Prediction of Successful ICSI Cycles by Oxidation-Reduction Potential (ORP) and Sperm DNA Fragmentation (SDF) Analysis

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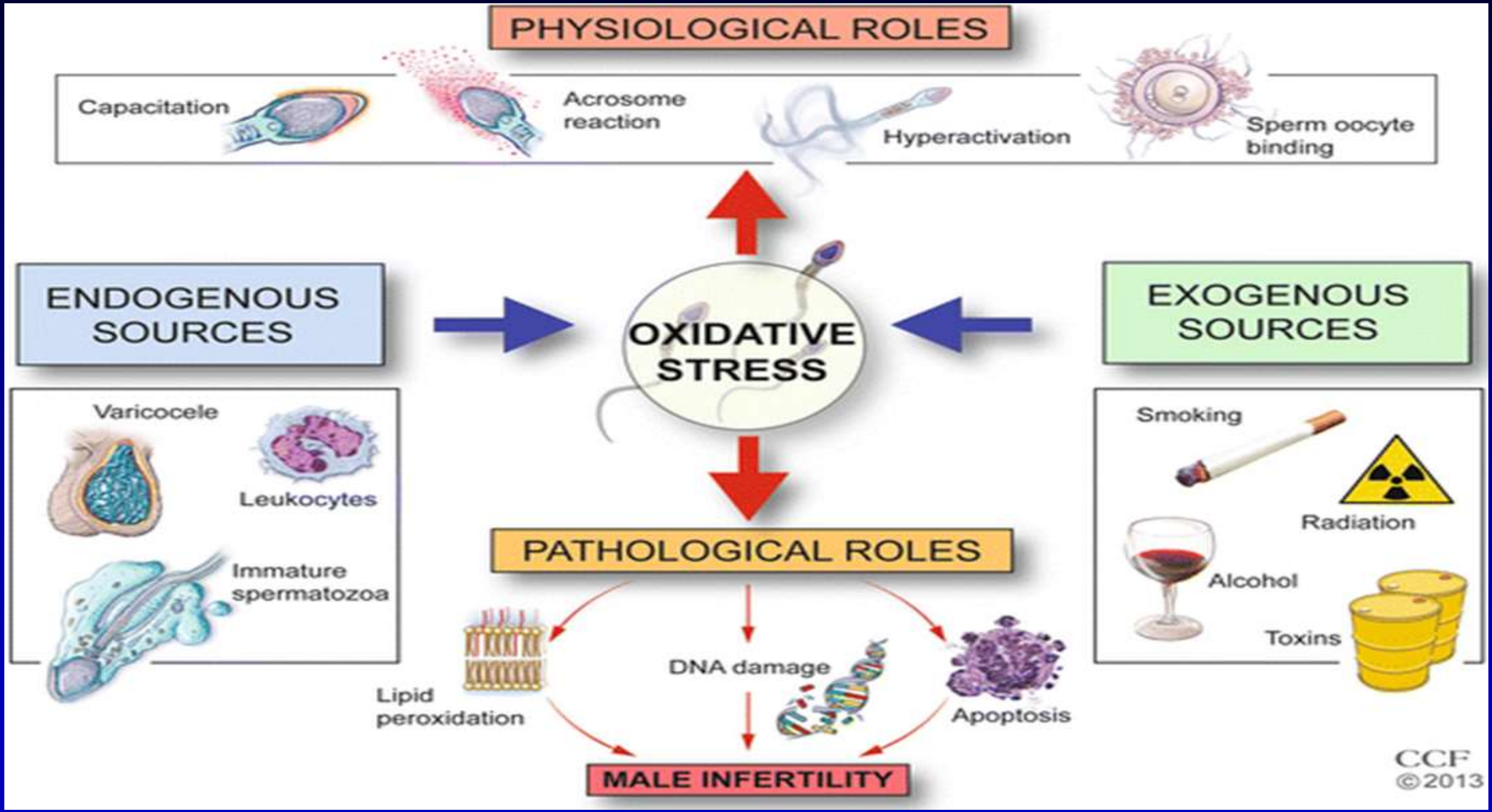
Disclosure

No Conflict of Interest

No financial relationships with any commercial or proprietary entity that produces healthcare-related products.

Sperm DNA Fragmentation and Oxidative Stress



Durairajanayagam, D., Dhillon, A.S., Salasin, R., Kashou, A. and Kothandaraman, N., 2017. Compendium of Oxidative Stress-Related Research from Cleveland Clinic (1993–2016). In Oxidative Stress in Human Reproduction (pp. 151-190). Springer, Cham.

Sperm DNA Fragmentation and Oxidative Stress

ARTICLE IN PRESS

ASRM PAGES

The clinical utility of sperm DNA integrity testing: a guideline

The Practice Committee of the American Society for Reproductive Medicine
American Society for Reproductive Medicine, Birmingham, Alabama

Human Reproduction, Vol.27, No.10 pp. 2908–2917, 2012
Advanced Access publication on July 12, 2012

human reproduction — META-ANALYSIS Andrology

The effect of sperm DNA fragmentation on miscarriage rates: a systematic review and meta-analysis

Lynne Robinson[1,*], Ioannis D. Gallos[1,2], Sarah J. Conner[1,2], Madhurima Rajkhowa[1], David Miller[3], Sheena Lewis[4], Jackson Kirkman-Brown[1,2], and Arri Coomarasamy[1,2]

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ORIGINAL ARTICLE

A systematic review and meta-analysis to determine the effect of sperm DNA damage on *in vitro* fertilization and intracytoplasmic sperm injection outcome

Luke Simon, Armand Zini, Alina Dyachenko, Antonio Ciampi, Douglas T Carrell

PLOS | ONE

COLLECTION REVIEW

Measuring Sperm DNA Fragmentation and Clinical Outcomes of Medically Assisted Reproduction: A Systematic Review and Meta-Analysis

Maartje Cissen[1], Madelon van Wely[2,*], Irma Scholten[2], Steven Mansell[3], Jan Peter de Bruin[1], Ben Willem Mol[4], Didi Braat[5], Sjoerd Repping[2], Geert Hamer[2]

Effect of sperm DNA fragmentation on the clinical outcomes for in vitro fertilization and intracytoplasmic sperm injection in women with different ovarian reserves

Arab Journal of Urology (2018) 16, 21–34

Arab Journal of Urology
(Official Journal of the Arab Association of Urology)

ETIOLOGY
ORIGINAL ARTICLE

Role of sperm DNA fragmentation in male factor infertility: A systematic review

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DIAGNOSIS
ORIGINAL ARTICLE

A systematic review on sperm DNA fragmentation in male factor infertility: Laboratory assessment

Manesh Kumar Panner Selvam, Ashok Agarwal*

American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH, USA

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Guideline

Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios

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Human Reproduction vol.13 no.4 pp.896–900, 1998

Reactive oxygen species: potential cause for DNA fragmentation in human spermatozoa

MODERN TRENDS

Edward E. Wallach, M.D.
Associate Editor

Sperm DNA fragmentation: mechanisms of origin, impact on reproductive outcome, and analysis

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Aims and Objectives

Investigating the clinical utilization of Sperm DNA Fragmentation (SDF) and Oxidative Reductive Potential (ORP) as a diagnostic and prognostic tool for patients undergoing ICSI cycles.

The following clinical outcomes will be evaluated

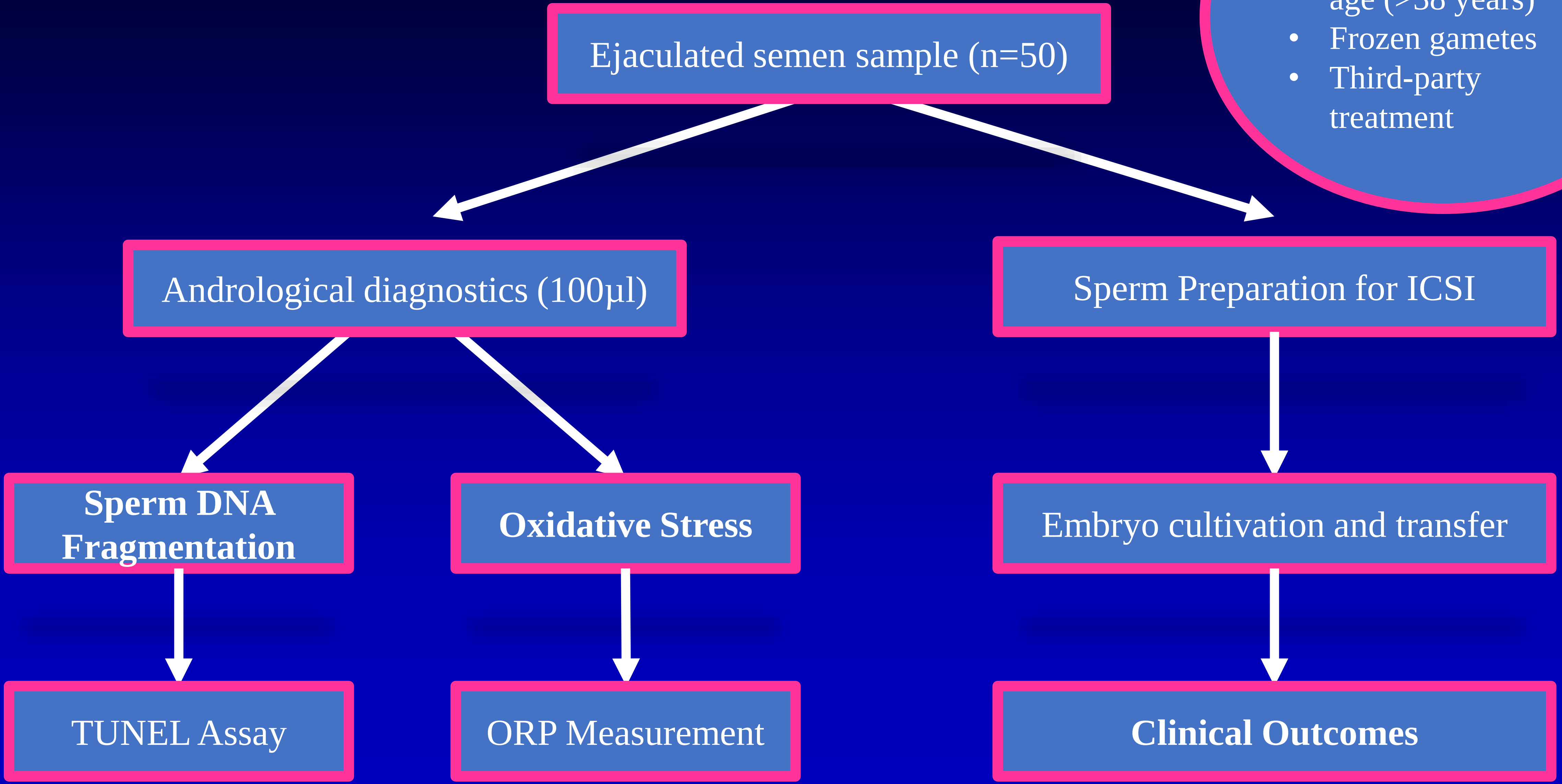
- Fertilization Rate
- Blastulation Rate
- Pregnancy
- Live Birth




Study Design

Exclusion Criteria

- Advanced maternal age (>38 years)
- Frozen gametes
- Third-party treatment



Methodology

The current preliminary study forms part of a larger PhD study, which has been ethically approved. A total of 50 patients undergoing ICSI as a treatment for male factor infertility was prospectively investigated.

Andrological component

SDF Detection

In Situ Cell Death Detection Kit, Fluorescein. ROCHE (11684795910)

ORP Detection

MiOXSYS System Aytu BioScience, Inc

Clinical component

- Fertilization rate = $\frac{No.of\ 2PN}{No\ of\ MII\ Oocytes\ injected}$ X100
- Blastulation rate = $\frac{No.of\ Blastocysts\ on\ Day\ 5}{No\ of\ MII\ Oocyte\ injected}$ X100
- Pregnancy = Positive βhCG, presence of gestational sac and fetal heart beat at ultrasound (Positive/Negative)
- Live birth = Positive/Negative

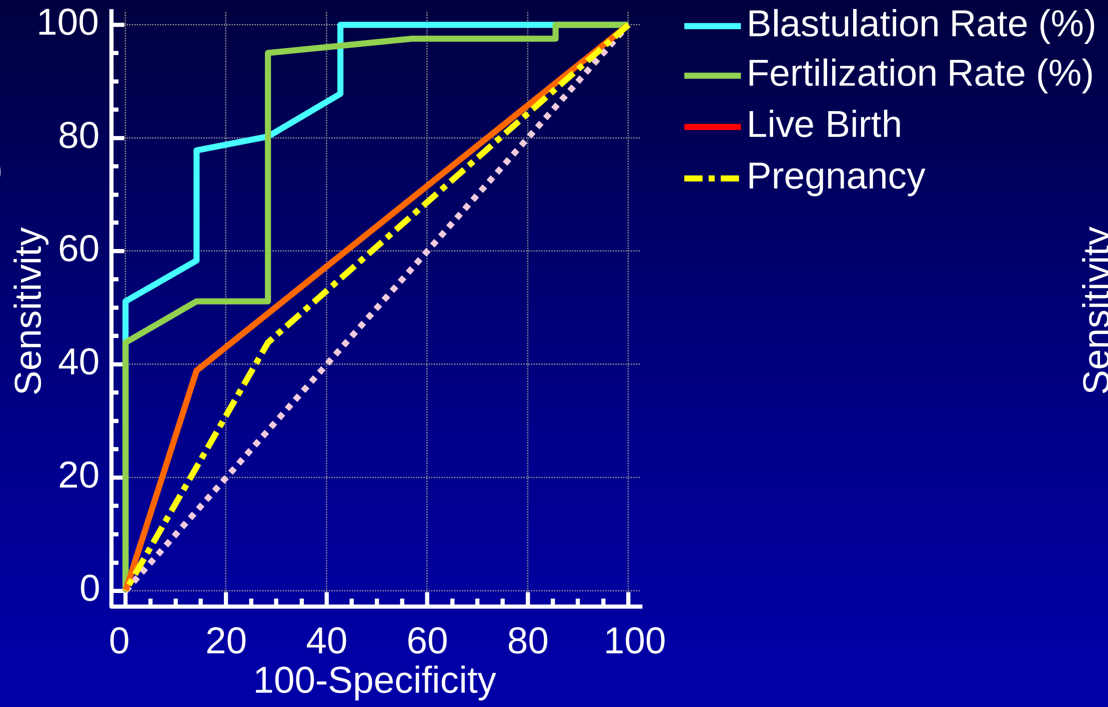
Results
Correlation table

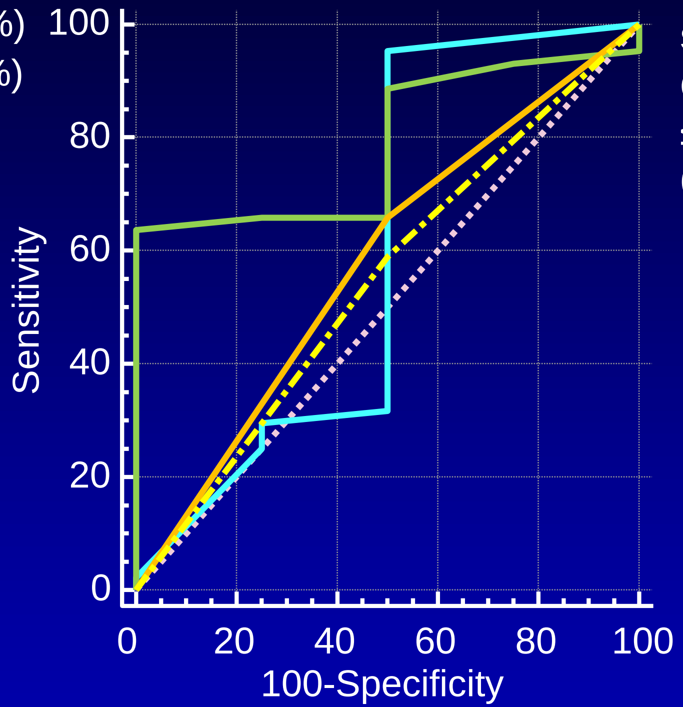
		Blastulation Rate (%)	Fertilization Rate (%)	Live Birth	Pregnancy	sORP ($mV/10^6$ sperm/mL)
Fertilization Rate (%)	Correlation coefficient Significance Level P	0.002 0.9910				
Live Birth	Correlation coefficient Significance Level P	**0.372** **0.0092**	0.177 0.2179			
Pregnancy	Correlation coefficient Significance Level P	**0.403** **0.0046**	0.167 0.2457	**0.880** **<0.0001**		
sORP ($mV/10^6$ sperm/mL)	Correlation coefficient Significance Level P	-0.257 0.0779	**-0.364** **0.0093**	**-0.447** **0.0010**	**-0.327** **0.0190**	
SDF (%)	Correlation coefficient Significance Level P	**-0.423** **0.0027**	**-0.506** **0.0002**	**-0.400** **0.0036**	**-0.296** **0.0347**	**0.528** **0.0001**

Spearman rank correlation coefficient

Comparison of ROC Curves for Various Variables with SDF and sORP

SDF
Cut-off:
<32%
(Henkel et al., 2004)





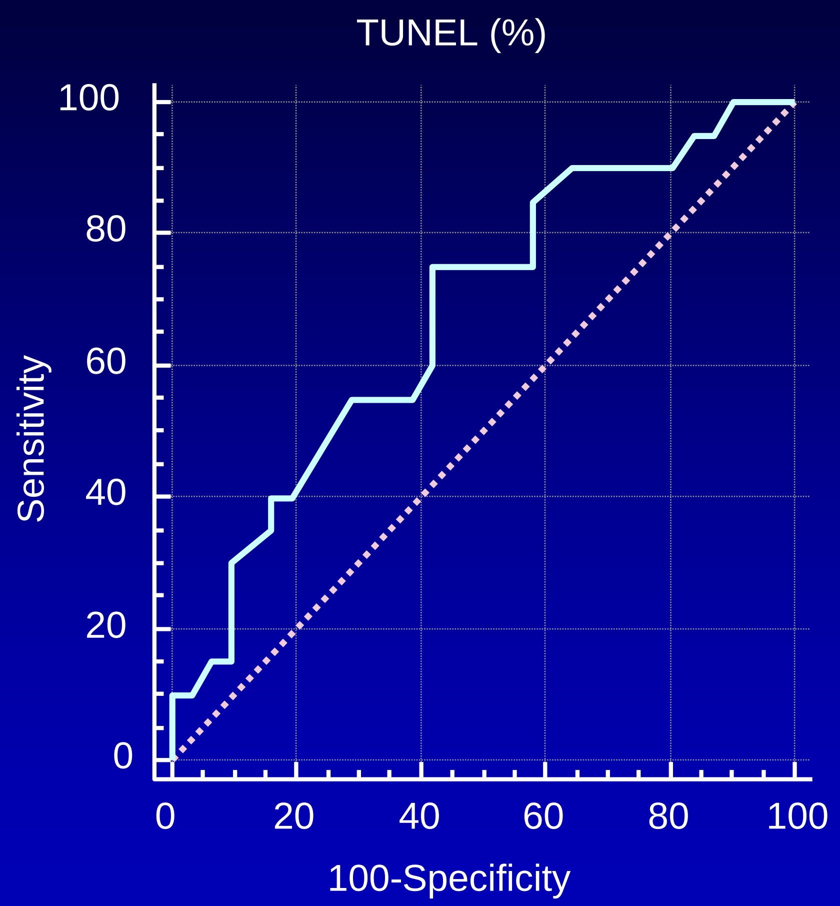
sORP
Cut-off:
≤1.36 mV/10^6 sperm/mL
(Agarwal et al., 2017)

Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Blastulation Rate (%)	0.883	>57.1	78.1	85.7	97.0	40.0	<0.0001
Fertilization Rate (%)	0.841	>40.0	92.9	75.0	95.1	66.7	0.0001
Live Birth	0.635	≤0	88.9	38.1	23.5	94.1	0.0449
Pregnancy	0.603	>0	42.9	77.8	90.0	22.6	0.2140

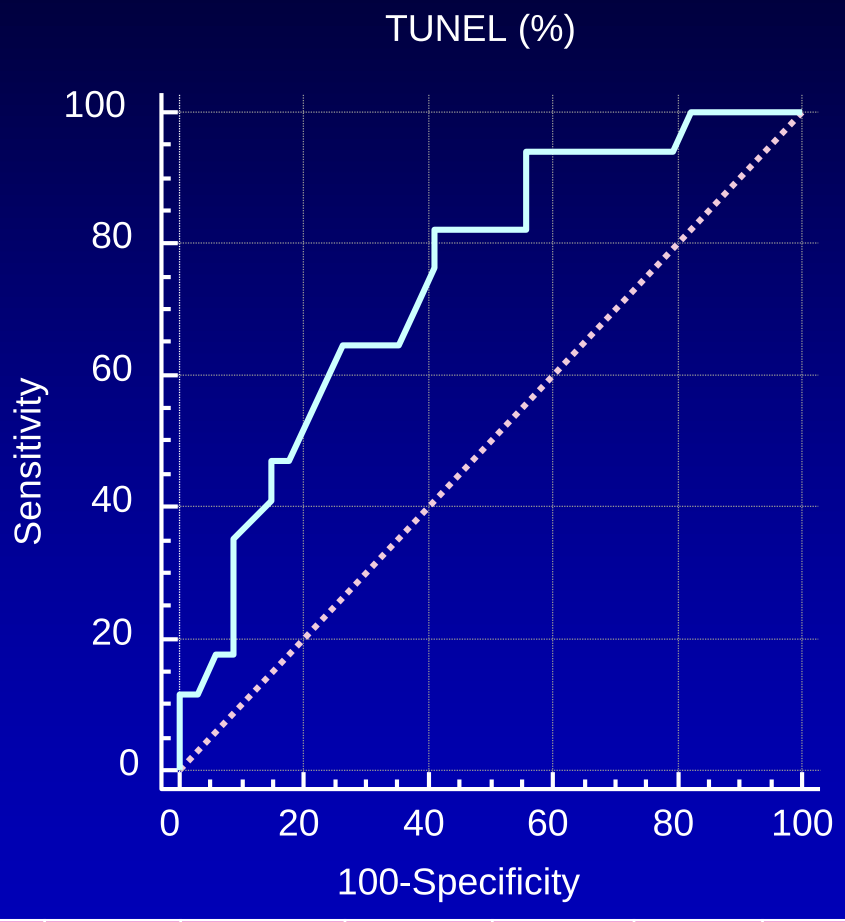
Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Fertilization Rate (%)	0.813	≤66.7	100.0	62.2	22.7	100.0	0.0002
Blastulation Rate (%)	0.599	<0	50.0	95.5	50.0	95.5	0.6552
Live Birth	0.537	>0	40.0	67.4	11.8	91.2	0.7717
Pregnancy	0.504	>0	40.0	60.9	10.0	90.3	0.9729

ROC Curve for SDF using TUNEL

Pregnancy



Live Birth



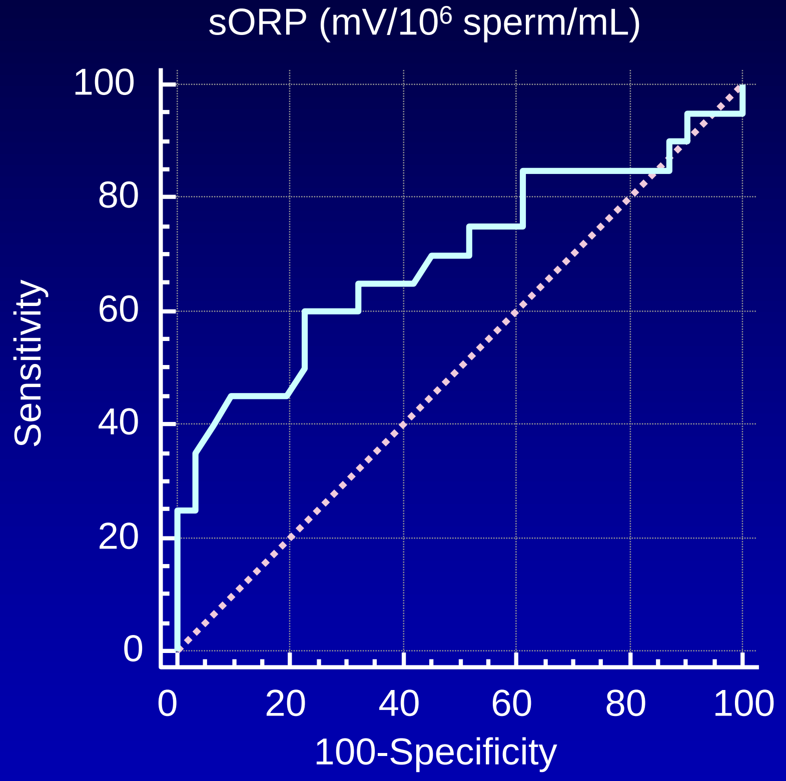
Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Pregnancy	0.675	**≤19.0**	75.0	58.1	53.6	78.3	0.0240

Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Live Birth	0.754	**≤19.0**	82.4	58.8	50.0	87.0	0.0007

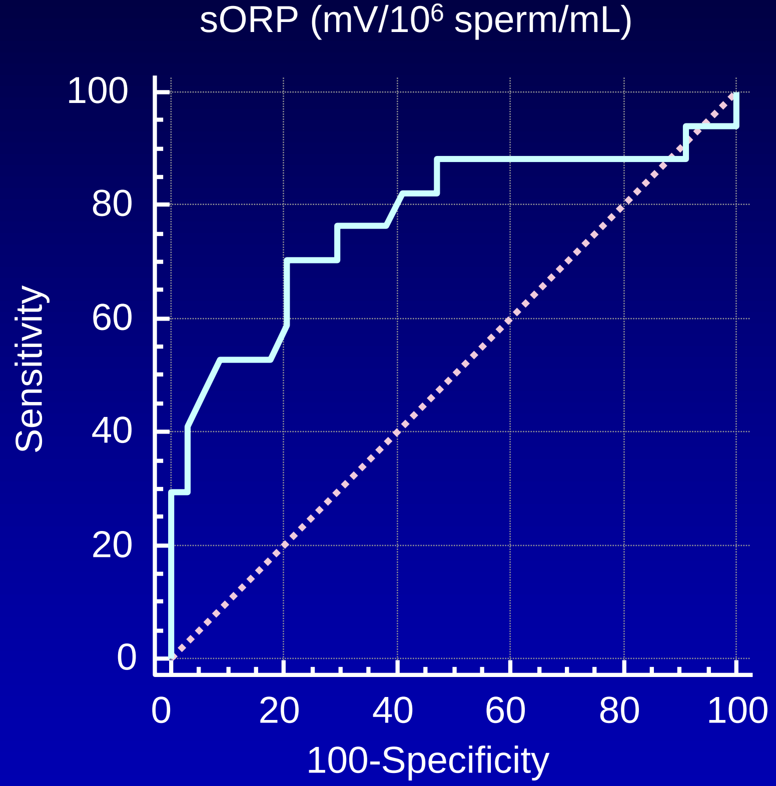
Comparison of both AUCs: **P=0.5079**

ROC Curve for sORP using MiOXSYS

Pregnancy



Live Birth



Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Pregnancy	0.694	**≤0.37**	60.0	77.4	63.2	75.0	0.0194

Variable	AUC	Cut-off	Sens.	Spec.	+PV	-PV	P-value
Live Birth	0.773	**≤0.37**	70.6	79.4	63.2	84.4	0.0007

Comparison of both AUCs: **P=0.4947**

Discussion

- The current study shows that both SDF and sORP are predictive of fertilization at the previously established cut-off values with a predictive power of 0.841 and 0.813, respectively

- SDF was also shown to be predictive of blastulation rate at the cut-off of 32% with a predictive power of 0.883 but not sORP.

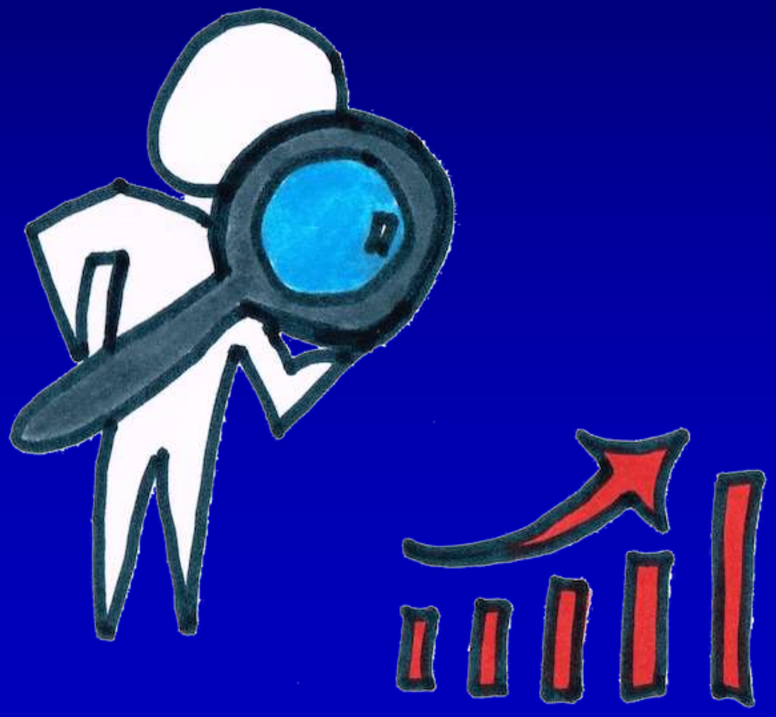
- The studies findings suggest that at a cut off of <19%, SDF could predict pregnancy and live birth.

- Similarly at a lower cut off for sORP ($<0.36 mvX10^6/ml$), the current data suggests that sORP could be used to predict Pregnancy and Live birth.

- This study is the first to establish the predictability of sORP as a diagnostic tool in a outcome based manner.

Limitations of study

It is important to note that the sample size of the current study is small, and further research is required to clearly establish the predictive capabilities of SDF and ORP in ICSI cycles.



Thank you