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Original Article

Clinical characteristics and assisted reproductive technology outcomes in infertile foreign brides: Comparison with native brides in south Taiwan

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Abstract

Objective: This study was conducted to determine if differences in clinical characteristics, embryonic development, and pregnancy outcomes exist between infertile foreign and native brides undergoing assisted reproductive technology (ART) treatment in a foreign-bride-immigrating country of Taiwan.

Material and Methods: A retrospective, case-control design was used to recruit consecutive infertile women seeking ART treatment for study. The treatment protocol consisted of controlled ovarian hyperstimulation with down-regulation and gonadotropin and ART method with conventional *in vitro* fertilization or intracytoplasmic sperm injection. Among the 1083 ART treatment cycles, 97 (9%) were from foreign brides and 986 (91%) from native brides. Records of those who received transfer of fresh embryos obtained by using husband sperm for fertilization were collected for analysis. A case-control design with adjustment of bride age was used to select the records of 86 infertile foreign and 172 native brides for the study. Infertility cause, bride age, retrieved oocyte number and maturity, fertilization rate, embryo score, and post-embryo transfer results were assessed.

Results: The foreign bride couples had significantly greater infertility due to tubal (36%) and combination (8.1%) factors than native bride couples (20.3% and 4.1%, respectively). Days of gonadotropin stimulation, number of oocytes retrieved, fertilization rate, embryo score, implantation rate, or clinical pregnancy rate, and live birth rate did not differ between the two groups.

Conclusion: The cause of infertile foreign bride couples requiring ART treatment had a higher percentage of tubal and combination factors, but similar ART outcomes.

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Keywords: assisted reproductive technology; foreign bride; infertility; native bride

Introduction

Ethnic differences regarding assisted reproductive technology (ART) treatment are always interesting issues in worldwide studies. Several studies reported the ethnic differences in infertility causes and ART outcomes between Asian, Caucasian, and African American couples [1–14], and their

results were diverse. Few studies explore the infertility differences among south Asian ethnic groups.

The population of foreign brides has grown in some developed countries in Asia in the past two decades. These foreign brides had never lived in the country to which they immigrated before marriage and therefore had no known genetic consanguinity with the native population. Some of these foreign brides confronted conception problems after marriage by seeking ART treatment. Foreign brides had their own growth environments, language, cultures, educations, and socioeconomic backgrounds that differed from those of native brides. There are no reports examining whether any clinical or embryonic

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differences existed between foreign brides and native brides after they married their native husbands. Accordingly, we aimed to determine if differences in clinical characteristics, embryonic development, and pregnancy outcomes existed between infertile foreign brides and native brides of similar ages undergoing ART treatment at a single medical center.

Materials and methods

Patient selection and study design

Infertile couples who underwent ART treatment with fresh embryo transfer at Chang Gung Memorial Hospital—Kaohsiung Medical Center in Taiwan from 2004 through 2008 were retrospectively reviewed. The causes of infertility were stratified into one of the following six groups: male factor, tubal factor, endometriosis, other female factor, combination factor (two or more of the above four), and unexplained factor. Couples with oocyte recipient or embryo freezing and thawing transfers were excluded.

The foreign brides were defined as those who had never been in Taiwan before marriage and thus, had no known genetic consanguinity with the native population. In accordance with Taiwan's regulations for human assisted reproduction, all couples had to have a documented marriage relationship before undergoing ART.

A total of 1083 cycles were reviewed in the study period. Among them, 97 (9%) were from foreign brides and 986 (91%) from native women. The mean age of the native brides was significantly older than that of the foreign brides. In order to exclude age bias, we designed a case-control study to select native brides whose ages were 1 year older or 1 year younger than those of the foreign brides. The foreign brides/native brides ratio was 1:2. According to the inclusion criteria, we recruited 86 foreign brides and 172 native brides; we then compared the demographic clinical characteristics of the two groups with respect to ART cycles. The institutional review board of the Ethics Committee of Chang Gung Memorial Hospital approved this study.

Protocols of ART

The ART protocols in this study included controlled ovarian hyperstimulation, which followed the standard down-regulation regimen, laboratory procedures for semen evaluation and preparation, oocyte manipulation, assessment of fertilization, embryo culture, and embryo transfer [15,16]. The use of conventional *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI) depended on individual infertility causes. ICSI was performed for couples with male factor infertility, which was defined according to World Health Organization criteria. Otherwise, conventional IVF was used for other couples. Those embryos with equal-sized blastomeres, eight cells on day 3 and less than 20% fragmentation were defined as good-quality embryos and were scored as 3. Those embryos with eight cells and 20% or more fragmentation or five or more cells of equal or unequal size regardless of fragmentation were

scored as 2. Those embryos with fewer than five cells of any size and fragmentation were scored as 1. The cumulative embryo score (ES) of the individual was the sum of the ESs of each transferred embryo [15]. Embryos were transferred either 3 or 5 days after oocyte retrieval, as per our established protocol [15,16].

Parameters of comparison

Parameters including maternal age, paternal age, maternal peak serum E₂ level, retrieved oocyte number and maturity, fertilization rate, embryo number and maturity, and implantation and pregnancy rates were compared between the foreign bride and native bride groups. Primary versus secondary infertility, infertility cause, body mass index (BMI), and infertility duration were also assessed.

Statistical analysis

Continuous data were summarized as means \pm SD. The Mann–Whitney rank sum test was used for comparison of means, and Fisher's exact test was used for comparison of proportions. The significance of group differences was evaluated using Student's *t* test. Statistical analyses were performed using SPSS (ver. 18.0; SPSS Inc., Chicago). All *p* values were two-sided, and *p* < 0.05 was considered statistically significant.

Results

The mean age of the native brides was 34.4 (\pm 4.4) years, which was significantly older than that of the foreign brides (29.8 \pm 4.9 years). After age adjustment, there was no significant difference in mean age between the foreign and native bride groups (30.7 vs. 30.8 years, *p* = 0.903).

Table 1 shows the details of infertility causes between the two groups. No differences in duration and primary/secondary causes of the infertility were found. Table 2 shows

Table 1

Comparison of infertility causes between 86 foreign bride couples and 172 native bride couples.

	Foreign bride	Native bride	<i>p</i>
Number of cycles	86	172	
Infertility % (<i>n</i>)			
Primary	65.1% (56/86)	73.3% (126/172)	0.159
Secondary	34.9% (30/86)	26.7% (46/172)	0.159
Infertility cause			
Tubal factor	36.0% (31/86)	20.3% (35/172)	0.006
Male factor ^a	33.7% (29/86)	32.6% (56/172)	0.926
Other female factor	8.1% (7/86)	15.1% (26/172)	0.079
Unexplained factor	11.6% (10/86)	20.9% (36/172)	0.066
Endometriosis	2.3% (2/86)	7.0% (12/172)	0.121
Combination factor ^b	8.1% (7/86)	4.1% (7/172)	0.045

^a Male factor was defined as WHO criteria 1999 (WHO laboratory manual for the examination of human semen and sperm–cervical mucus interaction. 4th ed. Cambridge: Cambridge University Press, 1999).

^b Combination factor means those who have at least two of the above infertility causes.

a comparison of the clinical characteristics of the two groups of couples before ART treatment. The mean age of husbands was significantly older in couples with foreign brides than in those with native brides (39.6 ± 7.2 vs. 33.4 ± 3.9 years, $p < 0.001$). The foreign brides had lower BMI (20.8 ± 2.5 vs. 21.9 ± 3.2 , $p = 0.008$). There was a higher incidence of tubal factor infertility among foreign brides (36.0% vs. 20.3%, $p = 0.006$). More combination factor was also found in the foreign bride group (8.1% vs. 4.1%, $p = 0.045$).

There were no significant differences in duration of infertility, days of follicular stimulation hormone (FSH) treatment, E₂ on hCG day, P on hCG day, number of oocytes retrieved, number of mature oocytes retrieved, use of ART method (conventional IVF or ICSI), zygotes with two pronuclei, fertilization rate, number of embryos transferred, cumulative ES, and mean ES per embryo. The clinical pregnancy, implantation, abortion, and live birth rates did not differ between the two groups.

Discussion

Our study demonstrated that foreign bride couples had a compatible live birth rate (36%, per fresh transfer cycle), based on a cohort ART treatment population in which foreign brides accounted for 9% of all infertile women. Although the

Table 2
Comparison of IVF cycles between 86 foreign bride couples and 172 native bride couples.

	Foreign bride couples	Native bride couples	<i>p</i>
Number of cycles	86	172	
Age of female partners (y)	30.7 ± 4.3	30.8 ± 4.4	0.903
Age of male partners (y)	39.6 ± 7.2	33.4 ± 3.9	<0.001
Body mass index (kg/m ²)	20.8 ± 2.5	21.9 ± 3.2	0.008
Duration of infertility (y)	3.3 ± 2.4	3.9 ± 2.7	0.088
Days of FSH treatment	9.1 ± 1.9	9.2 ± 1.8	0.704
E ₂ (pg/ml) on hCG day	2318.5 ± 1484.1	2005.1 ± 1424.8	0.109
P (ng/ml) on hCG day	1.5 ± 0.6	1.4 ± 0.7	0.389
Number of oocytes retrieved	8.2 ± 3.9	7.3 ± 4.2	0.106
Number of mature oocytes retrieved	4.5 ± 2.2	4.4 ± 2.6	0.700
ART method			
Conventional IVF	64.0% (55/86)	70.3% (121/172)	0.309
ICSI	36% (31/86)	29.7% (51/172)	0.309
Normal fertilization rate (%)	76.0	80.7	0.095
Number of embryos transferred	2.5 ± 0.9	2.3 ± 0.8	0.064
Cumulative embryo score	8.7 ± 3.4	8.4 ± 3.2	0.532
Mean embryo score per embryo	3.4 ± 1.1	3.5 ± 1.0	0.479
Clinical pregnancy rate per transfer % (<i>n</i>)	46.5% (40/86)	45.9% (79/172)	0.698
Implantation rate % (<i>n</i>)	25.3% (55/217)	27.9% (111/398)	0.707
Live birth rate per transfer % (<i>n</i>)	36.0% (31/86)	40.1% (69/172)	0.527
Abortion rate per transfer % (<i>n</i>)	10.5% (9/86)	5.8% (10/172)	0.220

ICSI = intracytoplasmic sperm injection; IVF = *in vitro* fertilization.

distribution of infertility causes in the foreign bride group varied, tubal factor was prominent, and the pregnancy outcome rate with the use of ART was similar to that of the native bride group.

Previous comparisons of the clinical characteristics of black women and white women in the United States showed that black women were heavier in body weight [5] and were also more likely to have uterine fibroids and tubal factor infertility [2–7]. ART outcomes between black and white women in the United States also differed. Bendikson et al [5] suggested there was no significant difference in IVF pregnancy outcomes between the two groups, whereas others reported that black women had higher clinical pregnancy rates [6], significant reduction in live birth rate, and increase in spontaneous abortion rate [2,3,7].

When comparing Asian women to white women, Lashen et al [11] concluded that Asian women's responses to controlled ovarian stimulation and IVF outcomes were comparable to their white peers, under the same IVF protocols. Other studies [12–14] reported that Asian women demonstrated lower fertilization rates, clinical pregnancy rates, and decreased live-birth rates compared to their white counterparts.

In this study, we focused on the comparison of foreign bride couples (marriage of a foreign bride and a native bridegroom) and native bride couples (marriage of both a native bride and bridegroom). The brides of two groups were different from their native countries with different ethnicity branches of Asians. Our study population should be considered different from those in previous studies that compared Asian infertile women with black and white women, without further investigations for the differences between ethnicity branches of Asian infertile females. Under this circumstance, the present study has its own unique considerations and findings for infertility clinics in a foreign-bride-immigrating country.

The age of the woman undergoing ART is the leading factor in determining the pregnancy outcome. We have made efforts to eliminate bias due to bride age on ART outcome in this comparison study. After adjusting for the women's ages, there were no significant differences in response to ART treatment between the foreign and native bride groups (Table 2). The parameters we compared included duration of infertility, days of FSH treatment, E₂ on hCG day, P on hCG day, number of oocytes retrieved, number of mature oocytes retrieved, number of embryos transferred, and cumulative ES. The clinical outcomes of the ART treatment also revealed no differences in terms of normal fertilization rate, clinical pregnancy rate, implantation rate, live birth rate, and abortion rate.

Interestingly, it is noteworthy that the men in the foreign bride couples group were significantly older and the women in the foreign bride group had significantly lower BMI in comparison to the native bride couples group. The demographic data demonstrated that bridegrooms who married foreign brides to have a family were older (mean: 39.6 ± 7.2) when sought ART treatment. Nevertheless, the man's age contributes little to the pregnancy prognosis in terms of ART therapy.

There was a similar tendency of a higher incidence of primary infertility, which means no previous pregnancy had

occurred in both groups (Table 1). The leading cause of infertility in the foreign bride group was tubal factor, whereas in the native bride group, male factor infertility as the major problem. We analyzed infertility causes further and found that tubal factor infertility and combination factor infertility were significantly higher in the foreign bride group. This observation was compatible with several studies [17–19] revealing that tubal factor infertility is the most common cause of general female infertility in developing countries. Tubal factor has a strong relationship with the prevalence of genital infections, such as Chlamydia, gonorrhea, and tuberculosis. Both the reason why foreign brides from developing countries had more tubal disorders and the timing when they got genital infections (either before or after immigration) in this study remain unknown and need to be explored.

There are some limitations in this study in addition to the inherent bias from the case-control study design. First, the foreign brides in our study were mostly from southeastern Asia and China, and surrounding areas, but it was difficult to distinguish their native countries and ethnicities by reviewing their charts or making telephone queries. Second, the number of foreign brides was relatively small in comparison to previous studies, which had larger sample sizes. Finally, the underlying causes and occurrence times of tubal disease, which might influence pregnancy outcomes, were not available and could not be analyzed in our study. In any subsequent study, it is mandatory to evaluate the health conditions, educational levels, and growth trends of foreign spouses. Moreover, the study data were rather preliminary, requiring multicenter studies to verify the final conclusions.

In conclusion, tubal factor was the leading cause for infertile foreign bride couples seeking ART treatment in a foreign-bride-immigrating country. The pregnancy outcomes were similar between the foreign and native bride couples.

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