ICM and TE quality significantly impact the live birth rate in euploid frozen blastocyst transfer cycles

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Study question

Is the live birth rate (LBR) in euploid frozen blastocyst transfer (FET) cycles affected by the quality of ICM (Inner cell mass) and TE (Trophectoderm)?

Material and Methods

Two-center retrospective observational study, including 977 euploid FET cycles between March 2017 and March 2020 at ART Fertility Clinics Muscat, Oman and Abu Dhabi, UAE. Trophectoderm biopsies were analyzed with Next Generation Sequencing (NGS). All blastocysts available on D5 or D6 with a quality ≥ BL3CC were subjected to TE biopsy for PGT-A analysis and LBR was recorded. Vitrification/warming of blastocysts was performed using Cryotop method (Kitazato). Bivariate and multivariate analysis were performed between LB outcomes and ICM and TE grade while controlling for confounding factors.

Results

A total of 977 single FET cycles were analyzed: 651 in hormone replacement therapy (HRT) and 326 in natural cycle regimen (NC) resulting in a 46.88% LBR. The mean patients' age was 33.80 years with a mean Body Mass Index (BMI) of 26.80 kg/m2. Though all qualities of ICM and TE were associated with LB, blastocyst ICM-A LBR was statistically significantly higher (57.3%) than ICM-B (48.4%) and ICM-C (22.1%) (p<0.001). Similarly, blastocyst TE-A LBR was statistically significantly higher (59.2%) than TE- B (48.6%) and TE- C (30.3%) (p<0.001). Miscarriage rate was similar in all groups.

The grade of ICM and TE were significantly associated with Anti-Mullerian-Hormone (AMH) and day of blastocyst biopsy. Mean AMH (ng/ml) was significantly higher in ICM groups (A: 3.78, B: 3.24, p<0.001) and TE group (A: 3.63, B: 3.38, p<0.05) compared to lower grade (ICM-C: 2.86, TE-C: 2.82).

In multivariate analysis, endometrial preparation for FET, BMI and AMH were the parameters influencing LBR: OR:1.45, [CI:1.07-1.96], (p<0.015) for NC; OR 0.96 [CI:0.93-0.99], (p=0.004) for BMI; OR 0.95 [CI:0.90-1.00], (p=0.033) for AMH. Both, ICM-C and TE-C, resulted in a significantly lower chance of LB [ICM: OR 0.32, CI:0.17-0.61, (p<0.001); TE: OR 0.44, CI:0.27-0.73, (p=0.002)], compared to grade A.

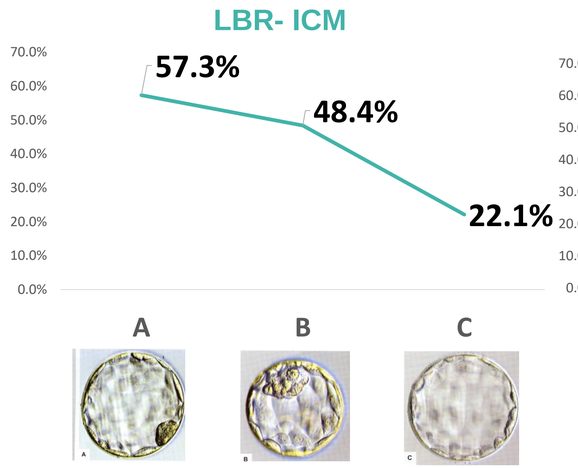

Figure 1: Graphic representing live birth rate (LBR) percentage according to inner cell mass (ICM) quality

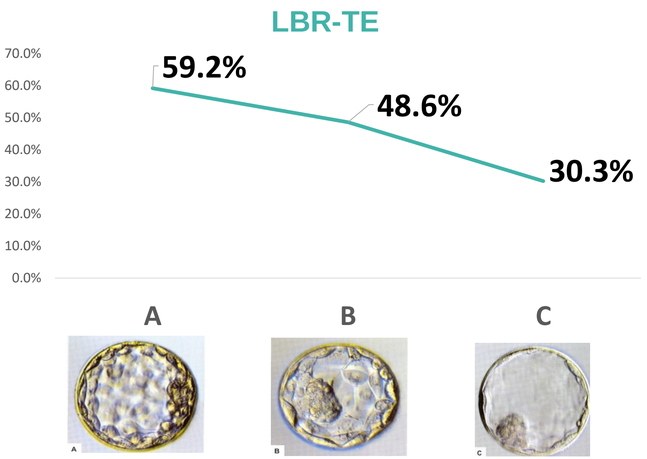

Figure 2: Graphic representing live birth rate (LBR) percentage according to trophectoderm (TE) quality

Livebirth	Odds Ratio	Std. Err.	P>z	[95% Conf.	Interval]
ICM A (reference)					
ICM B	0.78	0.14	0.171	0.54	1.12
ICM C	0.32	0.10	**<0.001**	0.17	0.61
TE A (reference)					
TE B	0.74	0.13	0.093	0.51	1.05
TE C	0.44	0.11	**0.002**	0.27	0.73

Table 1. Multivariate Regression analysis. Both grade ICM and TE significantly impact LB. Lower grade B and C showed lower chance of live birth compared to grade A blastocyst

Conclusion

ICM and TE significantly impacts the LBR with a decline of LB from 57.3% (ICM-A) to 48.5% (ICM-B) to 22.1% (ICM-C) (p<0.001).

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Poster number: P-677

Ongoing pregnancy rate (OPR) of day (D) 7 euploid blastocysts is inferior to D5/D6 euploid blastocysts in frozen embryo transfer (FET) cycles

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Objective

Do delayed-grown day (D) 7 euploid blastocysts have similar OPRs as D5 or D6 euploid blastocysts?

What is known already

Recently, high reproductive potential has been reported with D6 and D7 blastocysts. Usable D7 blastocysts represent nearly 5% of embryos in IVF with acceptable pregnancy and live birth rates, however, data are still limited.

Material and Method

A single center retrospective, observational study. Patients with frozen embryo transfer (FET) cycles, performed between March 2017 and March 2022 with euploid blastocyst were included in the study. Inclusion criteria were: autologous fresh or frozen sperm, fresh or vitrified oocytes and blastocysts graded ≥BL3CC (Gardner grading system) which underwent TE biopsy on D5, D6 or D7 for PGT-A by Next Generation Sequencing (NGS).

	Day 5	Day 6	Day 7	P value
Number of FET cycles	855	636	36	
Female age (in years)	33.2 ± 5.6	34.4 ± 5.3	35.9 ± 5.2	< 0.001
Male age (in years)	36.9 ± 7.1	37.9 ± 6.9	40.5 ± 6.1	0.001
AMH (ng/ml)	3.6 ± 3.5	2.9 ± 2.8	2.0 ± 1.7	0.087
BMI (kg/m2)	26.7 ± 4.9	27.2 ± 5.0	28.1 ± 4.6	< 0.001

Table 1: Patients' characteristics.

Results

The factors associated with a reduced OPR were: D7 euploid blastocyst FET cycles (OR= 0.19 [0.06-0.63]; p< 0.01), ICM grade C (OR= 0.29 [0.17-0.48]; p<0.001) and TE grade C (OR= 0.58 [0.38-0.89]; p=0.01). In patients >38 years, OPR was improved if a D7 euploid blastocyst FET cycles was performed compared to patients <38 years, however, was not statistically significant (OR= 2.33 [0.19-29.4], p= 0.51). Regardless of patient's age, OPR outcomes were higher with D5/D6 than with D7 euploid blastocysts.

	Day 5	Day 6	Day 7	P value
Pregnancy rate (%)	70.4	59.3	16.7	<0.001
Clinical pregnancy rate (%)	64.7	51.6	16.7	< 0.001
Ongoing pregnancy rate (%)	56	45.3	11.1	<0.001
Live birth rate (%)	48.7	35.5	11.1	<0.001
Clinical Miscarriage rate (%)	10.1	7.1	5.6	0.111

Table 2: Clinical outcomes for D5, D6 and D7 single euploid FET cycles.

Conclusion

Although OPR is lower with D7 euploid blastocysts than D5/D6, patients aged >38 years might benefit from a D7 euploid blastocysts FET cycle.

Considering age as a risk factor of having delayed-grown blastocysts in-vitro, culturing embryos till D7 can be a strategy to increase OPR in patients >38 years old.

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Does C-Section history affect the live birth outcomes after IVF in case of frozen embryo transfers

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Objective

Do previous Caesarean section deliveries (CD) affect reproductive outcomes in case of frozen embryo transfers (FET), including live births (LB), after IVF or ICSI?

Material and Method

This single center retrospective cohort study included a total of 412 single/double euploid FET cycles between March 2017 and October 2019. No embryo transfer was performed when intra cavitary fluid (ICF) was visible during the endometrial preparation for FET.

Patients with secondary infertility, having at least one euploid embryo after a previous IVF/ICSI-cycle with embryo vitrification, undergoing FET, were included. Clinical pregnancy rate (CPR), early pregnancy loss (EPL) and LBR were evaluated in patients after CD and after vaginal delivery (VD).

	Prev CS no	Prev CS yes	p-value
	N=237	N=175	
Age (years)	34.1 (5.0)	35.0 (4.6)	0.057
AMH (ng/ml)	2.5 (1.5)	2.6 (1.5)	0.85
BMI (kg/m2)	27.55 (0.3)	27.88 (0.4)	0.5
Infertility duration (years)	3.4 (3.3)	3.4 (2.8)	0.91
EMT (mm)	7.9 (1.4)	7.7 (1.3)	0.11

Table 1 Descriptive variables

Results

Patients in the CD group were significantly older than in the VD group (35.02±4.62 vs 34.11±5.03 years, respectively) (p=0.028) (Table 1).

In the multivariate regression model with embryo-quality, cycle-regimen, ET-difficulty, presence of blood/mucus, age, AMH, number of transferred embryos, only embryo quality remained significantly associated with LBR in CD-group (p=0.001).

In VD-group, cycle regimen was also significant parameter besides embryo quality (p=0.001, p=0.001 respectively). When CD and VD groups are categorized in terms of cycle regimen, CP and LBR were similar (p=0.828/p=0.618 in HRT; p=0.826/p=0.150 in NC).

Conclusion

This study confirmed that in patients after CD, the chance for CP and LBR is not compromised, when ICF is excluded during the endometrial preparation for FET. The existence of C-section scar may increase the ET-difficulty and the presence of the mucus on the transfer catheter.

		Categorical		
		Prev CS no	Prev CS yes	p-value
Embryos transferred (n)	SET	124 (52.3%)	103 (58.9%)	0.19
	DET	113 (47.7%)	72 (41.1%)	
Combined Embryo quality	1	67 (28.3%)	43 (24.6%)	0.59
	2	153 (64.6%)	116 (66.3%)	
	3	17 (7.2%)	16 (9.1%)	
Endometrial preparation regimen	NC	77 (32.5%)	82 (46.9%)	0.003
	HRT	160 (67.5%)	93 (53.1%)	
Presence of blood on ET catheter	no	187 (78.9%)	124 (70.9%)	0.061
	yes	50 (21.1%)	51 (29.1%)	
Presence of mucus on ET catheter	no	221 (93.2%)	148 (84.6%)	0.004
	yes	16 (6.8%)	27 (15.4%)	
Difficult ET procedure	no	216 (91.1%)	148 (84.6%)	0.04
	yes	21 (8.9%)	27 (15.4%)	
Positive pregnancy test	no	57 (24.1%)	46 (26.3%)	0.6
	yes	180 (75.9%)	129 (73.7%)	
Clinical pregnancy	no	69 (29.1%)	57 (32.6%)	0.45
	yes	168 (70.9%)	118 (67.4%)	
Live birth	no	94 (39.7%)	70 (40.0%)	0.94
	yes	143 (60.3%)	105 (60.0%)	

Table 2: Categorical variables

Poster number: P-377

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Reduction of gonadotropin-dosage towards the end of ovarian stimulation for IVF/ICSI improves ART-outcome in a subgroup of patients

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Objective

To identify in an unselected patient population those patients, who benefit from a gonadotropin stepdown towards the end of ovarian stimulation.

What is known already?

Ovarian stimulation with gonadotropins (Gn) for multi-follicular growth is a crucial part of IVF/ICSI-treatment. Intensive administration of gonadotropins might lead to progesterone elevation in the late follicular phase, impacting negatively the endometrial receptivity and possibly the embryo quality. During follicular growth, there is a shift from FSH- to LH-receptors in the late follicular phase, reducing susceptibility of the follicle towards systemic FSH-levels. In a good prognosis population, lower systemic FSH-levels on the trigger-day lead to significantly lower progesterone levels without reducing the number of retrieved/mature oocytes.

Material and Methods

Retrospective analysis of 1276 ovarian stimulation cycles, performed as GnRH (Gonadotropin-Releasing-Hormone)-antagonist protocol in an unselected patient population, between January 2018 and December 2020 at ART Fertility Clinic, Abu Dhabi, UAE.

Couples with an indication for ovarian stimulation for IVF/ICSI were included, independent of age or ovarian reserve parameters. Only GnRH antagonist cycles, with either rFSH or HP-HMG as sole medication for ovarian stimulation were included.

Results

A total of 1276 ovarian stimulation cycles were included, 495 (38.79%) with rFSH and 781 (61.21%) with HP-HMG as stimulation medication.

FSH group, aged 26 - ≤30 years: Despite no significant differences in the patient characteristics (AFC, BMI (Body Mass Index), mean age, FSH-starting dosage), a significantly higher number of oocytes (retrieved/mature) was obtained in the group with a decrease of Gn-dosage

HMG group, aged 36-≤40 years: Despite no significant differences in AFC, BMI, age and HMG-starting-dosage, a significantly higher number of oocytes (retrieved/mature) were obtained in the group with Gn-reduction. The progesterone-levels on trigger day in the non reduction-group was slightly higher (p<0.001), however, clinically insignificant.

	FSH cycles – age group 26 to 30 years			HMG cycles age group 36 - 40 years		
	Decrease of Gn-dosage NO	**Decrease of Gn-dosage YES**	**p-value**	**Decrease of Gn-dosage NO**	**Decrease of Gn-dosage YES**	**p-value**
	N=65	N=93		N=98	N=140	
AFC total	16.9 (6.6)	18.7 (6.7)	0.099	9.4 (6.4)	10.9 (5.7)	0.055
BMI	26.9 (4.6)	26.5 (5.0)	0.58	28.4 (4.6)	27.9 (4.4)	0.39
Patient Age	27.9 (1.3)	28.0 (1.5)	0.83	38.2 (1.3)	38.1 (1.4)	0.77
Starting dosage	228.8 (68.0)	239.1 (61.5)	0.32	384.4 (91.8)	401.4 (70.8)	0.11
End dose	228.8 (68.0)	149.9 (75.7)	<0.001	384.4 (91.8)	237.0 (96.6)	<0.001
Stimulation days	9.4 (1.0)	9.7 (1.2)	0.072	9.5 (1.6)	9.9 (1.7)	0.075
Total dosage	2130.4 (712.0)	2108.6 (568.7)	0.83	3594.5 (1077.1)	3552.9 (949.6)	0.75
Trigger E2	2285.9 (1177.2)	2924.6 (1182.7)	0.001	1663.2 (1137.9)	2369.8 (1119.3)	<0.001
Trigger P4	1.0 (1.3)	0.9 (0.6)	0.95	0.5 (0.3)	0.6 (0.4)	<0.001
COC	16.0 (7.1)	20.4 (8.3)	<0.001	7.2 (5.6)	9.8 (6.1)	<0.001
MII	12.5 (6.5)	15.8 (7.0)	0.004	5.7 (4.7)	7.9 (5.0)	<0.001

Table: significant outcome in FSH and HMG cycles in groups with Gn reduction NO / YES

Conclusion

In specific patient populations, Gn-dosage can be reduced towards the end of the follicular phase without impacting the oocyte yield and preventing progesterone-elevation despite higher oocyte yield. The Gn-reduction results in a more physiologic course of the Gn-levels during ovarian stimulation.

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P-569

PRIMARY SEX RATIO IS DECREASED IN EUPLOID EMBRYOS OF CONSANGUINE COUPLES AFTER IVF/ICSI WITH PGT-A

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Objective

What is the primary sex ratio outcome of embryos from consanguine couples as per PGT-A analysis during IVF/ICSI treatments?

Design

A total of 5135 blastocysts from 1836 IVF/ICSI cycles after preimplantation genetic testing on day 5 for aneuploidy (PGT-A) with NGS, from November 2016 to December 2020. Consanguinity was defined when couple were first-degree or second-degree cousins.

Materials and Methods

Blastocysts presenting normal sexual chromosome constitution with or without autosomal aneuploidies. Mosaic and non-informative embryos were excluded. Primary sex ratio (PSR) was observed for CG and NCG couples. Ethical approval was obtained from the Research Ethics Committee (REFA023b).

Table 1. Primary sex ratio (PSR) distribution of expanded blastocysts deriving from consanguine (CS, n=1138) and non consanguine (NCS, n=3997) couples following PGT-A on day 5.

	CS	NCS
XX	52.3%	51.2%
XY	47.7%	48.8%
PSR	*0.91 (P = 0.03)*	*0.95 (NS)*

Table 2. Primary sex ratio (PSR) distribution of normal euploid only blastocysts deriving from consanguine (CS, n=2264) and non consanguine (NCS, n=716) couples following PGT-A on day 5.

	CS	NCS
XX	53.4%	50.9%
XY	46.6%	49.1%
PSR	*0.87 (P = 0.01)*	*0.96 (NS)*

Results

In consanguine couples the age of female and male partner was 30.7±5.5 and 35.9 ±5.3 years old, respectively; while non consanguine couples were older (32.2±5.8 and 37.6±7.3 years old, respectively) (p<0.001).

Discussion

It is known that consanguine couples derive embryos with increased abnormalities in comparison to the general population. The fact that euploid embryos from consanguine couples seems to present a higher female constitution might incite us to investigate to what extent does heterozygosity for x-linked loci contribute to embryo survival.

Conclusion

The primary sex ratio (PSR) (males-to-females at time of conception) of euploid blastocysts on day 5 is decreased in consanguine couples.

Poster number: P-537

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Natural endometrial preparation for single euploid frozen embryo transfer increases the likelihood of live birth in obese patients

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INTRODUCTION

Several protocols to prepare the endometrium for frozen embryo transfer have been described with comparable clinical outcomes with no individual protocol demonstrated to be superior and no specific patient group defined that can benefit from a natural endometrial preparation.

Despite obesity being linked to adverse clinical outcomes, observational studies and clinical trials have traditionally included participants with normal weight. Therefore, studies focusing on endometrial preparation protocols for frozen embryo transfer that include obese patients are required.

MATERIALS AND METHODS

Retrospective dataset including 975 single euploid frozen embryo transfer cycles performed at two tertiary referral centers between 2017 and 2019. Primary outcome was live birth after natural and artificial endometrial preparation.

Participants were stratified into three groups, G1: Normal-weight ≤24.9, G2: Overweight 25 to 29.9, and G3: Obese ≥30.

PGT-A was performed after trophectoderm biopsy using NGS. Spontaneous LH rise from blood samples confirmed ovulation for natural preparation and embryo transfer occurred five days after initial progesterone elevation.

For artificial preparation, embryo transfer was performed after oral estradiol and 120-hour vaginal progesterone exposure. All participants received luteal phase support.

RESULTS

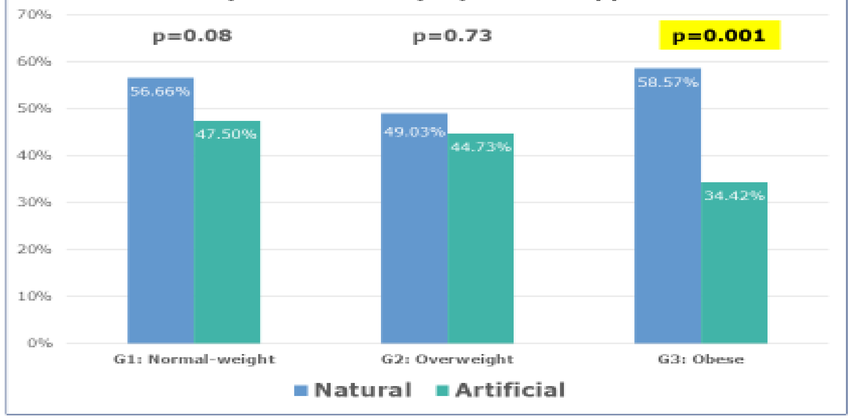
Descriptive analysis for age and implantation rate within BMI groups is shown in Table 1.

When a natural preparation was conducted live birth rates remained constant across BMI groups: G1 [56.66% (n=85/150)], G2 [49.03% (n=51/104)], and G3 [58.57% (n=41/70)].

Live birth rates decreased in G3 when an artificial endometrial preparation was performed: G1 [47.5% (n=114/240)], G2 [44.73% (n=102/228)], and G3 [34.42% (n=63/183)].

Univariate logistic regression analysis showed a statistically significant difference in live birth rates (Figure 1) when a natural endometrial preparation was conducted in G3 (OR 2.69, 95% CI 1.53-4.74; p=0.001), with no differences found in G1 (OR 1.45, 95% CI 0.96- 2.18; p=0.08) and G2 (OR 1.19, 95% CI 0.75-1.89; p=0.73).

Figure 1.
Live birth rates
by endometrial preparation approach



CONCLUSIONS

Obese women appear to be the patient group that can obtain benefit from a natural endometrial preparation for frozen embryo transfer by increasing the odds of live birth.

Table 1. Descriptive analysis for age and implantation rate per BMI group

BMI Group		Endometrial preparation: Natural	Endometrial preparation: Artificial	p value
G1: Normal-weight n=390		n=150	n=240	
	Age (years) Mean±SD	33.5±5.1	32.7±5.2	p=0.13
	Implantation Rate(%)	60	57.1	p=0.57
G2: Overweight n=332		n=104	n=228	
	Age (years) Mean±SD	34.5±4.9	33.9±5.8	p=0.39
	Implantation Rate(%)	54.8	55.7	p=0.88
G3: Obese n=253		n=70	n=183	
	Age (years) Mean±SD	35.6±4.9	34.3±5.6	p=0.1
	Implantation Rate(%)	64.3	51.4	p=0.07

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Identifying patients benefiting from delayed-matured oocytes insemination

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Objective

Are there any predictive factors supporting the decision of inseminating delayed-matured oocytes?

Design

This observational study was performed at ART Fertility Clinics, Abu Dhabi, UAE, between January 2019 and June 2021. A total of 5454 cumulus oocytes complexes (COC) were retrieved from 469 ovarian stimulation cycles. Out of the retrieved COCs, 3473 oocytes were immediate at metaphase II (MII-D0), and 915 were delayed-metaphase II oocytes (MII-D1).

Material and Method

Patients with primary and secondary infertility undergoing Controlled ovarian stimulation (COS) in standardized protocols for IVF/ICSI treatment were included. Ovum pick up performed 34-36h post final oocyte maturation trigger shot (TS). Insemination was done 39-41h post TS for the MII-D0, while MII-D1 ICSI was performed 63-68h post TS.

All cycles were planned for Preimplantation Genetic Testing for Aneuploidies (PGT-A) at blastocyst stage using Next Generation

Results

Fertilization rates significantly differed between MII-D0 and MII-D1 oocytes (69.54% vs 55.96%, p<0.001, respectively). Blastocyst utilization rates were significantly higher in MII-D0 group compared to MII-D1 group (59.47% vs 18.52%, p<0.001). However, no difference was observed in the rate of euploid blastocysts between MII-D0 and MII-D1 (46.3% vs 39.0%, p=0.163) (Figure 1).

As identified by univariant logistic regression analysis, the following parameters augmented the chances of obtaining at least 1 blastocyst for biopsy when MII-D1 were injected: AMH (OR 1.15, p<0.001), number of COCs collected (OR: 1.03, P=0.005), maturation rate on day0 (OR: 0.19, P=0.001). When the multivariant analysis model was applied, AMH and maturation rate on day0 remained significant factors predicting the success of inseminating delayed-matured oocytes (OR:1.15, [CI:1.00-1.32], p=0.045); OR:0.06, [CI:0.03-0.31], p<0.001, respectively), with cut off values of AMH >2.52 ng/ml and maturity rate of ≤59%, being identified by ROC analysis. (Table 1)

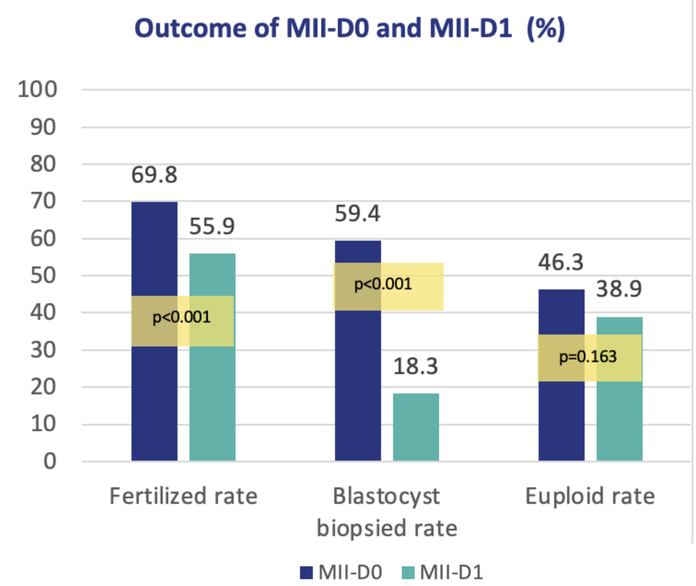

Figure 1: Outcomes of MII-D0 and MII-D1

ROC result for predicting Success						
Parameters	**Cut off value**	**AUC**	**95% CI**	**p**	**Sensitivity**	**Specificity**
Age	≤35	0.584	0.538 to 0.629	0.016	64.3	57.0
AMH	>2.55	0.636	0.594 to 0.684	<0.001	57.4	69.0
MR_day0	≤0.59	0.637	0.893 to 0.682	<0.001	61.4	60.0
Total maturation rate per cycle	≤0.83	0.571	0.528 to 0.619	0.058	55.7	58.0
fertilization rate MII	≤0.725	0.531	0.462 to 0.612	0.319	56.0	53.0

Table 1: ROC Curve and Cut-off Values

Conclusion

The results of this study might provide guidance to the IVF laboratories for targeting the patient population who would benefit from MII-D1 ICSI without adhering to unnecessary costs and workload.

Poster number: P-201

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Do ovarian reserve markers and female age predict euploidy rate in IVF/ICSI cycles?

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Objective

The value of Anti-Mullerian hormone (AMH) and antral follicular count (AFC) as quantitative markers of ovarian reserve is well established. However, their association with embryo ploidy remains controversial. We aimed to evaluate the association of maternal age, AMH and AFC with the rate of euploid blastocysts.

Material and Methods

Retrospective study of 10,556 blastocysts after preimplantation genetic testing for aneuploidy (PGT-A) with Next Generation Sequencing (NGS), obtained from 2,564 IVF/ICSI cycles of infertile couples at ART Fertility Clinics (UAE) from November 2016 to December 2020. Mosaic and non-informative embryos were excluded. Serum AMH was measured by Elecsys® assay (Roche®). Ethical approval was obtained from the Research Ethics Committee (REFA023b).

Results

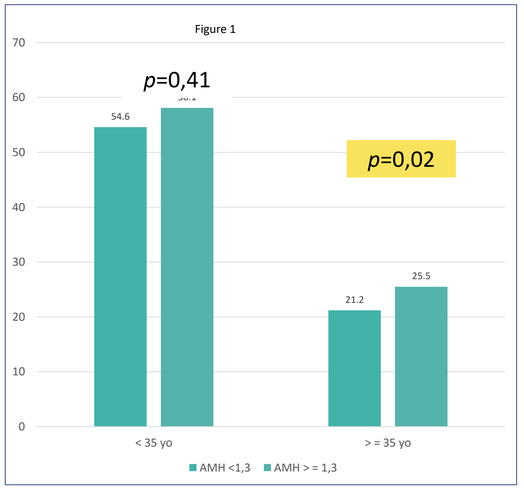
Patient characteristics are described in Table 1. A significant negative Pearson correlation coefficient was found between age and euploidy rate (ρ=-0.5398, p<0.001). AMH, AFC and total of MII showed a significant positive Pearson correlation coefficient with euploid rate (AMH: ρ=0.2076, p<0.001; AFC: ρ=0.2578, p<0.001; MII: ρ=0.2036, p<0.001) (Table 2). Linear regression analysis was conducted to evaluate the predictability of the variables on euploid rate. As expected, age clearly had a negative impact (Coef±SE=-3.10±0.10, p<0.0001). A positive effect was observed for AMH (Coef±SE=2.75±0.31, p<0.0001), AFC (Coef±SE=1.16±0.09, p<0.0001), MII (Coef±SE=1.10±0.10, p<0.0001) and 2PN embryos (Coef±SE=1.43±0.13, p<0.0001). When patients were evaluated per age categories, patients ≥35 years old with AMH<1.3 ng/mL showed significantly lower euploid rate compared to same age category and AMH>1.3 ng/mL (21.2% vs 25.5%, p=0.0192) (Figure 1).

Table 1

	Mean ± SD	Range
Age	34.72 ± 6.13	18-50
AMH (ng/ml)	2.52 ±2.70	0,01-23
AFC	11.57 ± 7.86	0-61
BMI (kg/m^2)	28.57 ± 4.83	14,3-44.9
MII inseminated (n)	10.11 ± 6.53	1-50
Blastocyst (n)	4.12 ± 3.21	1-26
Euploid rate per cycle %	39.42 ± 35.24	0-100

Table 2

	Correlation for euploidy rate		Linear regression for euploidy rate	
	Pearson´s coeff	p value	Coeff ± SE	p value
Age	- 0,5398	<0,001	-3,10 (±- 0,1)	<0,001
AMH	0,2076	<0,001	2,75 (±-0,31)	<0,001
AFC	0,2578	<0,001	1,16 (±-0,09)	<0,001



Conclusion

Age, AMH, AFC and total MII collected are significantly associated with the rate of euploid blastocysts. Patients ≥35 years and AMH>1,3ng/mL have a higher chance of having an euploid blastocyst than patients ≥35 years with AMH <1,3.

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Impact of systemic FSH levels on the embryo ploidy status in ovarian stimulation for IVF/ICSI

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Study Question: Does systemic serum FSH level per mature oocyte (FSH/MII) on the day of final oocyte maturation affect the ploidy status of the embryo cohort?

Introduction: In ovarian stimulation cycles, follicular phase **systemic FSH levels** have to be kept above a certain threshold to achieve and maintain **multifollicular growth**. This contrasts the natural pattern, where FSH declines steadily in the later follicular phase as a result of the increasing E2 level. Until now, it is unclear, whether this unphysiological pattern of the systemic FSH course has an influence on the **ploidy status** of the biopsied blastocysts.

Results: Patients had a mean **Age** (±SD) of 30.49 ± 4.99 years, **BMI** of 27.58 ± 5.14 kg/m2, **AMH** of 3.05 ng/ml and 17.54 ± 8.63 **oocytes** were collected at OPU. **FSH levels at DoT** revealed a wide range of systemic levels, from 2.12 – 47 IU/L.

Table 1. Significant correlations (blue negative and turquoise positive) found between Euploid Rate and stimulation parameters in the univariate (**A**) and multivariate analysis (**B**).

A

Euploid Rate	Univariate-Model 1				
	Coef.	Std. Err.	P>t	[95% Conf.	Interval]
FSH trigger	**-0.652**	0.234	*0.006	-1.112	-0.191
FSH (per MII)	**-3.194**	0.753	**0.000	-4.674	-1.715
E2 trigger (per 100)*	-0.059	0.114	0.604	-0.284	0.165
P4 trigger	2.125	1.478	0.151	-0.778	5.029
LH trigger	0.022	0.280	0.936	-0.527	0.572
E2 basal	-0.077	0.080	0.336	-0.233	0.080
P4 basal	12.554	9.742	0.198	-6.584	31.692
LH basal	0.073	0.395	0.853	-0.704	0.850
FSH basal	**-1.605**	0.650	*0.014	-2.883	-0.327
AFC basal	**0.416**	0.188	*0.027	0.047	0.785
Total follicle count at DoT	**0.507**	0.185	*0.006	0.145	0.869
Age	**-1.055**	0.243	**0.000	-1.532	-0.579
BMI	0.058	0.244	0.811	-0.421	0.537
AMH	0.244	0.407	0.549	-0.555	1.044
Duration of stimulation (days)	-0.477	0.789	0.546	-2.028	1.073
Stimulation dose (per 100)*	**-0.477**	0.163	*0.003	-0.796	-0.157

B

Euploid Rate	Multivariate-Model 2 (backward, eliminated vars p>0.2)				
	Coef.	Std. Err.	P>t	[95% Conf.	Interval]
FSH (per MII)	**-3.051**	1.060	*0.004	-5.134	-0.967
Age	**-0.940**	0.279	*0.001	-1.489	-0.391
AFC basal	0.038	0.246	0.878	-0.445	0.520

Variables of Significance (*p ≤ 0.05, **p ≤ 0.001).

Design, Material & Methods: Retrospective study including **582 cycles** between **March 2017-December 2020**. Patients with primary/secondary infertility and indication for ovarian stimulation for IVF/ICSI with PGT-A were included. All GnRH antagonist stimulation cycles used only **recombinant FSH** as gonadotropin.

Stimulation cycles were monitored by ultrasound and repeated measurement of **FSH**, **E2**, **P4** and **LH** throughout the cycle. The **FSH/MII ratio** was calculated as the ratio of the systemic FSH level on the day of trigger (DoT) to the total number of MII after denudation. Patients aged between 19-48. All embryos underwent **PGT-A by NGS** with trophectoderm biopsy. Patients with surgical sperm extraction or warmed oocytes were excluded.

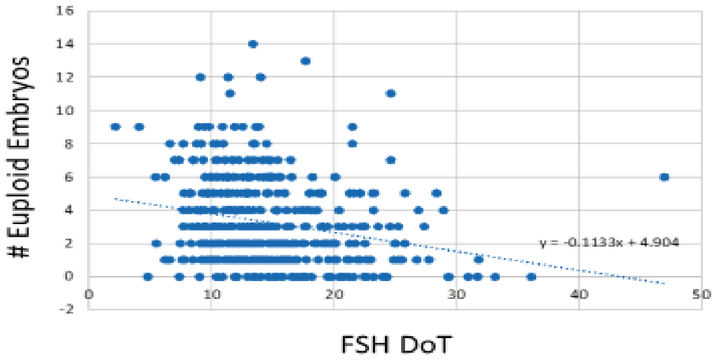

Figure 1. Relationship between FSH levels at DoT and total number of euploid embryos obtained per cycle.

Conclusion:

The retrospective character of this study can be seen as a limitation as well as the fact that the results cannot be translated to patients using either only HMG, or a combination of recombinant FSH and HMG for ovarian stimulation.

Higher **FSH/MII ratios** are associated with a decreased euploid rate in the embryo cohort. FSH level measurements should be introduced into ovarian stimulation monitoring, as the gonadotropin dosage might be adjusted according to its systemic level. This represents a further step on treatment individualization towards a more personalized medicine.

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Effect of endometrial thickness on biochemical pregnancy rate: an analysis of 1534 frozen euploid embryo transfers

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Objective

Higher Endometrial Thickness (EMT) prior to embryo transfer is associated with better clinical outcomes in general, like higher implantation and livebirth, and lower miscarriage rates. But up to our knowledge, no studies evaluated the effect of EMT on Biochemical Pregnancy (BP) per say. Can a thick endometrial lining measured prior to embryo transfer be considered a protective factor against BP?

Material and Methods

This is a two-center retrospective observational study including a total of 1534 euploid Frozen Embryo Transfer (FET) cycles between March 2017 and March 2020 at ART Fertility Clinics Muscat, Oman and Abu Dhabi, UAE. BP is defined as blood beta-hCG >15 mIU/ml on day 12 post FET, that is progressively decreasing, with no evidence of gestational sac on ultrasound.

The study group consisted of 112 cases of BP, while the control group consisted of the remaining 1422 FET's that led to different clinical outcomes. EMT was measured by transvaginal ultrasound on the day of progesterone rise (±1 day); that rise was either spontaneous in Natural Cycles (NC), or iatrogenic in Hormone Replacement Therapy (HRT) cycles. Euploidy status of the embryos was assessed by NGS analysis of trophectoderm biopsies. Bivariate and multivariate analyses were conducted.

Variables	Biochemical pregnancy (%)		
	No	Yes	p (t-test)
Age	33.4	33.26	0.4
BMI	27.06	27.67	0.1064
AMH	3.45	3.69	0.207
# of Embryos Transferred			
1	92.17	7.83	0.285
2	93.65	6.35	
Blastocyst Expansion			
BL3	92.88	7.12	0.957
BL4	92.87	7.13	
BL5	92.48	7.52	
ICM Grade			
A	93.37	6.63	0.325
B	92.96	7.04	
C	90.1	9.9	
Trophectoderm Grade			
A	92.62	7.38	0.055
B	93.85	6.15	
C	89.75	10.25	
Day of Biopsy			
5	92.59	7.41	0.605
6	93.2	6.8	
7	88	12	
Presence of Blood			
No	92.35	7.65	0.312
Yes	93.98	6.02	
Presence of Mucus			
No	92.27	7.73	0.099
Yes	95.52	4.48	
Cycle Preparation			
HRT	91.58	8.42	0.015
NC	95.01	4.99	
Parity			
Nulliparous	94.61	5.39	0.014
Previous Livebirth	91.3	8.7	

Table 1: Bivariate Analysis

Results

There was no difference in mean EMT between the study and the control groups (7.55 vs. 7.68 mm, p=0.154). Looking at the association of different variables with the rate of BP *(table 1)*, there was no effect of age, BMI, AMH, number of embryos transferred, degree of blastocyst expansion, inner cell mass or trophectoderm grade, day of biopsy, nor presence of blood or mucus on the transfer catheter. However, patients on HRT cycles had significantly higher rates of BP compared to NC (8.42% vs. 4.99%, p=0.015). Also, those with a previous livebirth had higher rates of BP compared to nulliparous women (8.7% vs. 5.39%, p=0.014).

The distribution of BP showed that 54.5% occurred with EMT <7.5 mm, 34.8% with EMT 7.5-9 mm, and 10.7% with EMT >9 mm. These represents respectively 8.16%, 6.68%, and 5.94% of the total sample. This decreasing trend of BP with increasing EMT didn't reach statistical significance (p=0.429). Univariate analysis comparing the risk of BP in FET's done with lower and higher EMT to those performed at 7.5-9 mm yielded similar conclusion: OR=1.24 [0.82-1.88] for <7.5 mm, and OR=0.88 [0.45-1.72] for >9 mm.

Controlling for different confounders, HRT cycles and multiparity remained as independent risk factors for BP *(table 2)*.

7.5-9 mm (reference)	Odds Ratio [95% CI]	Std. Err.	p>z
<7.5 mm	1.18 [0.77 – 1.80]	0.25	0.441
>9 mm	0.89 [0.45 – 1.76]	0.31	0.740
Cycle Preparation (HRT reference)			
NC	0.56 [0.35 – 0.88]	0.13	0.013
Nulliparity (reference)			
Previous Livebirth	1.79 [1.18 – 2.71]	0.38	0.007

Table 2: Multivariate Analysis

Conclusion

The risk of BP is independent of EMT, but rather dependent of the type of endometrial preparation and parity.

The reduced adverse clinical outcomes with NC shed light on the role of the corpus luteum in the early phases of implantation, and some potential secreted mediators other than progesterone. Besides, the effect of previous deliveries on the endometrium and its receptivity needs further investigation.

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