Effects of Chromosomal Abnormalities on Assisted Reproductive Technology: A Retrospective Cohort Study

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Abstract

Background: To ascertain whether couples with chromosomal abnormalities have a difference in cumulative clinical pregnancy rate and cumulative live birth rate among assisted reproductive technology population.

Methods: Design: A retrospective cohort study. Setting: Department of reproduction and infertility in Chengdu Women's and Children's Central Hospital.

Patients: A total of 112 couples were in exposed group with chromosomal abnormalities and 226 couples without chromosomal abnormalities in control group included in the study, totaling 338 cases. From 1st Jan 2017 to 31st Dec 2019. Control group (infertility couples without chromosomal abnormalities) was 1:2 matched by female age, type of infertility (primary, secondary), type of assisted reproductive technology (IVF, ICSI or IUI).

Results: Primary outcomes: cumulative clinical pregnancy rate and cumulative live birth rate. The results indicated that chromosomes abnormalities had no statistical difference in primary outcomes. Further analysis revealed exposed group (couples with chromosomal abnormalities) had less 2 pronuclear stage count. The times of embryo transfer by ICSI was less than IVF in exposed group. We found out only female age had an effect on the primary results and the threshold was 33.5 years old.

Conclusions: There were no significant differences in cumulative clinical pregnancy rate and cumulative live birth rate between two groups. But 2 pronuclear stage count, and the times of embryo transfer were affected by chromosomal abnormalities. It may be better to choose ICSI and PGT in this population.

Background

Infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse (clinical definition according to the World Health Organization (WHO)) [1]. The prevalence of infertility is high around the world, it is estimated that 1 out of 4 couples are infertile[2]. The latest epidemiological investigation in China showed that among 10742 women, prevalence of infertility was 25.0% (2680/10742) [3].

Chromosomal abnormalities, also known as chromosomal dysgenesis, include numerical and structural aberrations of any chromosome. Data from an infertility clinics have shown 1.3% of partners to have chromosomal abnormality[4]. Chromosomal abnormalities have been associated with infertility[5].

Chromosome anomalies are important, especially in early abortions. The majority of such abnormalities may be due to chromosomal non-disjunction, translocation, or another mutation. A balanced or unbalanced karyotype in one of the partners in a couple as a structural chromosomal abnormality (reciprocal or Robertsonian translocations etc.) may result in recurrent miscarriage, or physical and/or mental disorder in next generation. [6].
However, there were few articles to study whether couples with chromosomal abnormalities in assisted reproductive technology (ART) have a significant difference in pregnancy rate and times of embryo transfer.

As preimplantation genetic technologies (PGT) are increasingly used with in vitro fertilization includes three sub-categories of aneuploidies (PGT-A), for single gene / monogenic disorders (PGT-M), and PGT for chromosome structural rearrangements (PGT-SR). Genetic counseling and discussion of possible preimplantation genetic testing should be offered when a structural rearrangement (translocations, inversions, deletions, and insertions) is discovered in a parent. It is now able to differentiate inherited chromosome arrangement. This might help in deciding the best treatment options for PGT for chromosome structural rearrangements (PGT-SR) and minimize the risk of transmission of anomalies to the offspring.

Due to the limitation of economy and technical condition, western China, for example, some infertile patients refuse PGT after genetic counseling and ask for natural selection when they seeking for assisted reproductive technology. This research aims to discuss whether the outcomes will be different between couples with chromosomal abnormalities and couples without chromosomal abnormalities among ART population.

**Methods**

A retrospective cohort study 1:2 matched by female age, type of infertility (primary, secondary), and type of assisted reproductive technology intrauterine insemination (IUI)/ in vitro fertilization (IVF)/ Intracytoplasmic sperm injection (ICSI) were conducted. 4656 infertile couples came to our center (department of reproduction and infertility, Chengdu Women's and Children's Central Hospital) for assisted reproductive technology in the past 3 years (1st Jan 2017 to 31st Dec 2019), followed up by phone calls. The International System for Human Cytogenetic Nomenclature (ISCN, 2016)[7], was followed for defining the chromosomal abnormalities. Infertility according to WHO: a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Exposed group: Infertility couples with chromosomal abnormalities. Control group: Infertility couples without chromosomal abnormalities. Bias was mostly sampling error, to minimize the sampling error, we 1:2 matched data by female age, type of infertility (primary, secondary), type of assisted reproductive technology (IVF, ICSI or IUI). Outcomes were divided into groups by gender in couples with chromosomal abnormalities, and t-tests were used.

After adequate communication, more than one hundred couples (112/4656) with chromosomes abnormalities came to our center for assisted reproductive technology (ART) refuse PGT in the past 3 years (1st Jan 2017 to 31st Dec 2019). However, they were told that chorionic villus sampling (CVS) or amniocentesis should be done.

In our center, clinical and laboratory researchers were very stable (no staff changes) in the past three years, and we followed the standardized operating procedures, the pregnancy rate in three years was also
very stable. Therefore, we statistically analyzed the data of these three years to find out whether chromosomal abnormalities couples among an assisted reproductive technology population affect in cumulative clinical pregnancy rate and cumulative live birth rate compared with couples without chromosomal abnormalities.

Data extraction

We collect the following data from the electronic database of our center by two separate members. Quantitative variables were based on common causes of infertility: medical record number, female age, male age, chromosome karyotypes, type of infertility, type of ART, endometriosis, immune infertility (positive of anti-sperm antibody, anti-ovarian antibody, anti-endometrium antibody, or anti-cardiolipin antibody), salpingemphraxis (diagnosed by hysterosalpingography or laparoscopic surgery), endometrium abnormality( diagnosed by hysteroscopy), polycystic ovary syndrome (PCOS), years of infertility, Anti-Müllerian hormone(AMH) value, percentage of normal sperm, sperm donor. Primary outcomes: cumulative clinical pregnancy rate, cumulative live birth rate. Secondary outcomes were closely related to clinical outcomes: MII oocyte count, 2pn oocyte count (2 pronuclear stage), number of embryos, number of good-quality embryos. Embryo grading was performed by the same team of two highly trained embryologists, whom with over 10 years of experience by guidelines for assisted reproduction in China. (9–11). The outcomes were defined based on the International Committee for Monitoring Assisted Reproductive Technology and the World Health Organization revised glossary of ART terminology 2009.

[1] “cumulative clinical pregnancy” was defined as the detection of a gestational sac via transvaginal ultrasonography including the cycle when fresh embryos were transferred, and subsequent frozen/thawed ART cycles. “cumulative live birth” was defined as the complete expulsion or extraction of the fetus from his/her mother, followed by breaths or other evidence of life, such as a heartbeat, umbilical cord pulsation, or definite movements of voluntary muscles including the cycle when fresh embryos were transferred, and subsequent frozen/thawed ART cycles. All clinical pregnancy patients will continue to visit our clinic for 12 weeks. However, due to the transplant time of some patients, the cumulative clinical pregnancy rate and the live birth rate could not be fully counted. The day we collected the data, the patients had not got the pregnancy test or gave birth yet.

Statistical analysis

All data were entered into IBM SPSS Statistics 25. The statistical significance level was established at 0.05. Numeric variables were tested for their normality using the Kolmogorov-Smirnov test. Normally distributed variables are presented as the mean ± standard error of the mean and were compared using ANOVA. Continuous variables with non-normal distribution are expressed as the median with range and were compared using the non-parametric method (Kruskal-Wallis rank-sum test or Wilcoxon-Mann-Whitney test). Independent sample t-tests were used for continuous variables. Nominal variables are reported in the form of frequencies with percentages and were compared using the Chi-square test or Fisher’s exact test. The relationship between these factors and cumulative pregnancy rate/delivery of a
healthy baby (baby-take home rate) were studied using the conditional logistic regression, and the estimated odds ratios (OR) and their 95% confidence intervals (CI) are reported. Variables with p-values < 0.1 in the univariate analysis were allowed to participated in the multivariate stepwise logistic regression to explore the independent factors in predicting the pregnancy/deliver rate. The receiver-operating characteristic (ROC) curves were constructed for all independent predicting factors which are continuous variables, and the optimal threshold value was determined according to the Youden index.

**Results**

**Baseline characteristics**

Baseline characteristics of cases are shown in Table 1. Couples with chromosomal abnormalities were in the exposed group. The control group was matched by female age, type of infertility, and type of ART. Meanwhile male age, endometriosis, PCOS, etc. did not significantly differ between cases and controls. However, the sperm donor was more in chromosomal abnormalities couples.
Table 1
Baseline characteristics of study population

| Characteristic          | Exposed group Cases (N = 112) | Control group Cases (N = 224) | P value |
|-------------------------|-------------------------------|-------------------------------|---------|
| Type of infertility     |                               |                               |         |
| Primary                 | 67 (60%)                      | 130 (58%)                     | 0.814   |
| Secondary               | 45 (40%)                      | 94 (42%)                      |         |
| Type of ART             |                               |                               |         |
| IVF                     | 83 (74%)                      | 163 (73%)                     | 0.959   |
| ICSI                    | 22 (20%)                      | 47 (21%)                      |         |
| IUI                     | 7 (6%)                        | 14 (6%)                       |         |
| Female age              | 30.22 ± 4.159                 | 30.11 ± 4.025                 | 0.808   |
| Male age                | 32.32 ± 5.596                 | 32.28 ± 4.834                 | 0.946   |
| Endometrium abnormality | 19 (7%)                       | 27 (12%)                      | 0.240   |
| Endometriosis           | 10 (9%)                       | 16 (7%)                       | 0.665   |
| Immune infertility      | 2 (2%)                        | 8 (4%)                        | 0.506   |
| Salpingemphraxis        | 66 (59%)                      | 135 (60%)                     | 0.815   |
| PCOS                    | 23 (21%)                      | 45 (20%)                      | 1.000   |
| Year of infertility     | 3.75 ± 2.700                  | 3.20 ± 2.332                  | 0.055   |
| AMH                     | 4.34 ± 3.904                  | 4.28 ± 4.204                  | 0.915   |
| Percentage of normal sperm | 0.024 ± 0.160              | 0.041 ± 0.135                 | 0.188   |
| Sperm donor             | 6 (5%)                        | 2 (1%)                        | 0.018*  |

Note: *P<0.05

Values are presented as mean ± standard deviation or n (%).

ART = assisted reproductive technology; IVF=in vitro fertilization; ICSI=intracytoplasmic sperm injection; IUI=intrauterine insemination.

Types and numbers of chromosome anomalies

112 couples had chromosomal abnormalities, of which 66 were male (59%), 46 were female (41%). The types are divided into six categories, including: chromosome disorders: structural aberrations: chromosomal inversions (61/112), translocations(11/112), (rob) robertsonian translocations(4/112); sex abnormalities: 46,X,inv(Y)(p11;q11)(14/112), klinefelter syndrome 47,XXY(1/112), 47,XXX(1/112); Mosaic(14/112), others: 47,XY,+mar (5/112);(Fig. 1).
Clinical outcomes

Important clinical indicators for the success of ART including primary outcomes and secondary outcomes.

Our statistical results show that chromosomal abnormalities have no difference in primary outcomes. The overall cumulative clinical pregnancy rate was nearly the same between the two groups (74.1.0% vs 73.2, P 0.861). The overall cumulative live birth rate was also nearly the same between the two groups (62.1% vs 58.2, P = 0.886). (Table 2)

### Table 2

Primary clinical outcomes

| Characteristic                        | Exposed group      | Control group     | P value |
|---------------------------------------|--------------------|-------------------|---------|
|                                       | %(n/N)             | %(n/N)            |         |
| Cumulative clinical pregnancy rate    | Overall            | 74.1% (83/112)    | 73.2% (164/224) | 0.861   |
|                                       | IVF                | 77.9% (64/83)     | 77.1% (127/163) | 0.886   |
|                                       | ICSI               | 77.3% (17/22)     | 74.5% (35/47)  | 0.800   |
|                                       | IUI                | 28.6% (2/7)       | 14.3% (2/14)  | 0.574   |
| Cumulative live birth rate            | Overall            | 62.1% (54/95)     | 58.2% (114/196) | 0.521   |
|                                       | IVF                | 64.2% (43/67)     | 63.4% (90/142) | 0.911   |
|                                       | ICSI               | 71.4% (15/21)     | 55.0% (22/40)  | 0.212   |
|                                       | IUI                | 14.3% (1/7)       | 14.3% (2/14)  | 1.000   |

Note: Values are presented as %(n/N).

Statistical analysis of the secondary clinical outcomes showed there were no statistically significant differences in MII oocyte count, embryo count, and good-quality embryo count and times of embryo transfer (Table 3). However, 2pn oocyte count was lower in chromosomal abnormalities group(10.02 ± 6.095 vs 12.03 ± 7.753, p = 0.013). To further find out the reason, we analyzed by gender in couples with chromosomal abnormalities. There was no statistical difference between male and female groups in both primary and secondary outcomes(Table 4). Since 2PN oocyte count was lower in the chromosome abnormal group. Further analysis identified that the difference was due to the male group(9.95 ± 5.712 vs 10.11 ± 6.637, p = 0.024) (Table 5).
### Table 3
Secondary clinical outcomes

| Characteristic                  | Exposed group | Control group | P value |
|--------------------------------|---------------|---------------|---------|
|                                | n = 105       | n = 209       |         |
| MII oocyte count               | 14.48 ± 7.453 | 14.55 ± 8.592 | 0.940   |
| 2PN oocyte count               | 10.02 ± 6.095 | 12.03 ± 7.753 | 0.013*  |
| Embryo count                   | 5.90 ± 3.264  | 5.76 ± 3.437  | 0.731   |
| High quality embryo count      | 2.83 ± 2.796  | 2.96 ± 3.047  | 0.718   |
| The times of embryo transfer   | 1.41 ± 0.771  | 1.47 ± 0.764  | 0.573   |

*Note:* *P*<0.05

Values are presented as mean ± standard deviation.

2PN: 2 pronuclear stage (2PN)

### Table 4
Analysis by gender in couples with chromosomal abnormalities

| Outcomes                          | Male        | Female      | P value |
|-----------------------------------|-------------|-------------|---------|
| Cumulative clinical pregnancy rate| 47(71%)     | 33(77%)     | 0.523   |
| Cumulative live birth rate        | 20(50%)     | 19(59%)     | 0.428   |
| MII oocyte count                  | 14.30 ± 7.284 | 14.71 ± 7.748 | 0.783   |
| 2PN                              | 9.95 ± 5.712 | 10.11 ± 6.637 | 0.894   |
| Embryo count                      | 6.13 ± 3.197 | 5.58 ± 3.361 | 0.394   |
| High quality embryo count         | 2.77 ± 2.486 | 2.91 ± 3.197 | 0.795   |
| The times of embryo transfer      | 1.13 ± 0.505 | 1.03 ± 0.167 | 0.193   |

*Note:* Values are presented as mean ± standard deviation or n (%).
Table 5
Analysis by gender of 2PN oocyte count

| Male chromosome abnormal | Female chromosome abnormal | Control group | p<sup>1</sup> value | p<sup>2</sup> value |
|--------------------------|-----------------------------|---------------|---------------------|---------------------|
| 9.95 ± 5.712             | 10.11 ± 6.637               | 12.03 ± 7.753 | 0.024*              | 0.124              |

Note: *P < 0.05

Values are presented as mean ± standard deviation.

P<sup>1</sup> value: Male chromosome abnormal VS Control group

P<sup>2</sup> value: Female chromosome abnormal VS Control group

Independent Samples (Mann-Whitney U test) on secondary outcomes in the exposed group found out that the times of embryo transfer was less by ICSI than IVF. (Table 6).

Table 6
Assisted reproduction techniques for secondary outcomes in expose group

| Secondary outcomes          | IVF         | ICSI        | P value |
|-----------------------------|-------------|-------------|---------|
| MII oocyte count            | 14.48 ± 7.23| 14.45 ± 8.42| 0.988   |
| 2PN                         | 10.0 ± 6.06 | 9.77 ± 6.34 | 0.838   |
| Embryo count                | 6.07 ± 3.36 | 5.23 ± 2.86 | 0.282   |
| High quality embryo count   | 2.94 ± 2.81 | 2.4 ± 2.77  | 0.431   |
| The times of embryo transfer| 1.48 ± 0.84 | 1.12 ± 0.33 | 0.007*  |

Note: *P<0.05

Values are presented as mean ± standard deviation. IVF=in vitro fertilization; ICSI=intracytoplasmic sperm injection.

**Univariate analysis of the primary outcomes**

One-way ANOVA showed assisted reproduction techniques, salpingemphraxis, AMH, and female age had effects on the cumulative clinical pregnancy rate. Only assisted reproduction techniques and female age had effects on the cumulative live birth rate. (Table 7)
Table 7
Univariate analysis of the primary outcomes

| One-way ANOVA                  | Cumulative clinical pregnancy rate | Cumulative live birth rate |
|-------------------------------|------------------------------------|----------------------------|
|                               | P  | HR   | 95% CI      | P  | HR   | 95% CI      |
| Control group                 | 1.000 | Reference | 1.000 | Reference |
| Exposed group                 |     |       |             |     |       |             |
| Overall                       | 0.698 | 0.814 |               |     |       |             |
| Male                          | 0.748 | 0.905 | (0.492, 1.665) | 0.595 | 1.177 | (0.645, 2.148) |
| Female                        | 0.478 | 1.317 | (0.616, 2.818) | 0.651 | 1.182 | (0.574, 2.434) |
| Type of infertility           |     |       |             |     |       |             |
| Primary                       | 1.000 | Reference | 1.000 | Reference |
| Secondary                     | 0.338 | 0.784 | (0.476, 1.290) | 0.350 | 0.795 | (0.492, 1.285) |
| ART                           |     |       |             |     |       |             |
| Overall                       | 0.000* | 0.006* |               |     |       |             |
| IUI                           | 0.000* | 0.068 | (0.022, 0.210) | 0.000* | 0.095 | (0.027, 0.334) |
| IVF                           | 1.000 | Reference | 1.000 | Reference |
| ICSI                          | 0.690 | 0.881 | (0.022, 0.210) | 0.672 | 0.881 | (0.490, 1.583) |
| Endometriosis                 | 0.085 | 0.340 | (0.099, 1.161) | 0.148 | 0.492 | (0.188, 1.286) |
| Immune infertility            | 0.799 | 1.196 | (0.302, 4.729) | 0.809 | 1.179 | (0.310, 4.485) |
| Salpingemphraxis              | 0.021* | 0.561 | (0.343, 0.915) | 0.076 | 0.650 | (0.404, 1.046) |
| Endometrium abnormality       | 0.313 | 1.412 | (0.722, 2.762) | 0.107 | 1.757 | (0.886, 3.487) |
| PCOS                          | 0.536 | 0.822 | (0.441, 1.530) | 0.568 | 0.842 | (0.467, 1.518) |
| Year of infertility           | 0.236 | 0.945 | (0.860, 1.038) | 0.201 | 0.941 | (0.858, 1.033) |
| AMH                           | 0.042* | 1.074 | (1.003, 1.151) | 0.055 | 1.060 | (0.999, 1.125) |
| Male age                      | 0.079 | 0.960 | (0.916, 1.005) | 0.214 | 0.971 | (0.928, 1.017) |
| Female age                    | 0.001* | 0.899 | (0.847, 0.955) | 0.002* | 0.910 | (0.858, 0.965) |
| Percentage of normal sperm    | 0.298 | 0.348 | (0.048, 2.538) | 0.547 | 0.543 | (0.074, 3.960) |
| Sperm donor                   | 0.381 | 0.390 | (0.047, 3.212) | 0.717 | 0.728 | (0.131, 4.043) |

Note: *P<0.05

Data presented as p value and odds ratio (95% confidence interval). CI = confidence interval; HR = Hazard ratio. ART = assisted reproductive technology; IVF=in vitro fertilization; ICSI=intracytoplasmic sperm injection; IUI=intruterine insemination.
Multiple variables analysis of the primary outcomes

With the method of logistic regression variables. The input method was to put all the included factors into the model and calculate the p-value after adjustment. When the single factor $p < 0.1$ included age of male and female, type of infertility, salpingeumphraxis, and AMH, but only the female age and type of infertility were $p < 0.05$ after regression of all factors into the model, and the other factors were $p > 0.05$. (Table 8).

Table 8

| Multiple variables analysis | Cumulative clinical pregnancy rate | Cumulative live birth rate |
|----------------------------|-----------------------------------|---------------------------|
|                            | P       | HR          | 95% CI         | P       | HR          | 95% CI         |
| ART overall                | 0.000*  |             |                | 0.000*  |             |                |
| IUI                        | 0.000*  | 0.048       | (0.015,0.156)  | 0.000*  | 0.072       | (0.020, 0.261) |
| IVF                        | 1.000   | Reference   |                | 1.000   | Reference   |                |
| ISCI                       | 0.921   | 0.968       | (0.509,1.841)  | 0.905   | 0.964       | (0.529, 1.759) |
| Female age                 | 0.000*  | 0.872       | (0.818,0.930)  | 0.000*  | 0.889       | (0.836,0.946)  |

*Note:* Data presented as p value and odds ratio (95% confidence interval). CI = confidence interval; HR = Hazard ratio. ART = assisted reproductive technology; IVF=in vitro fertilization; ICSI=intracytoplasmic sperm injection; IUI=intrauterine insemination.

Analyzed the female age threshold

We statistically analyzed the female age threshold by the receiver operating characteristic (ROC) curve. The optimal threshold is determined by the age (Additional file 1 and additional file 2) at which the youden index reaches the maximum value[8]. The threshold of female age was 33.5 years old.

We did an analysis based on 34 years old. In the younger group (< 34 years old), the clinical pregnancy rate of the group was 78%, and the live birth rate was 65%. In the older group(≥ 34 years old) the clinical pregnancy rate was 55% and the live birth rate was 40%(P < 0.001). (Table 9)
Table 9
Analysis of female age threshold

|                           | < 34 years old | ≥ 34 years old | P value |
|---------------------------|----------------|----------------|---------|
| Cumulative clinical pregnancy rate | 78%            | 65%            | < 0.001 |
| Cumulative live birth rate  | 55%            | 40%            | < 0.001 |

Discussion

The prevalence of Infertility is rising year by year all over the world. It is estimated that 1 out of 4 couples are infertile[2]. Latest epidemiological investigations have shown prevalence of infertility to be 25% in China [3]. Chromosomal abnormalities were associated with infertility[5] and maybe the major recognized genetic causes for recurrent miscarriage[9]. A few couples (112/4656) with chromosomes abnormalities came to our center for assisted reproductive technology in the past 3 years (1st Jan 2017 to 31st Dec 2019). To figure out whether chromosomes abnormalities have any effect on our decision-making, we conducted this cohort study. The results indicated that chromosomes abnormalities without PGT had no statistical difference in primary outcomes (cumulative clinical pregnancy rate and cumulative live birth rate) between two groups. Further analysis revealed chromosomes abnormalities had less 2PN oocyte count, and had predominantly male influence. At baseline analysis, the number of sperm donors was statistically higher for couples with chromosomal abnormalities. This study found out that the times of embryo transfer were less in ICSI in the exposed group. For infertile couples with abnormal chromosomes, they may need more active ART, such as ICSI, and PGT-A.

Univariate analysis of the primary result showed assisted reproduction techniques, and the female age affected both cumulative clinical pregnancy rate and cumulative live birth rate. Salpingemphraxis and AMH only affected the cumulative clinical pregnancy rate. Multiple variables analysis of the primary result showed only the female age and assisted reproduction techniques were different statistically (p < 0.05).

Although male age and normal sperm percentage did not affect primary outcomes (cumulative clinical pregnancy rate and cumulative live birth rate), the male age was highly correlated with the fertilization and embryo count. Although there has been a significant decline in the fertility of both men and women globally, the male cause has not yet reached a threshold because of the very large sperm base of men. It remains to be further analyzed in the future.

Genetic counseling and discussion of possible preimplantation genetic testing should be offered when a structural rearrangement (translocations, inversions, deletions, and insertions) is discovered in a parent. However preimplantation genetic testing-structural rearrangements cannot differentiate between an embryo that has a normal karyotype, an embryo that carries a balanced form of the familial chromosome rearrangement and this testing method uses only a few trophectoderm cells. Because of these limitations, confirmation of preimplantation genetic testing-structural rearrangements results with chorionic villus
sampling (CVS) or amniocentesis should be offered[10]. However, the evidence suggests that the universal use of PGT-A is premature. We know that the technology is imperfect: PGT-A can erroneously call euploid embryos as aneuploidy[11] and we do not know what to do with apparently mosaic embryos[12]. Blockeel C et al, 2008 showed preimplantation genetic screening does not increase the implantation rates after IVF-intracytoplasmic sperm injection in women with repeated implantation failure[13]. Some studies have failed to find improvement in live birth rates for women younger than 37 years of age [14] [15] [16], so it seems unlikely that the added complexity and cost of this intervention can be justified in younger patients. An economic analysis of preimplantation genetic testing for aneuploidy by polar body biopsy in advanced maternal age showed PGT-A increased the cost greatly and suggested patients and doctors need to be aware of the high-cost implications of applying PGT-A[17]. Due to the limitation of economy and technical condition, western China, for example, some infertile patients refuse PGT after genetic counselling and opt for natural selection when seeking for assisted reproductive technology.

In this cohort study, we revealed chromosomes abnormalities had less 2PN oocyte count and the times of embryo transfer were less in ICSI in the exposed group. We statistically analyzed the female age threshold was 33.5 years old. Infertile couples with chromosomal abnormalities among the ART population, especially when the female age is over 33.5 years can be considered for PGT, and further research support is still needed.

The data we analyzed have a certain significance for the clinical decision-making of ART for couples with chromosomal abnormalities, and it provides a meaningful reference for patients and physicians in the selection of PGT.

Limitations of this study: It is a retrospective cohort study. Bias was mostly sampling error, to minimize the sampling error, we 1:2 matched data by female age, type of infertility, type of assisted reproductive technology. The age threshold may be different from big data. The data source is from a single-center, the sample size is still small, and the data does not include PGT. We need to further expand the sample size for sure.

**Conclusion**

There was no statistical difference in primary outcomes (cumulative clinical pregnancy rate and cumulative live birth rate) between two groups. However the secondary outcomes showed 2 pronuclear stage count was less in exposed group (couples with chromosomal abnormalities), and the times of embryo transfer by ICSI was less than IVF in exposed group. Therefore, in the case of infertile couples with chromosomal abnormalities, it may be better to choose ICSI and PGT in this population especially when the female age is over 33.5 years old.

**Abbreviations**
ART: assisted reproductive technology; PGT: preimplantation genetic technologies; IUI: intrauterine insemination; IVF: in vitro fertilization; ICSI: intracytoplasmic sperm injection; CVS: chorionic villus sampling; PCOS: polycystic ovary syndrome; AMH: Anti-Müllerian hormone.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Chengdu Women and Children's Central Hospital and all data were irreversibly anonymized, assuring protection of all patients’ information. Ethics approval number: No. 82019. Written informed consent was obtained from the participants when they presented for ART treatment. Each pair of couples with chromosomal abnormalities has been fully communicated to make them fully aware of and informed of their options (preimplantation genetic testing is optional), and the relevant informed consent has been signed. Couples with chromosomal abnormalities were fully informed that chorionic villus sampling (CVS) or amniocentesis should be done.

Availability of data and materials

The data that support the findings of this study are available from Chengdu Women and Children's Central Hospital but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Ethics Committee of Chengdu Women and Children's Central Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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None.

Authors’ contributions

Dr L.C. was involved in design and conduct of the study, data analysis, drafting the manuscript. Professor YH.L. was involved in supervised data analysis, and revised the manuscript. Professor F.W was involved in the design and conduct of the study, checked data extraction and revised the manuscript and validated the final version for submission. XT.Y, WD.T, H.X contributed to data interpretation. M.L was involved in data collection. All authors approved the final manuscript.
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Figures
Figure 1

Types and numbers of chromosome anomalies in couples with infertility

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