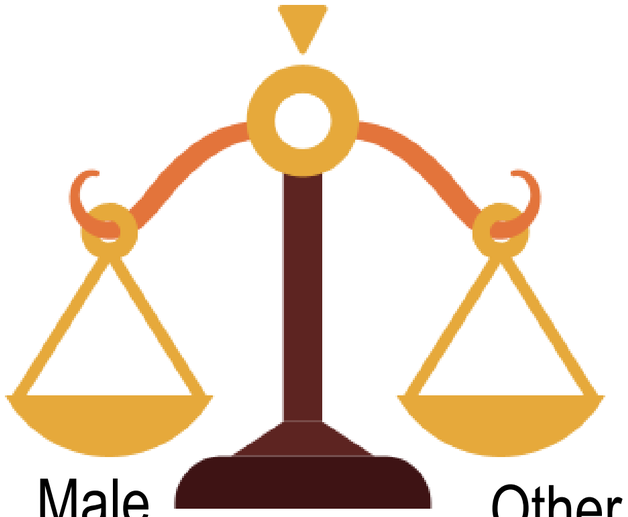
# THE IMPACT OF SPERM DNA FRAGMENTATION ON ICSI OUTCOMES DEPENDS ON OOCYTE QUALITY

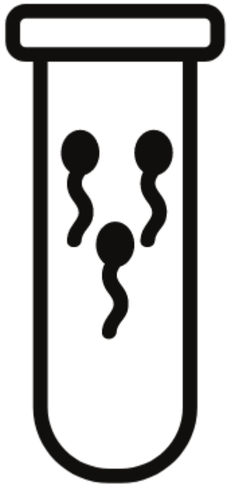
Daniela Paes de Almeida Ferreira Braga, Amanda Setti, Patrícia Guilherme, Rodrigo Rosa Provenza, Assumpto Iaconelli Jr., Edson Borges Jr.

# INTRODUCTION



Male factor

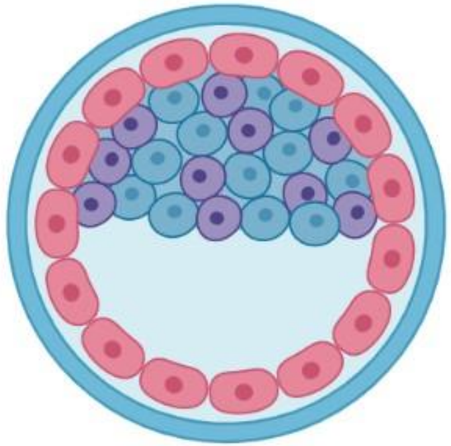
Other



Risk of transmission or induction of genetic and epigenetic conditions cannot be ignored

Parenthood may be achieved by assisted repro

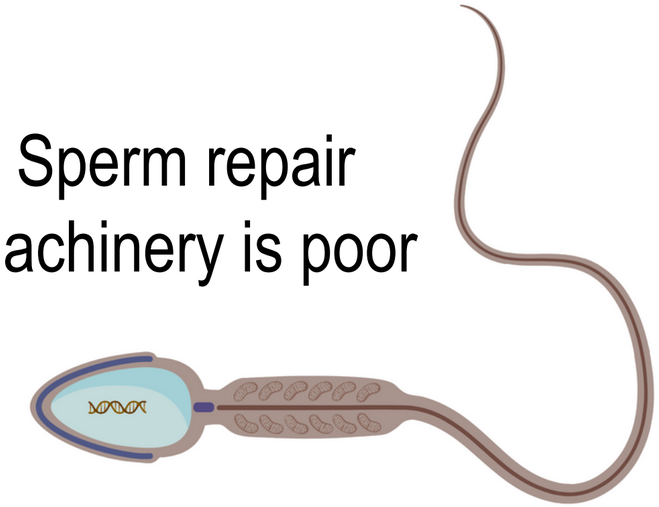
Unknown pathogenesis



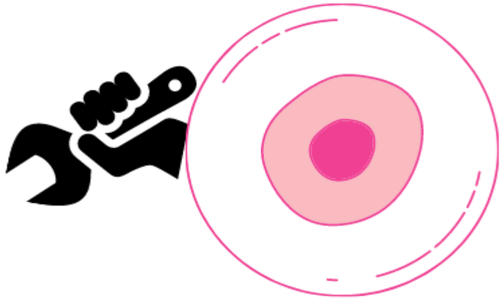
Sperm DNA damage, which is not amended by ICSI, compromises the embryo development

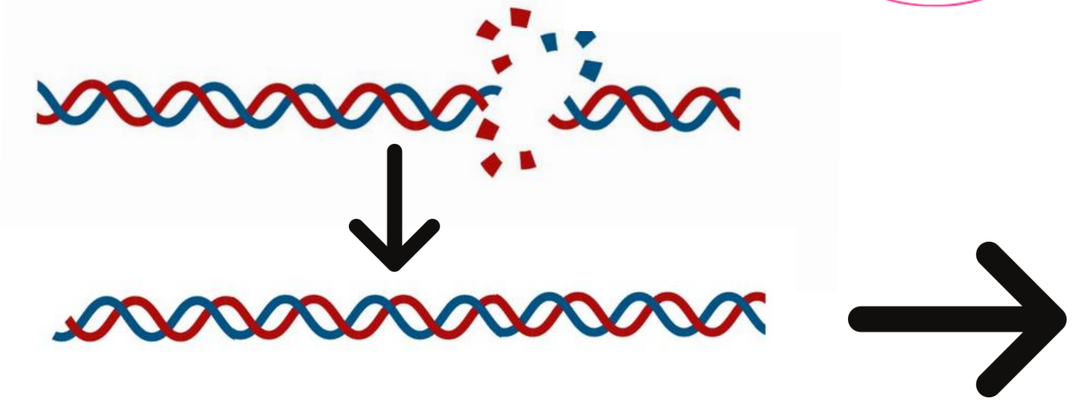
# INTRODUCTION

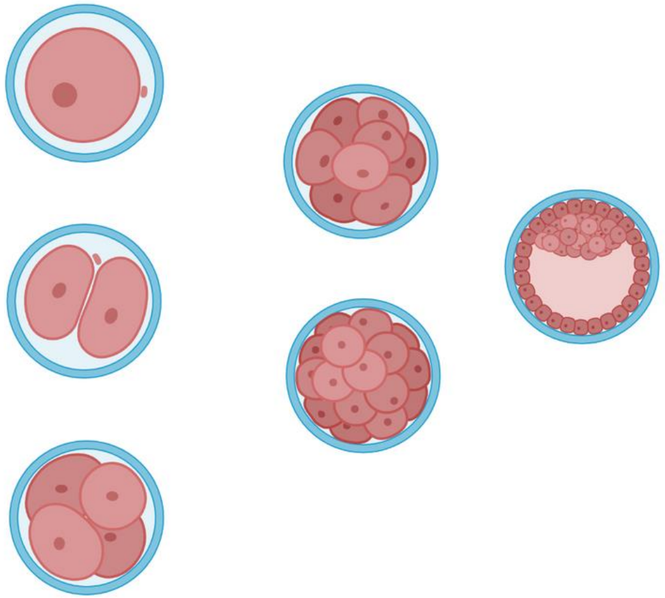
Sperm repair machinery is poor



The oocyte is responsible for repairing maternal and paternal genomes during embryo

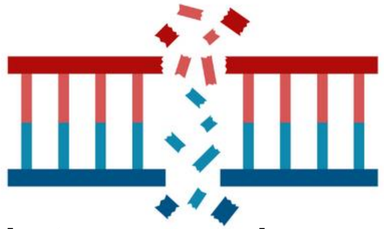






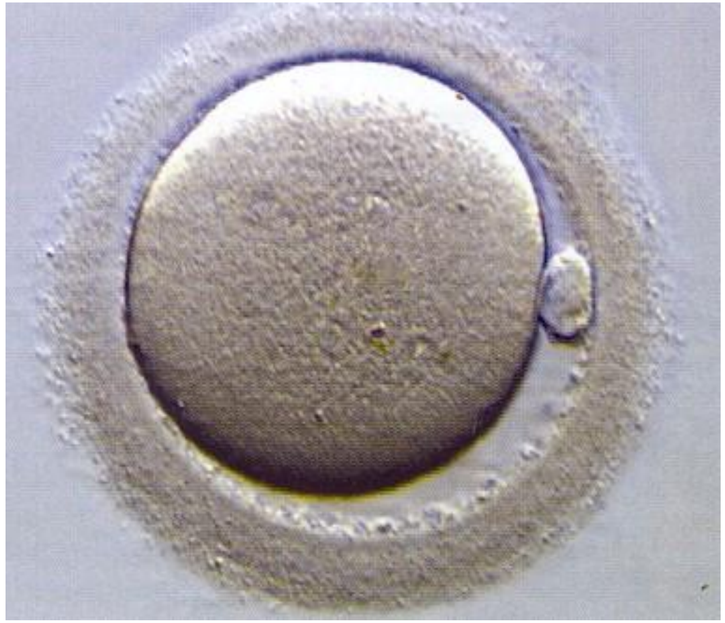
Sperm with DNA damage can fertilize oocytes and can still result in embryo development, due to the DNA repair ability of oocytes

# INTRODUCTION

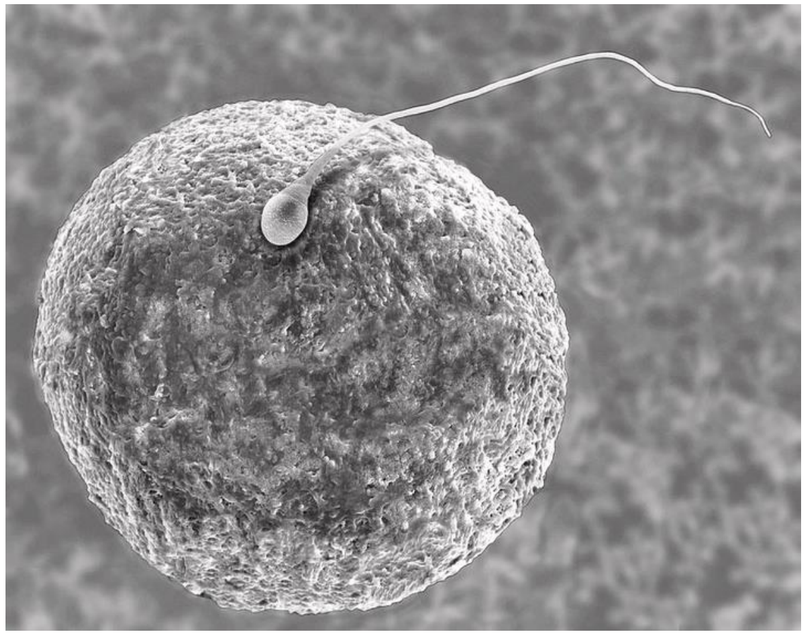


Nature or degree of DNA damage

Defects in the oocyte repair machinery



Oocyte quality can condition the negative impacts of SDF on pregnancy



Photograph by Dennis Kunkel Microscopy/scienc

# INTRODUCTION

ARTICLE IN PRESS

ORIGINAL ARTICLE: ASSISTED REPRODUCTION

## Oocyte ability to repair sperm DNA fragmentation: the impact of maternal age on intracytoplasmic sperm injection outcomes

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Older oocytes, when injected with sperm derived from samples with high SDF index, develop into embryos of poor quality

# INTRODUCTION


Considering the vital role played by the oocyte in the developmental process

## Hypothesis

Oocyte quality, as indicated by oocyte morphology, may influence the machinery responsible for DNA repair.

# OBJECTIVE

The goal of the present study was to investigate whether the impact of SDF on ICSI outcomes depends on the presence of oocyte dimorphisms

# MATERIAL AND METHODS


525 ICSI cycles

2,942 zygotes

<30% SDF n=1,468

≥30% SDF n=486

Presence of oocyte dimorphisms

ICSI outcomes

Generalized linear models Followed by Bonferroni

# MATERIAL AND METHODS

Pituitary blockage with GnRH antagonist and COS with FSH

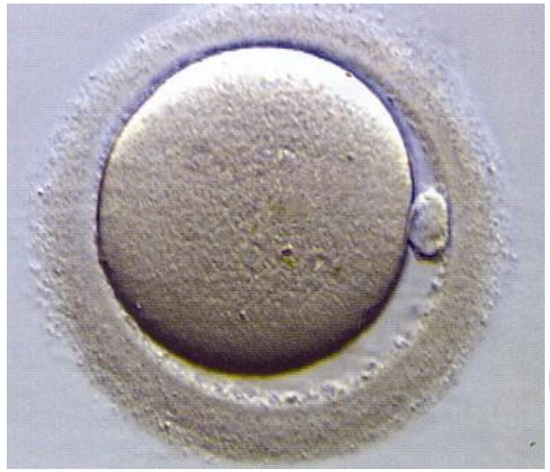
Incubation, denudation and nuclear maturation evaluation

Oocytes evaluated for morphology and ICSI performed according with Palermo et al (1992)

Embryo culture until day 5 (one or two blastocysts transferred)

# MATERIAL AND METHODS

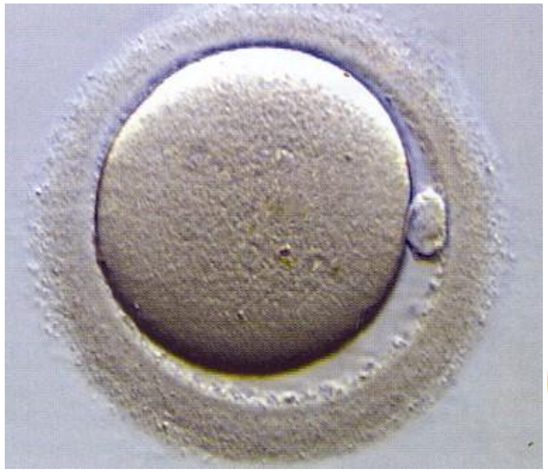
## Intracytoplasmic oocyte dimorphisms



- Centrally located cytoplasmic granulation
- Vacuoles in the ooplasm
- Dark cytoplasm
- Smooth endoplasmic reticulum clusters

# MATERIAL AND METHODS

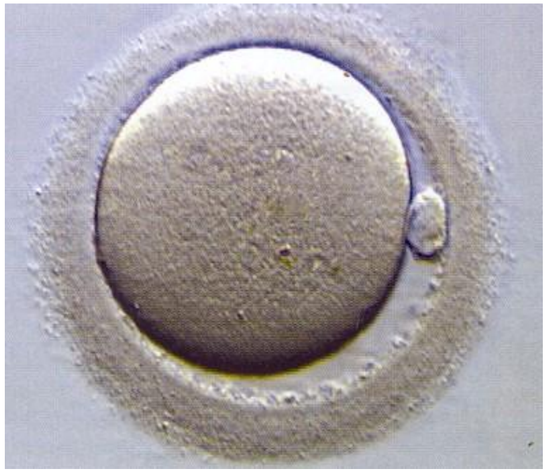
## Extracytoplasmic oocyte dimorphisms



- Large PVS
- Zona pellucida abnormalities
- PVS granularity
- Fragmented polar body

# MATERIAL AND METHODS

## Other oocyte dimorphisms



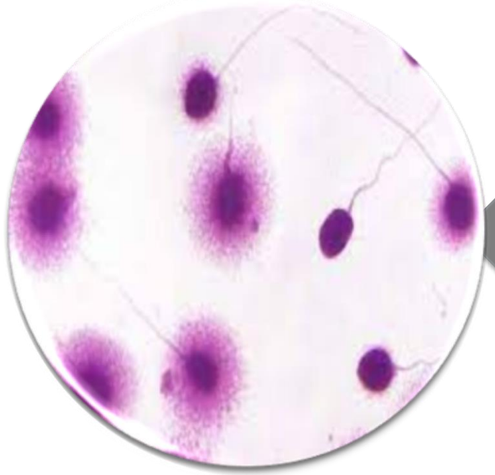
Shape abnormalities

Resistant membranes

Non-resistant membranes

# MATERIAL AND METHODS

Sperm preparation: 2-layered density gradient centrifugation technique



SDF was measured by using a sperm chromatin dispersion (SCD) test

FERTILITY MEDICAL GROUP

# RESULTS

A significant increase in the fertilization rate and high-quality embryo rate was noted for cycles with <30% SDF, when compared with cycles with ≥30% SDF, regardless of the presence of intracytoplasmic oocyte dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | CLCG + (n=313) | | CLCG – (n=2,629) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 90.7 ± 0.4[a] | 84.4 ± 0.8[b] | 92.3 ± 1.2[a] | 85.9 ± 1.49[b] | 0.026 |
| **High-quality D3-embryos (%)** | 41.0 ± 1.1 [a] | 34.0 ± 2.0[b] | 44.0 ± 2.9[a] | 37.0 ± 3.5[b] | 0.035 |
| | DC + (n=44) | | DC – (n=2,898) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 74.6 ± 3.2 [a] | 68.1 ± 3.3[b] | 91.2 ± 0.4[c] | 84.7 ± 0.8[d] | 0.01 |
| **High-quality D3-embryos (%)** | 30.0 ± 7.2 [a] | 24.0 ± 6.4[b] | 42.0 ± 1.1[a] | 35.0 ± 2.0[b] | 0.02 |
| | SERc + (n=110) | | SERc – (n=2,832) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 90.7 ± 0.4[a] | 84.2 ± 2.1[b] | 96.8 ± 2.0[a] | 84.1 ± 82.4[b] | <0.01 |
| **High-quality D3-embryos (%)** | 36.0 ± 4.8[a] | 30.0 ± 4.6[b] | 42.0 ±1.1[c] | 35.0 ± 4.6[a] | 0.013 |
| | Vacuoles in ooplasm + (n=136) | | Vacuoles in ooplasm - (n=2,881) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 89.5 ± 1.8[a] | 82.9 ±1.9[b] | 90.8 ± 0.44[c] | 84.1 ± 0.83[d] | <0.01 |
| **High-quality D3-embryos (%)** | 39.0 ± 4.4 [a] | 32.0 ± 4.3[b] | 41.0 ± 1.1[c] | 35.0 ± 1.9 [d] | 0.014 |

# RESULTS The association of oocyte dimorphisms and a high SDF index resulted in the lowest fertilization rate

| | Oocyte Dimorphisms | | | | |
|---|---|---|---|---|---|
| | CLCG + (n=313) | | CLCG – (n=2,629) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 90.7 ± 0.4[a] | 84.4 ± 0.8[b] | 92.3 ± 1.2[a] | 85.9 ± 1.49[b] | 0.026 |
| **High-quality D3-embryos (%)** | 41.0 ± 1.1 [a] | 34.0 ± 2.0[b] | 44.0 ± 2.9[a] | 37.0 ± 3.5[b] | 0.035 |
| | DC + (n=44) | | DC – (n=2,898) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 74.6 ± 3.2 [a] | 68.1 ± 3.3[b] | 91.2 ± 0.4[c] | 84.7 ± 0.8[d] | 0.01 |
| **High-quality D3-embryos (%)** | 30.0 ± 7.2 [a] | 24.0 ± 6.4[b] | 42.0 ± 1.1[a] | 35.0 ± 2.0[b] | 0.02 |
| | SERc + (n=110) | | SERc – (n=2,832) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 90.7 ± 0.4[a] | 84.2 ± 2.1[b] | 96.8 ± 2.0[a] | 84.1 ± 82.4[b] | <0.01 |
| **High-quality D3-embryos (%)** | 36.0 ± 4.8[a] | 30.0 ± 4.6[b] | 42.0 ±1.1[c] | 35.0 ± 4.6[a] | 0.013 |
| | Vacuoles in ooplasm + (n=136) | | Vacuoles in ooplasm - (n=2,881) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 89.5 ± 1.8[a] | 82.9 ±1.9[b] | 90.8 ± 0.44[c] | 84.1 ± 0.83[d] | <0.01 |
| **High-quality D3-embryos (%)** | 39.0 ± 4.4 [a] | 32.0 ± 4.3[b] | 41.0 ± 1.1[c] | 35.0 ± 1.9 [d] | 0.014 |

# RESULTS

Significantly higher fertilization and high-quality embryo rates were observed for cycles with <30% SDF than for cycles with ≥30% SDF, regardless of the presence of extra-cytoplasmic dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Large PVS + (n=626) | | Large PVS – (n=2,391) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 90.0 ± 4.7[a] | 85.4 ± 10.0[b] | 92.1 ± 8.8[a] | 83.6 ±8.5 [b] | <0.01 |
| **High-quality D3-embryos (%)** | 41.0 ±1.1[a] | 36.0 ± 2.5 [b] | 43.0 ± 2.1[a] | 34.0 ±2.0[b] | 0.011 |
| | Fragmented PB + (n=924) | | Fragmented PB – (n=2,093) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 89.1 ± 7.2[a] | 84.8 ± 8.6[b] | 90,5 ± 5.0[a] | 82.4 ±1.0 [b] | <0.01 |
| **High-quality D3-embryos (%)** | 42.0 ± 1.7[a] | 36.0 ± 2.3[b] | 41.0 ±1.2[a] | 34.0 ± 2.0 [b] | 0.013 |
| | NRM + (n=84) | | NRM – (n=2,793) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 82.8 ± 2.2 [a] | 76.0 ± 2.3[b] | 91.0 ± 0.4[c] | 84.2 ± 0.82[a] | <0.01 |
| **High-quality D3-embryos (%)** | 27.0 ± 4.4 [a] | 22.0 ± 4.4[b] | 42.0 ±1,1[c] | 35.0 ±1.9[d] | 0.011 |

# RESULTS

Significantly higher fertilization and high-quality embryo rates were observed for cycles with <30% SDF than for cycles with ≥30% SDF, regardless of the presence of extracytoplasmic dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | RM + (n=98) | | RM – (n=2,919) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 88.2 ± 2.1[a] | 81.6 ±2.2[b] | 90.8 ± 0.44[a] | 84.2 ± 0.8 [b] | <0.01 |
| **High-quality D3-embryos (%)** | 35.0 ± 5.0 [a] | 29.0 ± 5.2[b] | 41.0 ± 1.0[c] | 35.0 ±2.0[a] | 0.018 |
| | Shape abnormalities + (n=86) | | Shape abnormalities - (n=2,931) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 87.7 ± 2.3 [a] | 81.1 ±2.4[b] | 90.8 ± 0.44[c] | 84.1 ±0.82[a] | <0.01 |
| **High-quality D3-embryos (%)** | 37.0 ± 5.3[a] | 31.0 ± 5.1[b] | 41.0 ± 1.0[c] | 35.0 ± 1.9[a] | 0.013 |
| | ZP abnormalities + (n=236) | | ZP abnormalities - (n=2,781) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 88.4 ± 1.4[a] | 81.8 ± 1.5[b] | 90.9 ± 0.44[a] | 84.3 ± 0.83[b] | <0.01 |
| **High-quality D3-embryos (%)** | 40.0 ± 3.4[a] | 33.0 ± 3.4[b] | 41.0 ± 1.1[a] | 35.0 ± 1.9 [b] | 0.015 |

# RESULTS

The association of oocyte dimorphism and a high SDF index resulted in the lowest fertilization and/or high-quality embryo rates

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | **NRM + (n=84)** | | **NRM – (n=2,793)** | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 82.8 ± 2.2 [a] | 76.0 ± 2.3[b] | 91.0 ± 0.4[c] | 84.2 ± 0.82[a] | <0.01 |
| **High-quality D3-embryos (%)** | 27.0 ± 4.4 [a] | 22.0 ± 4.4[b] | 42.0 ±1,1[c] | 35.0 ±1.9[d] | 0.011 |
| | **Shape abnormalities + (n=86)** | | **Shape abnormalities - (n=2,931)** | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 87.7 ± 2.3 [a] | 81.1 ±2.4[b] | 90.8 ± 0.44[c] | 84.1 ±0.82[a] | <0.01 |
| **High-quality D3-embryos (%)** | 37.0 ± 5.3[a] | 31.0 ± 5.1[b] | 41.0 ± 1.0[c] | 35.0 ± 1.9[a] | 0.013 |
| | **RM + (n=98)** | | **RM – (n=2,919)** | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Fertilization (%)** | 88.2 ± 2.1[a] | 81.6 ±2.2[b] | 90.8 ± 0.44[a] | 84.2 ± 0.8 [b] | <0.01 |
| **High-quality D3-embryos (%)** | 35.0 ± 5.0 [a] | 29.0 ± 5.2[b] | 41.0 ± 1.0[c] | 35.0 ±2.0[a] | 0.018 |

# RESULTS

A decrease in implantation and pregnancy rates were noted for cycles with ≥30% SDF, when compared with cycles with <30% SDF, regardless of the presence of intracytoplasmic dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | CLCG + (n=62) | | CLCG – (n=561) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.9 ± 2.9[a] | 8.2 ± 3.4[b] | 20.1 ± 1.0[a] | 7.9 ± 1.6[b] | <0.01 |
| **Pregnancy (%)** | 21.0 ± 3.2[a] | 8.0. ± 1.9 [b] | 20.0 ± 1.1[a] | 7.0 ± 1.2 [b] | <0.01 |
| | DC + (n=8) | | DC – (n=615) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 19.7 ± 5.8[a] | 6.9 ± 6.0[b] | 20.2 ± 9.7[a] | 7.4 ± 1.6[b] | 0.01 |
| **Pregnancy (%)** | 19.7 ± 5.8[a] | 7.4 ± 1.7[b] | 20.2 ± 9.7[a] | 6.9 ± 6.0[b] | <0.01 |
| | SERc + (n=31) | | SERc – (n=592) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 23.4 ± 3.8[a] | 10.5 ± 4.0[b] | 20.0 ± 9.8[a] | 7.2 ± 1.7 [c] | <0.01 |
| **Pregnancy (%)** | 24.0 ± 4.8[a] | 9.0 ± 2.5[b] | 20.0 ± 1.1[a] | 7.0 ± 12.0[b] | 0.013 |
| | Vacuoles in ooplasm + (n=29) | | Vacuoles in ooplasm - (n=594) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.5 ± 9.8[a] | 7.8 ± 1.7[b] | 36.2 ± 4.3[c] | 13.0 ± 4.1[d] | <0.01 |
| **Pregnancy (%)** | 11.1 ± 3.9 [a] | 4.0 ± 1.6 [b] | 21.0 ± 11.1[c] | 8.0 ± 12.0[d] | <0.01 |

# RESULTS The associations of both male and female factors also impacted the clinical results

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | CLCG + (n=62) | | CLCG – (n=561) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.9 ± 2.9[a] | 8.2 ± 3.4[b] | 20.1 ± 1.0[a] | 7.9 ± 1.6[b] | <0.01 |
| **Pregnancy (%)** | 21.0 ± 3.2[a] | 8.0. ± 1.9 [b] | 20.0 ± 1.1[a] | 7.0 ± 1.2 [b] | <0.01 |
| | DC + (n=8) | | DC – (n=615) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 19.7 ± 5.8[a] | 6.9 ± 6.0[b] | 20.2 ± 9.7[a] | 7.4 ± 1.6[b] | 0.01 |
| **Pregnancy (%)** | 19.7 ± 5.8[a] | 7.4 ± 1.7[b] | 20.2 ± 9.7[a] | 6.9 ± 6.0[b] | <0.01 |
| | SERc + (n=31) | | SERc – (n=592) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 23.4 ± 3.8[a] | 10.5 ± 4.0[b] | 20.0 ± 9.8[a] | 7.2 ± 1.7 [c] | <0.01 |
| **Pregnancy (%)** | 24.0 ± 4.8[a] | 9.0 ± 2.5[b] | 20.0 ± 1.1[a] | 7.0 ± 12.0[b] | 0.013 |
| | Vacuoles in ooplasm + (n=29) | | Vacuoles in ooplasm - (n=594) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.5 ± 9.8[a] | 7.8 ± 1.7[b] | 36.2 ± 4.3[c] | 13.0 ± 4.1[d] | <0.01 |
| **Pregnancy (%)** | 11.1 ± 3.9 [a] | 4.0 ± 1.6 [b] | 21.0 ± 11.1[c] | 8.0 ± 12.0[d] | <0.01 |

# RESULTS

The effect of SDF on miscarriage rates was significantly influenced by the presence of CLCG

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | CLCG + (n=62) | | CLCG – (n=561) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 4.0 ± 3.1 [a] | 31.0 ± 8.3 [b] | 3.0 ± 8.8[a,c] | 12.0 ± 1.9[c] | 0.025 |
| | DC + (n=8) | | DC – (n=615) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 11.0 ± 1.9[a] | 28.0 ± 7.5 [b] | 0.0 ± 0.0 [c] | 0.0 ±0.0[c] | <0.01 |
| | SERc + (n=31) | | SERc – (n=592) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 12.0 ± 24.0[a] | 29 ± 19.0[b] | 0.0 ± 0.0[c] | 0.0 ± 0.0[c] | <0.01 |
| | Vacuoles in ooplasm + (n=29) | | Vacuoles in ooplasm - (n=594) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 11.0 ± 1.9 [a] | 29.0 ±7.6 [b] | 0.0 ± 0.0 [c] | 0.0 ± 0.0 [c] | <0.01 |

# RESULTS

Significant decrease in implantation and pregnancy rates for cycles with ≥30% SDF, when compared with cycles with <30% SDF, regardless of the presence of extracytoplasmic dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Large PVS + (n=57) | | Large PVS – (n=566) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 15.8 ± 22.4[a] | 5.9 ± 12.1[b] | 21.2 ± 13.2[c] | 7.9 ± 13.5[d] | <0.01 |
| **Pregnancy (%)** | 16.0 ± 2.1[a] | 6.0 ± 1.2[b] | 21.0 ± 1.2[c] | 8.0 ± 1.3[d] | 0.015 |
| | PVS granularity (n=207) | | PVS granularity (n=416) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.7 ± 1.3[a] | 17.9 ± 1.9[b] | 19.7 ± 1.2[a] | 6.9 ± 1.8[c] | <0.01 |
| **Pregnancy (%)** | 21.0 ± 1.5[a] | 8.0 ± 1.3[b] | 20.0 ± 1.4[a] | 7.0 ± 1.2[c] | <0.01 |
| | Fragmented PB + (n=199) | | Fragmented PB – (n=424) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 17.2 ± 1.6[a] | 4.3 ± 2.1[b] | 21.4 ± 1.1[a] | 8.5 ± 1.7[c] | <0.01 |
| **Pregnancy (%)** | 17.0 ± 1.7 [a] | 6.0 ± 1.1[b] | 22.0 ± 1.3[a] | 8.0 ± 1.1[c] | 0.013 |

# RESULTS

Significant decrease in implantation and pregnancy rates for cycles with ≥30% SDF, when compared with cycles with <30% SDF, regardless of the presence of extracytoplasmic dimorphisms

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | NRM + (n=28) | | NRM – (n=595) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 16.1 ± 5.3[a] | 5.9 ± 4.8[b] | 20.3 ± 9.8[a] | 7.5 ± 1.6[b] | <0.01 |
| **Pregnancy (%)** | 16.1 ± 0.56[a] | 5.9 ± 0.2[b] | 20.3 ± 0.11[a] | 7.4 ± 0.12[b] | <0.01 |
| | RM + (n=24) | | RM – (n=599) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 15.4 ± 4.3[a] | 2.6 ± 4.5[b] | 20.4 ± 9.8[a] | 7.6 ± 1.7[b] | <0.01 |
| **Pregnancy (%)** | 15.0 ± 4.7[a] | 6.0 ± 2.1[b] | 20.0 ± 1.1[a] | 8.0 ± 1.0[b] | 0.018 |
| | Shape abnormalities + (n=30) | | Shape abnormalities - (n=593) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 28.0 ± 4.8[a] | 16.2 ± 5.0[b] | 19.9 ± 8.4[a] | 7.2 ± 1.7[b] | <0.01 |
| **Pregnancy (%)** | 30.0 ± 6.2[a] | 12.0 ± 3.6[b] | 20.0 ± 1.1[a] | 7.0 ± 1.2[b] | 0.013 |
| | ZP abnormalities + (n=62) | | ZP abnormalities - (n=561) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 8.4 ± 0.24[a] | 3.2 ± 0.1[b] | 21.2 ± 0.12[a] | 3.2 ± 0.10[b] | <0.01 |

# RESULTS

The presence of large PVS, NRM, RM, shape abnormalities and ZP abnormalities resulted in decreased rates of implantation and pregnancy for both SDF index groups

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Large PVS + (n=57) | | Large PVS – (n=566) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 15.8 ± 22.4[a] | 5.9 ± 12.1[b] | 21.2 ± 13.2[c] | 7.9 ± 13.5[d] | <0.01 |
| **Pregnancy (%)** | 16.0 ± 2.1[a] | 6.0 ± 1.2[b] | 21.0 ± 1.2[c] | 8.0 ± 1.3[d] | 0.015 |
| | NRM + (n=28) | | NRM – (n=595) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 16.1 ± 5.3[a] | 5.9 ± 4.8[b] | 20.3 ± 9.8[a] | 7.5 ± 1.6[b] | <0.01 |
| **Pregnancy (%)** | 16.1 ± 0.56[a] | 5.9 ± 0.2[b] | 20.3 ± 0.11[a] | 7.4 ± 0.12[b] | <0.01 |
| | RM + (n=24) | | RM – (n=599) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 15.4 ± 4.3[a] | 2.6 ± 4.5[b] | 20.4 ± 9.8[a] | 7.6 ± 1.7[b] | <0.01 |
| **Pregnancy (%)** | 15.0 ± 4.7[a] | 6.0 ± 2.1[b] | 20.0 ± 1.1[a] | 8.0 ± 1.0[b] | 0.018 |

# RESULTS

The presence of large PVS, NRM, RM, shape abnormalities and ZP abnormalities resulted in decreased rates of implantation and pregnancy for both SDF index groups

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Shape abnormalities + (n=30) | | Shape abnormalities - (n=593) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 28.0 ± 4.8[a] | 16.2 ± 5.0[b] | 19.9 ± 8.4[a] | 7.2 ± 1.7[b] | <0.01 |
| **Pregnancy (%)** | 30.0 ± 6.2[a] | 12.0 ± 3.6[b] | 20.0 ± 1.1[a] | 7.0 ± 1.2[b] | 0.013 |
| | ZP abnormalities + (n=62) | | ZP abnormalities - (n=561) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 8.4 ± 0.24[a] | 3.2 ± 0.1[b] | 21.2 ± 0.12[a] | 3.2 ± 0.10[b] | <0.01 |
| **Pregnancy (%)** | 9.0 ± 2.4[a] | 3.0 ± 1.0[b] | 21.0 ± 1.1[a] | 8.0 ± 1.3[b] | 0.015 |

# RESULTS

The association of a higher SDF index with the presence of oocyte dimorphisms impacted the clinical results for oocytes presenting large PVS, PVS granularity and fragmented PB

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Large PVS + (n=57) | | Large PVS – (n=566) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 15.8 ± 22.4[a] | 5.9 ± 12.1[b] | 21.2 ± 13.2[c] | 7.9 ± 13.5[d] | <0.01 |
| **Pregnancy (%)** | 16.0 ± 2.1[a] | 6.0 ± 1.2[b] | 21.0 ± 1.2[c] | 8.0 ± 1.3[d] | 0.015 |
| | PVS granularity (n=207) | | PVS granularity (n=416) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 20.7 ± 1.3[a] | 17.9 ± 1.9[b] | 19.7 ± 1.2[a] | 6.9 ± 1.8[c] | <0.01 |
| **Pregnancy (%)** | 21.0 ± 1.5[a] | 8.0 ± 1.3[b] | 20.0 ± 1.4[a] | 7.0 ± 1.2[c] | <0.01 |
| | Fragmented PB + (n=199) | | Fragmented PB – (n=424) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Implantation (%)** | 17.2 ± 1.6[a] | 4.3 ± 2.1[b] | 21.4 ± 1.1[a] | 8.5 ± 1.7[c] | <0.01 |
| **Pregnancy (%)** | 17.0 ± 1.7 [a] | 6.0 ± 1.1[b] | 22.0 ± 1.3[a] | 8.0 ± 1.1[c] | 0.013 |

# RESULTS

The effect of SDF on miscarriage rates was significantly influenced by the presence of large PVS and NRM

| | **Oocyte Dimorphisms** | | | | |
|---|---|---|---|---|---|
| | Large PVS + (n=57) | | Large PVS – (n=566) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 6.0 ±3.1[a] | 30.0 ±8.1[b] | 17.0 ± 8.7[a,b] | 12.0 ± 2.0[a,b] | 0.581 |
| | NRM + (n=28) | | NRM – (n=595) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 5.8 ± 19.7[a] | 30.0 ± 15.2[b] | 11.0 ± 18.0[a,b] | 22.0 ± 7.4[a,b] | 0.378 |
| | RM + (n=24) | | RM – (n=599) | | |
| **Groups** | <30% SDF | ≥30% SDF | <30% SDF | ≥30% SDF | p |
| **Miscarriage (%)** | 4.6 ± 18.6[a] | 8.0 ± 13.5[b] | 4.6 ± 18.6[a] | 3.0 ± 8.3[b] | 0.378 |

# CONCLUSION

The association of low oocyte quality and high SDF indexes may compromise the clinical outcomes specially the miscarriage rate.

# WIDER IMPLICATIONS OF THE FINDINGS

The findings presented here are particularly important for informing patients about the crucial role of both male and female factors when facing ART cycles.

The negative impacts of a high degree of DNA fragmentation on clinical outcomes can be overcome by using high-quality oocytes.

Our evidence supports the hypothesis that defective oocytes lose their ability to cope with SDF and avoid pregnancy loss due to DNA damage in sperm.

As oocyte defects usually cannot be modified, the in vivo improvement of spermatozoa before ART should be stimulated.

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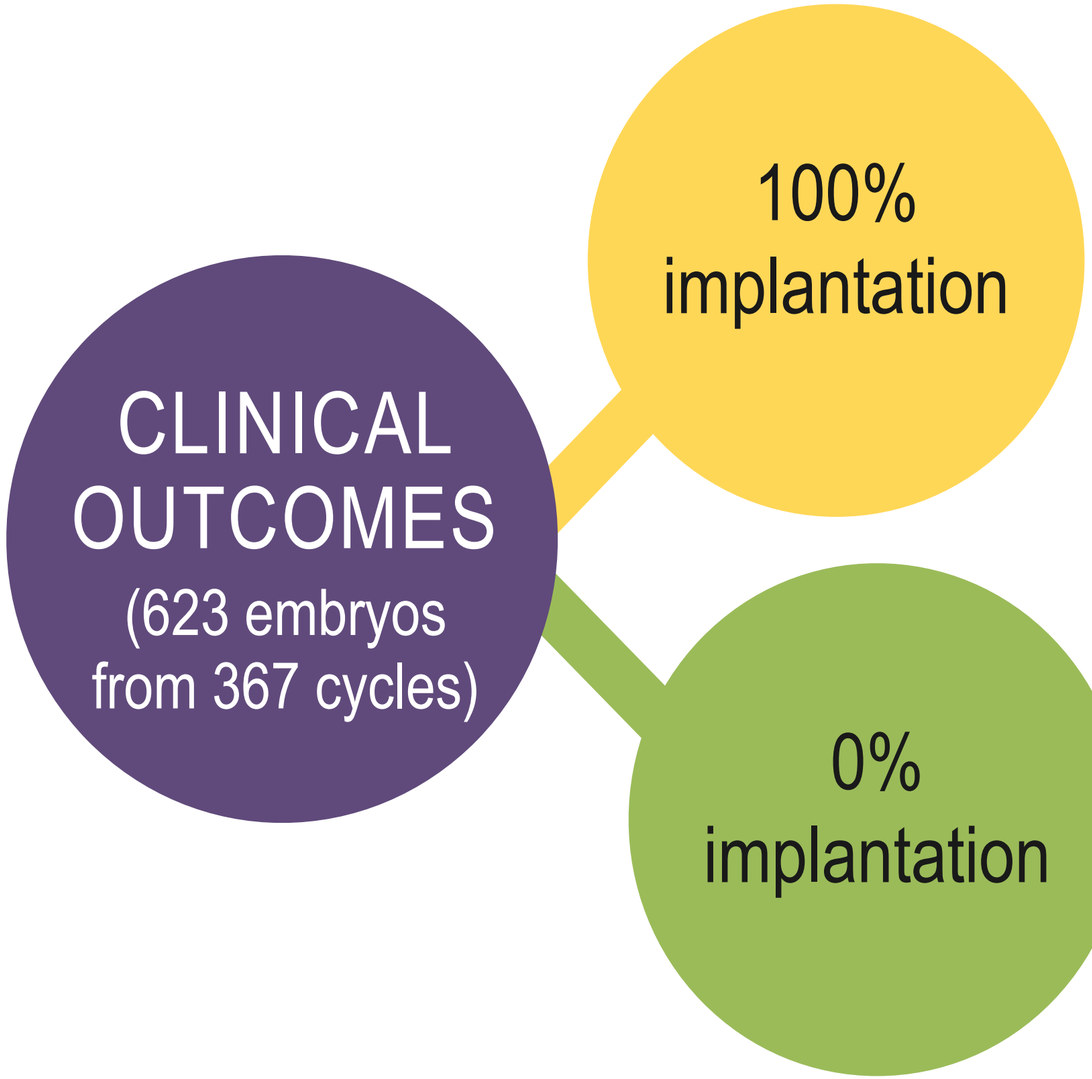
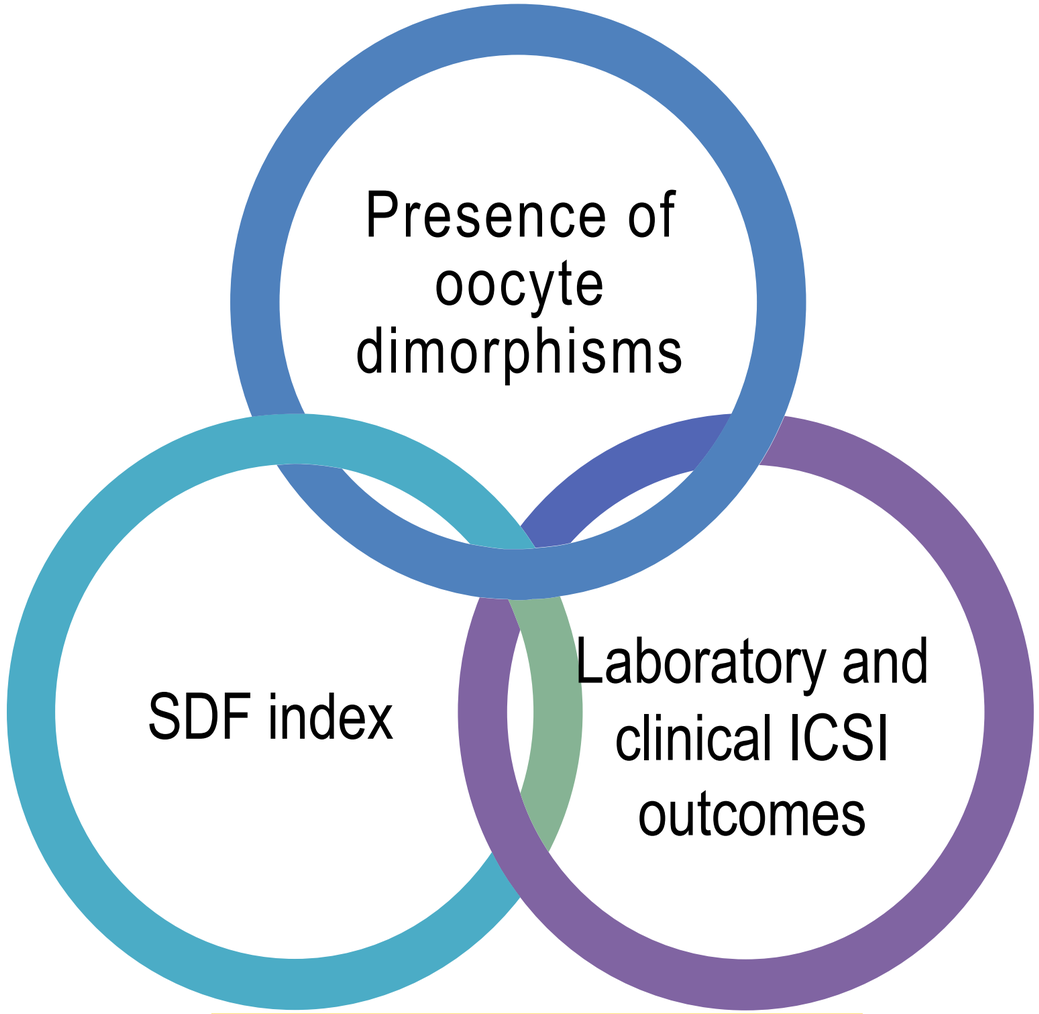
# MATERIAL AND METHODS




Generalized linear models
Followed by Bonferroni