Endometrial thickness, endometrial preparation protocol and number of euploid embryos transferred, significantly impact the live birth in frozen embryo transfer cycles

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Study question

Is the live birth rate (LBR) in euploid frozen embryo transfer (FET) cycles affected by the endometrial thickness (EMT)?

Design

This was a two-center retrospective observational study including euploid FET cycles between March 2017 and March 2020 at ART Fertility Clinics Muscat, Oman and Abu Dhabi, UAE.

Material and Methods

Trophectoderm biopsies were analyzed with Next Generation Sequencing (NGS). Vitrification/warming of blastocysts was performed using Cryotop method (Kitazato). EMT was measured by vaginal ultrasound prior initiating the progesterone administration (± 1 day) and LBR was recorded. Univariate analysis was performed for the categorical variables to compare patients with live birth with no live birth. The significant variables were used to build a multinomial regression model.

Results

A total of 1522 FET cycles were analyzed: 975 single embryo transfer (SET) and 547 double embryo transfer (DET). The mean age of the patients was 33.38 years with a mean BMI of 27.1 kg/m^2. FET were performed in EMT ranging from 3 to 15 mm and 50.52% resulted in a live birth. Though potentially all ranges of EMT were associated with LB, the median EMT in patients with LB was significantly higher than the median EMT of patients without LB (7.6 mm vs. 7.4 mm; p < 0.001) (Fig.1).

The dataset was stratified into two groups based on the median EMT (7.5 mm): < 7.5 mm (n=744 cycles) and ≥ 7.5 mm (n=778 cycles). A significantly higher live birth rate was observed in ≥ 7.5 mm group (46.24% vs. 54.63%. p=0.0012) (Fig.2).

In multivariate analysis, EMT, FET endometrial preparation protocol, and number of embryos transferred were the main parameters influencing the chance to achieve LB: OR 1.10 [1.01-1.19], p<0.015 for the EMT; OR 1.84 [1.47-2.30], p<0.0001 for Natural Cycle protocol and OR 1.55 [1.25-1.93], p<0.0001 for DET. Intercept 0.18 [0.07-0.44] p<0.0002. Female age did not reach significance: OR 1.02 [1.00-1.04], p=0.056 (Fig.3).

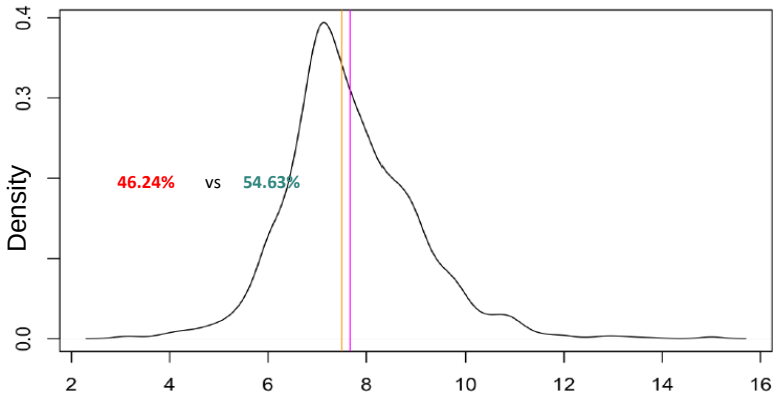

Figure 2. The density of distribution for EMT in X axis (N=1522. Median= 7.5 mm, orange line. Mean = 7.7 mm, pink line.

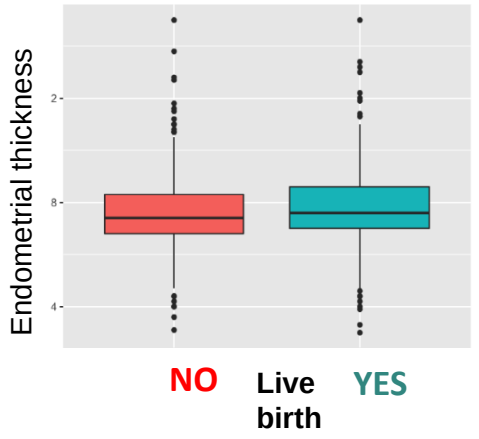

Figure 1: Box-Plot graph representing EMT in the group of live birth and no live birth.

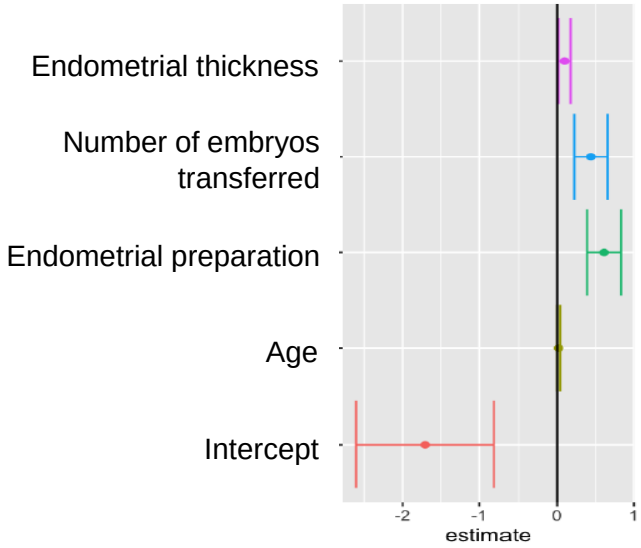

Figure 3: Multinomial regression model to predict live birth.

Conclusion

Patients with an endometrial thickness above the median (7.5 mm), have a significantly higher chance to obtain a livebirth.

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Antimüllerian Hormone (AMH) as a predictive marker of cycle ploidy outcome

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Objective

To determine whether AMH value is a predictive marker of blastocyst formation and/or cycle ploidy outcome.

Design

A retrospective analysis was performed between March 2017 and July 2020 at ART Fertility Clinics (Abu Dhabi) including all couples that were triggered for final oocyte maturation and planned for Preimplantation Genetic Testing for Aneuploidies (PGT-A). Patients were stratified into four age categories [≤30, 31-35, 36-40, >40 years]. For each age category patients were further divided into three AMH groups: ≤0.65ng/ml, 0.65-1.3ng/ml, 1.31-6.25ng/ml (reference group).

Materials and Methods

Trophectoderm biopsy samples were subjected to Next Generation Sequencing. AMH serum levels (ng/ml) were determined using the commercial fully automated Elecsys® (Roche) assay. Patients with a Progesterone rise of >1.5ng/ml on the day of final oocyte maturation and patients with AMH values >6.25ng/ml were excluded from the analysis. Per patient who was triggered, the chance to have at least one euploid blastocyst in that cycle, was calculated.

Results

A total of 1.300 couples were included. The mean values were maternal age 35.6±6.2 years, AMH 2.1 ±1.5ng/ml and body mass index 27.5±5.0 kg/m^2.

The chance to have at least one blastocyst biopsied per cycle was affected in all patients with extreme low AMH (≤0.65ng/ml), compared to the reference group and irrespective of age **(Figure 1).**

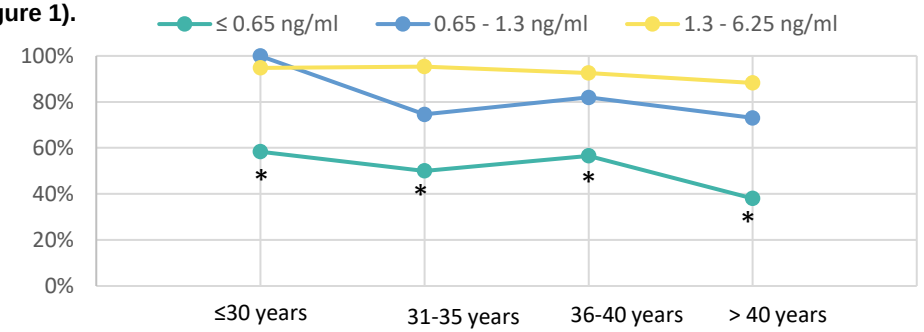

Figure 1- Probability (%) to have at least one blastocyst biopsied. * p<0.001 AMH

In all age categories, patients with ≤0.65 ng/ml AMH values had a significantly reduced probability of having a euploid blastocyst compared to the reference group (1.31-6.25 ng/ml) **(Table 1).**

Age/AMH	≤0.65ng/ml	0.65-1.3ng/ml	1.31-6.25ng/ml	OR [CI 95%]	p value
≤30 years	41.67%	85.19%	88.89%	0.01 [0.03-0.30]	p<0.001
31-35 years	43.75%	52.73%	88.09%	0.10 [0.05-0.23]	p<0.001
36-40 years	21.74%	56.63%	77.67%	0.08 [0.04-0.15]	p<0.001
>40 years	6.45%	22.22%	29.42%	0.16 [0.08-0.36]	p<0.001

Table 1- Probability (%) to have at least one euploid blastocyst. OR=Odds ratio, CI= confidence of interval.

The chance to have at least one blastocyst biopsied per cycle was affected in all patients with extreme low AMH (≤0.65ng/ml), compared to the reference group and irrespective of age, p<0.001. Woman within AMH range of 0.65-1.3ng/ml presented the same decreased probability of having a euploid blastocyst only when 31-35 (52.73%, n=55) or 36-40 years old (56.63%, n=83) (OR 0.15 [0.08-0.29], p<0.001 and OR 0.37 [0.22-0.64], p<0.001, respectively **(Figure 2**).

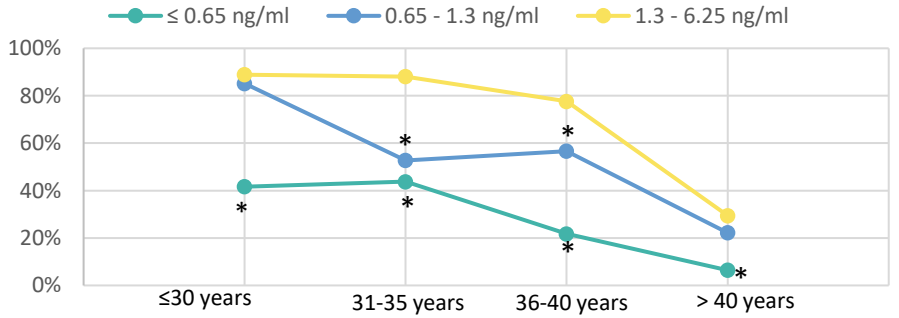

Figure 2- Probability (%) to have at least one euploid blastocyst. * (p<0.001)

Conclusion

AMH is a clear biomarker of oocyte-embryo competence. Incorporation of AMH-specific counseling recommendations into clinical practice guidelines, could lead to a more informed guidance on cycle ploidy outcomes, rather than age alone.

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Blastocyst biopsy day does have an impact on clinical pregnancies in different frozen embryo transfer (FET) regimens: natural cycle (NC) versus hormone replacement therapy (HRT).

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Study question

Do euploid blastocysts biopsied on day (D) 5 or D6 differ in clinical pregnancy rates (CPR) when single FET is performed in NC or HRT cycles?

Participants/materials, setting, methods

An observational retrospective study was performed including 1027 single euploid FET with blastocysts biopsied on D5 or D6. In NCs, vaginal progesterone (P4) was administrated after ovulation. For HRT cycles, oral estradiol was administrated starting on day 2 or 3 of menses. When endometrial thickness was at least 6 mm, P4 was added. All FET were performed on the 5th day of P4 administration as shown in Figure 1. Clinical pregnancy was recorded with the presence of an intrauterine gestational sac.

Main results and the role of chance

Women's mean age was 33.8 ± 5.5 years. The distribution of D5 and D6 and the endometrial preparation (EP) of the FET cycles is shown in Table 1.

Table 1: Distribution of EP protocols on D5 and D6.

FET characteristics	Cycles (N=1027)
D5 FET cycles (n)	651
NC (%)	37.6
HRT (%)	62.4
D6 FET cycles (n)	376
NC (%)	43.1
HRT (%)	56.9

CPR and miscarriages rates (MR) of FET cycles according to the day of biopsy (D5 vs. D6) or type of endometrial preparation protocol used (NC vs. HRT) are shown in Table 2 and Table 3.

Figure 1: Endometrial preparation (EP) protocols: NC (left) and HRT (right).

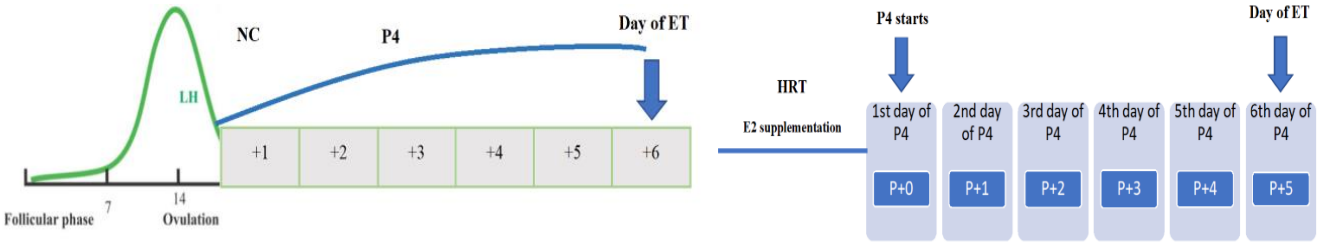


Table 2: Clinical pregnancy rates (CPR).

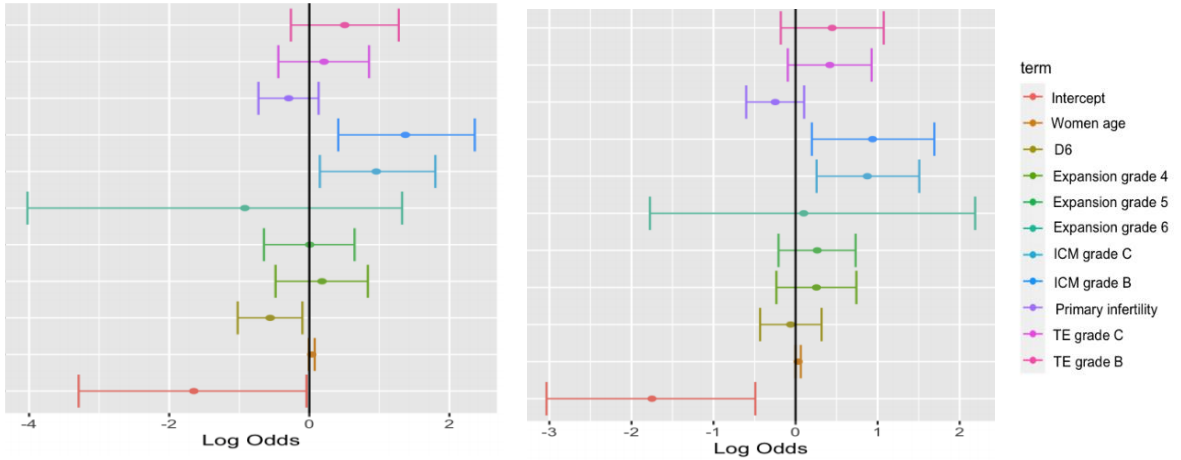
CPR %	D5	D6	OR [95% CI]	p value
NC	66.9%	50.5%	0.49 [0.32–0.75]	<0.001
HRT	64.3%	58.4%	0.78 [0.54–1.11]	0.164

Table 3: Miscarriage rates (MR).

MR %	D5	D6	OR [95% CI]	p value
NC	10.9%	3.7%	0.23 [0.04–0.83]	0.019
HRT	18.7%	20.8%	1.01 [0.58–1.71]	1.007

From a multilogistic regression model including confounding factors (Figure 2), day of blastocyst biopsy and inner cell mass (ICM) in NC and exclusively ICM in HRT cycles were statistically significant.

Figure 2: Multilogistic regression model for NC (left) and HRT (right).



Summary Answer

In FET cycles, EP protocols should be based on the day of blastocyst biopsy as euploid D5 blastocysts have higher CPR than D6 in NC, while outcomes are comparable in HRT cycles.

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P-359 Blastocyst quality, transfer difficulty and endometrial thickness affect clinical pregnancy after frozen embryo transfer (FET) of euploid blastocysts in the upper uterine cavity.

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Objective

To study which factors affect the clinical pregnancy rate (CPR) after single euploid frozen embryo transfers (FET), when the blastocyst is transferred in the upper uterine cavity area.

Design

This single center retrospective cohort study included a total of 603 single euploid FET cycles, in which the embryo was transferred in the upper half of the uterine cavity, between January 2019 and November 2020 in ART Fertility Clinic Abu Dhabi, UAE. Trophectoderm biopsy samples were subjected to Next Generation Sequencing to screen the ploidy state. Vitrification and warming were performed using the Cryotop method (Kitazato, Biopharma).

Materials and Methods

Embryo transfer was performed under abdominal ultrasound guidance. After the embryo was released, the full length of the uterine cavity (from the highest point of the endometrial reflex in the fundus region until the inner cervical os) and the longitudinal distance between the fundal endometrial surface and the air bubble, were measured. The following explanatory variables were analyzed to evaluate their influence on the clinical pregnancy: age, Anti Müllerian hormone (AMH), body mass index (BMI), endometrial thickness (EMT), quality of the blastocyst (Top, good, fair and poor), difficulty of the transfer (requirement of additional instrumentation), presence of mucus or blood on the transfer catheter, day 5 or day 6 biopsy, type of endometrial preparation.

Results

The patients were on average 33.9 (range 19-46) years old. The FET was performed in a Natural Cycle (NC) (n=278) or in a Hormonal Replacement Therapy (HRT) cycle (n=325). Of the 603 transfers which had been performed in the upper half of the uterus, 412 (68.3%) resulted in a pregnancy and 311 (51.5%) in a clinical pregnancy. After bivariate analysis, the clinical pregnancy rate was significantly higher for high quality blastocysts (grade 1-2 versus 3-4) ($p<0.001$), after embryo transfers without the need for additional instrumentation ($p=0.001$) and for higher EMT ($p=0.027$).

After performing a multivariate logistic regression analysis to consider the effect of all explanatory variables, the clinical pregnancy was affected by the EMT: OR 1.20 [1.05-1.37], p=0.007; transfer difficulty: OR 0.44 [0.25-0.79], p=0.006; blastocyst quality 3: OR 0.38 [0.18-0.79], p=0.01 and blastocyst quality 4: OR 0.15 [0.06-0.37], p<0.0001 (Table 1). Age did not affect the clinical pregnancy after transferring a single euploid blastocyst: OR 1.03 [1.00-1.06], p=0.052.

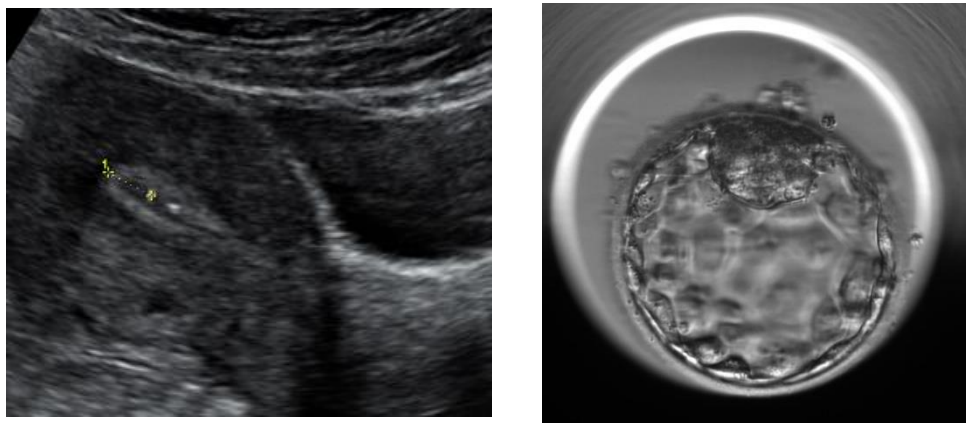

Figure 1: Embryo transfer in the upper uterine cavity (left) and Top-quality blastocyst (right).

	OR	95%CI	P value
Endometrial Thickness	1.202	[1.052-1.372]	0.007
Embryo quality, Good	0.860	[0.505-1.464]	0.60
Embryo quality, Fair	0.383	[0.184-0.796]	0.01
Embryo quality, Poor	0.153	[0.063-0.368]	<0.0001
ET Difficulty	0.448	[0.253-0.793]	0.006

Table 1: Multivariate logistic regression analysis OR = odds ratio, 95% CI = 95% confidence interval. For embryo quality comparison, top quality embryo is our reference.

Conclusion

Optimization of clinical pregnancy outcomes after FET depends on multiple factors. Even after transfer of euploid blastocysts in the upper uterine cavity, the endometrial thickness, transfer difficulty and blastocyst quality will still affect the clinical pregnancy outcomes.

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Ovarian reserve parameters and ovarian stimulation outcome for IVF/ICSI are influenced by ethnicity

P-723

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Objective

To compare whether ovarian reserve parameters and the outcome of ovarian stimulation for IVF / ICSI is influenced by ethnicity.

Design

Prospective observational study, performed in 10 infertility centers worldwide (Europe (4 centers), Middle East North Africa (MENA) region (2 centers), Iran (2 centers), South America (1 center), India (1 center)) between May 2019 and September 2020, evaluating ovarian reserve and outcome parameters of ovarian stimulation treatments for IVF/ICSI.

Materials and Methods

Couples with primary / secondary infertility and an indication for an IVF/ICSI treatment were included into this study. Besides anamnestic data regarding the history of the infertility and self-reported ethnicity (Arab, Caucasian, Hispanic, Others, Persian and South Asian), data obtained during the basic fertility assessment on the ovarian reserve parameters (Antral follicle count (AFC) and Anti-Müllerian-Hormone (AMH)) as well as stimulation parameters from the ovarian stimulation treatment were collected and analyzed.

Results

ETHNICITY	NUMBER / % N = 1033	AMH (ng/ml) mean, SD and [95%CI]	AFC (n) mean, SD and [95%CI]	RETRIEVED OOCYTES (n) mean, SD and [95%CI]
ARAB	222 / 21.5	3.33±0.19 [2.95-3.71]	15.52±0.53 [14.49-16.55]	14.08±0.61 [12.88-15.27]
CAUCASIAN	164 / 15.9	2.03±0.25 [1.55-2.52]	12.00±0.67 [10.69-13.31]	9.84±0.71 [8.44-11.24]
HISPANIC	52 / 5	2.43±0.74 [0.97-3.88]	12.69±1.08 [10.57-14.81]	7.94±1.26 [5.48-10.41]
OTHERS	12 / 1.2	2.76±0.96 [0.88-4.64]	15.11±2.60 [10.01-20.21]	9.92±2.62 [4.78-15.05]
PERSIAN	345/ 33.4	3.10±0.16 [2.79-3.41]	13.58±0.42 [12.75-14.41]	10.83±0.49 [9.87-11.79]
SOUTH ASIAN	238 / 23	3.62±0.19 [3.25-3.98]	13.49±0.51 [12.49-14.48	17.06±0.59 [15.90-18.21

Univariate analysis of AMH, AFC and retrieved oocytes with the ethnicities revealed highly statistically significant differences for AMH and retrieved oocytes ($p < 0.001$, respectively) and significant differences for AFC ($p = 0.0014$).

As age is a major confounder for the ovarian reserve, multivariate analyses were performed. After adjusting for age, AMH was significantly different between Arab-Persian, Arab-South Asian and Arab-Caucasian ($p < 0.001$, $p < 0.001$, $p = 0.002$) and AFC statistically significant between Arab and all other ethnicities. For retrieved oocytes, besides age, also the stimulation-dosage and -duration was taken into account. Highly statistically significant differences were found for the groups Arab-Persian and Arab-Caucasian and no differences towards the other ethnical groups.

Conclusion

Ethnicity influences ovarian reserve parameters and the outcome of ovarian stimulation for IVF / ICSI

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Preimplantation Genetic Testing for Aneuploidies (PGT-A) and pregnancy outcome

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Study question

Frozen embryo transfer (FET) of euploid blastocysts in hormone replacement therapy (HRT) or natural cycle (NC): are there differences in obstetric, fetal and neonatal outcomes?

Study Design

An observational, retrospective study was conducted between March 2015 and November 2019 in patients with singleton pregnancies after ART with PGT-A/FET/HRT and NC. A total number of 353 patients from two fertility centres (ART Fertility Clinics Dubai and Abu Dhabi, UAE), were included. They were divided into two groups according to the endometrial preparation for FET: group A: HRT (n=225) and group B: NC (n=128). The following pregnancy outcomes were recorded: Gestational Diabetes Mellitus (GDM), preeclampsia and hypertension, obstetric cholestasis, placental abnormalities, mode of delivery, preterm delivery, gestational age at delivery, birth weight, fetal abnormalities and admission to Neonatal Intensive Care Unit (NICU).

Results

There were no statistically significant differences in maternal and demographic characteristics of the studied groups. The mean maternal age was 34.05 (20-45) and 34.26 (23-47) years for group A and B, respectively. The mean BMI was 28.31kg/m² (17.93-43.76) versus 27.93 (17.32-43.18). The ratio of nulliparous versus multiparous patients was 1:1 for both groups. Majority of the patients in both groups were of Arab ethnicity. The number of patients recorded as smokers was low and comparable in the groups. The mean gestational age at the time of delivery was comparable: 37.64 gestational weeks (24-41) versus 37.76 (26-41). The Caesarean section rate was around 50% for both groups. The rate of preterm delivery was comparable in both groups (16.9% and 18.8% for group A and B, respectively).

There was no detectable difference in the distribution of the birth weight in both groups with a median weight of 3000 grams of which 13.6% were low birth weight. In the studied groups, 30.5% had pregnancy complications with no observed statistically significant differences when the groups were compared (table 1). There was no increased incidence of fetal abnormalities. Admission to NICU was comparable and was related to prematurity.

	Group A (n= 225)	Group B (n=128)	p - value
Gestational diabetes mellitus n (%)	45 (20%)	33 (25.8%)	0.23
Preeclampsia, Hypertension n (%)	14 (6.2%)	10 (7.8%)	0.66
Obstetrics cholestasis n (%)	1 (0.4%)	2 (1.6%)	0.29
Placenta abnormalities n(%)	3 (1.3%)	0	0.55

Table 1. Pregnancy complications.

Conclusion

In patients with FET of a euploid blastocyst after PGT-A, the type of FET treatment preparation (HRT or NC) has no significant effect on pregnancy complications, birth weight and fetal abnormalities.

The findings of the present study could be used to improve prenatal counselling for women undergoing ART with PGT-A.

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P-21-0906

Should intracytoplasmic sperm injection (ICSI) on delayed mature oocytes become a routine practice in the IVF Laboratory?

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Objective

To determine wither delayed mature oocytes result in similar euploid blastocyst rates as their immediate mature sibling oocytes .

Design

A single center retrospective sibling oocyte study was performed between January 2019 and December 2020 at ART Fertility clinics Abu Dhabi, UAE. A total of 345 PGT-A cycles, with at least one delayed mature oocyte inseminated by ICSI, were included: 2506 immediate mature oocytes and 669 delayed mature oocytes.

Material and Methods

Following controlled ovarian stimulation, MII oocytes at time of denudation were inseminated by ICSI/IVF (immediate mature). Immature oocytes (MI/GV) were cultured for 16-24 hours in fertilization medium and injected the next day if mature (delayed mature). Trophectoderm biopsy was performed on day 5/6/7 and samples were subjected to Next Generation Sequencing to screen the ploidy state of the blastocyst.

Results

The characteristics of the 345 cycles are presented in **Table 1**. On the day of oocyte retrieval (day 0), 2506 MIIs were inseminated, while 669 delayed mature oocytes were inseminated on day 1. Normal fertilization rate was significantly higher for the immediate mature oocytes compared to delayed mature oocytes (68% vs 56%, p<0.0001). Similarly, usable blastocyst rate was significantly higher for immediate mature oocytes (59% vs 19%, p<0.0001).

Group characteristics	Cycles (N=345)
Mean age (years old)	36.2±6.12
Mean BMI	27.9±5.0
Mean AMH	2.4±3.0
Day 0 Metaphase II (Immediate MII)	2506
Delayed Marure oocytes	669

Table 1: Cycle characteristics: Patient's age, BMI and AMH are expressed as mean±standard deviation.

A significantly higher good quality blastocyst formation rate was obtained on day 5 for immediate mature oocytes (65% vs 27%, p<0.0001) as well as the rate of good quality blastocysts on the day of biopsy (76% vs 62%, p=0.015). The euploid rate of blastocysts biopsied on day 5/6/7 originating from immediate mature oocytes or sibling delayed mature oocytes, showed no significant difference (p=0.388) **(Figure 1)**.

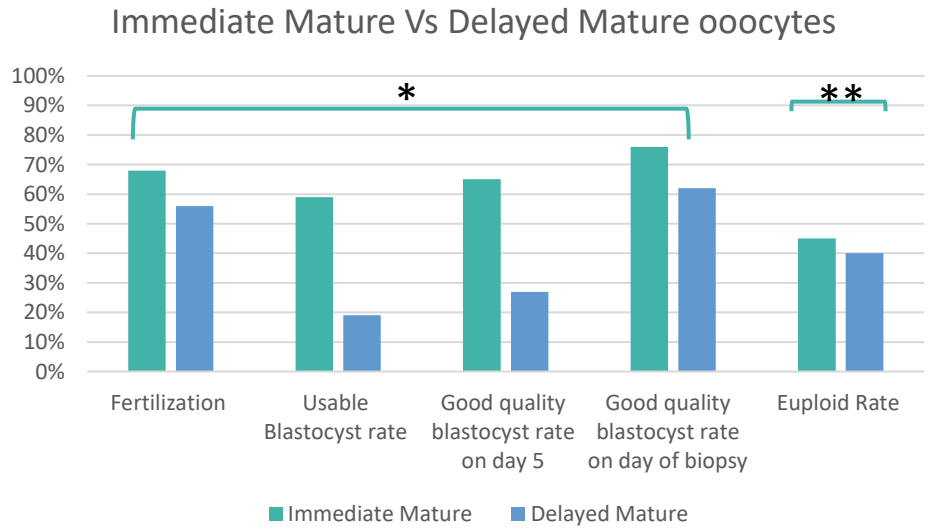

Figure 1: Fertilization, blastocyst development and euploid rate of immediate mature oocytes vs delayed mature oocytes. * p<0.0001, ** p=0.015,

Conclusion

Insemination of delayed mature oocytes by ICSI, should be considered as a tool to increase patients' chances of obtaining a euploid embryo, especially in cases where low yield of euploid blastocysts is expected.

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The ratio of serum progesterone (P4) to the number of follicles (P4/Follicle) is a more objective parameter for euploidy rate as compared to systemic progesterone.

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Study question

Does the ratio of serum progesterone (P4) to the number of follicles (P4/Follicle) on the day of final oocyte maturation affect the ploidy status of the embryos?

Participants/materials, setting, methods

This retrospective study was performed at ART Fertility Clinics Abu Dhabi, UAE and Muscat, Oman. Which have included 975 cycles. Serum P4 was measured on the last ultrasound prior triggering for final oocyte maturation. The P4/Follicle ratio was calculated as the ratio of P4 on trigger day to the number of follicles > 10 mm on the last ultrasound. Serum P4 and P4/Follicle ratio were then analyzed using linear and univariate regression model to find potential correlation with the number of oocytes retrieved, number of mature oocytes, embryo quality (day 3 and 5), and euploid rate.

Main results and the role of chance

Mean serum P4 on trigger day was 0.83±0.005 ng/ml, On the other hand, the mean P4/Follicle ratio was 0.056±0.00041 ng/ml. A higher serum P4 values were observed as the number of oocytes retrieved (NOR) and the number of mature oocytes increased(NMO)(Table 1), while the number of oocytes retrieved and the number of mature decreased with the higher P4/Follicle (Table 2).

	β	Standard Error	P-value
NOR	0.026	0.00055	<0.001
NMO	0.022	0.00076	<0.001

Table 1: Univariate analysis of P4 with NOR and NMO

	β	Standard Error	P-value
NOR	-0.001	54.77E-05	<0.001
NMO	-0.001	6.17E-05	<0.001

Table 2: Univariate analysis of P4 /Follicle with NOR and NMO

While day 3 embryos were not affected by serum P4 or P4/Follicle ratio, the blastocyst quality was negatively affected by both increasing serum P4 levels and the P4/Follicle ratio (β=-0.012 p<0.05, β=-0.002, p<0.001, respectively)(Figure 1).

Euploid rates were positively correlated in cycles with increased serum P4 β=0.18,(Table 3) p<0.001), while negatively correlated in cycles with a high P4/Follicle ratio (β=-0.015, p<0.001) (Table 4).

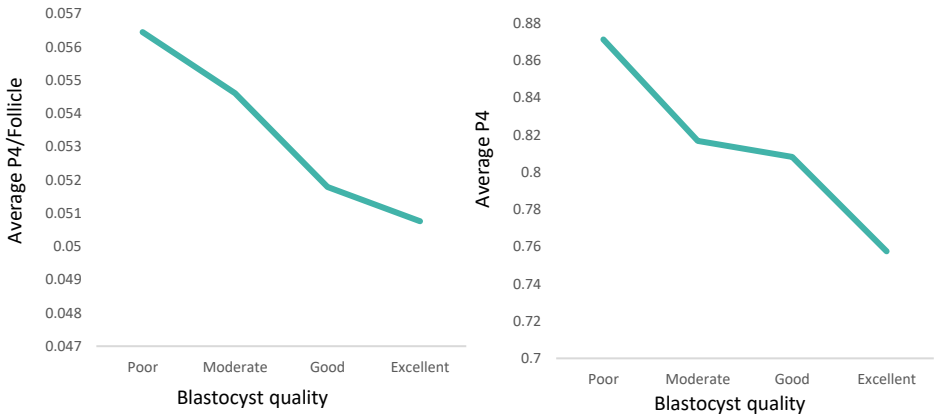

Figure 1: A graoh showing the negative impact of the Average value of P4/Follicle(Left) and the average P4 values to the right with the blastocyst quality

After adjusting for potential confounders, only P4/Follicle remained as a significant negative factor for euploid rate (β=-0.004, p<0.001, 95% CI: -0.007- -0.001, p<0.001), which was not observed for serum P4 (p=0.46).

	β	Standard Error	P-value
Euploid rate	0.18	0.0156	<0.001

Table 3: Univariate analysis of P4 with the Euploid rate

	β	Standard Error	P-value
Euploid rate	-0.015	0.0012	<0.001

Table 4: Univariate analysis of P4/Follicle with the Euploid rate

Summary Answer

A high P4/Follicle ratio negatively affects the euploid rate of the embryos..

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FEMALE PARENTAL CONSANGUINITY IS ASSOCIATED WITH A REDUCED OVARIAN RESERVE

Abu Dhabi, United Arab Emirates.

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OBJECTIVE: Consanguineous marriages have high prevalence in the Arabian Peninsula societies. We sought to investigate whether parental consanguinity is associated with a reduced ovarian reserve, comparing both ovarian reserve markers, Anti-Mullerian hormone (AMH) and antral follicle count (AFC), in daughters from consanguineous marriages to daughters from non-consanguineous marriages.

MATERIALS AND METHODS: Retrospective large-scale observational study including 2482 women, aged 19-49 years, from the Arabian Peninsula who had AMH and AFC measured as part of their fertility assessment at ART Fertility Clinics (UAE), from May 2015 to November 2019. Consanguinity was defined as women whose parents were first-degree or second-degree cousins. Ovarian reserve was evaluated by AFC with transvaginal ultrasound and serum AMH (Elecsys, Cobas, Roche®) for all participants. Women with adnexal surgical history (n=284) were excluded, and 2198 women were included for analysis. Ethical approval was obtained from the Research Ethics Committee (REFA040).

	Total group (n=2198)	Non-consanguine group (n=1593, 72.47%)	Consanguine group (n=605, 27.53%)
Age Mean±SD	34.52±6.67	34.78 ± 6.64	33.74 ± 6.64
Age Median (Min–Max)	35 (19-49)	34.83 (19-49)	33.75 (19-49)
AMH Mean±SD	2.64±2.9	2.65 ± 2.91	2.62 ± 2.88
AMH Median (Min–Max)	1.86 (0.01-23.80)	1.84 (0.01-23)	1.90 (0.01-23.8)
AFC Mean±SD	12.99±9.48	13.07 ± 9.39	12.78 ± 9.73
AFC Median (Min–Max)	11 (0-80)	11.00 (0-60)	11.00 (0-80)

Table 1. Descriptive analysis for age, AMH and AFC.

RESULTS: Descriptive analysis for age, AMH and AFC for the total group is described in Table 1. Consanguine group were significantly younger compared with the non-consanguine group (p<0.0001). Both groups were similar in BMI, years of infertility, type of infertility (primary/secondary), dress code (Hijab/Niqab) and smoking status. As expected, AMH and AFC exhibit an age-dependent decline. To evaluate differences on ovarian reserve, a multivariate analysis was performed including age, consanguinity and AMH/AFC. Women from the consanguine group showed significantly lower levels of AMH and AFC compared with non-consanguineous women (Figure 1), and the highest differences were found for women ≤35 years of age (Table 2).

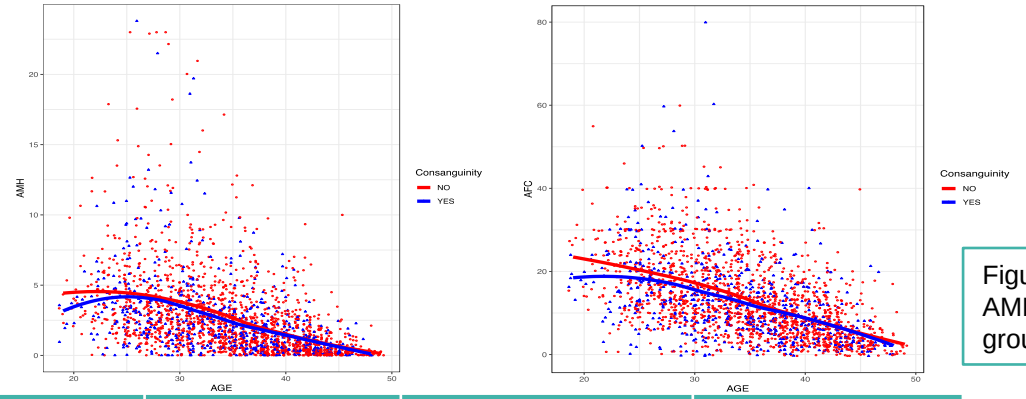

Figure 1. Age-dependent AMH/AFC decline for both groups.

	Total group (n=2198)		Age ≤35 years old (n=1188)		Age>35 years old (n=1010)	
	R^2	p	R^2	p	R^2	p
AMH (ng/mL)	0.26	0.036*	0.05	0.035*	0.16	0.504
AFC (n)	0.29	0.003*	0.08	0.001*	0.16	0.463

Table 2. Multivariate analysis between consanguine and non-consanguine groups. *Significant p values.

CONCLUSIONS: Female parental consanguinity is associated with a reduced ovarian reserve in the studied population. Medical advice, focused on genetic counselling, risk prediction, and earlier intervention is recommended.

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Sibling oocytes cultured in a time-lapse versus benchtop incubator: limited exposure of embryos outside the incubator improves outcomes.

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Study Question

Does the limited exposure of embryos outside the incubator, during evaluation and changeover, have an impact on the blastocyst development, blastocyst quality and euploid outcomes?

Study design

An observational sibling oocyte study was performed at ART Fertility Clinics, Abu Dhabi between March 2018 and April 2020 and included data of 796 mature oocytes injected from 42 stimulation cycles. Sibling oocytes were randomly split between 2 different incubators if at least 16 mature oocytes were available for ICSI: 12 oocytes were assigned to the twelve wells of the Embryoscope™ (ES) and the remaining oocytes were cultured in a conventional benchtop incubator, G185 K-System (KS). Only cycles with PGT-A through NGS on trophectoderm biopsies were included.

Results

Five hundred and three (63.2%) oocytes were cultured in ES and 293 (36.8%) in KS. The fertilization and cleavage rates were similar between incubators. Total useable blastocyst rate (64.8% *vs* 49.6%, *p*<0.001) was significantly higher for embryos cultured in ES **(Figure 1)**, mainly due to a higher percentage of blastocysts biopsied on day 5 in ES (67.8% *vs* 57.0%, *p*=0.037), with improved quality (p=0.008). There was no difference in the total euploid rate between ES and KS (59.9% *vs* 50.4%, *p*=0.314), but a significantly higher euploid rate was seen for blastocysts cultured in ES and biopsied on day 5 (63.5% *vs* 37.4%, *p*=0.001) **(Table 1)**.

	Embryoscope		K-System		p value
	Mean %	SD	Mean %	SD	
Usable Blastocyst rate	64.8	26.1	49.6	29.8	<0.001*
Euploid rate	59.9	26.4	50.4	40.2	0.314
Day 5 Euploid rate	63.5	29.0	37.4	44.1	0.001*
Day 6 Euploid rate	40.9	40.7	26.6	40.0	0.08
Day 7 Euploid rate	0	0	3.6	17.1	0.182

Table 1: Usable blastocyst and euploid rate, stratified per day of biopsy, per cycle.

Day 3 embryo quality and total biopsied blastocyst quality was not different between incubators. No difference was observed in the total usable blastocyst development from good (p=0.0832) and poor (p=0.112) quality day 3 cleavage stage embryos. However, when stratifying according to the day of blastocyst development, poor quality embryos on day 3 showed superior blastocyst formation on day 5 when cultured in ES (64.1% vs 39.1% for day 5 and 35.9% vs 60.9% for day 6, p=0.005). Accordingly, blastocyst formation from poor quality embryos on day 3, was shifted to day 6 for embryos cultured in KS. This difference in the day of blastocyst development was not observed for good quality cleavage stage embryos (p=0.917).

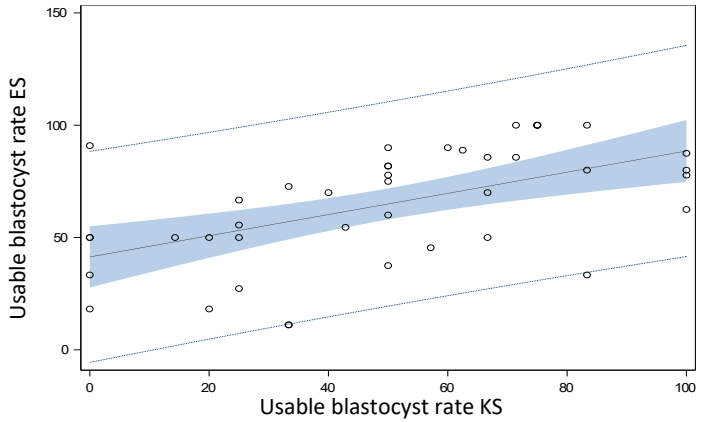

Figure 1: Linear regression with 95% confidence limits and 95% prediction limits of the usable blastocyst rate per cycle.

Conclusion

Exposure of embryos outside the incubator, negatively impacts the number, quality and euploidy rate of day 5 blastocysts.

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