Robust evidence reveals the reliable rate of normal/balanced embryos for identifying reciprocal translocation and Robertsonian translocation carriers

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Research Article

Summary

We aimed to evaluate the reliable rate of normal/balanced embryos for reciprocal translocation and Robertsonian translocation carriers and to provide convincing evidence for clinical staff to conduct genetic counselling regarding common structural rearrangements to alleviate patient anxiety. The characteristics of 39,459 embryos that were sourced from unpublished data and literature were analyzed. The samples consisted of 17,536 embryo karyotypes that were not published and 21,923 embryo karyotypes obtained from the literature. Using the PubMed, Cochrane Library, Web of Science, and Embase databases, specific keywords were used to screen the literature for reciprocal translocation and Robertsonian translocation. The ratio of normal/balanced embryos in the overall data was calculated and analyzed, and we grouped the results according to gender to confirm if there were gender differences. We also divided the data into the cleavage stage and blastocyst stage according to the biopsy period to verify if there was a difference in the ratio of normal/balanced embryos. By combining the unpublished data and data derived from the literature, the average rates of normal/balanced embryos for reciprocal translocation and Robertsonian translocation carriers were observed to be 26.96% (7953/29,495) and 41.59% (4144/9964), respectively. Reciprocal translocation and Robertson translocation exhibited higher rates in male carriers than they did in female carriers (49.60% vs. 37.44%; 29.84% vs. 27.67%). Additionally, the data for both translocations exhibited differences in the normal/balanced embryo ratios between the cleavage and blastocyst stages of carriers for both Robertsonian translocation and reciprocal translocation (36.07% vs 43.43%; 24.88% vs 27.67%). The differences between the two location types were statistically significant ($P < 0.05$). The normal/balanced ratio of embryos in carriers of reciprocal and RobT was higher than the theoretical ratio, and the values ranged from 26.96% to 41.59%. Moreover, the male carriers possessed a higher number of embryos that were normal or balanced. The ratio of normal/balanced embryos in the blastocyst stage was higher than that in the cleavage stage. The results of this study provide a reliable suggestion for future clinic genetic consulting regarding the rate of normal/balanced embryos of reciprocal translocation and Robertsonian translocation carriers.

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Introduction

In couples of childbearing age, reciprocal translocation (RecT) and Robertsonian translocation (RobT) are the two major chromosomal abnormalities responsible for the high occurrence of abortion (Xu *et al.*, 2017). Its incidence is higher in newborns and couples of childbearing age and ranges from 0.1% to 0.2% and 0.4%, respectively (Alfarawati *et al.*, 2012). According to published studies, the miscarriage rates for RecT and RobT are ~2–5% (Zhai *et al.*, 2022). RecT is caused by the translocation of two chromosome segments on both sides of the breakpoint and can occur in all chromosomes. The formation of RobT is related to the centromere region and involves the long-arm connection of two chromosomes that were restricted to chromosomes 13, 14, 15, and 21 (Xu *et al.*, 2017; Zhai *et al.*, 2022). Previous studies have revealed the occurrence of RecT/RobT during gamete formation (including oocytes or sperm), therefore indicating that the onset of most RecT/RobT was novel.

The intrinsic characteristic of RecT/RobT is the change in chromosome fragments; however, the majority of patients did not exhibit a loss of key genes. Therefore, RecT/RobT carriers do not possess any genetic diseases (Findikli *et al.*, 2019). Most RecT/RobT carriers were detected using chromosomal karyotype analysis of peripheral blood for recurrent abortion and infertility. However, RecT/RobT carriers can exhibit a higher frequency of chromosomal abnormalities in oocytes and sperm, ultimately resulting in offspring with congenital diseases such as Down's syndrome and Pato syndrome (Xu *et al.*, 2017). According to the adjacent and 3:1 theory for

RobT carriers, they may possess 1/6 normal and 1/6 balanced gametes (Liu *et al.*, 2020), and this results in phenotypically normal offspring based on the normal and balanced gametes possessing normal expression of genes from the entire genome (Jin *et al.*, 2010). For RecT, to ensure proper alignment of translocated chromosomes and homologous sequences, quadrivalents were formed and generated alternately, an adjacent-1, adjacent-2, 3:1, and 4:0 segregation could be performed (Kushnick, 1992; Yuan *et al.*, 2021). Therefore, 1/18 normal and 1/18 balanced gametes were ultimately formed, and the remaining 16/18 unbalanced gametes would theoretically cause recurrent abortion in RecT carrier couples. Sex can also exert different effects on the formation of normal, carrier, and unbalanced gametes (Ko *et al.*, 2010; Zhang *et al.*, 2018). Preimplantation genetic testing (PGT) for aneuploidies (PGT-A) and structural rearrangement (PGT-SR) can select embryos by performing a genetic test to identify and abandon those with chromosomal abnormalities and transfer the normal embryos to the uterus of patients with IVF in a suitable situation, and this can improve the outcomes of IVF (Xu *et al.*, 2017; Zhang *et al.*, 2018; Findikli *et al.*, 2019; Shi *et al.*, 2021).

However, the theoretical rate of normal/balanced gametes for RecT/RobT carriers did not represent the true situation of normal/balanced gametes and embryos of these carriers, as several of the theoretical gametes were eliminated directly during the formation stage. Therefore, the rate of normal/balanced embryos in RecT/RobT carriers was not consistent with the theoretical results. The normal/balanced embryo rates among patients with RecT/RobT were observed to be different in previous studies (Boynukalin *et al.*, 2021; Yuan *et al.*, 2021; Zhai *et al.*, 2022), and it remains controversial if sex could affect the rate of normal/balanced embryos of patients with RecT/RobT. Certain scholars believe that there are differences in the normal/balanced ratio results among different embryos during the biopsy period (Beyer and Willats, 2017; Wang *et al.*, 2019). The normal/balanced embryo ratio during the cleavage stage is lower than that during the blastocyst stage, and this can ensure that doctors provide more accurate genetic counselling services. Consequently, the genetic consultation of RecT/RobT carriers has primarily been based on the theoretical rate of gametes that was much lower than the reported normal/balanced embryos of patients with RecT/RobT, and this may also cause anxiety in patients. Accordingly, in this study the rates of normal/balanced embryos of 39,063 embryos were analyzed, and among 39,063 embryos, 9568 RobT carriers and 29,495 RecT carriers were included. Additionally, sex was considered in our study to reveal the plausible effect of sex on the rate of normal/balanced embryos in patients with RecT or RobT, and we verified the difference in the normal/balanced embryo ratio between the cleavage and blastocyst stages.

Materials and methods

Editorial policies and ethical considerations

This study was approved by the reproductive ethics board of the First Affiliated Hospital of Kunming Medical University, and informed consent was obtained from all patients.

To determine the normal/balanced embryo rate of patients with RecT/RobT with PGT, 9568 embryos from RobT carriers and 29,495 embryos from RecT carriers were analyzed. In this study, 4158 embryos from 856 RobT carriers and 13,378 embryos from 2924 RecT carriers were newly reported and provided by the Department of Medical Genetics of the Yikon Genomics Company

in Jiangsu Suzhou, China. As presented in Tables 1 and 2, 5410 embryos from RobT carriers and 16,117 RecT carriers were retrieved from the literature (Tables 1 and 2). RecT and RobT carriers with preimplantation genetic testing (PGT)/preimplantation genetic diagnosis (PGD) were used as keywords to screen the literature in the PubMed, Cochrane Library, Web of Science, and Embase databases, respectively, and October 2022 was deemed as the deadline for the published literature. The abstract of each study was read, and balanced/normal embryo data of RecT and RobT carriers with PGT were retrieved from the literature to evaluate the rate of normal/balanced embryos from patients with RecT/RobT with PGT that were analyzed in this study. To further reveal the effect of sex, 856 RobT carriers and 2924 RecT carriers were grouped according to sex. Of the 856 RobT carriers, 420 were male and 436 were female. Similarly, 2924 RecT carriers included 1336 male and 1558 female carriers. Additionally, to verify the effect of the biopsy period on embryo karyotype, we divided all embryo data into two groups based on the biopsy period (cleavage stage and blastocyst stage). The cleavage and blastocyst stage embryos from both groups are recorded in detail in Table 5. Some of the embryonic karyotypes were not included for two reasons: they were obtained using methods other than biopsy; there were no detailed records of the biopsy period in the literature.

Statistical analysis

The ratio of normal to balanced embryos to the total embryos was recorded and calculated. The numbers of normal/balanced and unbalanced embryos were compared using the chi-squared test. A *P*-value < 0.05 was considered statistically significant in this study.

Results

General characteristics of the subjects

Normal/balanced embryos possess the common gene expression of the entire human genome, and this would not result in any clinical characteristics in patients. These types of embryos could be used for translation of couples suffering from RobT/RecT, despite the possibility that the offspring of the balanced carrier embryo could experience complications such as recurrent abortion. However, most RobT/RecT carriers with PGT might not possess sufficient embryos for transfer. Therefore, balanced embryos were also considered for transplantation. To determine the rate of normal/balanced embryos of RobT/RecT carriers and provide reliable genetic evidence for genetic consultation in clinics, 3780 patients with RobT/RecT were recruited for this study (856 RobT carriers and 2924 RecT carriers). In total, 4158 RobT carriers and 13,378 embryos RecT carrier embryos were identified. Averages of 4.86 (2924/856) embryos of RobT carriers and 4.56 (13,178/2924) embryos for each RecT carrier were subjected to PGT-A/PGT-SR. The average number of embryos in RobT carriers was higher than that in RecT carriers with PGT.

The rate of normal/balanced embryos from RobT/RecT carriers

The transfer of normal/balanced embryos from RobT/RecT carriers with PGT produced offspring without a phenotype. Therefore, normal/balanced embryos were present. However, the rate of normal/balanced embryos exhibited a large range of fluctuations, and this was not conducive for clinicians in regard to performing genetic counselling. Accordingly, to determine the probability of normal/balanced embryos in RobT/RecT carriers,

Table 1. Basic information obtained from the literature on RobT carriers

ID	Year	Study type	Country	Biopsy period	Detection platform	No. of embryos	Normal/ Balanced	Proportion	References
2	2002	Clinical trials	Portugal	Blastomere	FISH	44	23	52.27%	(Alves et al., 2002)
3	2002	Clinical trials	America	Blastomere	FISH	111	26	23.42%	(Gianaroli et al., 2002)
4	2003	Clinical trials	America	Blastomere/ Trophoblast	FISH	151	51	33.77%	(Verlinsky et al., 2002)
6	2004	Clinical trials	Korea	Blastomere	FISH	130	29	22.31%	(Kyu Lim et al., 2004)
8	2004	Clinical trials	China	Blastomere	FISH	10	1	10.00%	(Xu et al., 2004)
9	2008	Clinical trials	China	Blastomere	FISH	133	44	33.08%	(Yu-li et al., 2008)
11	2009	Clinical trials	China	Blastomere	FISH	107	31	28.97%	(Li et al., 2009)
12	2010	Clinical trials	France	Blastomere	PCR	124	82	66.13%	(Fiorentino et al., 2010)
13	2010	Clinical trials	America	Blastomere/ Trophoblast	FISH	265	141	53.21%	(Kuliev et al., 2010)
14	2011	Clinical trials	America	Blastomere	FISH	270	68	25.19%	(Mardešić et al., 2011)
15	2011	Clinical trials	China	NA	FISH	167	64	38.32%	(Xu et al., 2011)
16	2013	Retrospective	China	Blastomere	SNP	1422	469	32.98%	(Tan et al., 2013)
17	2014	Retrospective	America	Blastomere/ Trophoblast	SNP/aCGH	396	186	46.97%	(Tobler et al., 2014)
22	2016	Retrospective	Turkey	Blastomere	FISH	177	141	79.66%	(Tulay et al., 2016)
24	2017	Retrospective	Australia	Blastomere/ Trophoblast	FISH	1040	471	45.29%	(Beyer and Willats, 2017)
25	2017	Retrospective	China	Trophoblast	SNP	379	160	42.22%	(Wang et al., 2017)
26	2017	Clinical trials	China	Blastomere/ Trophoblast	array-CGH	73	13	17.81%	(Zhou et al., 2017)
27	2018	Retrospective	China	Blastomere/ Trophoblast	aCGH	197	52	26.40%	(Xie et al., 2018)
32	2021	Retrospective	Turkey	Trophoblast	FISH	156	57	36.54%	(Boynukalin et al., 2021)
34	2021	Clinical trials	China	Trophoblast	FISH	136	60	44.12%	(Liu et al., 2020)
36	2021	Retrospective	China	Trophoblast	NGS	181	114	62.98%	(Yuan et al., 2021)
37	2022	Retrospective	China	Trophoblast	NGS	137	44	32.12%	(Zhai et al., 2022)
Total						5806	2327	40.08%	

NA, Not available.

the rate was analyzed among 39,063 embryos from patients with PGT. Among 856 RobT carriers, in total, 4158 embryos were retrieved with 1817 embryos characterized as normal/balanced embryos, and the rate of normal/balanced embryos was 43.70% (1817/4158) for RobT carriers. The limited embryos from the literature may not reflect the plausible rate of normal/balanced carrier embryos among all the embryos from RobT/RecT carriers. Therefore, the data for normal/balanced embryos were retrieved from the literature as presented in Table 3. By combining with the datasets from the literature, 2141 normal/balanced embryos were identified from 5140 embryos, and the rate of normal/balanced embryos was 39.57% (2141/5140). The total rate of normal/balanced embryos was 41.37% (3958/9568), and this was much higher than that based on the theory of gamete production.

Stratified analysis of normal/balanced embryo distribution based on carrier gender

It is well established that male RecT/RobT carriers produce a larger number of gametes each month compared with those of females,

and this may cause less of an effect on normal or balanced embryos. Therefore, male RecT/RobT carriers may exhibit a higher proportion of normal/balanced embryos than female carriers. To explore if sex could affect the rate of normal/balanced embryos from RecT/RobT carriers, RecT/RobT carriers were grouped according to sex. Our data revealed that the rate of normal/balanced embryos in male RobT carriers was higher than that in female RobT carriers (49.60% vs. 37.44%), and a significant difference was detected between the two subgroups ($P < 0.01$) as presented in Table 4. Furthermore, the RecT carriers of PGT were also divided into male and female groups, and the data indicated a similar rate to that of RobT carriers (29.84% vs. 27.67%) (Table 4).

Stratified analysis of normal/balanced embryo distribution of the biopsy period

Embryo cells from the third and fifth/sixth day of development were selected for biopsy during the cleavage and blastocyst stages, respectively. The number of fertilized egg cells on the third day of development was relatively small (only 6–8). Therefore, to reduce

Table 2. Basic information obtained from the literature on Rec. T carriers

ID	Year	Study type	Country	Biopsy period	Detection platform	No. of embryos	Normal/ Balanced	Proportion	References
1	2000	Retrospective	America	Blastomere	FISH	32	7	21.88%	(Munné et al., 2000)
3	2002	Clinical trials	America	Blastomere	FISH	61	7	11.48%	(Gianaroli et al., 2002)
4	2003	Clinical trials	America	Blastomere	FISH	596	158	26.51%	(Verlinsky et al., 2002)
5	2004	Clinical trials	America	Blastomere	FISH	18	4	22.22%	(McKenzie et al., 2003)
6	2004	Clinical trials	Korea	Blastomere	FISH	710	164	23.10%	(Kyu Lim et al., 2004)
7	2004	Retrospective	America	Blastomere	FISH	56	1	1.79%	(Sampson et al., 2004)
9	2008	Clinical trials	China	Blastomere	FISH	92	14	15.22%	(Yu-li et al., 2008)
10	2008	Clinical trials	Poland	Blastomere	FISH	8	3	37.50%	(Wiland et al., 2008)
11	2009	Clinical trials	China	Blastomere	FISH	16	1	6.25%	(Li et al., 2009)
12	2010	Clinical trials	France	Blastomere	PCR	117	45	38.46%	(Fiorentino et al., 2010)
13	2010	Clinical trials	America	Blastomere	FISH	722	277	38.37%	(Kuliev et al., 2010)
14	2011	Clinical trials	America	Blastomere	FISH	359	59	16.43%	(Mardesić et al., 2011)
15	2011	Clinical trials	China	NA	FISH	154	32	20.78%	(Xu et al., 2011)
16	2013	Retrospective	China	Blastomere	SNP/FISH	2757	626	22.71%	(Tan et al., 2013)
17	2014	Retrospective	America	Blastomere/ Trophoblast	SNP/aCGH	102	40	39.22%	(Tobler et al., 2014)
18	2015	Retrospective	Italy	Blastomere/ Trophoblast	NGS	145	20	13.79%	(Bono et al., 2015)
19	2015	Retrospective	America	Trophoblast	FISH	1501	555	36.98%	(Celestine et al., 2015)
20	2015	Retrospective	UK	NA	SNP	20	8	40.00%	(Sarasa et al., 2015)
21	2015	Clinical trials	Turkey	Blastomere	FISH	135	16	11.85%	(Tulay et al., 2015)
22	2016	Retrospective	Turkey	Blastomere	FISH	383	63	16.45%	(Tulay et al., 2016)
23	2017	Retrospective	Israel	Blastomere	FISH	270	61	22.59%	(Amir et al., 2019)
24	2017	Retrospective	Australia	Blastomere/ Trophoblast	FISH	1777	436	24.54%	(Beyer and Willats, 2017)
25	2017	Retrospective	China	Trophoblast	SNP	1053	283	26.88%	(Wang et al., 2017)
26	2017	Clinical trials	China	Blastomere/ Trophoblast	array-CGH/ FISH	62	10	16.13%	(Zhou et al., 2017)
27	2018	Retrospective	China	Blastomere/ Trophoblast	aCGH/SNP	318	59	18.55%	(Xie et al., 2018)
28	2019	Clinical trials	China	Trophoblast	FISH	400	109	27.25%	(Liu et al., 2020)
29	2019	Retrospective	France	Blastomere	FISH	427	177	41.45%	(Lammers et al., 2019)
30	2019	Clinical trials	China	Trophoblast	NGS	378	122	32.28%	(Wang et al., 2019)
31	2019	Clinical trials	China	Trophoblast	SNP	18	10	55.56%	(Zhang et al., 2019)
32	2021	Retrospective	Turkey	Trophoblast	NGS	376	112	29.79%	(Boynukalin et al., 2021)
33	2021	Clinical trials	China	Trophoblast	FISH	1935	286	14.78%	(Li et al., 2021)
34	2021	Clinical trials	China	Trophoblast	NGS	252	70	27.78%	(Liu et al., 2020)
35	2021	Clinical trials	China	Trophoblast	CCS/SNP	12	6	50.00%	(Pei et al., 2021)
36	2021	Retrospective	China	Trophoblast	NGS	580	207	35.69%	(Yuan et al., 2021)
37	2022	Retrospective	China	Trophoblast	NGS	275	59	21.45%	(Zhai et al., 2022)
	Total					16117	4107	25.48%	

NA, Not available.

Table 3. The rate of abnormal and normal phenotype embryos from RobT carriers and RecT carriers

Diagnosis of couple	Source of the data	Number of the embryos	Unbalanced chromosome embryos	Rate of unbalanced chromosome embryos	Normal/Balanced chromosome embryos*	Rate of normal/balanced chromosome embryos
RobT	This study	4158	2341	56.30%	1817	43.70%
	Literatures	5806	3479	59.92%	2327	40.08%
	Total	9964			4144	41.59%
RecT	This study	13,378	9532	71.25%	3846	28.75%
	Literatures	16,117	12,010	74.52%	4107	25.48%
	Total	29,495			7953	26.96%

*Chromosome normal or balanced embryos from RobT and RecT carriers.

Table 4. The rate of abnormal and normal phenotype embryos from RobT carriers and RecT carriers

	Number of the embryos	Number of unbalanced chromosome embryos	Rate of unbalanced chromosome embryos	Number of normal/balanced chromosome embryos*	Rate of normal/ balanced chromosome embryos	χ^2	P
Male with RobT	2139	1078	50.40%	1061	49.60%	62.406	0.000
Female with RobT	2019	1263	62.56%	756	37.44%		
Male with RecT	6690	4694	70.16%	1996	29.84%	7.687	0.006
Female with RecT	6687	4837	72.33%	1850	27.67%		

*Chromosome normal or balanced embryos from RobT and RecT carriers.

Table 5. The rate of normal/balanced embryos selected for biopsy during blastomere or trophoblast stages

Chromosome abnormality type	Biopsy period	N. of embryos	N. of Normal/Balanced chromosome embryos*	Proportion	χ^2	P
RobT	Blastomere	2534	914	36.07%	36.526	0.000
	Trophoblast	4571	1985	43.43%		
RecT	Blastomere	6769	1684	24.88%	19.008	0.000
	Trophoblast	18064	4998	27.67%		

*Chromosome normal or balanced embryos from RobT and RecT carriers.

the effect on the embryo, only a small number of cells can be biopsied, and this leads to low accuracy of the results. On the fifth/sixth day of development there were more trophoblast cells, and 5–10 cells can be selected for biopsy, therefore greatly improving the accuracy and success rate of the results. Additionally, certain studies have reported that the normal/balanced rate of embryos in the blastocyst stage biopsy is slightly higher than that in the cleavage stage, and this is consistent with the results of the present study. There were 2534 cleavage-stage embryos in the Robertson translocation group. Of these, 914 were normal/balanced. There were 4571 embryos in the blastocyst stage, and of these 1985 were normal/balanced. For RecT, there were, in total, 6769 cleavage stage embryos and, of these, 1684 were normal/balanced embryos. In total, 18,064 embryos were in the blastocyst stage and, of these, 4998 were normal/balanced. The proportions of normal/balanced embryos at different biopsy periods in both groups were statistically significant (36.07% vs. 43.43% and 24.88% vs. 27.67%, respectively).

Discussion

Carrying RecT or RobT is the major reason for abortion and infertility due to the risk of generating imbalanced chromosome gametes. Natural pregnancy combined with prenatal diagnosis after pregnancy, oocyte or sperm donation, and PGT are different strategies to produce a phenotypically normal infant with a normal or balanced chromosome karyotype. Additionally, PGT has been widely approved by the carriers of RecT/RobT for producing phenotypically normal and genetic material that is consistent with that of the parents. However, most PGT procedures were performed by genetic diagnosis of blastula trophoblast cells for the blastosphere, and the culture of embryos from the cleavage-stage to the blastocyst stage led to the loss of embryos. This enhances the anxiety of patients with PGT during assisted reproductive technology (ART) and also increases the difficulty for doctors who perform genetic counselling. Due to the lack of large-scale datasets for normal/balanced embryos from

RecT/RobT carriers with PGT, the theoretical probability rate of normal/balanced gametes of these carriers remains uncertain. For example, RobT carriers could possess 1/6 gametes with normal chromosomes, 1/6 gametes with balanced chromosomes, and 4/6 gametes with unbalanced chromosomes. RecT carriers would possess 1/18 gametes with normal chromosomes, 1/18 gametes with balanced chromosomes, and 16/18 gametes with unbalanced chromosomes. The unbalanced gametes would cause recurrent abortions. Accordingly, we aimed to provide robust genetic evidence supporting the proportion of normal/balanced gametes in RobT/RecT carriers and to determine if gender was a factor affecting the proportion of normal/balanced gametes in RobT/RecT carriers.

In total, 4158 embryos from 856 patients were obtained from RobT carriers with PGT, and this was slightly higher than the 13,378 embryos obtained from 2924 RecT carriers with PGT. Furthermore, in this study 4158 embryos from RobT carriers and 13,378 embryos from 2924 RecT carriers were analyzed, and our data revealed that each RobT carrier possessed 4.86 (2924/856) embryos and 4.56 (13,378/2924) embryos for each RecT carrier. Patients with RecT possessed fewer embryos than did RobT PGT carriers. Further analyses indicated that ~41.37% (3958/9568) of RobT carriers with PGT possessed normal/balanced embryos, and this was higher than that for RecT carriers (26.96%; 7953/29495). Interestingly, the proportion of RobT carriers with PGT in this study was 43.70% (1817/4158), and this was higher than that reported in the literature (39.57%; 2141/5410). The consistent rate of normal/balanced embryos for RobT carriers with PGT from datasets in this study and the literature supported the reliable evidence that RobT carriers may exhibit a rate for obtaining ~41.37% embryos for embryo transplantation, and this was consistent with that in previous studies (44.1%; 60/136; Liu *et al.*, 2020). The pattern for RecT carriers was similar, in which the total rate of normal/balanced embryos for RecT carriers with PGT was 26.96% (7953/29,495), and the rate from datasets in this work was 28.75% (3846/13,378) and was consistent with datasets from literature (25.48%; 4107/16,117). Additionally, this rate is similar to that reported in recent studies (70/252, 27.8%). The rate of normal/balanced embryos in RobT/RecT carriers with PGT was higher than the theoretical value of synaptonemal complex segregation for RobT (2/6, 33.33% vs. 3958/9568; 41.37%) and RecT (2/18, 11.11% vs. 7953/29,495; 26.96%). Natural selection may play a crucial role during the processes of gametogenesis and embryogenesis (Mateu-Brull *et al.*, 2019; Liu *et al.*, 2020), and the higher ratio of normal/balanced embryos for RobT carriers (41.37%; 3958/9568) compared with that of RecT carriers (26.96%; 7953/29,495) may be caused by the higher alternate segregation of RobT carriers compared with that of RecT carriers (Liu *et al.*, 2020). Specifically, both RobT carriers and RecT carriers exhibit a greater chance of obtaining a transferable embryo compared with the theoretical value, and this provides reliable genetic evidence for clinical genetic consulting for RobT/RecT carriers with the aim of performing PGT.

To further determine if sex could affect the rate of normal/balanced embryos, the 856 RobT carriers and 2924 RecT carriers were divided into two groups according to their sex. For RobT carriers, our data indicated that male carriers possess more normal/balanced embryos than female carriers (49.60% vs. 37.44). A significant difference between the two groups was detected with $P = 0.000$ ($P < 0.05$), and this indicated that male carriers possess a higher number of transferable embryos than do female carriers. However, for RecT carriers a higher transferable embryo rate was observed in 29.84% (1996/6690) of male carriers than was observed in female carriers (27.67%; 1850/6687) with $P = 0.006$ ($P < 0.05$). These data also indicated a higher number of transferable embryos in male RecT carriers. Our data illustrated that male carriers possess more normal/balanced embryos than do female RobT and RecT carriers. This is consistent with the results of a previous study (Liu *et al.*, 2020). Therefore, the gender of the carrier should be considered when performing genetic consulting for patients with the aim of PGT. Additionally, according to the results of biopsy period grouping, the normal/balanced ratio of embryos in the blastocyst stage was higher than that in the cleavage stage (36.07% vs 43.43%; 24.88% vs 27.67%) in both groups of carriers for both RobT and RecT, therefore indicating a higher likelihood of obtaining normal/balanced embryos through blastocyst stage biopsy. This phenomenon may be explained by the observation that the process of embryo development from days 3 to 5/6 naturally eliminated poor-quality embryos.

However, the absence of patient information for data retrieved from the literature, including the age of RobT/RecT carriers, the number of patients participating in the research, and the clinical outcomes of PGT, restricts a better understanding of the clinical outcomes of PGT. Additionally, mosaic embryos with a low proportion of unbalanced chromosomes or a high proportion of unbalanced chromosomes were included in the datasets of this study and those from the literature, and this could be caused by technology such as fluorescence *in situ* hybridization (FISH) used for performing genetic diagnosis in the literature.

In conclusion, the performance of PGT could diagnose the normal/balanced embryos of RobT/RecT carriers, and this could reduce the clinical pregnancy rate of the carriers. However, the conventional genetic consulting of RobT/RecT carriers was primarily explained with theoretical values of 2/6 and 2/18, and this did not reflect the real ratios of the normal/balanced embryos and may cause anxiety to carriers. The plausible ratios were illustrated in previous studies and ranged from 1.79% to 55.56% for RecT carriers (Sampson *et al.*, 2004; Zhang *et al.*, 2019) and from 10.00% to 79.66% for RobT carriers (Tulay *et al.*, 2016; Xu *et al.*, 2004). The small sample size was the major factor responsible for causing the fluctuations in the normal/balanced embryo rate of RobT/RecT carriers. Consequently, to provide reliable genetic datasets for genetic consulting, the large-scale embryos of RobT/RecT carriers were collected and analyzed in this study. The datasets illustrated that the rates of normal/balanced embryos were 41.37% among 9568 embryos from RobT carriers and 26.96% from 29,495 embryos from RecT. The rates were much higher than the theoretical values of 2/6 and 2/18. The male carriers for both RobT and RecT exhibited a higher rate of normal/balanced embryos compared with that of female groups, and the ratio of normal/balanced embryos in the blastocyst stage was higher than that in the cleavage stage. This supplied robust genetic evidence for performing genetic consulting for RobT/RecT carriers with PGT.

Competing interests. The authors declare no conflicts of interest.

Ethical standard. The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional committees on human experimentation and the Declaration of Helsinki of 1975 as revised in 2008.

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