MSOME I+II: A NEW CUT-OFF VALUE FOR MALE INFERTILITY AND EMBRYO DEVELOPMENT PREDICTION ON INTRACYTOPLASMIC SPERM INJECTION CYCLES

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1 FERTILITY MEDICAL GROUP

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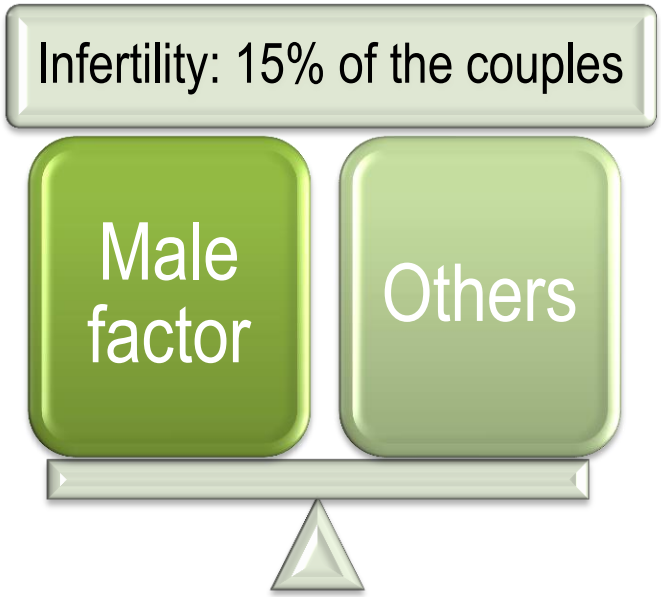
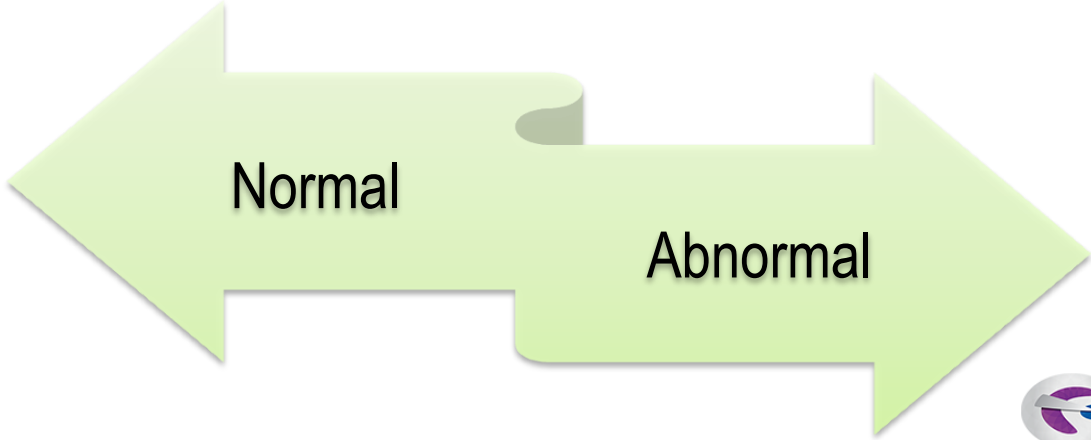
INTRODUCTION

- ✓ It is estimated that 72.4 million couples globally experience fertility problems



World Health Organization (WHO)

- Sperm count
- Sperm motility
- Sperm morphology



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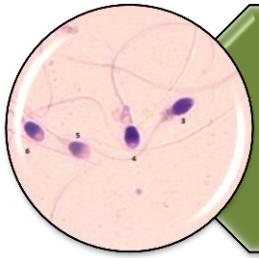
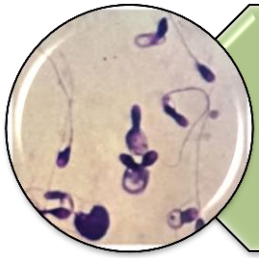
INTRODUCTION

Sperm morphological assessment



Fixed stained cells



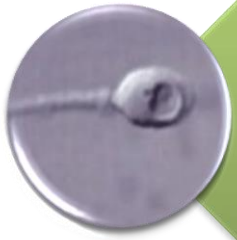
Detection of major abnormalities

Dependent on the method, operator, and optical system

INTRODUCTION

Motile Sperm Organelle Morphology Examination

Unstained, Real-time, observation of spermatozoa



High magnification

x6,300 – x13,000

Inverted microscope with NIC and video magnification

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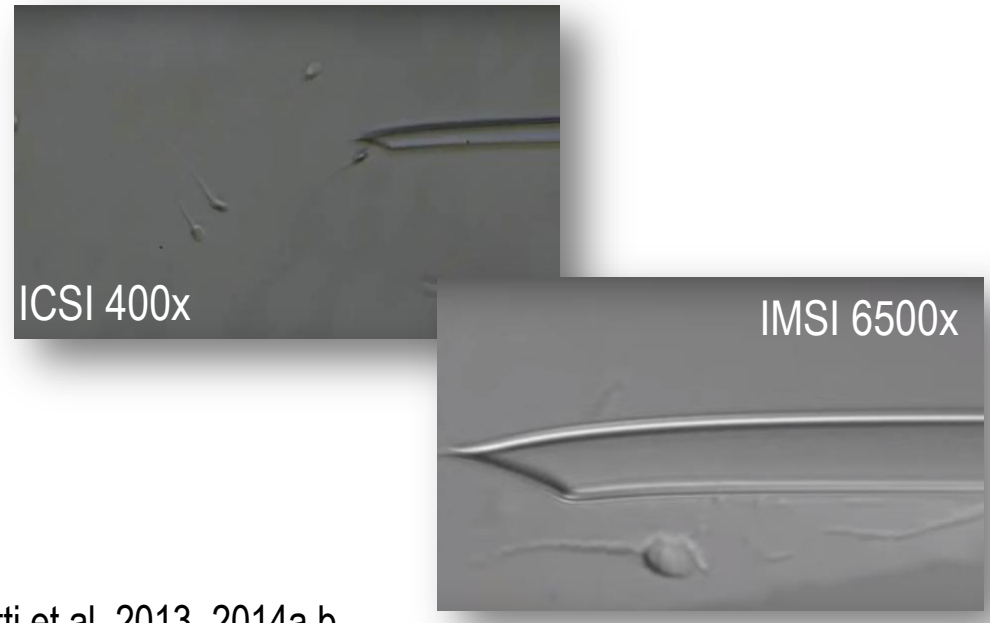
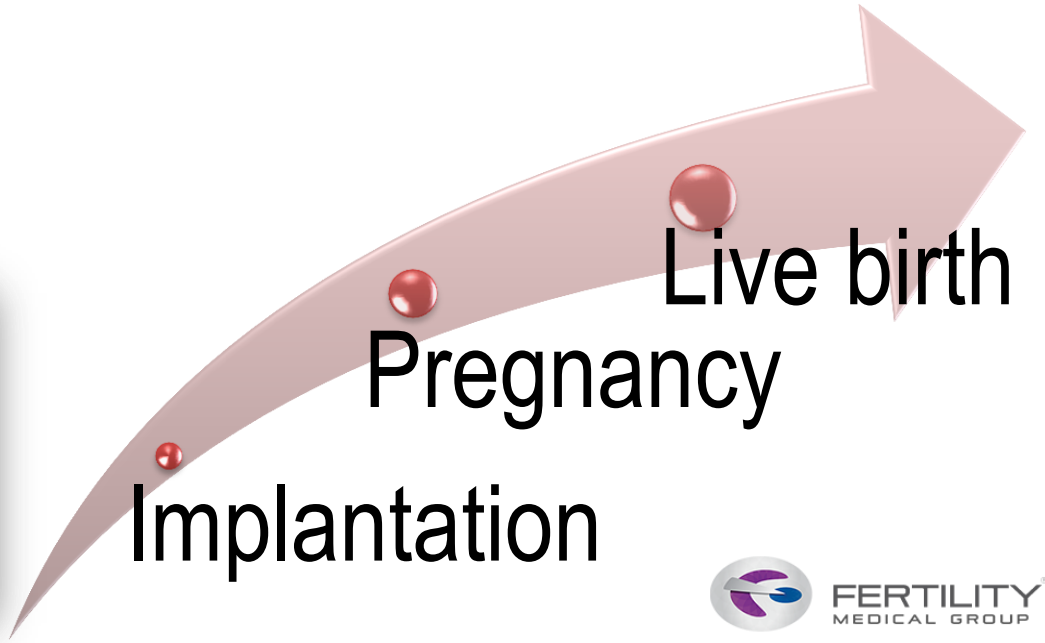
INTRODUCTION

Motile **S**perm **O**rganelle **M**orphology **E**xamination

Intracytoplasmic **M**orphologically Selected **S**perm **I**njection





Setti et al. 2013, 2014a,b

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INTRODUCTION

Direct correlation with male infertility?

Direct correlation with seminal characteristics?

Direct correlation with ICSI outcomes?

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OBJECTIVE

To investigate if MSOME can bring additional information to semen analysis, in terms of better definition of male infertility

To investigate if MSOME classification is a better prognosis to ICSI success compared with standard seminal analysis

To define a MSOME cutoff value for successful blastocyst formation

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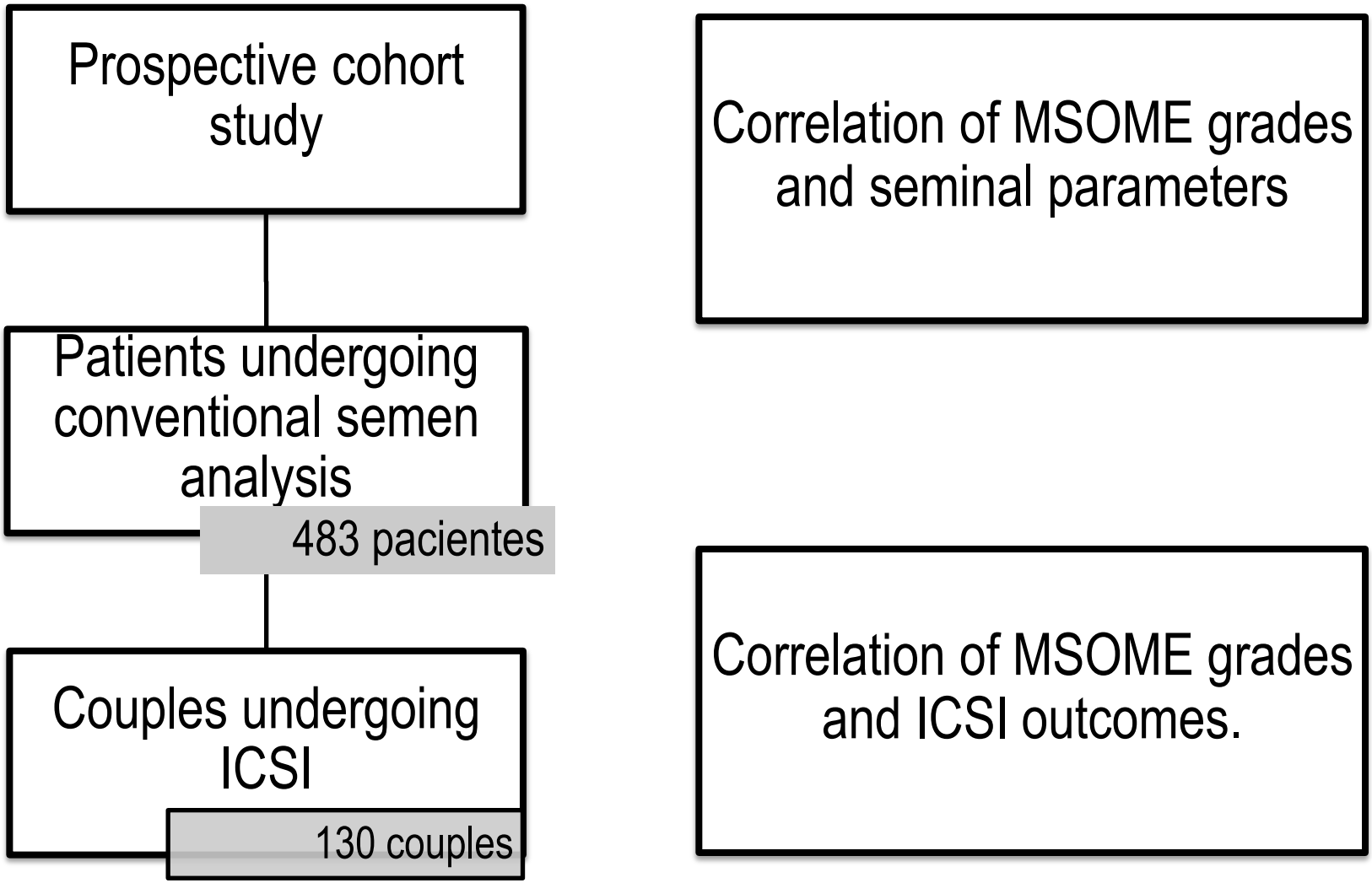
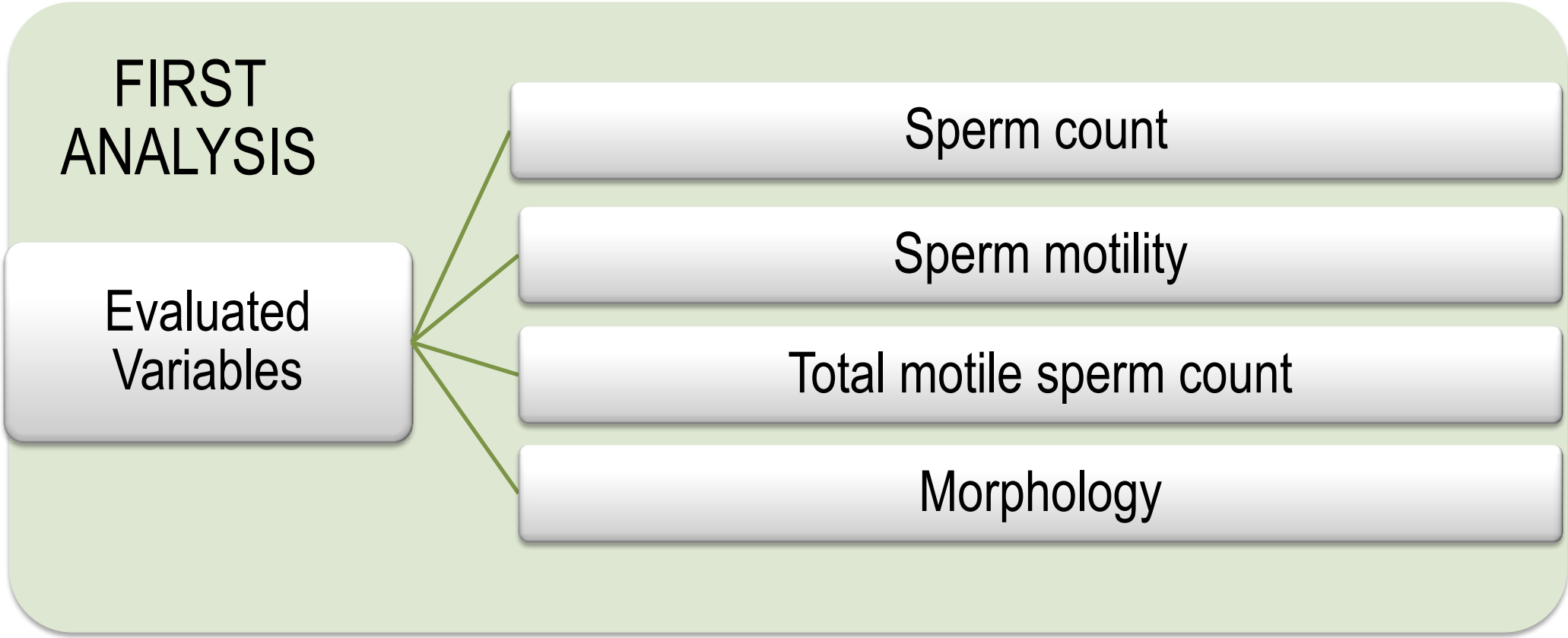
MATERIALS AND METHODS

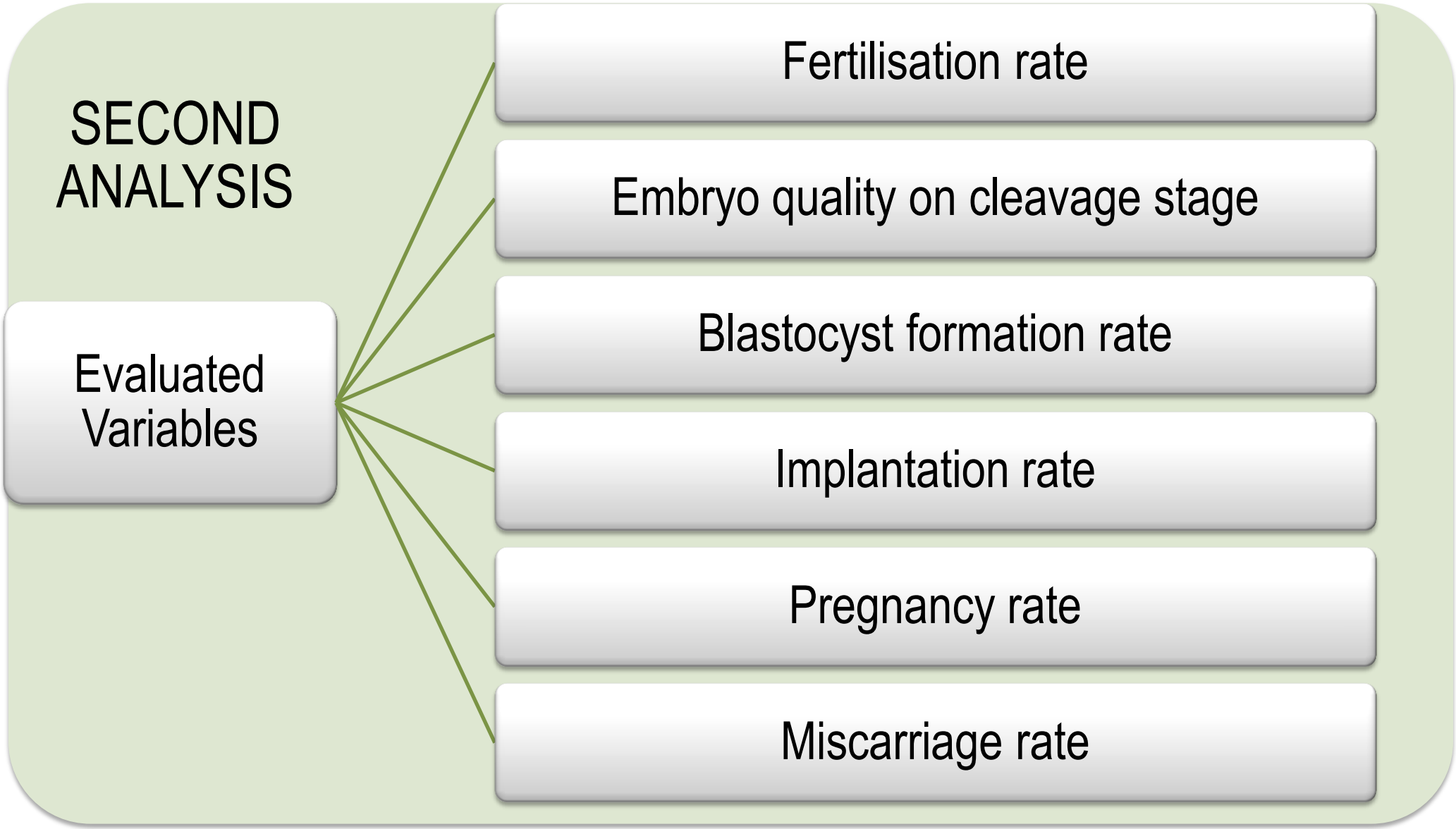
- STUDY DESIGN



MATERIALS AND METHODS



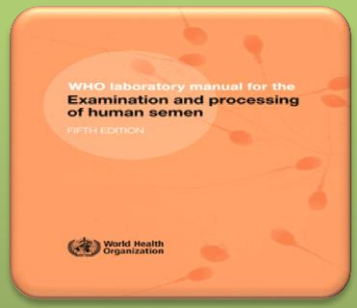
MATERIALS AND METHODS



MATERIALS AND METHODS

Ovarian stimulation

- rFSH
- GnRH antagonist
- rhCG to trigger final follicular maturation



Semen analysis

- Semen samples collected in the lab by masturbation
- Threshold values (WHO 2010)
- MSOME

Semen preparation

- 2-layered density gradient centrifugation

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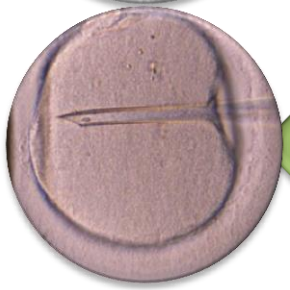
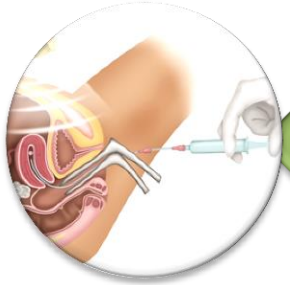
MATERIALS AND METHODS

Incubation, denudation and nuclear maturation evaluation



ICSI - (Palermo et al., 1992)

Embryo culture until day 5



One or two blastocysts transferred

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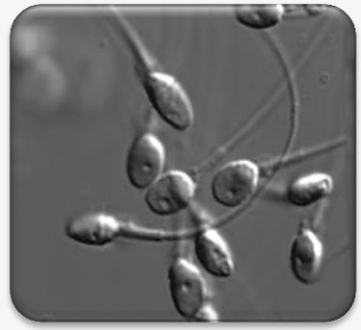
MATERIALS AND METHODS

- MOTILE SPERM ORGANELLE MORPHOLOGY EXAMINATION

Aliquot of sperm cell transferred to a microdroplet of 8% PVP in a glass dish



200 sperm cells per sample analyzed under x6,600

Presence and size of vacuoles were recorded

(Vanderzwalmen et al. 2008)

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MATERIALS AND METHODS

- MSOME: SPERM CLASSIFICATION (Vanderzwalmen et al., 2008)

Grade I:

- Normal form
- No vacuoles

Grade II:

- Normal form
- ≤ 2 small vacuoles

Grade III:

- Normal form
- > 2 small vacuoles or at least one large vacuole

Grade IV:

- Abnormal head shapes or other abnormalities
- Large vacuole

Grade I+II: normal spermatozoa parameter

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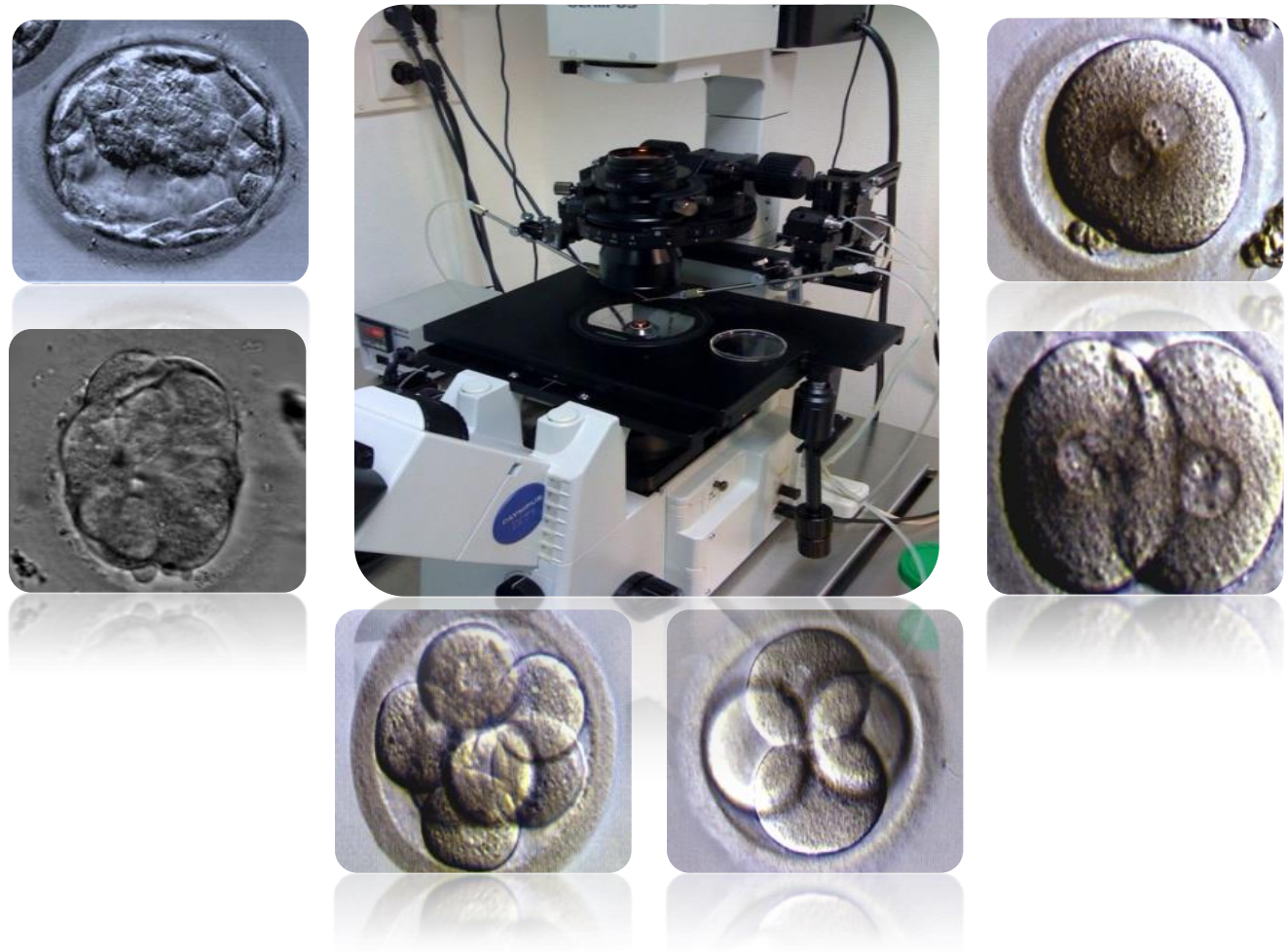
MATERIALS AND METHODS

- EMBRYO MORPHOLOGY AND EMBRYO TRANSFER



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RESULTS/DISCUSSION

Linear regression analysis of the association between sperm parameters and MSOME

SEMEN PARAMETER	MSOME I+II		MSOME III		MSOME IV	
	β	p	β	p	β	p
Volume	-0.031	0.508	-0.029	0.539	0.025	0.592
Concentration	0.281	<0.001	0.022	0.630	-0.252	<0.001
Total sperm count	0.224	<0.001	-0.013	0.782	-0.193	<0.001
Total motility	0.178	<0.001	-0.012	0.791	-0.175	<0.001
Progressive motility	0.192	<0.001	0.008	0.856	-0.188	<0.001
Morphology	0.341	<0.001	0.136	0.003	-0.350	<0.001
TMSC	0.210	<0.001	-0.017	0.716	-0.180	<0.001

RESULTS/DISCUSSION

Descriptive statistics for semen analysis according to male infertility classification

	N	T	AT	OT	OAT	p
Volume (ml)	3.25 ± 1.95 [a]	3.14 ± 1.59 [b]	4.23 ± 3.11 [a]	2.12 ± 1.17 [c]	2.13 ± 1.34 [c]	<0.001
Concentration (x10^6/ml)	96.82 ± 47.48 [a]	73.33 ± 49.74 [b]	39.68 ± 22.74 [c]	10.95 ± 12.02 [d]	14.12 ± 19.28 [d]	<0.001
Total sperm count (x10^6)	298.9 ± 210.6 [a]	214.4 ± 174.7 [b]	155.5 ± 128.4 [b]	16.69 ± 10.83 [c]	17.40 ± 12.94 [c]	<0.001
Total motility (%)	66.21 ± 9.84 [a]	64.17 ± 10.87 [a]	35.75 ±8.58 [c]	57.79 ± 11.03 [b]	33.17 ± 9.86 [c]	<0.001
Progressive motility (%)	58.05 ± 10.94 [a]	55.71 ± 12.43 [a]	24.66 ± 4.58 [c]	47.44 ± 11.09 [b]	21.95 ± 7.54 [c]	<0.001
Morphology (%)	4.44 ± 0.64 [a]	1.27 ± 1.00 [b]	1.00 ± 1.25 [c]	0.85 ± 0.93 [c]	0.34 ± 0.71 [c]	<0.001
TMSC	179.4 ± 143.0 [a]	123.3 ± 112.7 [b]	38.15 ± 31.14 [c]	8.04 ± 5.66 [d]	4.21 ± 3.40 [d]	<0.001
MSOME I+II (%)	14.10 ± 7.01 [a]	9.46 ± 6.33 [b]	8.93 ± 16.93 [b]	6.92 ± 5.38 [c]	3.95 ± 3.78 [c]	<0.001
MSOME III (%)	5.81 ± 3.74	5.30 ± 3.87	5.27 ± 6.18	5.18 ± 4.44	4.78 ± 4.12	0.911
MSOME IV (%)	80.07 ± 8.58 [a]	85.22 ± 8.41[b]	87.42 ± 12.24[b]	87.74 ± 7.74[b]	91.26 ± 6.81[c]	<0.001

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RESULTS/DISCUSSION

Analyses of effect of WHO seminal classification on ICSI outcomes (n = 483)

	N	T	AT	OT	OAT	p
Fertilization rate	86.23 ± 7.30	87.58 ± 2.08	79.12 ± 8.98	83.36 ± 4.67	86.17 ± 6.29	0.846
High-quality embryos rate	47.15 ± 30.12	40.23 ± 17.28	38.75 ± 1.76	35.32 ± 16.31	57.40 ± 25.05	0.414
Blastocyst rate	46.80 ± 32.10	45.14 ± 34.32	26.66 ± 46.18	34.70 ± 38.85	32.58 ± 40.49	0.603
Implantation rate	4.67 ± 20.72	20.32 ± 4.95	50.88 ± 26.35	30.11 ± 14.09	10.46 ± 14.93	0.227
Cancelation rate	55.5%	33.7%	60.0%	47.0%	30.0%	0.433
Pregnancy rate	25.0%	29.3%	50.0%	40.0%	28.6%	0.661

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RESULTS/DISCUSSION

Logistic regression analyses of MSOME grades correlation with ICSI outcomes

	MSOME I+II		MSOME III		MSOME IV	
	β	*p*	β	*p*	β	*p*
Fertilization rate	0.197	0.044	0.150	0.134	-0.192	0.052
High-quality embryos rate	0.306	0.013	0.379	0.002	-0.378	0.002
Blastocyst rate	0.248	0.047	0.008	0.954	-0.195	0.130
Implantation rate	-0.098	0.405	-0.137	0.252	0.138	0.244
	95% CI	***p***	**95% CI**	***p***	**95% CI**	***p***
Cancelation rate	0.95; 1.07	0.817	0.94; 1.12	0.557	0.95; 1.03	0.716
Pregnancy rate	0.90; 1.05	0.493	0.84;1.09	0.528	0.96; 1.09	0.396

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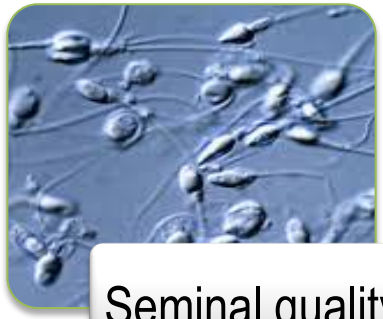
RESULTS/DISCUSSION



Seminal quality

Blatocyst formation

Roc curve based on the blastocyst formation rate

>50%

≤ 50%

MSOME value

Normal sperm samples

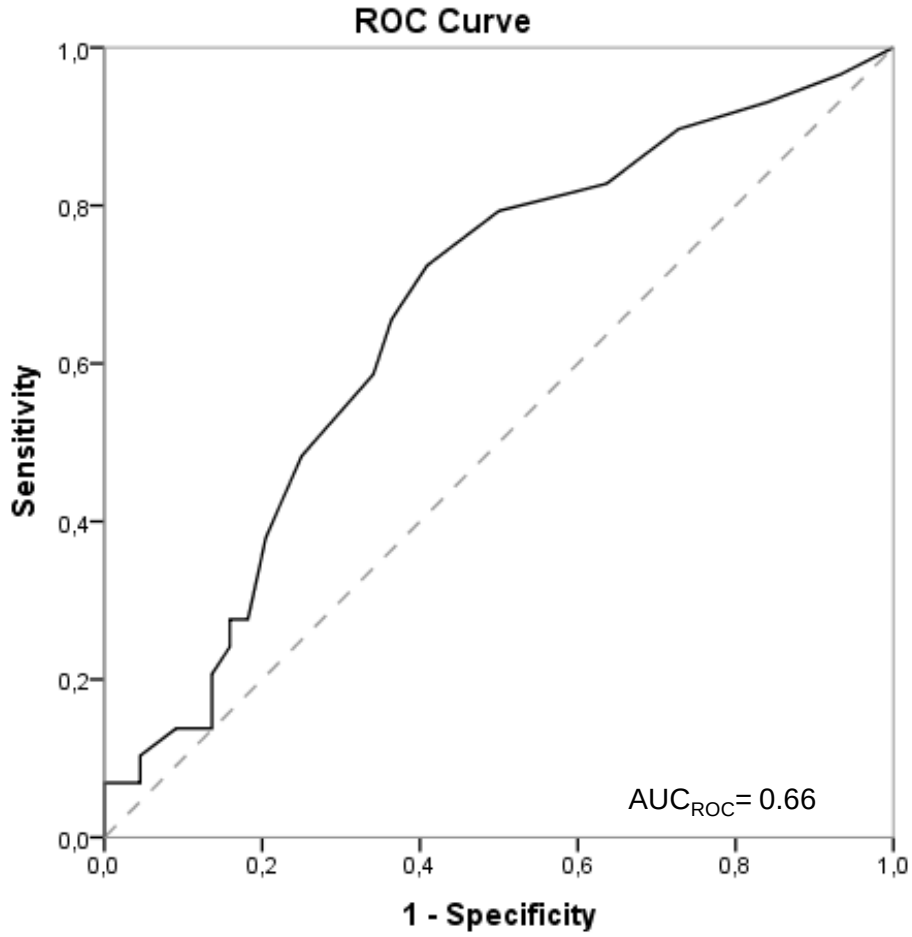
Abnormal sperm samples

MSOME I + II

ROC

RESULTS/DISCUSSION

ROC Curve of MSOME grades I+II and blastocyst formation rate (below or equal and above 50%)



AUC: 0,66

MSOME I+II

cut-off: 5,5%

sensitivity of 0.72

specificity of 0.41

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RESULTS/DISCUSSION

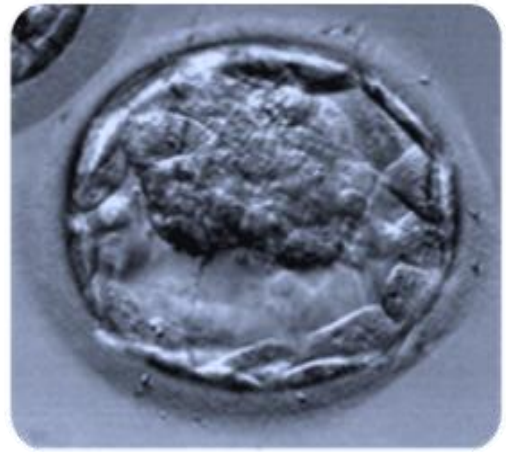
Descriptive statistic of ICSI outcomes per MSOME I+II normality classification

	Normal (MSOME I+II ≥5.5%)	Abnormal (MSOME I+II <5.5%)	p
Female age (years)	36.18 ± 4.29	36.66 ± 3.58	0.527
Total dose of FSH administered (IU)	2346.38 ± 680.43	2422.61 ± 704.55	0.560
Number of follicles	14.28 ± 12.49	14.06 ± 10.97	0.925
Number of retrieved oocytes	9.92 ± 9.95	10.81 ± 7.74	0.608
Fertilization rate	86.94 ± 19.04	84.59 ± 14.79	0.708
High-quality embryos rate	41.78 ± 16.04	38.40 ± 21.73	0.463
Blastocyst rate	50.14 ± 5.05	28.53 ± 5.69	0.005
Implantation rate (%)	20.10 ± 35.59	24.24 ± 37.05	0.618
Pregnancy rate (%)	28.26	36.36	0.472

RESULTS/DISCUSSION

Normal seminal parameter by MSOME
resulted in around 20% more blastocysts on Day 5.

Sperm functionality



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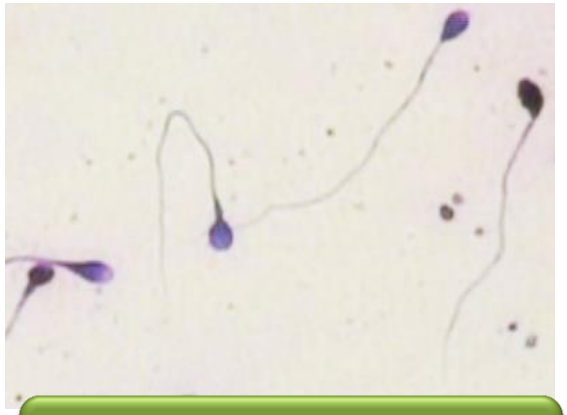
RESULTS/DISCUSSION

Descriptive statistic of seminal parameters per MSOME I+II normality classification

	Normal (MSOME I+II ≥5.5%)	Abnormal (MSOME I+II <5.5%)	p
Male age (years)	36.95 ± 6.94	36.88 ± 7.26	0.911
Ejaculatory abstinence (days)	4.22 ± 2.60	3.98 ± 2.16	0.307
Seminal volume (mL)	3.01 ± 1.70	3.00 ± 1.90	0.582
Seminal Concentration (x 10^6/ml)	74.46 ± 54.10	42.15 ± 35.65	<0.001
Total sperm count (x 10^6)	215.97 ± 184.55	129.42 ± 152.23	<0.001
Total sperm motility (%)	65.65 ± 12.56	55.92 ± 16.08	<0.001
Progressive sperm motility (%)	53.78 ± 14.02	46.82 ± 17.35	<0.001
Sperm Morphology (%)	1.75 ± 1.36	0.82 ± 1.07	<0.001
TMSC	121.93 ± 118.04	69.16 ± 97.11	<0.001

RESULTS/DISCUSSION



WHO

VS

MSOME

Stricter

Only 37% of patients with abnormal semen samples as per the WHO 2010 parameters had abnormal MSOME classification

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RESULTS/DISCUSSION

Long-term stability of MSOME readings of patients that repeated semen analysis within a year

	First analysis	Second analysis	p
Ejaculatory abstinence (days)	4.02 ± 2.13	3.98 ± 1.73	0.895
Seminal volume (mL)	2.90 ± 1.90	2.93 ± 2.00	0.899
Seminal Concentration (x 10^6/ml)	62.56 ± 51.75	57.82 ± 61.18	0.459
Total sperm count (x 10^6)	183.81 ± 185.14	172.90 ± 226.83	0.709
Total sperm motility (%)	61.96 ± 16.32	62.65 ± 17.05	0.717
Progressive sperm motility (%)	53.15 ± 17.49	53.54 ± 18.03	0.871
Sperm Morphology (%)	1.11 ± 0.97	1.43 ± 1.44	0.175
TMSC	108.34 ± 123.27	99.27 ± 136.81	0.590
MSOME Grades I+II (%)	8.69 ± 6.33	9.29 ± 6.85	0.088
MSOME Grade III (%)	4.72 ± 3.92	5.39 ± 4.15	0.358
MSOME Grade IV (%)	86.67 ± 8.48	85.28 ± 8.96	0.085

CONCLUSION

MSOME brings additional information to semen analysis, in terms of better definition of male infertility

MSOME classification is able to predict ICSI success, better than conventional seminal parameters

A MSOME I+II cut-off ≥ 5.5% for successful blastocyst formation is suggested

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WIDER IMPLICATION OF FINDINGS

The future use of MSOME as a routine method may be reliable for assessing male infertility and its impact on ICSI

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