MEDDOCS Open Access Publisher

ISSN 2641-6522

Annals of Obstetrics and Gynecology

Open Access | Research Article

The Pregnancy Outcomes of Patients with Antinuclear Antibodies or Antiphospholipid Antibodies Positive Undergo *In Vitro* Fertilization

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Received: Apr 30, 2023

Accepted: May 19, 2023

Published Online: May 26, 2023

Journal: Annals of Obstetrics and Gynecology

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Antiphospholipid antibodies; Antinuclear antibodies; In vitro fertilization; Infertility.

Abstract

Objectives: To explore the prevalence of Antinuclear Antibodies (ANA) and antiphospholipid antibodies (aPLs) in infertile women who experienced In Vitro Fertilization (IVF) failure and to investigate the impact of ANA and aPLs on the pregnancy outcomes of IVF in these patients.

Methods: A total of 2727 infertile patients underwent IVF at the Reproductive Center of Peking University People's Hospital from January 2016 to December 2016 were included in this study. Patients who experienced IVF failure at least once underwent ANA and aPLs tests. Finally, 425 patients were included in this study and were followed up until December 2021. The prevalence of ANA and aPLs and the association between those antibodies and IVF-ET outcomes (including the embryo implantation rate, the clinical pregnancy rate and the live birth rate) were assessed.

Results: ANA was positive in 52 (14.2%) of the 365 patients and the prevalence of ANA at titers of 1:40, 1:80, 1:160, and 1:320 was 9.3%, 2.7%, 0.8% and 1.4%, respectively. The positivity of anticardiolipin antibody (aCL), anti-β2-glycoprotein I antibody (aβ2GPI), and lupus anticoagulant (LAC) were 3.0%, 2.8%, and 1.3% among 411 women, respectively. The IVF-ET outcomes were all comparable in both the ANA-positive and negative groups, as well as in the aPLs-positive and negative groups. Aspirin increased the probability of live birth (OR 1.868, 95% CI 1.110 to 3.142, $P = 0.019$) and clinical pregnancy (OR 2.262, 95% CI 1.328 to 3.850, $P = 0.003$) after adjustment for laboratory confounders.

Conclusion: The presence of ANA or aPLs do not result in adverse IVF outcomes in patients who experienced fertilization failure. Aspirin increase the probability of good IVF outcomes.

Cite this article: Yuke H, Ziyi S, Yuchao Z, Peng Z, Cai X, et al. The Pregnancy Outcomes of Patients With Antinuclear Antibodies or Antiphospholipid Antibodies Positive Undergo *In Vitro* Fertilization. Ann Obstet Gynecol. 2023; 6(1): 1048.

Introduction

Infertility is one of the three major diseases affecting human life and health in the 21st century by World Health Organization [1]. The prevalence of infertility among couples of reproductive age is about 10%-15%, which is increasing year by year [2-4]. *In-Vitro* Fertilization and Embryo Transfer (IVF-ET) is an effective therapy for infertility. Despite the remarkable development of IVF-ET, a large proportion of IVF attempts have failed [5].

Previous studies have suggested that autoimmunity, including cellular and humoral immunity, is an essential factor in infertility [4,5]. Thus, many investigators focused on the relationship between autoantibodies and IVF-ET outcomes [6,7]. Antinuclear antibodies (ANA) and antiphospholipid antibodies (aPLs) are two widely investigated antibodies [7,8]. However, there is no consensus as to the association of ANA and/or aPLs and IVF outcomes [9-11].

Adjuvant aspirin has been shown in previous trials to enhance the live birth rate in patients with recurrent implantation failure [12-14]. However, there are still conflicting opinions that aspirin does not help improve clinical pregnancy rates, embryo implantation rates and live birth rates [15,16]. Aspirin as an adjunct to IVF is therefore controversial. There has also been little research on whether aspirin should be used before IVF in patients with the presence of ANA or aPLs.

The aim of this study is to explore the prevalence of ANA and aPLs in infertile women who had experienced fertilization failure and to study the association between autoantibodies and IVF-ET outcomes.

Methods

Study design and population

This was an observational cohort study. A total of 2727 infertile women undergo IVF-ET from January 2016 to December 2016 were screened. Patients who failed at least one IVF-ET cycle were tested for ANA profile and aPLs [anticardiolipin antibody (aCL), anti-β2-glycoprotein I antibody (aβ2GPI), and lupus anticoagulant (LA)]. The exclusion criteria were as follows: male infertility, uterine factor infertility (uterine malformation, endometritis, intrauterine adhesion), or female chromosomal abnormalities. Finally, 425 patients were included in the study **(Figure 1)** and were followed up until December 2021. Of the enrolled patients, 365 individuals underwent ANA test, and 411 underwent aPLs test. The correlation between autoantibodies and IVF-ET outcomes was analyzed.

Patients with undifferentiated connective tissue disease (UCTD) [17,18], Sjögren's syndrome (SS) [9], Rheumatoid Arthritis (RA) [20], Systemic Lupus Erythematosus (SLE) [21], and antiphospholipid syndrome (APS) [22] were diagnosed according to the current classification criteria, respectively.

Detection of serum ANA and aPLs

Immunofluorescence (IF) assay was used to detect ANA in serum using diagnostic kits (EUROIMMUN, Lubeck, Germany). Biochips coated with monkey liver cells and human epithelial (HEp-2) cells were used to determine serum ANA. The dilution factors were as follows: 1:40, 1:80, 1:160, 1:320 and 1:640. The ANA was considered positive with characteristic fluorescent signal and a dilution ratio ≥ 1:40. An assessment was carried out using the International Consensus on ANA Patterns (ICAP) criteria [23]. Immunoblotting Test (IBT) was used to detect anti-Extractable Nuclear Antigens (ENA) antibodies by diagnostic kits (EUROIMMUN, Lubeck, Germany). Enzyme Linked Immunosorbent Assay (ELISA) was used to detect anti-dsDNA antibody (ORGANTEC, Germany).

IgG/IgM/IgA aCL, IgG/IgM/IgA aβ2GPI were determined by ELISA (EUROIMMUN, Lubeck, Germany). The local cut-off value for aCL was > 12 IU/mL and aβ2GPI was > 27 RU/mL [24]. The LA assay was performed using Stago STA Compact Hemostasis System and the simplified Dilute Russell's Viper Venom Test (dRVVT) ratios >1.2 were considered positive [24].

Data collection

Age, age at menarche, duration of infertility, number of pregnancies were collected as baseline data. The parameters related to IVF included number of controlled ovarian hyperstimulation cycles, total and average number of retrieved oocytes, total and average number of available embryos, number of available blastocysts and good-quality blastocysts, total and average number of good-quality embryos, number of embryo transfer cycles, number of fresh embryo transfer cycles, number of frozen-thawed embryo transfer cycles, number of transferred blastocysts, number of embryo implantation failures, number of biochemical pregnancies, number of clinical pregnancies, number of miscarriages, and number of live births. The fetal outcomes including average fetal weight, average fetal length and neonatal malformation were also collected.

The IVF-ET outcomes

IVF-ET outcomes included the embryo implantation rate, the clinical pregnancy rate and the live birth rate. Embryo implantation rate was defined as the number of gestational sacs observed divided by the number of embryos transferred [25]. Clinical pregnancy was defined as ultrasonographic visualization of intrauterine gestational sac and fetal heartbeat at 28-35 days after embryo transfer [25]. Live birth was defined as delivery of any viable infant ≥ 28 weeks gestation [26]. Biochemical pregnancy was defined as β-hCG level > 25 IU/L on the fourteenth day after embryo transfer [26]. Spontaneous miscarriage was defined as loss of an intra-uterine pregnancy prior to 22 completed weeks of gestational age [25].

Statistical analysis

Continuous variables were demonstrated as mean ± Standard Deviation (SD). Categorized variables were shown as frequency or percentage. Levene's test for homogeneity of variance and the Kolmogorov–Smirnov test for normality were used. The $\chi 2$ test was used for categorical variables, while t-test was used to analyze continuous variables that followed a normal distribution. Binary logistic regression analysis was applied to assess the associations between IVF-ET outcomes, autoantibodies and treatments. Differences were considered statistically significant when $P < 0.05$. Statistical Package for Social Science (SPSS 26.0) was used to analyze all data.

Results

The mean age of these infertile patients was 34.4 ± 4.7 years. The mean age at menarche was 13.4 ± 1.3 years. The mean duration of infertility was 3.8 ± 2.9 years. The mean follow-up was 19.7 ± 10.9 months.

The ANA positivity and IVF outcome

ANA was positive in 14.2% (52/365) patients. Among ANA

positive patients, the titers of 1:40, 1:80, 1:160 and 1:320 were 9.3%, 2.7%, 0.8% and 1.4%, respectively. Of the ANA-positive samples detected by indirect immunofluorescence (IIF), 37.1% was speckled pattern, 32.9% was homogeneous pattern, 12.9% was cytoplasmic pattern, 8.6% was centromere pattern, 5.7% was nucleolar pattern, 2.9% was membranous pattern **(Table 1)**.

The positive rate of anti-dsDNA, anti-SSA antibody, anti-Ro52 antibody, anti-centromere antibody, anti-RNP antibody, anti-ribosomal antibody, anti-SSB antibody, anti-nucleosome antibody in these patients were 5.8%, 5.8%, 5.8%, 3.8%, 1.9%, 1.9%, 1.9%, 1.9%, respectively **(Table 1)**.

The baseline clinical characteristics were comparable between ANA-positive (n = 52) and ANA-negative groups (n = 313). The embryo implantation rate (19.3% vs. 23.0%, *P* = 0.235), the biochemical pregnancy rate (36.4% vs. 41.8%, *P* = 0.293), the clinical pregnancy rate (32.7% vs. 34.4%, *P* = 0.729) and the live birth rate (24.3% vs. 20.4%, *P* = 0.350) were all similar between the two groups **(Table 2)**.

The aPLs positivity and IVF outcomes

The positive rates of aCL, aβ2GPI, and LA were 3.0%, 2.8%, and 1.3%, respectively. Twenty-four patients were single positive (5.8%), two were double-positive (0.5%) and none were triple-positive.

The clinical pregnancy rate (33.9% vs. 34.0%, *P* = 0.988), the embryo implantation rate (22.4% vs. 29.0%, *P* = 0.984), the biochemical pregnancy rate (35.5% vs. 41.3%, *P* = 0.367), and the live birth rate (12.9% vs. 21.2%, *P* = 0.120) were comparable between the aPLs-positive and aPLs-negative group **(Table 3)**.

Diagnosis of autoimmune diseases

Among these autoantibody-positive patients, 12 patients were diagnosed with UCTD, 2 with SS, 2 with RA, 2 with SLE, and 1 with APS. Two SLE patients were diagnosed before IVF, and the other 18 patients were diagnosed by rheumatologist after IVF failure.

The Medications and IVF outcomes

Of the patients, 313 (73.6%) were prescribed medications. Aspirin, Low Molecular Weight Heparin (LMWH), Hydroxychloroquine (HCQ), and glucocorticoids (GCs) accounted for 69.6%, 37.2%, 8.0%, and 8.0%, respectively.

We found that aspirin use (73.8% vs. 63.0%, *P* = 0.019) was higher in patients with a successful clinical pregnancy, while use of LMWH (73.8% vs. 63.0%, *P* = 0.019), HCQ (6.8% vs. 9.9%, *P* = 0.263), and GCs (7.2% vs. 9.3%, *P* = 0.453) was equivalent to that of patients without a clinical pregnancy. If live birth was considered as the basis of grouping, the proportion of patients in the live birth group using LMWH (29.9% vs. 43.9%, *P* = 0.003), HCQ (4.4% vs. 11.3%, *P* = 0.009) and GCs (4.4% vs. 11.3%, *P* = 0.009) is lower than that in the non-live birth group, and there was no significant difference in aspirin use (72.1% vs. 67.4%, *P* = 0.229) between the two groups **(Table 4/5)**.

Binary logistic regression analysis included factors with P < 0.1 in univariate analysis and factors associated with IVF outcomes reported in previous research, such as ANA, aPLs, aspirin, LMWH, HCQ, and GCs [14,27-30]. Aspirin increased the probability of live birth (OR 1.868, 95% CI 1.110 to 3.142, *P* = 0.019) and clinical pregnancy (OR 2.262, 95% CI 1.328 to 3.850, *P* = 0.003) after adjustment for laboratory confounders. LMWH (OR 0.474, 95% CI 0.288 to 0.780, *P* = 0.003; OR 0.549, 95% CI 0.328 to 0.921, *P* = 0.023), HCQ (OR 0.566, 95% CI 0.209 to 1.534, *P* = 0.263; OR 0.632, 95% CI 0.253 to 1.582, *P* = 0.327) and GCs (OR 0.601, 95% CI 0.234 to 1.543, *P* = 0.290; OR 1.273, 95% CI 0.519 to 3.123, *P* = 0.598) did not improve IVF outcomes, including live birth and clinical pregnancy **(Table 6/7)**.

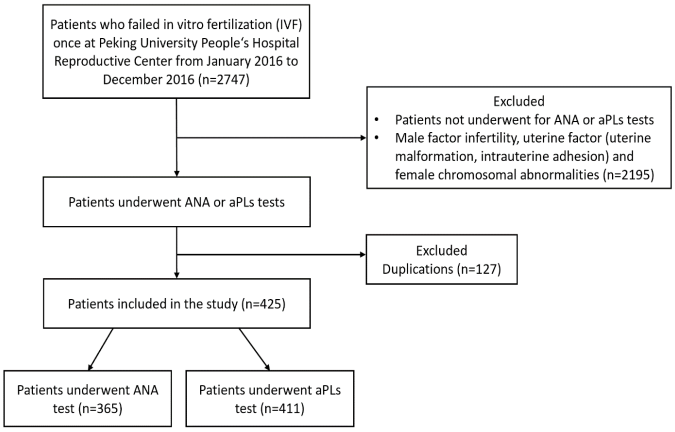

Figure 1: Flow diagram of the study.
ANA: Antinuclear Antibody; **aPLs:** antiphospholipid antibodies.

Table 1: Fluorescence karyotype and target antigen analysis in ANA-positive patients.

Variables	Value
ANA-fluorescence karyotype	
Speckled pattern, n (%)	26 (37.1)
Homogeneous pattern, n (%)	23 (32.9)
Cytoplasmic pattern, n (%)	9 (12.9)
Centromere pattern, n (%)	6 (8.6)
Nucleolar pattern, n (%)	4 (5.7)
Membranous pattern, n (%)	2 (2.9)
ANA-target antigen	
Not identified, n (%)	44 (84.6)
Anti-dsDNA antibody, n (%)	3 (5.8)
Anti-SSA antibody, n (%)	3 (5.8)
Anti-Ro52 antibody, n (%)	3 (5.8)
Anti-centromere antibody, n (%)	2 (3.8)
Anti-RNP antibody, n (%)	1 (1.9)
Anti-ribosomal antibody, n (%)	1 (1.9)
Anti-SSB antibody, n (%)	1 (1.9)
Anti-nucleosome antibody, n (%)	1 (1.9)

ANA: Antinuclear Antibody; dsDNA: double-stranded DNA; **RNP:** Ribonuclear Protein.

Table 2: Comparison of infertility characteristics and IVF outcomes between ANA- positive and ANA-negative women.

Variables	ANA-positive group (n = 52)	ANA-negative group (n = 313)	*P*
Age, yrs	34.4 ± 4.9	34.3 ± 4.7	0.825
Age at menarche, yrs	13.2 ± 1.1	13.5 ± 1.3	0.225
Duration of infertility, yrs	3.2 ± 2.4	3.8 ± 2.9	0.122
No. of controlled ovarian hyperstimulation cycles	1.9 ± 1.8	1.9 ± 1.4	0.989
Total No. of retrieved oocytes	14.2 ± 8.5	15.3 ± 9.8	0.451
Average No. of retrieved oocytes	10.1 ± 7.4	10.0 ± 6.9	0.93
Total No. of available embryos	5.4 ± 2.7	6.2 ± 4.2	0.2
Average No. of available embryos	4.0 ± 2.7	4.2 ± 3.7	0.683
Total No. of good-quality embryos	0.9 ± 1.7	1.2 ± 1.5	0.368
Average No. of good-quality embryos	0.7 ± 1.6	0.9 ± 1.2	0.216
No. of ET cycles	2.1 ± 1.0	2.4 ± 1.4	0.104
No. of fresh embryo transfer cycles	0.4 ± 0.7	0.4 ± 0.6	0.821
No. of FET cycles	1.7 ± 0.9	2.0 ± 1.3	0.118
No. of transferred embryos	3.9 ± 1.9	4.4 ± 2.6	0.11
No. of transferred blastocysts	1.2 ± 1.4	1.7 ± 1.8	0.061
No. of clinical pregnancies	0.7 ± 0.6	0.8 ± 0.7	0.175
No. of live births	0.5 ± 0.5	0.5 ± 0.5	0.833
Average fetal weight (g)	3311 ± 818	3081 ± 769	0.197
Average fetal length (cm)	49.5 ± 3.6	48.7 ± 3.6	0.308
Embryo implantation rate, n (%)	39/202 (19.3%)	316/1371 (23.0%)	0.235
Biochemical pregnancy rate, n (%)	39/107 (36.4%)	311/744 (41.8%)	0.293
Clinical pregnancy rate, n (%)	35/107 (32.7%)	256/744 (34.4%)	0.729
Live birth rate, n (%)	26/107 (24.3%)	152/744 (20.4%)	0.35
Clinical pregnancy, n (%)	30/52 (57.7%)	199/313 (63.6%)	0.416
Live birth, n (%)	25/52 (48.1%)	151/313 (48.2%)	0.982

FET: Frozen-Thawed Embryo Transfer; **ET:** Embryo Transfer; **ANA:** Antinuclear Antibody; Unless otherwise indicated, numbers are mean ± standard deviation. Data shown are median (95% confidence interval). The Chi-square test was performed for categorical variables and the t-test was performed for continuous variables. For ordinal and numerical variables variable, a *P*-value <.05 was considered significant.

Table 3: Comparison of infertility characteristics and IVF outcomes between aPLs- positive and aPLs-negative women.

Variables	aPLs-positive group (n = 26)	aPLs-negative group (n = 385)	*P*
Age, yrs	35.2 ± 5.7	34. 3 ± 4.6	0.345
Age at menarche, yrs	13.5 ± 1.6	13.4 ± 1.3	0.796
No. of pregnancies	1.0 ± 1.3	0.9 ± 1.2	0.621
Duration of infertility, yrs	3.5 ± 3.1	3.8 ± 2.9	0.624
No. of controlled ovarian hyperstimulation cycles	2.3 ± 2.3	2.0 ± 1.6	0.384
Total No. of retrieved oocytes	15.1 ± 8.5	14.7 ± 9.5	0.821
Average No. of retrieved oocytes	7.6 ± 4.0	9.9 ± 7.0	0.39
Total No. of available embryos	5.9 ± 3.7	6.0 ± 4.0	0.808
Average No. of available embryos	3.1 ± 2.2	4.1 ± 3.5	0.594
Total No. of good-quality embryos	1.6 ± 2.3	1.2 ± 1.5	0.392
Average No. of good-quality embryos	1.1 ± 2.1	0.8 ± 1.2	0.418
No. of ET cycles	2.4 ± 1.3	2.3 ± 1.4	0.852
No. of fresh embryo transfer cycles	0.3 ± 0.7	0.4 ± 0.6	0.697
No. of FET cycles	2.0 ± 1.4	2.0 ± 1.3	0.702
No. of transferred embryos	3.9 ± 1.9	4.4 ± 2.6	0.708

No. of transferred blastocysts	1.3 ± 1.6	1.6 ± 1.7	0.556
No. of biochemical pregnancies	0.8 ± 0.9	1.0 ± 0.8	0.486
No. of clinical pregnancies	0.8 ± 0.8	0.8 ± 0.7	0.916
No. of miscarriages	0.5 ± 0.7	0.3 ± 0.5	0.07
No. of live births	0.3 ± 0.5	0.5 ± 0.5	0.079
Average fetal weight (g)	2924 ± 505	3109 ± 775	0.563
Average fetal length (cm)	48.6 ± 2.1	48.8 ± 3.7	0.885
Embryo implantation rate, n (%)	26/116 (22.4%)	370/1275 (29.0%)	0.984
Biochemical pregnancy rate, n (%)	22/62 (35.5%)	371/898 (41.3%)	0.367
Clinical pregnancy rate, n (%)	21/62 (33.9%)	305/898 (34.0%)	0.988
Live birth rate, n (%)	8/62 (12.9%)	190/898 (21.2%)	0.12
Clinical pregnancy, n (%)	16/26 (61.5%)	239/385 (62.1%)	0.956
Live birth, n (%)	8/26 (30.8%)	190/385 (49.4%)	0.066

FET: Frozen-Thawed Embryo Transfer; **ET:** Embryo Transfer; **aPLs:** Antiphospholipid Antibodies. Unless otherwise indicated, numbers are mean ± standard deviation. Data shown are median (95% confidence interval). The Chi-square test was performed for categorical variables and the t-test was performed for continuous variables. For ordinal and numerical variables variable, a P-value <.05 was considered significant.

Table 4: Treatments of women with or without clinical pregnancy.

Variables	Clinical pregnancy group (n = 263)	Non-clinical pregnancy group (n = 162)	*P*
Treatment			
Yes (n = 313)	207/263 (78.7%)	106/162 (65.4%)	0.003*
No (n = 112)	56/263 (21.3%)	56/162 (34.6%)	
Aspirin	194/263 (73.8%)	102/162 (63.0%)	0.019*
LMWH	94/263 (35.7%)	64/162 (39.5%)	0.435
HCQ	18/263 (6.8%)	16/162 (9.9%)	0.263
GCs	19/263 (7.2%)	15/162 (9.3%)	0.453

LMWH: Low Molecular Weight Heparin; **GCs:** Glucocorticoids; **HCQ:** Hydroxychloroquine. * *P*<0.05

Table 5: Treatments of women with or without live birth.

Variables	Live birth group (n = 204)	Non-live birth group (n = 221)	*P*
Treatment			
Yes (n = 313)	157/204 (77.0%)	156/221 (70.6%)	0.136
No (n = 112)	47/204 (23.0%)	65/221 (29.4%)	
Aspirin	147/204 (72.1%)	149/221 (67.4%)	0.229
LMWH	61/204 (29.9%)	97/221 (43.9%)	0.003*
HCQ	9/204 (4.4%)	25/221 (11.3%)	0.009*
GCs	9/204 (4.4%)	25/221 (11.3%)	0.009*

LMWH: Low Molecular Weight Heparin; **GCs:** Glucocorticoids; **HCQ:** Hydroxychloroquine. * *P*<0.05

Table 6: Binary logistic regression analysis between live birth group and non-live birth group.

Variables	B	SE	OR	95% CI	*P*
Model I					
ANA	-0.022	0.311	0.978	(0.531, 1.801)	0.943
aPLs	-0.896	0.496	0.408	(0.154, 1.080)	0.071
Model II					
ANA	0.046	0.327	1.047	(0.552, 1.987)	0.889
aPLs	-0.828	0.514	0.437	(0.160, 1.196)	0.107
Aspirin	0.625	0.265	1.868	(1.110, 3.142)	0.019*
LMWH	-0.746	0.254	0.474	(0.288, 0.780)	0.003*
HCQ	-0.569	0.509	0.566	(0.209, 1.534)	0.263
GCs	-0.51	0.482	0.601	(0.234, 1.543)	0.29

ANA: Antinuclear Antibody; **aPLs:** Antiphospholipid Antibodies; **LMWH:** Low Molecular Weight Heparin; **GCs:** Glucocorticoids; **HCQ:** Hydroxychloroquine. * *P*<0.05.

Table 7: Binary logistic regression analysis between clinical pregnancy group and non- clinical pregnancy group.

Variables	B	SE	OR	95% CI	*P*
Model I					
ANA	-0.274	0.313	0.76	(0.411, 1.405)	0.382
aPLs	-0.011	0.466	0.99	(0.397, 2.464)	0.982
Model II					
ANA	-0.249	0.325	0.78	(0.412, 1.476)	0.445
aPLs	-0.002	0.478	0.998	(0.391, 2.550)	0.997
Aspirin	0.816	0.271	2.262	(1.328, 3.850)	0.003*
LMWH	-0.599	0.264	0.549	(0.328, 0.921)	0.023*
HCQ	-0.458	0.468	0.632	(0.253, 1.582)	0.327
GCs	0.242	0.458	1.273	(0.519, 3.123)	0.598

ANA: Antinuclear Antibody; **aPLs:** antiphospholipid antibodies; **LMWH:** Low Molecular Weight Heparin; **GCs:** Glucocorticoids; **HCQ:** Hydroxychloroquine * *P*<0.05.

Discussion

In this study, we did not find any association between autoantibodies and IVF outcomes. The role of autoantibodies in IVF has been discussed for almost three decades. Nonetheless, studies are still scarce and widely controversial [31]. The prevalence of ANA in the present study was similar to previous study [6]. The positive rate of ANA was 10.7% among 1720 women undergoing first IVF or intracytoplasmic sperm injection (IVF/ICSI) [6].

The relationship between ANA and IVF outcomes are controversial. Some studies found no relationship between ANA positive and ANA negative groups [6]. However, in a meta-analysis, ANA was associated with poor pregnancy outcomes in infertile women undergoing IVF treatment [11]. Studies have revealed that the presence of ANA might hinder oocytes maturation and embryo development, thus affecting the fertilization rate, the number of good-quality embryos and the implantation process, resulting in IVF/ICSI failure [27,28,32]. However, ANA did not reduce the cumulative pregnancy rate [33].

In clinical practice, physicians try to treat patients with high titers of ANA. Prednisone coupled with HCQ, according to Rui Gao et al' s research, could increase the implantation rate, biochemical pregnancy rate, and clinical pregnancy rate of ANA positive female patients, as well as lower the miscarriage rate [30]. Low dose corticosteroid, or low-dose aspirin plus prednisone could also serve as a treatment option in ANA positive patients [8,34,35]. In our real-world study, we did not see any association between ANA and IVF outcomes, this may because of the treatment in clinical practice.

The prevalence of aPLs was 5.8% among Chinese women with one failed IVF attempt in this research, which was similar to the study conducted by Hong et al. in Korea [36]. The positive rate of aPLs was determined by the definition of infertile population. The proportion of positive aPLs in infertile patients has been reported to be highly variable ranged from 16.0% to 42.1% [37-41]. Khizroeva et al. reported a higher frequency of aPLs circulation in IVF-failure group than IVF-success group (42.1% vs. 19.1%) [41]. The prevalence of each type of aPLs was also low considering other previous studies. Most patients could benefit from APS treatment and do not need IVF-ET procedure.

In the present study, the clinical pregnancy rate, the live birth rate, the biochemical pregnancy rate, and the embryo implantation rate were similar in the aPLs-positive and aPLs-negative groups. Thus, the presence of aPLs may not be associated with adverse IVF outcomes. These results consist with previous investigations which investigate the association between aPLs and IVF outcomes. There was no effect of aPL on IVF outcomes [42].

Aspirin, LMWH, and hydroxychloroquine have been widely used in obstetric APS, unexplained recurrent miscarriage caused by immune factors and connective tissue disease (CTD) [43-47]. According to our research data, aspirin increased the probability of live birth and clinical pregnancy after adjustment for laboratory confounders. However, we did not find the association between LMWH, HCQ, GCs and IVF-ET outcomes.

Our research has some limitations. One of the main limitations of this study is the relatively small sample size of the ANA-positive group and the aPLs-positive group. Moreover, the study is a single-center observational study and lacks universality. Further, sufficiently robust and large-scale multi-center prospective studies are needed.

Conclusions

In conclusion, the presence of ANA or aPLs may not result in adverse IVF-ET outcomes. Aspirin increase the probability of good IVF-ET outcomes, including clinical pregnancy and live birth.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

YK. H, ZY. S, YC. Z, Z. P, X. C, Y. X, Q. L, XW. Z and C. L conceived and designed the project. YK. H. and ZY. S collected and input the clinical and laboratory data. YK. H completed the statistical analyses. YK. H and C.L conducted table and figure predations. YK.H, ZY. S and C.L wrote the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript. All authors discussed the results and contributed to the final manuscript.

Compliance with ethics guidelines

All procedures related to human investigations were performed in accordance with the ethical standards of the responsible committee on human experimentation (Peking University People's Hospital, Beijing, 2019PHB252) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all participants included in the study.

Key Summary Points

Why carry out this study?

Many researchers focused on the connection between autoantibodies (such as ANA and aPLs) and IVF-ET outcomes. Nevertheless, there is no agreement on it.

The objective of this study is to explore the prevalence of ANA and aPLs in infertile women who have had fertilization failure, as well as the correlation between autoantibodies and IVF-ET outcomes.

What was learned from this study?

In patients who had fertilization failure, the presence of ANA or aPLs does not result in poor IVF outcomes.

Funding

This study was supported by the research project from the Beijing Natural Science Foundation (Grant No.7192211), China international medical foundation (Grant No.Z-2018-40-2101) and National Natural Science Foundation of China (No.2101000418).

Acknowledgments

We would like to thank all the rheumatologists, gynaecologists and patients that participated in this study.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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