, type of infertility, ART indications, and type of ART (adjusted odds ratio [aOR] 2.04, 95% CI 1.06–3.92). First-trimester FPG was also an independent predictor for GDM (aOR 1.54, 95% CI 1.01–2.34).

**4. DISCUSSION**

In this study, the prevalence of GDM in women with PCOS was significantly higher than in those without PCOS (37% vs. 26.5%, p=0.02). These results contradict a recently published small study in Vietnam [17], which found that the prevalence of GDM did not differ between women with PCOS and those without PCOS (33.7% vs 22.7%, p>0.05), possibly because of lack of statistical power (98 women with PCOS vs. 119 without PCOS). However, the increased prevalence of GDM in women with PCOS that was observed in this study is consistent with the results of several studies [1, 3, 7, 8], all of which concluded that women with a diagnosis of PCOS had a higher risk of GDM than women with no such diagnosis.

The most common PCOS phenotype in this study was phenotype D (OA+PCO), followed by phenotype A (HA+OA+PCO), phenotype C (HA+PCO), and phenotype B (HA+OA), which is consistent with a study conducted in Indonesian women [18]. The current study did not reveal any statistically significant differences in the prevalence of GDM between the four phenotype groups, a finding similar to some previous studies [19-20]. However, there have been studies that have found the prevalence of GDM to be significantly higher in the PCOS phenotypes with hyperandrogenism compared to normo-androgenic PCOS [11, 12, 21]. This study confirms, along with a study conducted in Indonesian women, that South East Asian women are less hyperandrogenic than

Western women [10, 13, 18, 22]. To our knowledge, this is the first study comparing the prevalence of GDM between four PCOS phenotype groups in Vietnamese women.

However, our sample size was relatively small for each phenotype group, therefore, there is a need for a larger study in Vietnamese women, to further investigate GDM risk in different PCOS phenotypes.

In the crude analysis, factors that affected risk of GDM were pre-pregnancy BMI, PCOS and first-trimester FPG. However, after adjustment for potential confounders, BMI no longer significantly affected GDM. Vietnamese women with PCOS tend to be lean [23-24]. A study in Chinese women, found that lean women with PCOS had a higher risk of GDM than lean controls [8]. However, research has also shown that a pre-pregnancy BMI >25 was the most important predictor for GDM [7], although in this study PCOS was also a statistically significant risk factor for GDM in women with a high pre-pregnancy BMI.

Women with PCOS had a higher risk of GDM after adjustment for potential confounders (age, pre-pregnancy BMI, type of infertility, ART indications, and type of ART), indicating that PCOS is an independent risk factor for GDM. This is consistent with previous studies, with PCOS shown to be an independent predictor of GDM (aOR=2.9, 95% CI 2.0-4.1) [8], or to be a significant risk factor for the development of GDM [1, 25]. First-trimester FPG was also an independent predictor for GDM, which is also consistent with previous studies [26-27].

There are several advantages of this study. First, this retrospective cohort study followed patients from their first diagnosis of PCOS to the subsequent development of GDM. Additionally, strict criteria were employed for the diagnosis of PCOS, and patients were classified as having GDM on the basis of objective laboratory examinations rather than by a physician's subjective diagnosis. Furthermore, all the women in our study conceived through ART, eliminating the confounding effects of ART on the development of GDM.

Our study has some limitations. As this was a retrospective cohort study, we were unable to accurately assess clinical hyperandrogenism, relying instead on biochemical indicators. We were also unable to collect information of other risk factors: first-degree relative with diabetes, socio-economic status and smoking. Additionally, the retrospective design is associated with limitations in terms of completeness of record keeping and the results might not be representative for our study population.

**Table 4.** Odds ratio for gestational diabetes mellitus

| Parameter | Univariable OR (95% CI; p-value) | Multivariable aOR (95% CI; p-value) |
|---|---|---|
| Age | 1.04 (0.98-1.10); 0.18 | 1.05 (0.99-1.12); 0.10 |
| Pre-pregnancy BMI | 1.10 (1.02-1.19); 0.02 | 1.08 (1.00-1.17); 0.07 |
| PCOS | | |
| Non-PCOS | Reference | Reference |
| PCOS | 1.63 (1.06-2.50); 0.02 | 2.04 (1.06-3.92); 0.03 |
| Type of infertility | | |
| Primary | Reference | Reference |
| Secondary | 1.52 (0.97-2.38); 0.07 | 1.42 (0.86-2.34); 0.17 |
| ART indications | | |
| Male factor | Reference | Reference |
| Tubal factor | 1.16 (0.62-2.16); 0.64 | 1.72 (0.78-3.83); 0.18 |
| Endometriosis | 0.99 (0.29-3.42); 0.99 | 2.06 (0.52-8.18); 0.30 |
| Ovulatory disorders | 1.27 (0.73-2.2); 0.4 | 1.30 (0.73-2.34); 0.37 |
| Unexplained | 1.03 (0.49-2.17); 0.93 | 2.17 (0.85-5.52); 0.10 |
| Others | 7.45 (0.74-74.56); 0.09 | 7.14 (0.67-76.11); 0.10 |
| Type of ART | | |
| ICSI – fresh ET | Reference | Reference |
| ICSI – frozen ET | 1.27 (0.49-3.30); 0.62 | 1.43 (0.53-3.88); 0.49 |
| IVM – fresh ET | 2.17 (0.68-6.90); 0.19 | 2.22 (0.66-7.48); 0.20 |
| IVM – frozen ET | 2.42 (0.86-6.82); 0.09 | 2.30 (0.76-6.93); 0.14 |
| First-trimester FPG | 1.56 (1.05-2.34); 0.03 | 1.54 (1.01-2.34); 0.04 |

*aOR, adjusted odds ratio; ART, assisted reproductive technology; CI, confidence interval; ET, embryo transfer; FPG, fasting plasma glucose; ICSI, intracytoplasmic sperm injection; IVM, in-vitro maturation of oocytes; OR, odds ratio; PCOS, polycystic ovary syndrome.*

## 5. CONCLUSION

This study revealed that among women undergoing ART, women with a diagnosis of PCOS are at increased risk of GDM compared to those without PCOS. PCOS was a significant risk factor for GDM, independent of age, pre-pregnancy BMI, type of infertility, ART indications, and type of ART. Women with PCOS should be informed of an increased risk of GDM and may require closer antenatal surveillance. There were no differences in the prevalence of GDM between the four PCOS phenotypes although larger sample-size studies may be needed to validate this finding.

## ACKNOWLEDGEMENTS

## DECLARATION OF CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

## REFERENCES

1.  Pan ML, Chen LR, Tsao HM, Chen KH. Relationship between Polycystic Ovarian Syndrome and Subsequent Gestational Diabetes Mellitus: A Nationwide Population-Based Study. PloS one. 2015;10(10):e0140544.

2.  Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC medicine. 2010;8:41.

3.  Xiao Q, Cui YY, Lu J, Zhang GZ, Zeng FL. Risk for Gestational Diabetes Mellitus and Adverse Birth Outcomes in Chinese Women with Polycystic Ovary Syndrome. International journal of endocrinology. 2016;2016:5787104.

4.  Rotterdam EA-SPCWG. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81(1):19-25.

5.  Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes care. 1999;22(1):141-6.

6.  Cassar S, Misso ML, Hopkins WG, Shaw CS, Teede HJ, Stepto NK. Insulin resistance in polycystic ovary syndrome: a systematic review and meta-analysis of euglycaemic-hyperinsulinaemic clamp studies. Human reproduction (Oxford, England). 2016;31(11):2619-31.

7.  Mikola M, Hiilesmaa V, Halttunen M, Suhonen L, Tiitinen A. Obstetric outcome in women with polycystic ovarian syndrome. Human reproduction (Oxford, England). 2001;16(2):226-9.

8.  Wang Y, Zhao X, Zhao H, Ding H, Tan J, Chen J, et al. Risks for gestational diabetes mellitus and pregnancy-induced hypertension are increased in polycystic ovary syndrome. BioMed research international. 2013;2013:182582.

9.  Yu HF, Chen HS, Rao DP, Gong J. Association between polycystic ovary syndrome and the risk of pregnancy complications: A PRISMA-compliant systematic review and meta-analysis. Medicine. 2016;95(51):e4863.

10. Pehlivanov B, Orbetzova M. Characteristics of different phenotypes of polycystic ovary syndrome in a Bulgarian population. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology. 2007;23(10):604-9.

11. Bil E, Dilbaz B, Cirik DA, Ozelci R, Ozkaya E, Dilbaz S. Metabolic syndrome and metabolic risk profile according to polycystic ovary syndrome phenotype. The journal of obstetrics and gynaecology research. 2016;42(7):837-43.

12. Moghetti P, Tosi F, Bonin C, Di Sarra D, Fiers T, Kaufman JM, et al. Divergences in insulin resistance between the different phenotypes of the polycystic ovary syndrome. The Journal of clinical endocrinology and metabolism. 2013;98(4):E628-37.

13. Dewailly D, Catteau-Jonard S, Reyss AC, Leroy M, Pigny P. Oligoanovulation with polycystic ovaries but not overt hyperandrogenism. The Journal of clinical endocrinology and metabolism. 2006;91(10):3922-7.

14. Li R, Zhang Q, Yang D, Li S, Lu S, Wu X, et al. Prevalence of polycystic ovary syndrome in women in China: a large community-based study. Human reproduction (Oxford, England). 2013;28(9):2562-9.

15. Balen AH, Morley LC, Misso M, Franks S, Legro RS, Wijeyaratne CN, et al. The management of anovulatory infertility in women with polycystic ovary syndrome: an analysis of the evidence to support the development of global WHO guidance. Human reproduction update. 2016;22(6):687-708.

16. Agarwal MM. Gestational diabetes mellitus: An update on the current international diagnostic criteria. World Journal of Diabetes. 2015;6(6):782-91.

17. Yen HTN, Quan PT, Vinh DQ, Lan VTN. Risk of gestational diabetes mellitus in women with polycystic ovary syndrome conceived through assisted reproductive technology. Y hoc thanh pho Ho Chi Minh. 2018;22(1):5-7.

18. Wiweko B, Maidarti M, Priangga MD, Shafira N, Fernando D, Sumapraja K, et al. Anti-mullerian hormone as a diagnostic and prognostic tool for PCOS patients. Journal of Assisted Reproduction and Genetics. 2014;31(10):1311-6.

19. Ashrafi M, Sheikhan F, Arabipoor A, Rouhana N, Hosseini R, Zolfaghari Z. Gestational Diabetes Mellitus and Metabolic Disorder Among the Different Phenotypes of Polycystic Ovary Syndrome. Oman Medical Journal. 2017;32(3):214-20.

20. Jamil AS, Alalaf SK, Al-Tawil NG, Al-Shawaf T. A case-control observational study of insulin resistance and metabolic syndrome among the four phenotypes of polycystic ovary syndrome based on Rotterdam criteria. Reproductive health. 2015;12:7.

21. de Wilde MA, Lamain-de Ruiter M, Veltman-Verhulst SM, Kwee A, Laven JS, Lambalk CB, et al. Increased rates of complications in singleton pregnancies of women previously diagnosed with polycystic ovary syndrome predominantly in the hyperandrogenic phenotype. Fertility and sterility. 2017;108(2):333-40.

22. Welt CK, Gudmundsson JA, Arason G, Adams J, Palsdottir H, Gudlaugsdottir G, et al. Characterizing discrete subsets of polycystic ovary syndrome as defined by the Rotterdam criteria: the impact of weight on phenotype and metabolic features. The Journal of clinical endocrinology and metabolism. 2006;91(12):4842-8.

23. Ho VNA, Pham TD, Le AH, Ho TM, Vuong LN. Live birth rate after human chorionic gonadotropin priming in vitro maturation in women with polycystic ovary syndrome. Journal of ovarian research. 2018;11(1):70.

24. Lan VT, Norman RJ, Nhu GH, Tuan PH, Tuong HM. Ovulation induction using low-dose step-up rFSH in Vietnamese women with polycystic ovary syndrome. Reproductive biomedicine online. 2009;18(4):516-21.

25. Sterling L, Liu J, Okun N, Sakhuja A, Sierra S, Greenblatt E. Pregnancy outcomes in women with polycystic ovary syndrome undergoing in vitro fertilization. Fertility and sterility. 2016;105(3):791-7.e2.

26. Hao M, Lin L. Fasting plasma glucose and body mass index during the first trimester of pregnancy as predictors of gestational diabetes mellitus in a Chinese population. Endocr J. 2017;64(5):561-9.

27. de Wilde MA, Veltman-Verhulst SM, Goverde AJ, Lambalk CB, Laven JS, Franx A, et al. Preconception predictors of gestational diabetes: a multicentre prospective cohort study on the predominant complication of pregnancy in polycystic ovary syndrome. Hum Reprod. 2014;29(6):1327-36.