Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2024, 14, 18-28
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Association between the Different Phenotypes of Polycystic Ovary Syndrome and the Outcome in *in Vitro* Fertilization at Human Reproductive Center Paul et Chantal Biya-Yaoundé

Ngono Akam Vanina[1,2*], Ngah Minala[1], Belinga Etienne[1,2], Voundi Voundi[1,2], Mpono Pascale[1,2], Nyada Serges[1,2], Onana Y. Kasia[1], Cho Joselyne[1], Kasia Florence[1], Adjessa Abega[1], Kasia Jean Marie[1,2]

[1]Gynaecological Endoscopic Surgery and Human Reproductive Teaching Hospital, Yaoundé, Cameroon
[2]Department of Gynecology and Obstetrics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1, Yaoundé, Cameroon
Email: *vakam24@yahoo.fr

How to cite this paper: Vanina, N.A., Minala, N., Etienne, B., Voundi, V., Pascale, M., Serges, N., Kasia, O.Y., Joselyne, C., Florence, K., Abega, A. and Marie, K.J. (2024) Association between the Different Phenotypes of Polycystic Ovary Syndrome and the Outcome in *in Vitro* Fertilization at Human Reproductive Center Paul et Chantal Biya-Yaoundé. *Open Journal of Obstetrics and Gynecology*, **14**, 18-28.
https://doi.org/10.4236/ojog.2024.141003

Received: October 24, 2023
Accepted: January 9, 2024
Published: January 12, 2024

Abstract

Background: *In Vitro* Fertilization/Intracytoplasmic Sperm Injection (IVF/ICSI) represents the final step in the management of Polycystic Ovarian Syndrome (PCOS). Our objective was to study the association between PCOS phenotypes and IVF/ICSI results in women admitted to Gynaecological Endoscopic Surgery and Human Reproductive Teaching Hospital (CHRACERH). **Material and Method:** We carried out a cohort study with historical-prospective data collection over a period of seven years (January 2016 to March 2023) at Chracerh. PCOS patients were subdivided into 4 subgroups A, B, C and D. **Results:** We recruited 128 patients including 64 PCOS patients divided into four phenotypes and 64 non-PCOS patients constituting the control group. Phenotype D without hyperandrogenism had used the lowest dose of gonadotropins, *i.e.* 1939.7 ± 454.3 IU, and had produced a greater quantity of estradiol on the day ovulation was triggered (6529.8 ± 4324.8 ng/ml). The average number of punctured follicles and mature oocytes were higher in the phenotype D group. Ovarian hyperstimulation syndrome (OHSS) occurred mainly in phenotype D (3/35), with an estimated prevalence of 2.3%. The fertilization rate seemed lower in the hyperandrogenic phenotypes A, B, C compared to the group without hyperandrogenism without significant difference (p = 0.461). The biological pregnancy rate and live birth rate were comparable between the different groups. **Conclusion:** Phenotype D used less dose of gonadotropins. Biological pregnancy and live birth rates were comparable between the different phenotypes.

Keywords

Phenotype, Polycystic Ovarian Syndrome, IVF/ICSI, Prognosis, CHRACERH

1. Introduction

Polycystic Ovary Syndrome (PCOS) is the most common endocrine pathology in women of childbearing age. Its overall prevalence in the world is between 6% and 21% [1] [2]. It is characterized to varying degrees by the association of clinical and/or biological hyperandrogenism (HA), ovulation disorders (OA) and the presence of polycystic ovaries on ultrasound (PCO). We thus distinguish four phenotypes. PCOS is the major cause of anovulatory infertility [3] [4] [5] [6]; *In Vitro* Fertilization (IVF) constitutes the final stage of care for this group of patients and according to several authors, the outcome in IVF/ICSI (*In Vitro* Fertilization/Intracytoplasmic Sperm Injection) would depend on the PCOS phenotype [3] [6] [7] [8]. Thus, given the recurrence of cases of PCOS admitted for ovarian stimulation for IVF/ICSI at the Hospital Center for Research and Application in Endoscopic Surgery and Human Reproduction (CHRACERH) and the fact that no study on this subject has been carried out in our context which we proposed to carry out this study.

2. Materials and Methods

This was a cohort study with historical-prospective data collection which took place at CHRACERH-Yaoundé-Cameroon. It took place over a period ranging from 1st of January 2016 to the 30th of May 2023, *i.e.*, a period of 7 years and 4 months. After obtaining approval from the ethics committee of Faculty of Medicine and Biomedical Science of the University of Yaounde I (Ref N 00273/12th, May 2023), and authorizations from the competent authorities, we recruited patients admitted to IVF/ICSI with ovarian stimulation at CHRACERH during the period. The data collected was reported in the previously established technical sheet.

The "exposed" group consisted of PCOS patients meeting the Rotterdam criteria who had a usable file or who had agreed to participate in the study. The "control" group constituted the files of patients who did not have signs of PCOS. The PCOS group was THEN subdivided into four subgroups corresponding to the following PCOS phenotypes: Phenotype A (HA, hyperandrogenism + ovulation disorders, OA+ polycystic ovaries, PCO on ultrasound), Phenotype B (HA + OA), Phenotype C (HA+PCO) and Phenotype D (OA + PCO) (See **Figure 1**).

The variables of interest were socio-demographic and clinical, assessment of ovarian reserve, and IVF outcome.

Stimulation protocol: patients were placed either on an antagonist protocol or on an agonist protocol depending on the availability of drugs. The dose of gonadotropin required depended on the ovarian reserve and varied from 150 to

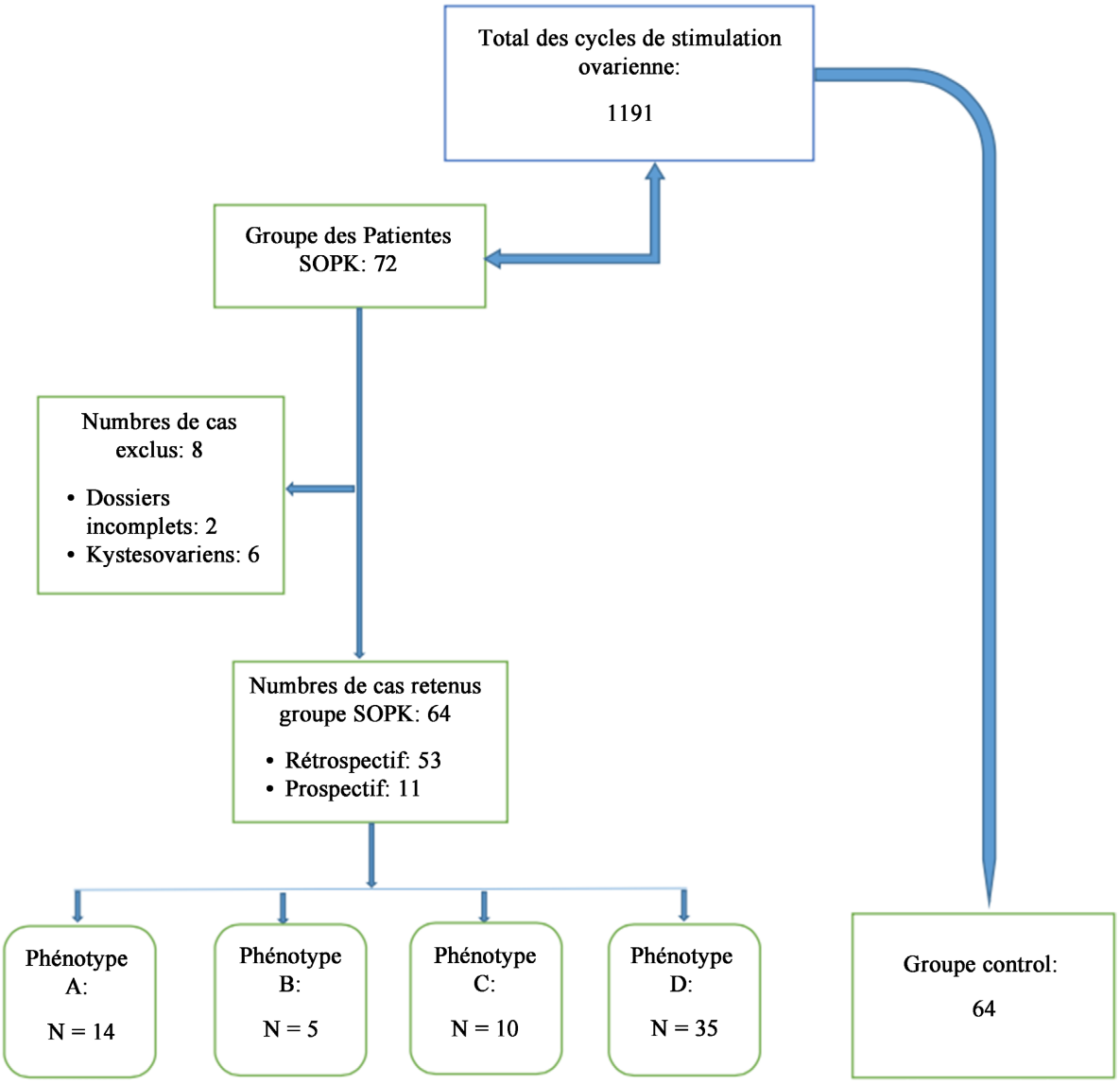

Figure 1. Flowchart of patients.

300 IU. The doses must be revised downwards depending on the evolution. Thus, the monitoring of IVF cycles consisted of regular monitoring by endovaginal ultrasound carried out by a gynecologist or a radiologist with an ACUSON X150 type ultrasound device (**Figure 2**).

Aimed at counting antral follicles and measuring the thickness of the endometrium and by measuring the level of estradiol, progesterone from the 5th-6th day of the cycle depending on the protocol. Dosage of serum estradiol (E2) and progesterone (P4) carried out by a biologist on a Cobass e 411 HITACHI type device (**Figure 3**).

Then every 2 - 3 days depending on progress, until at least 2 follicles of 17 mm are obtained. Triggering was based on an intramuscular injection of 10,000 IU of Human Chorionic Gonadotropin (HCG) for the agonist protocols and triptorelin (decpeptyl) 0.1 mg or HCG in the case of the antagonist protocol. The oocyte

Figure 2. ACUSON X150 type ultrasound device.

Figure 3. Cobas e 411 HITACHI immunoassay device.

retrieval was carried out 36 hours later. The luteal phase was supported by daily intake of micronized progesterone 600 mg/day vaginally from the day of oocyte retrieval until the pregnancy test (12 days later). The embryo transfer was most often carried out on D2 or D3 after the puncture under ultrasound control. It could be carried out in the same cycle or postponed to a later cycle due either to the high progesterone level on the day of initiation or risk of hyperstimulation. Pregnancy was initially diagnosed by a positive plasma HCG level on day 12 after embryo transfer. The data were entered and coded in CS Pro version 6.2 software; then imported and analyzed in IBM SPSS version 23.0 software for statistical analysis. Comparisons between PCOS phenotypes were made by ANOVA tests (LSD post-hoc Tukey test) for continuous variables and the Chi Square test (or the Fisher's Exact test) for categorical variables. Results were expressed as mean ±

standard deviation for continuous variables and as frequencies for categorical variables. P values less than 0.05 were considered statistically significant.

3. Result

3.1. Clinical Characteristics of Patients

The average age of the patients was comparable in the different phenotypes. The average ages ranged from 29.1 ± 4.0 to 33.6 ± 4.8 (p = 0.066). The phenotypes with hyperandrogenism (B > A > C) had higher BMI (respectively 35.47 ± 7.3 > 28.26 ± 4.0 > 25.87 ± 2.3 kg/m^2) than the D phenotype without hyperandrogenism (25.83 ± 4.8). Phenotypes with the ultrasound criterion for PCOS (A, C, D) had AMH and CFA statistically higher than the control group (p < 0.001). The phenotypes with ovulation disorders (A, B and D) had an LH/FSH ratio not only > 1 but also statistically higher than the control group (p = 0.011) (Table 1).

3.2. Therapeutic Characteristics

During stimulation, the total dose of gonadotropins was significantly lower in phenotype D (without hyperandrogenism) compared to the control group (p = 0.002). Among the groups with ovulation disorders (A, B, D), it is the one without ultrasound signs (phenotype B) which received a higher dose of gonadotropins (p = 0.002). The estradiol level on the day ovulation was triggered was highest in the group without hyperandrogenism (phenotype D) compared to the control group (p = 0.018) (Table 2).

3.3. Therapeutic Evaluation

The average numbers of collected follicles and mature oocytes were higher in phenotypes with PCOS ultrasound criteria A, C and D without significant difference. As for the maturation rate, it was comparable between the different groups (p = 0.061) (Table 3). Although the difference was not statistically significant, only the group without hyperandrogenism presented ovarian hyperstimulation syndrome (OHSS), *i.e.*, 3/35 (8.6%) and 1/35 (2.9%). This allowed

Table 1. Clinical characteristics of patients.

Variables	PCOS Phenotypes				Controls (N = 64)	P
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Mean Ag	33.6 ± 4.8	33.2 ± 3.7	29.1 ± 4.0	30.5 ± 4.3	32.4 ± 4.2	0.066
BMI** (Kg/m^2)	28.26 ± 4.0^{b}	35.47 ± 7.3^{a,c,d,e}	25.87 ± 2.3^{b}	25.83 ± 4.8^{b}	26.62 ± 3.7^{b}	0.000
AMH level	5.12 ± 2.7^{e}	2.92 ± 1.1^{d}	5.25 ± 1.9^{e}	6.72 ± 2.9^{b,e}	2.33 ± 1.1^{a,c,d}	0.000
LH/FSH	2.0 ± 1.2^{e}	1.5 ± 1.8^{e}	1.0 ± 0.2	1.4 ± 1.1^{e}	0.7 ± 0.4^{a,b,d}	0.011
CFA	35.5 ± 15.1^{b,e}	10.0 ± 4.6^{a,c,d}	32.2 ± 10.0^{b,e}	36.6 ± 9.2^{b,e}	13.3 ± 6.5^{a,c,d}	0.000

[a]Significant difference with phenotype A; [b]Significant difference with phenotype B; [c]Significant difference with phenotype C; [d]Significant difference with phenotype D; [e]Significant difference with the control group.

Table 2. Therapeutic characteristics of patients.

Variables	PCOS Phenotypes				Controles (N = 64)	p
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Stimulation protocol						
Short agonist	9 (64.3)	4 (80.0)	7 (70.0)	17 (48.6)	60 (93.7)	0.001
Antagonist	5 (35.7)	1 (20.0)	3 (30.0)	18 (51.4)	4 (6.3)	
Total dose of gonadotropine	1903.6 ± 704.1[b]	2925.5 ± 725.2[a,d]	2010.0 ± 793.6	1939.7 ± 454.3[b,e]	2334.3 ± 690.8[d]	0.002
Duration of stimulation	11.3 ± 2.1	13.4 ± 1.9	11.3 ± 2.4	11.7 ± 1.8	12.1 ± 2.0	0.175
Total estradiol on the triggering day	5508.6 ± 5208.6	3536.8 ± 1155.3	5052.3 ± 4122.0	6529.8 ± 4324.8[e]	4242.7 ± 2473.8[d]	0.018

[a]Significant difference with phenotype A; [b]Significant difference with phenotype B; [c]Significant difference with phenotype C; [d]Significant difference with phenotype D; [e]Significant difference with the control group.

Table 3. Response to ovarian stimulation.

Variables	PCOS phenotypes				Controles (N = 64)	p
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Number of punctured follicles	15.5 ± 5.68	13.4 ± 6.1	18.0 ± 10.1[e]	20.6 ± 12.4[e]	9.5 ± 4.6[c,d]	0.000
Type of response						
Hypo-response	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.8)	0.267
Normo-response	7 (50.0)	4 (80.0)	4 (40.0)	13 (37.1)	52 (81.3)	0.000
Hyper-response	7 (50.0)	1 (20.0)	6 (60.0)	22 (62.9)	6 (9.4)	0.000
M2 oocytes	10.9 ± 5.4	9.0 ± 2.6	10.5 ± 7.2	12.0 ± 7.6[e]	6.7 ± 3.5[d]	0.004
Maturation rate (in %)	70.6 ± 19.9	65.3 ± 15.6	63.1 ± 27.9	61.7 ± 19.9	73.9 ± 19.8	0.061
M1 oocytes	0.6 ± 0.9	1.8 ± 2.1	2.6 ± 3.7	1.8 ± 3.5	0.7 ± 1.0	0.247
Number of VGs	1.8 ± 2.8	0.6 ± 0.9	2.8 ± 3.3	2.5 ± 4.1	0.6 ± 1.3	0.057
Rate of immaturity (in %)	14.4 ± 19.2	15.0 ± 15.4	29.2 ± 23.3	18.7 ± 18.6	13.6 ± 16.3	0.121

Variables	PCOS Phenotypes				Controles (N = 64)	p
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Age of embryo transfer						
D2	6 (46.2)	4 (80.0)	7 (70.0)	13 (38.2)	32 (50.0)	0.90
D3	5 (38.5)	1 (20.0)	2 (20.0)	9 (26.5)	25 (39.1)	
D5	2 (15.4)	0 (0.0)	1 (10.0)	12 (35.3)	7 (10.9)	
Type of embryo transfered						
Fresh	10 (76.9)	3 (60.0)	7 (70.0)	29 (85.3)	59 (92.2)	0.102
Frozen	3 (23.1)	2 (40.0)	3 (30.0)	5 (14.7)	5 (7.8)	
Rate of positive BHCG after transfer	4 (30.8)	1 (20.0)	4 (40.0)	14 (41.2)	14 (21.9)	0.310
Ultrasound pregnancies	2 (15.4)	0 (0.0)	2 (20.0)	11 (32.4)	11 (17.2)	0.304

us to determine a prevalence of OHSS estimated at 2.3% (3/128).

3.4. IVF-ICSI Outcome

Phenotype A patient had a fertilization failure (1/14 or 7.14%) and a phenotype D patient had all her embryos degenerated (1/35 or 2.85%) and therefore had no embryo transfer. The fertilization rate seemed lower in the phenotypes with hyperandrogenism A, B, C (63.3% ± 30.7%; 65.9% ± 15.18% and 67.2% ± 16.2% respectively) compared to the phenotype D without hyperandrogenism (75.7% ± 19.3%) without significant difference (p = 0.461). The average number of top-quality embryos was comparable between the different groups (p = 0.207) (Table 4).

Once the embryos were obtained and transferred, the biological pregnancy rates were comparable in the different groups: 30.8%, 20.0%, 40.0%, 41.2% and 21.9% respectively in phenotypes A, B, C, D and the control group (p = 0.310) (Table 5).

4. Discussion

Age was comparable in the different phenotypes. These results were close to

Table 4. Outcome in IVF-ICSI.

Variables	PCOS Phenotypes				Controles (N = 64)	p
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Fertility rate (in %)	63.3 ± 30.7	65.9 ± 15.18	67.2 ± 16.2	75.7 ± 19.3	72.8 ± 24.2	0.461
Number degenerated	1.0 ± 0.9	1.0 ± 0.7	1.3 ± 1.5	1.2 ± 1.5[e]	0.5 ± 1.0[d]	0.038
Number of top quality embryo	3.2 ± 2.4	2.8 ± 1.3	3.8 ± 2.0	3.6 ± 1.8	2.8 ± 1.8	0.207
Percentage of top quality embryo (in %)	71.8 ± 32.0	56.7 ± 22.1	80.0 ± 23.0	72.8 ± 30.1	73.0 ± 27.4	0.677

Table 5. Distribution of phenotypes according to the results after transfer.

Variables	PCOS Phenotypes				Controles (N = 64)	p
	A (N = 14)	B (N = 5)	C (N = 10)	D (N = 35)		
Age of embryo transfer						
D2	6 (46.2)	4 (80.0)	7 (70.0)	13 (38.2)	32 (50.0)	
D3	5 (38.5)	1 (20.0)	2 (20.0)	9 (26.5)	25 (39.1)	0.90
D5	2 (15.4)	0 (0.0)	1 (10.0)	12 (35.3)	7 (10.9)	
Type of embryo transfered						
Fresh	10 (76.9)	3 (60.0)	7 (70.0)	29 (85.3)	59 (92.2)	0.102
Frozen	3 (23.1)	2 (40.0)	3 (30.0)	5 (14.7)	5 (7.8)	
Rate of positive BHCG after transfer	4 (30.8)	1 (20.0)	4 (40.0)	14 (41.2)	14 (21.9)	0.310
Ultrasound pregnancies	2 (15.4)	0 (0.0)	2 (20.0)	11 (32.4)	11 (17.2)	0.304

those of the study by Wang *et al.* carried out in China in 2022 which found an average age of between 28.87 ± 3.02 and 29.49 ± 3.46 (p = 0.095) [3]. PCOS phenotypes with hyperandrogenism (B > A > C) had a higher BMI than the D phenotype without hyperandrogenism. These results were consistent with those found in Belgium by Mackens *et al.* with a significantly higher BMI in phenotypes with hyperandrogenism (p < 0.001) [8]; this can be justified by the pathophysiology of PCOS involving hyperandrogenism in the occurrence of obesity (metabolic syndrome) by mechanism of insulin resistance (and reactive hyperinsulinemia with adipogenesis) and obesity itself increasing hyperandrogenism. Concerning the different phenotypes, the phenotypes presenting the ultrasound criterion for PCOS (A, C and D) had a significantly higher ovarian reserve than phenotype B without ultrasound criterion. These data are in strong agreement with those found in Iran by Ramezanali *et al.* who found an AMH varying between 5.8 ± 2.4 and 6.8 ± 2.8 ng/ml and a CFA (from 33.2 ± 3.9 to 35.4 ± 4.8) [7], in Italy by Cela *et al.* (AMH: 7.78 ± 2.63 to 10.57 ± 0.79 ng/ml and a CFA: 25.89 ± 8.19 to 36.43 ± 8.18) [5] and in China by Wang *et al.* (AMH: 8.86 ± 4.37 to 12.35 ± 6.03 ng/ml and CFA ranging from 27.74 ± 8.62 to 33.73 ± 11.64) [3]; The duration of stimulation was comparable between the different groups. These results confirmed those of Wang *et al.* with stimulation durations of between 10.04 ± 2.40 and 10.55 ± 2.52 days [3]. Studies by Cela in Italy and Ramezanali in Iran also found similar results but with shorter average durations varying between 9.34 ± 1.87 and 11.75 ± 2.06 days and between 10.1 ± 2.3 and 10.4 ± 2.1 days respectively [6] [7].

The total dose of gonadotropins used during ovarian stimulation was lower in phenotype D. These results agree with those of Cela *et al.* who found a lower total dose of gonadotropins used (1377.92 ± 618.0 IU) in phenotype D. Hyperandrogenism may alter folliculogenesis by disrupting the meiotic cell cycle of the oocyte, leading to premature cessation of oocyte development. This mechanism compromises oocyte maturation and the complete acquisition of its skills. The exact mechanisms of this maturation defect in PCOS remain poorly understood compared to other phenotypes [6]; but do not corroborate those of Wang *et al.* in whom the total doses were comparable in the different phenotypes [3].

The estradiol level on the day of ovulation triggering was higher in phenotypes with ultrasound criterion (A, C and D). The studies by Cela and Wang also went in the same direction, but found lower doses respectively ranging from 1479.77 ± 828.05 to 2034.25 ± 1732.5 ng/ml and from 4168.88 ± 2488.18 to 4882.83 ± 2918.41 ng/ml. This discrepancy is explained by the use of the short agonist protocol "microflare" in a large proportion of PCOS patients due to the unavailability of antagonists at the given times.

The numbers of follicles collected after puncture and mature oocytes obtained after decoronization appeared to be lower in the phenotypes with hyperandrogenism A, B, C without significant difference. These results follow the same trend as those of Cela *et al.* with lower numbers of follicles ranging from 7.1 ± 2.56 to

8.54 ± 3.59 follicles and 3.58 ± 1.50 to 5.11 ± 1.45 M2 in hyperandrogenic phenotypes (A, B, C) versus 9.36 ± 4.36 follicles and 6.84 ± 3.15 M2 in phenotype D without hyperandrogenism [6]. However, Wang *et al.* reported comparable results between the different phenotypes.

The results did not show any differences in terms of immature oocytes in the different phenotypes. But the number of immature oocytes were significantly higher in the group of PCOS patients (2.22 ± 3.60 VG and 1.70 ± 3.10 M1) compared to the control group (0.64 ± 1.32 VG and 0.80 ± 1.03 M1) ($p < 0.001$). These results can be justified by data from the literature which states that hyperandrogenism alters folliculogenesis and compromises oocyte maturation [9]-[15].

Ovarian hyperstimulation syndrome occurred mainly in phenotype D without hyperandrogenism. These data are similar to those found in the literature reporting that the occurrence of OHSS varies between 3% - 8% [8]; but a study conducted in France by Isnard *et al.* on ovarian stimulation with gonadotropins in patients with female polycystic ovarian syndrome reported two cases of OHSS with a lower prevalence of 1.1% which could be explained by the exclusive use of the antagonist protocol.

The fertilization rate was lower in phenotypes A, B, C with hyperandrogenism without significant difference ($p = 0.461$). This result could be explained by the fact that hyperandrogenism alters the quality of oocytes [11] [12] [13] [14] [15]. But once the embryos were obtained, the average number of top quality embryos was comparable between the different phenotypes ($p = 0.207$). The same results were found by Wang *et al.*, Ramezanali *et al.* and by Cela *et al.* Biological pregnancy rates were comparable in the different groups. These results were similar to those of Ramezanali *et al.* which found biological pregnancy rates of 32.5%, 26.4%, 36.8%, 53.3% and 45.1% in phenotypes A, B, C, D.

5. Conclusion

Phenotypes D and A were respectively the most represented. Age was comparable between the different groups. BMI was higher in phenotypes with hyperandrogenism. Ovarian reserve was significantly higher in phenotypes with ultrasound criterion (A, C, D). Ovarian hyperstimulation syndrome occurred mainly in phenotype D. Phenotype D seemed to have a higher pregnancy rate. This raises the question of systematic treatment of hyperandrogenism before or during ovarian simulation in these PCOS phenotypes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Lizneva, D., Suturina, L., Walker, W., Brakta, S., Gavrilova-Jordan, L. and Azziz, R.

(2016) Criteria, Prevalence, and Phenotypes of Polycystic Ovary Syndrome. *Fertility and Sterility*, **106**, 6-15. https://doi.org/10.1016/j.fertnstert.2016.05.003

[2] Azziz, R., Woods, K.S., Reyna, R., Key, T.J., Knochenhauer, E.S. and Yildiz, B.O. (2004) The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population. *The Journal of Clinical Endocrinology & Metabolism*, **89**, 2745-2749. https://doi.org/10.1210/jc.2003-032046

[3] Wang, Q., Wang, H., Li, P., Li, X., Wang, Z., Yan, L., *et al.* (2022) Association of Polycystic Ovary Syndrome Phenotypes with Adverse Pregnancy Outcomes after *In-Vitro* Fertilization/Intracytoplasmic Sperm Injection. *Front Endocrinol*, **13**. https://doi.org/10.3389/fendo.2022.889029 https://www.frontiersin.org/articles/10.3389/fendo.2022.889029

[4] Giampaolino, P., Morra, I., Della Corte, L., Sparice, S., Di Carlo, C., Nappi, C., *et al.* (2017) Serum Anti-Mullerian Hormone Levels after Ovarian Drilling for the Second-Line Treatment of Polycystic Ovary Syndrome: A Pilot-Randomized Study Comparing Laparoscopy and Transvaginal Hydrolaparoscopy. *Gynecological Endocrinology*, **33**, 26-29. https://doi.org/10.1080/09513590.2016.1188280

[5] Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2008) Consensus on Infertility Treatment Related to Polycystic Ovary Syndrome. *Fertility and Sterility*, **89**, 505-522. https://doi.org/10.1016/j.fertnstert.2007.09.041

[6] Giampaolino, P., De Rosa, N., Della Corte, L., Morra, I., Mercorio, A., Nappi, C., *et al.* (2018) Operative Transvaginal Hydrolaparoscopy Improve Ovulation Rate after Clomiphene Failure in Polycystic Ovary Syndrome. *Gynecol Endocrinol Off J Int Soc.*, **34**, 32-35. https://doi.org/10.1080/09513590.2017.1412429

[7] Cela, V., Obino, M.E.R., Alberga, Y., Pinelli, S., Sergiampietri, C., Casarosa, E., *et al.* (2018) Ovarian Response to Controlled Ovarian Stimulation in Women with Different Polycystic Ovary Syndrome Phenotypes. *Gynecological Endocrinology*, **34**, 518-523. https://doi.org/10.1080/09513590.2017.1323204

[8] Ramezanali, F., Ashrafi, M., Mandana, H., Arabipoor, A., Jalali, S. and Moini, A. (2016) Assisted Reproductive Outcomes in Women with Different Polycystic Ovary Syndrome Phenotypes: The Predictive Value of Anti-Mullerian Hormone. *Reproductive BioMedicine*, **32**, 503-512. https://doi.org/10.1016/j.rbmo.2016.01.010

[9] Brodin, T., Bergh, T., Berglund, L., Hadziosmanovic, N. and Holte, J. (2009) High Basal LH Levels in Combination with Low Basal FSH Levels Are Associated with High Success Rates at Assisted Reproduction. *Human Reproduction*, **24**, 2755-2759. https://doi.org/10.1093/humrep/dep254

[10] Mackens, S., Pareyn, S., Drakopoulos, P., Deckers, T., Mostinckx, L., Blockeel, C., *et al.* (2020) Outcome of *In-Vitro* Oocyte Maturation in Patients with PCOS: Does Phenotype Have an Impact? *Human Reproduction*, **35**, 2272-2279. https://doi.org/10.1093/humrep/deaa190

[11] Le Gouez, A., Naudin, B., Grynberg, M. and Mercier, F.J. (2011) Le syndrome hyperstimulation ovarienne. *Annales Françaises d'Anesthésie et de Réanimation*, **30**, 353-362. https://doi.org/10.1016/j.annfar.2010.11.026

[12] Madill, J.J., Mullen, N.B. and Harrison, B.P. (2008) Ovarian Hyperstimulation Syndrome: A Potentially Fatal Complication of Early Pregnancy. *Journal of Emergency Medicine*, **35**, 283-286. https://doi.org/10.1016/j.jemermed.2007.11.074

[13] Patel, S.S. and Carr, B.R. (2008) Oocyte Quality in Adult Polycystic Ovary Syndrome. *Seminars in Reproductive Medicine*, **26**, 196-203. https://doi.org/10.1055/s-2008-1042958

[14] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004)

Revised 2003 Consensus on Diagnostic Criteria and Long-Term Health Risks Related to Polycystic Ovary Syndrome. *Fertility and Sterility*, **81**, 19-25. https://doi.org/10.1016/j.fertnstert.2003.10.004

[15] Wood, J.R., Ho, C.K., Nelson-Degrave, V.L., McAllister, J.M. and Strauss III, J.F. (2004) The Molecular Signature of Polycystic Ovary Syndrome (PCOS) Theca Cells Defined by Gene Expression Profiling. *Journal of Reproductive Immunology*, **63**, 51-60. https://doi.org/10.1016/j.jri.2004.01.010