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REGULAR ARTICLE

Impact of egg donation deliveries from domestic and overseas sources on maternal care: a questionnaire survey of Japanese perinatal physicians

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Abstract
Objectives Recent demographic changes, such as marriage at later ages and delayed childbearing, have contributed to the increased demand for ovum donation. The purpose of the present study was to evaluate the frequency and impact of egg donation deliveries on maternal care using a questionnaire survey of Japanese perinatal care providers.
Methods A quantitative survey was conducted from October to November 2012 using self-administered anonymous questionnaires. We asked 2,693 obstetrics clinics/hospitals throughout Japan to complete the survey: 679 questionnaires were returned (response rate, 25.2 %).
Results Of the respondents, 15.8 % answered that they had handled egg donation deliveries in the past. With regards to the country in which patients received egg donation services, the most frequent was the United States, including Hawaii. Asian countries, such as Thailand, Korea, and Singapore, were also reported; only two cases in Japan were reported. "Advanced age/menopause" was the most frequent reason for egg donation, and the mean age at egg donation delivery, because of advanced age/menopause, was 48.3 years.
Conclusions Our findings will increase public awareness of the legal issues related to assisted reproductive technology and cross-border reproductive care, as well as care of the mother and child in pregnancies resulting from reproductive technologies such as egg donation overseas. People should be aware of the issues involved in egg donation abroad and the resulting deliveries, and should implement specific care for women bearing children at later ages.

Keywords Japanese patients · Egg donation delivery · Infertility · Obstetricians · Late childbearing

Introduction

Recent demographic changes, such as marriage at later ages and delayed childbearing, have contributed to the increased demand for assisted reproductive technology (ART) in Japan. Indeed, in Japan, around 600 accredited in vitro fertilization (IVF) clinics performed over 200,000 IVF cycles in 2009 [1].

The dissemination of ART in Japan has contributed to an increase in child deliveries at advanced ages. Advanced maternal age, defined as 35 years or older at the estimated delivery date, has become increasingly common in Japan. The number of live births in women aged 45–49 years and older in Japan increased from 244 to 802 between 1985 and 2011. The number of deliveries by women older than 50 years rose from only one in 1985 to 41 in 2011 [2].

This increase in childbearing at later ages has been supported not only by the increasing use of IVF but also by an increase in infertile patients who receive donor-egg IVF. Ova donated by younger women enable older women to conceive. According to statistical data from the Centers for Disease Control and Prevention [3], the live birth rate of women who had undergone standard, non-donor IVF decreases with increasing age. Conversely, the live birth rate of women who had undergone donor-egg IVF was approximately stable with age. Even postmenopausal women can conceive if the ovum comes from a younger

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woman. Thus, egg donation may contribute to an increased frequency of very late childbirth.

The use of donor eggs in infertility treatment has contributed to the availability of procreative choices for older women. At the same time, this practice remains controversial. Several countries have legal restrictions on such procedures, whereas commerce in donor oocytes is flourishing in other countries.

No comprehensive ART legislation exists in Japan, and regulation of third-party reproduction is left to professional bodies or is based on governmental reports. Regarding egg donation, the Japan Society of Obstetrics and Gynecology (JSOG) published guidelines in 2004 [4], as did the Japan Society for Reproductive Medicine (JSRM) in 2009 [5]. Both state that commercial egg donation should be prohibited, and only 'altruistic' donation should be permitted. The Japanese Institution for Standardizing Assisted Reproductive Technology (JISART) was organized by the private sector in 2003 in the context of a lack of altruistic egg donors. JISART formulated its own guidelines, and its member clinics established a voluntary egg donation program among relatives (e.g., sisters) of recipients [6]. However, only 18 egg donations were reported between 2008 and 2011. JISART is the only organization that discloses its operations; the number of egg donations received by other clinics in Japan is unknown.

However, it is difficult for patients to access donor eggs for IVF in Japan. Consequently, increasing numbers of Japanese women have traveled overseas. This phenomenon has been referred to as "reproductive tourism" [7] and "cross-border reproductive care" [8, 9]. Japanese patients unable to access to donor eggs have usually traveled to the United States, but increasing numbers of Japanese women also travel to Asian countries, such as India, Thailand, Malaysia, and South Korea.

With the development of reproductive tourism, Japanese perinatal specialists now encounter an increasing number of Japanese patients who have undergone embryo transfer abroad and then returned to Japan for delivery. They must deal with patients who face possible medical risks associated with advanced maternal age and egg donation.

The purpose of the present study was to evaluate the frequency and impact of egg donation delivery on maternal care, based on data from questionnaires completed by Japanese perinatal care providers. Many previous surveys focused primarily on the attitudes of infertility specialists regarding ART and third-party reproduction [10–13]. Such studies have discussed access to ART: which women access ART services, what types of technologies should be provided, and whether the right to identify children born from third-party reproduction should be accepted. To date, however, few studies have reported on the attitudes, opinions, and perceptions of perinatal specialists who must offer perinatal care to patients seeking reproductive services from ART and third-party providers. This study focused on perinatal care specialists' attitudes toward, opinions about, and perceptions of ART [14–16], the frequency and the details of egg donation delivery [17] and cross-border reproductive care [18].

Materials and methods

Data collection and analysis

The present study was approved by the Ethics Committee of the Kanazawa Graduate School of Medical Sciences (No. 1274).

A quantitative survey was conducted using a self-administered anonymous questionnaire. From October to November 2012, we asked 2,693 obstetrics clinics/hospitals throughout Japan to complete our survey. The list of clinics/hospitals was drawn from the website http://shusanki.org/area.html. The list contains all the facilities where women can deliver in Japan. Completed questionnaires were sealed in a white envelope and returned to the hospital or mailed directly to the researchers by each respondent. The questionnaire in English is available at the website http://saisentan.w3.kanazawa-u.ac.jp/image/syuusanki_en.pdf (password: SGRH), and the Japanese version at http://saisentan.w3.kanazawa-u.ac.jp/image/suvey_Investigation.pdf (password: SGRH).

Calculations, including descriptive analyses, were performed using the SPSS software (ver. 19.0 for Mac). To evaluate differences between categories, a χ^2 test was used. To examine differences in mean values between more than two groups of variables, ANOVA was used. p values <0.05 were deemed to indicate statistical significance.

Assessment

Demographic characteristics of obstetricians (age, gender, marital status, and years of experience in obstetrics) and institutional background (NICU, institutional type, and number of deliveries per year) were obtained.

The past experience of respondents with egg donation pregnancies was evaluated. The question was "Have you had any patients who became pregnant via egg donation?" The response could be "Yes" or "No."

Next, respondents were asked how they would handle an egg donation pregnancy case. The four options were "Provide no special care," (meaning no extra/different care specific to egg donation delivery), "Refer to another hospital," "Provide special care, such as hospitalization," and "Refuse delivery."

Recognition of the involved risks was assessed with the following question: "Do you think pregnancy via egg donation carries risks for the recipient (regardless of age)?" The response could be "Yes," "No," or "Do not know."

We inquired about the annual number of egg donation deliveries performed during the previous 5 years (2007–2011). Each respondent was asked to describe the 10 most recent cases in detail (including the reason for egg donation and the country where the reproductive services were provided).

Regarding age-related matters, respondents were asked whether there should be an age limit for the ovum recipient. The answers were "Agree with an age limit," "Disagree with an age limit," or "Disagree with egg donation." If they agreed with an age limit for the recipient, respondents were also asked what the limit should be. Moreover, respondents were asked the age of the oldest patient for whom they performed a delivery, and what the upper age limit for a safe delivery should be.

Results

Individual characteristics and institutional background information

In this study, 679 questionnaires were returned, for a response rate of 25.2 %. The clinics covered six major regions in Japan. The distribution and response rates (%) according to region were as follows: 87 (30.6 %) in the Chugoku and Shikoku regions, 124 (26.2 %) in the Chubu region, 125 (26.0 %) in the Kinki region, 78 (24.0 %) in the Hokkaido and Tohoku regions, 124 (23.8 %) in the Kanto region, and 97 (22.8 %) in the Kyushu and Okinawa regions. The distribution and response rates according to institutional type were as follows: obstetrics and gynecology (OB/GYN) clinics, $n = 357$ and 52.6 %; OB/GYN departments at general hospitals, $n = 211$ and 31.1 %; OB/GYN departments at university hospitals, $n = 47$ and 6.9 %; and perinatal medical centers $n = 46$ and 6.8 %.

Individual characteristics and institutional background information are presented in Table 1. The distribution of the participants' ages was as follows: 50–59 (40.9 %), 40–49 (27.0 %), 60–69 (22.1 %), 30–39 (5.6 %), 70–79 (4.3 %), and 20–29 (0.1 %). In total, 593 (87.5 %) were males, and most of the respondents (93.1 %) were married. The mean experience (±standard deviation, SD) in perinatal care was 27.3 ± 9.2 years. Regarding the institutional number of deliveries per year, most (62.1 %) had 100-499, and 25.7 % had 500-999. The percentage of hospitals/clinics with a neonatal intensive care unit (NICU) was 19.6 %.

Table 1 Individual characteristics and institutional characteristics ($n = 679$)

		n	%
Gender	Male	593	87.5
Marital status	Married	632	93.1
Age	20–29	1	0.1
	30–39	38	5.6
	40–49	183	27.0
	50–59	278	40.9
	60–69	150	22.1
	≥70	29	4.3
Years of experience in obstetrics	<10	14	2.0
27.3 (± 9.2)	10–20	105	15.5
	20–30	273	40.2
	30–40	209	30.8
	≥40	78	11.5
NICU	Yes	133	19.6
Type of medical institution	OB/GYN Clinic[a]	357	52.6
	OB/GYN Department at University Hospital	47	6.9
	OB/GYN Department at General Hospital	211	31.1
	Perinatal Medical Center	46	6.8
	Other	18	2.6
Number of deliveries per year	<100	48	7.2
	100–499	420	62.1
	500–999	174	25.7
	1,000–1,999	32	4.7
	>2,000	2	0.3

[a] Obstetric and gynecology clinic

Past experience, attitudes towards patients, and recognition of risks

Participants were asked about their past experiences with egg donation delivery (Fig. 1). Of all respondents, 107 (15.8 %) responded that they had experience with an egg donation delivery. However, more than 80 % (83.8 %) had no such experience. Among them, 60.0 % of respondents affiliated with a university hospital and 56.8 % of respondents affiliated with a perinatal medical center had experience with egg donation deliveries. Thus, approximately one in six obstetricians had previously encountered deliveries resulting from donor-egg IVF.

Respondents were also asked how they proceeded once an egg donation pregnancy was identified. There was a difference between obstetricians who had previously handled an egg donation delivery and those who had not ($p < 0.001$; Table 2). Among respondents who had experience with egg donation delivery, more than 80 %

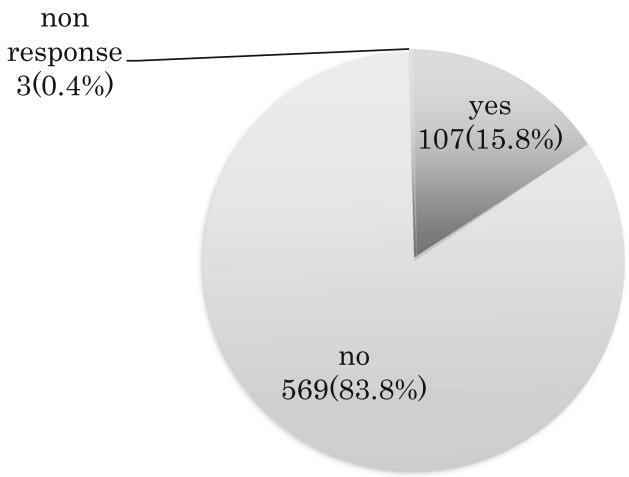


Fig. 1 Have you had any patients who were pregnant via egg donation?

responded that they provided no special care for the patient. In contrast, among respondents who had no experience with egg donation delivery, 56.4 % responded that they would offer no special care to the patient, 26 % responded that they would refer the patient to another hospital/clinic, 4.7 % responded that they would refuse the patient, and 3.7 % responded that they would hospitalize and provide special patient management.

Regarding recognition of the risks associated with egg donation delivery, more than half of respondents (54.3 %) with experience with egg donation delivery agreed that the procedure was risky. In contrast, of the respondents with no experience of egg donation delivery, 42.8 % responded "Do not know" ($p < 0.001$; Table 2).

Egg donation delivery cases

The number of egg donation deliveries reported by obstetricians was 20 in 2007, whereas 63 were reported in 2011 (Table 3); thus, a threefold increase occurred in the 5-year period. Respondents were asked to describe 91 of the 169 cases in detail. In total, 107 reasons for egg donation were reported and are described here. For 53 cases, "advanced age/menopause" was the reason reported for egg donation. Repeated failure of IVF was described for 17 cases, premature menopause for 13 cases, and unknown cause for 19 cases. Regarding the country in which patients received egg donation services, the most frequent was the United States, including Hawaii (91 cases) (57). Asian countries, such as Thailand (7), Korea (6), and Singapore (1), were also reported. Only two cases were reported in Japan. Regarding the number of deliveries of fetuses, 33 % of the 91 cases were multiple pregnancies (Table 3).

Association of age with procedure safety

The age of the oldest patient for whom the respondents had experienced a delivery ranged from 36 to 60 years (mode, 45 years). Moreover, more than half of the respondents (61.5 %) had experienced a delivery from a patient older than 45 years (Table 4). The age of the oldest patient differed according to institution type. The average age of the

Table 2 Attitudes toward and perceptions of egg donation delivery among respondents

	Doctors with experience with deliveries for patients receiving egg donation	Doctors without experience with deliveries for patients receiving egg donation	Total
Response to patients who were pregnant through egg donation†			
Provide no special care	84 (80.8)	291 (56.4)	375 (60.5)
Refer to other hospitals	8 (7.7)	134 (26.0)	142 (22.9)
Provide special care such as hospitalization	8 (7.7)	19 (3.7)	27 (4.4)
Refuse delivery	1 (1.0)	24 (4.7)	25 (4.0)
Other	3 (2.8)	48 (9.2)	51 (8.2)
Total	104 (100.0)	516 (100.0)	620 (100.0)
Do you think pregnancy via egg donation carries risks for the recipient (regardless of age)?§			
Yes	57 (54.3)	240 (44.8)	297 (46.3)
No	19 (18.1)	63 (11.7)	82 (12.8)
Do not know	27 (25.7)	230 (42.8)	257 (40.0)
Other	2 (1.9)	4 (0.7)	6 (0.9)
Total	105 (100.0)	537 (100.0)	642 (100.0)

† Chi square test: $p < 0.001$

§ Chi square test: $p < 0.001$

oldest patient at perinatal medical centers was 48.4 years, and that at university-affiliated hospitals was 48.6 years. These two ages were higher than those of both general hospitals (45.6 years) and free-standing private clinics (44.6 years; Fig. 2, $p < 0.001$).

According to the physicians' opinions, the upper age limit for safe delivery ranged from 30 to 53 years. More than half of the respondents (53.7 %) answered that the safe delivery age was up to 45 years old, while 189 (30.1 %) responded up to 40 years old (Table 4).

Regarding ovum donation, over half of the respondents (54.6 %) agreed with limiting the age for ovum recipients. In contrast, 33.2 % of respondents were against egg donation itself. There was a significant difference between male and female respondents regarding age limits. More female (71.8 %) than male (52.1 %) respondents agreed with an age limit (Fig. 3).

The upper age limit for ovum recipients was determined among respondents who agreed with limiting ovum donation by age ($n = 343$). The age limit ranged from 29 to 55 years. Of the respondents, 126 (36.7 %) responded that ovum donation should be performed in recipients aged 45 years or younger and 100 (29.2 %) responded that ovum donation should be performed in recipients aged 40 years or younger (Table 4).

Table 3 Egg donation delivery cases

Number of pregnancies via egg donation	($n = 169$)
2007	20
2008	23
2009	26
2010	37
2011	63
Reasons for egg donation (%)	($n = 107$)
Advanced age/menopause	53
Repeated failure of IVF	17
Premature menopause (including Turner syndrome)	13
Anovulation	2
Ovariectomy	2
Other (ovarian dysfunction by kidney transplant)	1
Unknown	19
Total was not 91 because of multiple answers	
Country where patients received egg donation services	($n = 91$)
Number of patients by destination country	
US (Hawaii 3)	57
Thailand	7
Korea	6
Japan	2
Singapore	1
Russia	1
Unknown	17
Number of fetus	
Single	61
Twin	28
Triplet	2

Discussion

In the present study, one of six respondents (15.8 %) reported experience with egg donation delivery. Moreover, the total number of egg donation deliveries during the previous 5 years was 169. However, this might represent only a small subset of cases because some women may choose not to inform their perinatal physicians, and the overall response rate was only 25.2 %. Moreover, egg donation delivery at an older age might occur more frequently in university hospitals and perinatal medical centers; however, the response rates at these types of institution were low. This could have resulted in underestimating egg donation delivery cases and creating bias regarding the age of egg donation delivery. Although the precise number of egg donation deliveries in Japan is unknown, it may have increased in recent years in accordance with the increase in late childbearing generally. In

Table 4 Respondents' experiences with and perceptions of maternal age

	Lowest	Highest	Mean (±SD)	Mode	Up to 35 (%)	Up to 40 (%)	Up to 45 (%)	Up to 50 (%)	Over 50 (%)
Oldest maternal age at delivery (670)	36	60	45.3 (±2.9)	45	0	9 (1.3)	395 (59.0)	228 (34.0)	38 (5.7)
Upper age limit for safe delivery (628)	30	53	43.2 (±3.5)	45	22 (3.5)	189 (30.1)	337 (53.7)	79 (12.6)	1 (0.1)
Upper age limit for ovum recipients (343)	29	55	41.5 (±5.1)	45	64 (18.7)	100 (29.2)	126 (36.7)	33 (9.6)	20 (5.8)
Age at egg donation delivery (91)	26	58	44.6 (±7.0)	46	14 (15.4)	6 (6.6)	18 (19.8)	38 (41.8)	15 (16.4)
Age at egg donation delivery (advanced age/menopause) (53)	39	58	48.3 (±3.6)	47	0	2 (3.8)	9 (17.0)	29 (54.7)	13 (24.5)

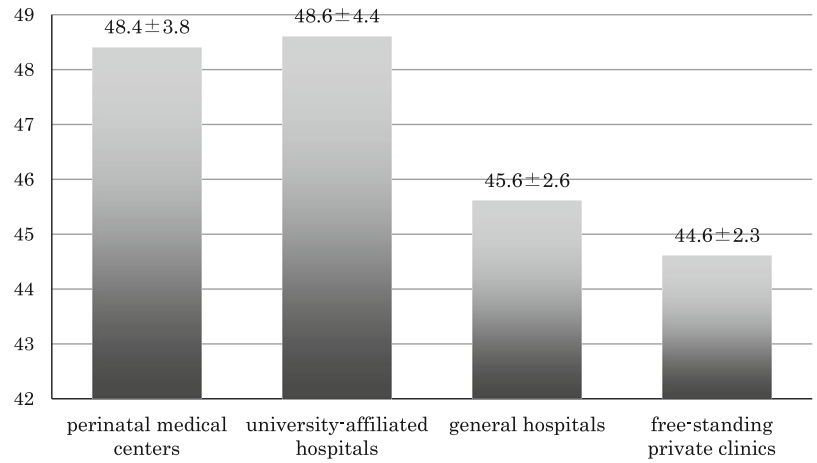
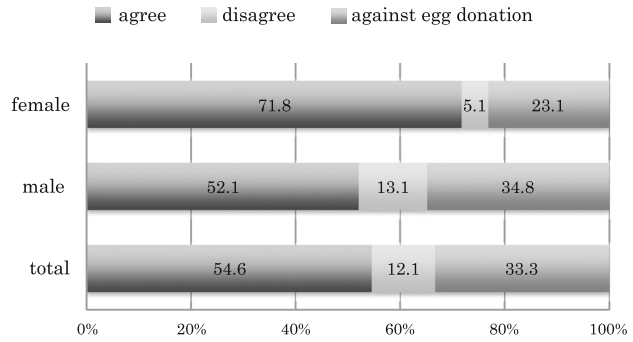


Fig. 2 The average age of the oldest patient

statistical test: one way ANOVA ($p<0.001$)



statistical test: chi-square ($p=0.004$)

Fig. 3 Age limit for egg donation

the present study, the number of egg donation deliveries increased linearly during the previous 5 years (Table 2). Measures to protect maternal and child health resulting from egg donation deliveries should be implemented immediately.

The reason that women hesitate to reveal that they have undergone an egg donation procedure is that infertility is stigmatized in Japanese society, and few egg donations are performed domestically. Consequently, although egg donation is not illegal in Japan, the status of egg donation procedures remains ambiguous to many. Thus, women who have received IVF with donor eggs may feel unable to report the fact to their perinatal doctors. Another reason may be that several clinics/hospitals refuse to provide delivery services if a pregnancy resulted from ovum donation. In the present study, 4.7 % of perinatal professionals with no experience of egg donation cases responded that they would refuse to accept such women. In contrast, of the physicians with experience of egg donation delivery, none reported providing special care. This result must be interpreted with caution. Japanese perinatal physicians affiliated with a university hospital or perinatal medical center treat many pregnant women with high-risk factors, such as older age; thus, they may have answered "give no special care" for this question. Based on these facts, specific guidelines for the care of egg donation deliveries should be established in Japan.

Egg donation by younger women enables older women to conceive. Thus, a proportion of egg donation deliveries tended to involve women who had children later in life. In the present study, more than half of the reported cases responded with "advanced age/menopause" as the reason for egg donation. Moreover, in the present study, the mean age of women who underwent an egg donation procedure at an advanced age was 48 years. This was higher than 45 years, which many physicians regarded as the age limit for delivery safety. Previous studies have explored whether egg donation delivery increases the risk of pregnancy-induced hypertension (PIH) [19]. In addition to donated-egg pregnancy, there may be other medical risk factors related to older age, such as miscarriage and placenta previa. In the present study, more than half of physicians (54.3 %) regarded egg donation delivery as risky, particularly among those who had experience with egg donation procedures. However, if patients do not disclose their status, clinicians cannot prepare for any extra risk associated with ovum donation. Thus, concealing having undergone an egg donation procedure may be risky behavior too.

In the present study, more than half of the respondents (54.7 %) agreed with limiting the age of ovum recipients. Domestically, egg donation is permitted for medical reasons, such as premature menopause, Turner syndrome, and anovulation, but not for advanced age alone. However, the advanced age threshold is difficult to identify. In reality, in the present study, the mean age of egg donation delivery

due to advanced age was 48 years. Thus, if the Japanese government does not permit egg donation delivery because of advanced age, reproductive tourism will thrive and the deliveries at advanced ages will continue.

Cross-border reproductive care is motivated by several reasons. The major reason may be simply that people cannot obtain certain reproductive services domestically. A social trend towards increasingly late childbearing in Japan, coupled with the unavailability of donor eggs in this country, has contributed to increased demand for egg donation. Because very little ovum donation is conducted in Japan, many infertile patients go abroad, including the United States and Asian countries, and most of these patients give birth after their return to Japan.

Travel to seek third-party reproductive care such as egg donation is associated with medical, ethical, legal, and social problems. In terms of medical problems, reproductive tourism is associated with risks such as multiple pregnancies [18], and pregnancy at older ages. For example, of the 91 egg donation delivery cases reported in the present study, 28 cases were twins and 2 were triplets (Table 3). Regarding age, "Advanced age/menopause" was the most frequent reason for egg donation in the present study, and the mean age at egg donation delivery was 48.3 years for this reason, although 87.3 % of respondents answered that the maximum age for safe delivery is up to 45 years old. As a result, measures to protect maternal and child health in the context of egg donation delivery should be implemented. In terms of social problems, unclear gamete donation records are common abroad. In terms of ethical problems, such travel might result in harm to economically vulnerable women. Moreover, legal problems may arise if there is any legal discrepancy between the two countries involved. Thus, policies regarding third-party reproductive care, such as age limit for egg donation delivery and ART and a legal system governing egg donation, including rights of the born child, should be developed.

The present study has several limitations and strengths. First, our overall response rate was low and the sample size was small. The response rate of perinatal medical centers was particularly low, and perinatal medical centers are likely especially important for egg donation deliveries. This may have introduced selection bias into the data, leading to misrepresentation of the extent of egg donation pregnancies and misinterpretation of the results, such as the total number of physicians who have delivery experience of egg donated pregnant women and the mean age at egg donation delivery. This may have caused underestimating egg donation delivery cases and a lower mean age for egg donation delivery cases. Thus, the results of the present study may not be representative of the overall frequency of egg donation deliveries in Japan. Nevertheless, delivery resulting from ovum donation, both domestically and overseas, is an urgent issue in Japan where, with trends towards marriage at later ages and delayed childbearing, demand for ART continues to increase. This is the first reported comprehensive nationwide study of Japanese obstetricians regarding egg donation delivery.

In summary, there are many issues regarding future perinatal care related to ART, including whether permission should be required for egg donation procedures due to advanced age, whether egg donation delivery should be performed domestically when pregnancy resulted from cross-border reproductive care, and what constitutes the provision of adequate maternal and child care in such cases. Hopefully, our findings will increase public awareness of the lack of care and legal systems related to ART, reproductive tourism, and care of the mother and child in cases of pregnancies resulting from reproductive technology.

Conflict of interest The authors declare that they have no conflict of interest.

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