Original Article

Role of Female Age in Regulating the Effect of Sperm DNA Fragmentation on the Live Birth Rates in Intracytoplasmic Sperm Injection Cycles with Own and Donor Oocytes

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ABSTRACT

Background: Sperm DNA integrity assessment has been progressively used as an unfettered measure of sperm as it proffers more prognostic and diagnostic information than routine semen analysis. The contentious effect of sperm DNA fragmentation (SDF) on clinical outcomes can be attributed to female factors such as age, oocyte quality and ovarian reserve. **Aims:** The study is mainly aimed to know the influence of SDF on the live birth rates in intracytoplasmic sperm injection (ICSI) cycles with own and donor oocytes. Second, to know the role of female age in regulating the effect of SDF on the live birth rates in ICSI cycles with own and donor oocytes. **Setting and Design:** A prospective cohort study was done at our tertiary care centre attached to the reproductive medicine unit in medical college. **Materials and Methods:** The study included 356 patients who underwent first ICSI cycles either with own or donor-oocytes along with day 5 fresh embryo transfers only. The main outcome measures were live birth rates and miscarriage rates. **Statistical Analysis Used:** Chi-squared test was used to compare the categorical variables between the groups. The receiver operating characteristic curve was developed to correlate the female age with the live birth rate. **Results:** A significant decrease in the live birth rates (42.85% vs. 26.15%, $P = 0.023$) and an increase in the miscarriage rates (12.30% vs. 34.61%, $P = 0.013$) were observed in the high-SDF group ICSI cycles of own-oocyte patients. However, there was no significant difference in the live birth rates and miscarriage rates in the low- and high-SDF groups of donor oocyte ICSI cycle patients ($P > 0.05$). The own-oocyte ICSI cycle patients were further stratified based on the female age. In the female age group ≤30 years there was no significant difference in the live birth and miscarriage rates ($P > 0.05$) similar to donor oocyte ICSI cycles. Whereas, there was a significant difference in the live birth rates in the females of age >30 years (13.79% vs. 34.37%, $P = 0.040$). **Conclusion:** In conclusion, high-SDF has a negative influence on the live birth rates and a positive influence on the miscarriage rates in patients with own-oocyte ICSI cycles. A similar influence was not observed in patients with donor-oocyte ICSI cycles and in young female patients (age ≤30 years) with own-oocyte ICSI cycles.

Keywords: *Intracytoplasmic sperm injection, live birth rates, own and donor oocyte, sperm DNA fragmentation*

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Received: 23-10-2021 **Revised:** 27-02-2022
Accepted: 27-02-2022 **Published:** 31-03-2022

Access this article online

Quick Response Code:

Website:
www.jhrsonline.org

DOI:
10.4103/jhrs.jhrs_150_21

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How to cite this article: Repalle D, Saritha KV, Bhandari S, Chittora M, Choudhary J. Role of female age in regulating the effect of sperm DNA fragmentation on the live birth rates in intracytoplasmic sperm injection cycles with own and donor oocytes. J Hum Reprod Sci 2022;15:64-71.

Introduction

Sperm DNA integrity assessment has been progressively used as an unfettered measure of sperm as it proffers more prognostic and diagnostic information than routine semen analysis.[1-4] The effect of sperm DNA fragmentation (SDF) on clinical outcomes in *in vitro* fertilisation (IVF) and/or intracytoplasmic sperm injection (ICSI) cycles is controversial, as some reported a negative effect[5-12] and other studies contradicted with no effect.[13-15] SDF may not affect the fertilisation potential of sperm.[1,12] However, SDF was related to a late paternal effect and may increase the risk of miscarriage.[16] The clinical correlation of SDF is limited to pregnancy rates only.[8,9,13] In the opinion of a recent meta-analysis, very few studies correlated SDF with live birth rates in cycles of ICSI.[7]

The contentious effect of SDF on clinical outcomes can be attributed to female factors like age, oocyte quality and ovarian reserve.[9,17,18] The mature sperm do not possess the capacity to repair their DNA as transcription and translation are halted. However, oocytes can repair the SDF to some extent depending on the oocyte quality.[19,20] Age swaps gene expression patterns in cumulus cells requisite for quality of oocyte.[21] As the female age controls oocyte quality, it has to be considered in studies related to SDF and its influence on clinical outcomes in IVF or/and ICSI cycles.[9] The study is mainly aimed to understand the effect of SDF on the live birth rates in ICSI cycles with own and donor oocytes. Secondary outcome measure is the role of female age in regulating the effect of SDF on the live birth rates in ICSI cycles with own and donor oocytes.

Methods

Study population

A prospective study from 356 patients undergoing their first ICSI cycles and day 5 fresh embryo transfer exclusively with either own (n = 198) or donor (n = 158) oocytes between August 2017 and December 2019 at our tertiary care center attached to the reproductive medicine unit in medical college were included. Institutional Ethics Committee (IEC) approved this study (IEC NO: SAIMS/IEC/2017/02/03). Written consent was taken from all the couples and all the study participants were treated in accordance to Helsinki Declaration (2013). Patients with uterine factor infertility, male patients with surgically retrieved sperms and severe oligozoospermia (count <1 M/ml), and patients with life-threatening diseases, day 2/3 fresh embryo transfers, previous standard IVF cycles, ICSI with vitrified/warmed oocytes, preimplantation genetic testing, frozen sperm were excluded from this study [Figure 1].

Oocyte donation was anonymous and donors were between the ages of 21 and 35 years (mean age 27.82 ± 2.44 years). The donor's recruitment, confidentiality and screening were done according to the Indian Council for Medical Research (ICMR) guidelines (updated on 10 December, 2018).[22] All the patients in both the own and donor oocyte groups were categorised into two groups based on SDF rates. I. Low-SDF (SDF ≤30%) group and II. High-SDF (SDF >30%) group.[8,23-26] Clinical, as well as embryological outcomes, were correlated between these two groups. Sample size calculation done using G * Power 3.1.9.7 (Franz Faul, universitat kiel) indicated that 138 cycles would be adequate to demonstrate a 20% proportion difference with 80% power and 5% significance level considering the miscarriage rate as the primary outcome.

Semen analysis and processing

Patients collected semen samples in sterile, nontoxic containers by masturbation after sexual abstinence of 2–3 days. After 30 min of liquefaction, semen samples were evaluated for count, motility and morphology according to WHO 2010 criteria.[27] Semen samples were prepared using the double-layer density gradient (V-Grad 80%–40%, Vitromed, Germany). Discontinuous gradient centrifugation. SDF was evaluated on post-wash samples with acridine orange test (AOT).

Acridine orange test

The AOT is an established method for assessing the DNA integrity of the sperm of infertile men.[28-30] The

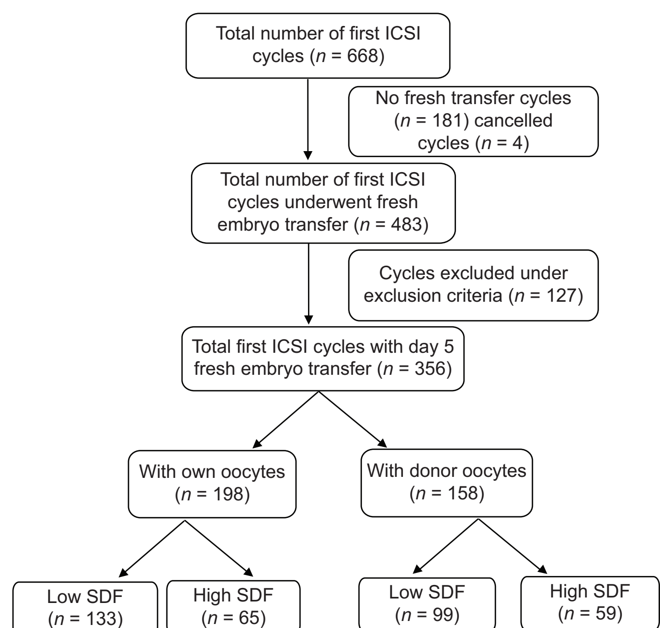

Figure 1: Flow chart for inclusion of patients

SDF was assessed with the AOT method according to Tejada *et al*.,[28] Green fluorescence represents normal intact sperm, whereas red indicates fragmented and denatured sperm.[28,31] At least 200 sperms were assessed in each slide of two replicates to calculate the average SDF. Slides were fixed on the very same day of semen processing and SDF was evaluated on the next day using acridine orange staining. One highly skilled and trained andrologist evaluated all the slides for consistency and to prevent interpersonal variability. Each stained slide was observed right away after staining to reduce the variation of fluorescence intensity. Clinical assessments of SDF need to be performed on the total motile fraction of sperm rather than raw ejaculate sperm by AOT, as the raw semen carry a huge number of degenerated and dead sperm with damaged DNA.[32]

Assisted reproductive technology procedure

The patients and donors had controlled ovarian stimulation with gonadotrophin-releasing hormone (GnRH) agonists or GnRH antagonist protocols described elsewhere.[13] Only patients with optimum endometrium (>7 mm) underwent fresh embryo transfer after oocyte retrieval micronised progesterone was administered daily vaginally (Crinone 8% gel, Merck.) and intramuscularly (Hald 100 mg, Intas) on alternate days till the pregnancy test was confirmed negative or continued during the first trimester if the pregnancy test was positive.

In recipient patients of donor oocyte cycles, oral estradiol valerate (Evadiol, Intas) was used in a step-by-step increasing dose pattern with a starting dose of 2 mg/day and a maximum dose of 6 mg/day for the preparation of endometrium. Patients with optimum endometrial lining and thickness (>7 mm) underwent embryo transfer otherwise transfer was cancelled. Micronised progesterone (Crinone 8% gel, Merck) was administered daily vaginally and intramuscularly (Hald 100 mg, Intas) on alternate days from the day of donor oocyte pickup and continued till the pregnancy test was confirmed negative or continued for another 3 months if the pregnancy test was positive.

The ICSI procedure was performed according to Palermo *et al*.[33] The obtained embryos were cultured till day 5 post-ICSI at 37°C with 6% CO_2, 5% O_2 and the rest N_2 for embryo transfer. Day 3 embryos were graded as A, B and C based on blastomere number, fragmentation percentage, and multinucleation.[34] Grade A: Good embryo with stage-specific 6–8 blastomeres, <10% fragmentation, and no multinucleation grade B: Fair embryo with stage-specific 6–8 blastomeres, 10%–25% fragmentation and no multinucleation and grade C: Poor embryo with non-stage specific blastomeres, severe fragmentation (>25%) and presence of multinucleation. Day 5 blastocysts were graded according to Gardner and Schoolcraft.[35] Expansion of the blastocysts graded as 3, 4, 5 and 6, which were corresponding to full, expanded, hatching and hatched blastocyst. Both trophectoderm and inner cell mass were graded as A, B and C where A represents intact good number of cells, B represents loosely grouped cells, and C represents scarce cells.[35] Blastocysts with grade ≥3AA were considered good quality.

On day 5, one or two embryos were transferred with the help of a soft catheter (Cook, Australia). Serum β human chorionic gonadotropin was observed after 14 days of the transfer to confirm the pregnancy test positive. An intrauterine sac with the presence of a foetal heartbeat was considered a clinical pregnancy. The implantation rate was calculated as the proportion of gestational sacs with cardiac activity determined by ultrasound divided by the total number of embryos transferred. Miscarriage was defined as a pregnancy loss after an intrauterine pregnancy had been detected by ultrasound before 20 weeks of gestation. The live birth rate was calculated as the presence of a live birth (either single or multiple live births) after a fresh embryo transfer cycle.

Statistical analysis of data

Categorical variables like clinical outcomes between groups were shown as proportions and scrutinised using the Chi-square test. Characteristics of patients between groups were shown as continuous variables and scrutinised using the independent-test. The receiver operating characteristic (ROC) curve was developed to correlate the female age with the live birth rate in own and donor oocyte ICSI cycle groups. Statistical significance was set at $P < .05$. Statistical analysis was executed in the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, USA) for windows version 28.0.

Results

The causes of infertility in patients with own-oocyte ICSI cycles were unexplained in 63, male factor in 28, ovarian factor in 9, tubal factor in 52, mixed in 25, polycystic ovary syndrome in 21. In donor oocyte ICSI cycles, poor ovarian reserve (POR) in 93, POR with male factor in 32, POR with tubal factor in 23 and POR with mixed in 10 patients.

Characteristics of patients between low- and high-sperm DNA fragmentation groups in own and donor oocyte cycles

Sperm parameters were similar between the low- and high-SDF groups in both own and donor oocyte ICSI cycle groups except for the SDF rates (P = 0.000) [Table 1]. Patient characteristics such as female age, male age, number of oocytes retrieved

and number of mature MII oocytes were also similar in low- and high-SDF groups in both own and donor oocytes ICSI cycle groups [Table 1].

Comparison of embryological and clinical outcomes between low- and high-sperm DNA fragmentation groups with own-oocyte intracytoplasmic sperm injection cycles

Out of 198 patients in own-oocyte ICSI cycles, 133 were in the low-SDF and 65 were in the high-SDF group. A striking decrease in the live birth rate ($P = 0.023$) and increase in the miscarriage rate ($P = 0.013$) was seen in the high-SDF group compared to the low SDF group. Other clinical and embryological outcomes were similar in both groups [Table 2].

Comparison of embryological and clinical outcomes between low- and high-sperm DNA fragmentation groups with donor oocyte intracytoplasmic sperm injection cycles

Out of 158 patients in donor-oocyte ICSI cycles, 99 were in the low-SDF and 59 were in the high-SDF group. When the clinical outcomes were compared between the low- and high-SDF groups, there was no significant difference between the groups. Among the laboratory outcomes, except for the good quality blastocyst rate ($P = 0.027$), all were similar between the groups [Table 3].

In patients with own-oocyte ICSI cycle, female age was an independent predictor of the live birth rate, area under the curve (AUC) was 0.628 (95% confidence interval [CI] = 0.551–0.704; $P = 0.003$) [Figure 2a]. The female age cut-off value for achieving a live birth was 30.5 years, the sensitivity was 70.3% and the specificity was 54.0% [Figure 2a]. In the donor-oocyte ICSI cycle patients, female age was not a predictor of the live birth rate, AUC was 0.532 (95% CI = 0.442–0.622; $P = 0.493$). The cut-off values of female age were not able to be calculated [Figure 2b].

Comparison of embryological and clinical outcomes between low- and high-sperm DNA fragmentation groups in the own oocyte intracytoplasmic sperm injection cycles stratified based on the female age

Based on the female age cut-off value, the own-oocyte ICSI cycle patients were stratified further into two groups I. Female age ≤30 years ($n = 105$), II. Female

Table 1: Characteristics of patients between low and high sperm deoxyribonucleic acid fragmentation groups in own and donor oocyte cycles

Characteristics	Own oocyte ICSI cycles		*P*	Donor oocyte ICSI cycles		*P*
	Low SDF	High SDF		Low SDF	High SDF	
Number of patients (*n*)	133	65		99	59	
SDF rate	14.64±8.76	52.13±15.26	<0.001[a]	14.41±8.56	53.22±17.71	<0.001[a]
Sperm count (×10^6/mL)	34.75±17.66	33.98±18.65	0.778	31.40±16.90	30.13±15.08	0.635
Sperm motility (%)	54.01±16.21	53.10±14.39	0.702	53.69±17.35	53.86±17.48	0.953
Sperm morphology (%)	4.42±1.35	4.49±1.41	0.732	4.42±1.17	4.40±1.34	0.932
Female age (years)	30.63±4.25	30.29±4.46	0.605	35.69±5.02	35.84±5.05	0.856
Male age (years)	34.92±5.17	34.52±4.62	0.596	39.47±5.82	40.35±5.59	0.352
Number of oocytes retrieved	13.21±5.17	12.27±4.34	0.211	14.80±4.92	14.55±4.67	0.755
Number of MII oocytes	10.90±5.17	9.70±3.96	0.103	11.93±4.41	12.01±4.21	0.914

[a]$P<0.001$, All the values are represented as mean±standard deviation if not otherwise specified. ICSI: Intracytoplasmic sperm injection, DNA: Deoxyribonucleic acid, SDF: Sperm DNA fragmentation, MII: Metaphase II oocytes

Table 2: Comparison of embryological and clinical outcomes between low and high sperm deoxyribonucleic acid fragmentation groups in own oocyte intracytoplasmic sperm injection cycles

Characteristics	Low-SDF group	High-SDF group	*P*
Number of transfers (*n*)	133	65	
Fertilization rate	84.67±16.93	83.38±15.55	0.606
Cleavage rate	81.94±17.78	79.65±19.30	0.409
Good quality embryos at day 3 rate	40.24±23.86	37.54±25.68	0.466
Blastocyst rate	42.69±19.39	44.31±21.74	0.595
Good quality blastocyst rate	20.36±13.62	20.17±17.83	0.936
Clinical pregnancy rate, *n* (%)	65/133 (48.87)	26/65 (40.0)	0.239
Live birth rate, *n* (%)	57/133 (42.85)	17/65 (26.15)	0.023[a]
Miscarriage rate, *n* (%)	8/65 (12.30)	9/26 (34.61)	0.013[a]
Implantation rate	28.94±32.68	23.84±32.00	0.300

[a]$P<0.05$, All the values are represented as mean±SD if not otherwise specified. SD: Standard deviation, DNA: Deoxyribonucleic acid, SDF: Sperm DNA fragmentation

age >30 years (n = 93). In the female age ≤30 years, 69 patients were in low-SDF group and 36 patients were in the high-SDF group. There was no significant difference in the live birth rates between the low- and high-SDF groups [Table 4]. In the female age >30 years, 64 patients were in the low-SDF group and 29 patients were in the high-SDF group. There was a significant decrease in the live birth rate in the high-SDF group compared to the low-SDF group [P = 0.040, Table 4]. Other clinical and embryological outcomes were similar in the low- and high-SDF groups in both the female age groups.

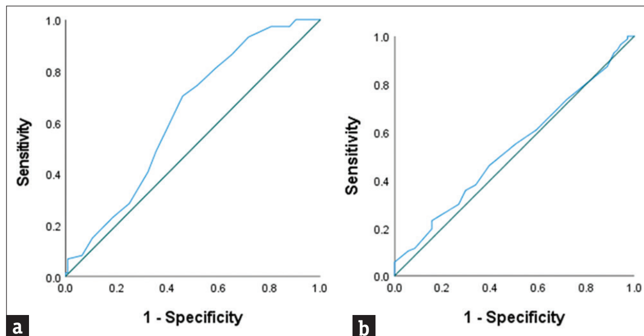

Figure 2: Receiver operating characteristic curve for female age as predictor of the live birth rate in own and donor oocyte intracytoplasmic sperm injection cycles. (a) Female age was correlated to the live birth rate in own-oocyte intracytoplasmic sperm injection cycles. The area under the curve was 0.628 (0.551–0.704) (P = 0.003). The cut-off value of female age for achieving a live birth was 30.5 years; the sensitivity was 70.3% and the specificity was 54.0%. (b) Female age was not correlated to the live birth rate in donor-oocyte intracytoplasmic sperm injection cycles. The area under the curve was 0.532 (0.442–0.622) (P = 0.493)

Discussion

In this study, we focussed on the effect of SDF on the live birth rate and miscarriage rate. There was a 1.5-fold striking decline in the live birth rate and a 2.5-fold rise in the miscarriage rate in the high SDF group compared to the low-SDF group in own-oocyte ICSI cycles [Table 2]. However, in the donor-oocyte ICSI cycles, no significant correlation of SDF with the clinical outcomes was observed. Even in the two high-SDF groups of own and donor oocytes, there was striking difference in the live birth rates. This conveys that oocyte quality has a vital role in regulating the effect of SDF on clinical outcomes.

Table 3: Comparison of embryological and clinical outcomes between low and high sperm deoxyribonucleic acid fragmentation groups in donor oocyte intracytoplasmic sperm injection cycles

Characteristics	Low-SDF group	High-SDF group	P
Number of transfers (n)	99	59	
Fertilisation rate	86.18±14.82	83.55±13.87	0.270
Cleavage rate	82.71±16.52	80.45±17.02	0.411
Good quality embryos at day 3 rate	47.95±23.78	40.95±21.19	0.064
Blastocyst rate	51.51±18.22	46.68±19.17	0.116
Good quality blastocyst rate	29.46±16.73	23.79±12.91	0.027[a]
Clinical pregnancy rate, n (%)	68/99 (68.68)	44/59 (74.57)	0.430
Live birth rate, n (%)	53/99 (53.53)	34/59 (57.62)	0.616
Miscarriage rate, n (%)	15/68 (22.05)	10/44 (22.72)	0.933
Implantation rate	47.47±38.04	55.93±39.48	0.185

[a]$P<0.05$, All the values are represented as mean±SD if not otherwise specified. SD: Standard deviation, DNA: Deoxyribonucleic acid, SDF: Sperm DNA fragmentation

Table 4: Comparison of embryological and clinical outcomes between low and high sperm deoxyribonucleic acid fragmentation groups in own oocyte intracytoplasmic sperm injection cycles stratified according to female age

Characteristics	Female age ≤30 years (n=105)		P	Female age >30 years (n=93)		P
	Low SDF	High SDF		Low SDF	High SDF	
Number of transfers (n)	69	36		64	29	
Fertilisation rate	86.81±13.18	81.58±16.56	0.081	82.36±20.07	85.62±1417	0.433
Cleavage rate	84.21±14.19	78.35±22.09	0.102	79.50±20.81	83.75±14.50	0.323
Good quality embryos at day 3 rate	43.25±16.22	42.65±14.37	0.852	40.60±15.22	41.24±15.43	0.852
Blastocyst rate	44.07±20.16	44.67±20.50	0.886	41.19±18.56	43.86±23.56	0.557
Good quality blastocyst rate	21.42±13.11	20.32±14.67	0.697	19.21±14.15	19.98±21.40	0.837
Clinical pregnancy rate, n (%)	37/69 (53.62)	17/36 (47.22)	0.533	28/64 (43.75)	9/29 (31.03)	0.246
Live birth rate, n (%)	35/69 (50.72)	13/36 (36.11)	0.154	22/64 (34.37)	4/29 (13.79)	0.040[a]
Miscarriage rate, n (%)	2/69 (2.89)	4/36 (11.11)	0.085	6/64 (9.37)	5/29 (17.24)	0.277
Implantation rate	31.88±33.17	29.16±34.58	0.695	25.78±32.11	17.24±27.63	0.219

[a]$P<0.05$, All the values are represented as mean±SD if not otherwise specified. SD: Standard deviation, DNA: Deoxyribonucleic acid, SDF: Sperm DNA fragmentation

Few studies have evaluated the effect of SDF on clinical outcomes like pregnancy and miscarriage in own and donor oocyte cycles.[13,17] One study observed a negative effect of SDF on pregnancy rates in own-oocyte cycles and no effect in the cycles of donor-oocytes whereas, the other study not observe any effect of SDF on clinical pregnancy, miscarriage, and implantation rates in both own and donor oocyte cycles. The effect of SDF on pregnancy in cycles of ICSI is due to the late paternal effect.[16] The late paternal effect leads to decreased implantation or early embryonic loss after implantation affecting live birth rates. Various meta-analyses have confirmed the positive correlation of SDF with the miscarriage rate after natural and assisted reproductive technology (ART) conceptions.[5,7,12] Hence, the prime parameters for assessing the influence of SDF on reproductive outcomes are live birth and miscarriage rates.

Female age plays a major role in determining oocyte quality.[36] According to a recent study, SDF did not affect the outcomes of pregnancy when the female age was ≤30 years. Whereas in females with age >30 years, high-SDF negatively affected the pregnancy outcomes.[9] So in this study, the ROC curve was developed to predict the role of female age on the live birth rate in own-oocyte ICSI cycles. We obtained a cut-off age of 30.5 years for achieving live birth. Whereas, the ROC curve results in the donor-oocyte ICSI cycles showed that neither the female age nor the donor age (details not mentioned) can predict the live birth rates. The own-oocyte ICSI cycle patients were further stratified based on the female age cut-off value. The live birth rates were similar in the low- and high-SDF groups in the female age ≤30 years group and as expected there was a 2.5 fold decrease in the live birth rate in the female age >30 years group.

Female age affects the genes related to "DNA repair" and "response to DNA damage" and they are upregulated in the oocytes of older females. The upregulation may be a compensatory mechanism to tolerate the increased DNA damage and assist the repair role in older age.[37] In older female oocytes, the capacity to repair the damaged DNA of sperm may decrease with increased age. Another study reported that oocytes of younger females (<35 years) can repair up to 40% of sperm DNA damage, whereas the older female's oocytes are not capable of repair efficiently.[38]

A recent study reported that the delay in the human embryo morphokinetics in young and healthy donor-oocyte ICSI cycles was related to the high-SDF. This delay produced noticeable slowdown in progression to the two-cell stage which reinforces the recognition of SDF at early checkpoints, particularly at the S phase.[39] SDF does not alter the blastocyst arrival rate, which specifies that the slow embryos at the initial stage catch up later and continue the development.[39] In this study, the blastocyst rate was similar in both the low- and high-SDF groups in own and donor oocyte cycles. Whereas, the good quality blastocyst rate was remarkably higher in the low-SDF group compared to the high-SDF group in the donor oocyte ICSI cycles. This was not observed in the own-oocyte ICSI cycles group possibly due to the lesser number of overall available blastocysts compared to the donor-oocytes group.

ICSI cycles were suggested to have higher take-home baby rates in high-SDF couples compared to IVF cycles.[40] A recent meta-analysis by Osman also suggested that in ICSI cycles, the negative effect of SDF on live birth rates was not observed in female factor analysed studies.[7] When female age was >30 years, the SDF affects the clinical outcomes (pregnancy and miscarriage) of couples with IVF but not with ICSI cycles.[9] Whether ICSI is favourable in high-SDF cases is still questionable as other studies reported higher miscarriage rates with ICSI cycles.[5,12]

In this study, all the couples underwent ICSI cycles irrespective of SDF rate. In most of the studies, SDF was evaluated before ART cycles and was allotted to IVF and ICSI cycles based on SDF values or samples were frozen and/or evaluated at the time of necessity.[9,10,18,41-43] In this study, SDF was evaluated on the actual sperm used for ICSI cycles and clinically correlated without any bias to improve the outcome.

SDF can be measured by two types of assays: those that can directly measure the extent of DNA fragmentation with the use of probes and dyes and those that measure the susceptibility of DNA to denaturation, which is higher in fragmented DNA.[8] The AOT belongs to the second type of assay and the higher frequency of men with raised SDF in this study group probably reflects the sensitivity of the AOT method. The inverse effect of SDF by the AOT method on pregnancy and implantation rates was perceived in the group with high-SDF (>30%) in ICSI cycles.[26] The SDF assessed by AOT has clinical significance in patients with repeated early pregnancy loss.[44] The AOT method is simple, inexpensive and convenient to do routinely in-house. The principle of AOT is similar to sperm chromatin structure assay (SCSA) except for the number of sperms counted. We have been doing the AOT method for assessing SDF since 2012 for various research projects.[45] Even though AOT is not robust as SCSA, the cells can be differentiated easily and the SDF rate can be evaluated technically. The controversial aspect of the AOT method

being the threshold values for the test at 30%–50% for clinical correlations.[26,30,46] In this study at a threshold value of 30%, the high-SDF is inversely correlated with the live birth rate and positively correlated with the miscarriage rate in own-oocyte ICSI cycles.

Despite the valuable results obtained in the study, we wish to highlight the limitations of the study. The smaller sample size due to the prospective nature of the study and for a 15% proportion difference in the live birth rate, the sample size would increase to 178 samples, which we could not achieve in the donor oocyte group. The AOT method used may not be robust like the golden standard SCSA method, but as already mentioned above the AOT method is comparable to the SCSA method.

Conclusion

High-SDF has a negative influence on the live birth rate and a positive influence on the miscarriage rate in patients of own-oocyte ICSI cycles. The negative influence of SDF on clinical outcomes was not observed in patients of the donor-oocyte ICSI cycles and in young female patients (female age ≤30 years) with own-oocyte ICSI cycles. Our findings suggest that SDF testing before ART cycles is especially useful in counselling the couples of advanced female age and high-SDF seeking ICSI with own-oocytes.

Data availability statement

The data used in the study is available with the corresponding author and the authors are willing to share the data upon reasonable request.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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