



OVO

CLINIQUE

IVF CYCLE OUTCOMES ACCORDING TO ANTI-MÜLLERIAN HORMONE (AMH) : IS QUALITY BEHIND THE QUANTITY?

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INTRODUCTION

Quebec's governmental assisted reproductive technology (ART) program poses new challenges for physicians. Up to now, there have been few markers for the individual evaluation of oocyte quality.

AMH is a known quantitative biomarker of the ovarian reserve [1-4]. Nevertheless, its ability to determine the oocyte competence is a matter of debate [2,5].

OBJECTIVE

To evaluate the impact of serum AMH levels (ng/ml) on stimulated IVF implantation and pregnancy rates.

METHODS

We conducted a retrospective study including 637 patients undergoing stimulated IVF protocols at the **clinique ovo** (Montreal University affiliated center) between January 2009 and December 2011. Only non-polycystic ovary patients at their first IVF attempt were considered for the analysis.

Cycle outcomes were analysed according to **AMH percentiles** (<25th, 25-75th and >75th) based on the AMH normogram per patients' age of our infertile population.

STATISTICS

The statistical analysis was performed with a univariate followed by a multivariate analysis adjusted for confounding factors such as age, total exogenous FSH dosage and number of eggs retrieved.

RESULTS

Population characteristics

AMH percentile (ng/ml)	< 25 ^{eme} (≤ 0.46)	25-75 ^{eme} (0.47-1.76)	> 75 ^{eme} (≥ 1.77)	Valeur p
Number of patients, n (%)	136 (21.4)	334 (52.4)	167 (26.2)	
Average Age, Mean, (SD)	38.04 (3.4)	36.6 (3.9)	34.3 (4.4)	<0.001*
AFC	7.0 (3.1)	12.2 (4.7)	16.5 (4.4)	<0.001*
Baseline FSH (mIU/ml)	9.7 (4.3)	7.5 (2.0)	6.5 (1.5)	<0.001*
Total gonadotropin used (UI)	5 190 (2 100)	4 364 (1 541)	3 003 (1 322)	<0.001*

*Kruskal wallis

IVF outcomes, Multivariate analysis

AMH percentile (ng/ml)	< 25 ^{eme} (≤ 0.46)	25-75 ^{eme} (0.47-1.76)	> 75 ^{eme} (≥ 1.77)
	OR (IC95%)	Reference	OR (IC95%)
Cancelled cycle	6.54 (2.71-15.76)	1	0.15 (0.02-1.24)
Embryo transfers performed	0.48 (0.31-0.74)	1	1.10 (0.69-1.75)
Ongoing pregnancy per started Cycle	0.56 (0.31-0.99)	1	1.09 (0.70-1.69)
Miscarriages	1.25 (0.43-3.67)	1	1.30 (0.57-2.97)
Frozen embryos (%)	0.40 (0.24-0.65)	1	1.54 (1.04-2.28)

*Fisher exact test, ** Chi square

The multivariate analysis demonstrated that women with AMH levels <25th percentile (<0.47 ng/ml), were twice less likely to obtain an ongoing pregnancy per IVF started cycle (OR 0.56, 95% CI 0.31-0.99) and had a decreased embryo transfer (OR = 0.48, 95% CI 0.31-0.74) and freezing rate (OR 0.40, 95% CI 0.24-0.65) compared to the reference population (≥25th percentile - AMH≤75th percentile).

Significant lower implantation rate (0.26 Vs 0.45, P 0.04) was observed in patients under 35 years of age, with AMH levels <25th percentile (<1 ng/ml) compared to the reference population.

IVF outcomes, Univariate analysis

AMH percentile (ng/ml)	< 25 ^{eme} (≤ 0.46)	25-75 ^{eme} (0.47-1.76)	> 75 ^{eme} (≥ 1.77)	Valeur p
Number of patients, n (%)	136 (21.4)	334 (52.4)	167 (26.2)	
Cancelled cycle, n (%)	18 (13.2)	9 (2.7)	1 (0.6)	<0.001*
Mature oocytes per patient, Mean (SD)	4.3 (2.7)	7.2 (4.2)	10.0 (4.9)	<0.001
Embryo transfers performed, n (%)	88 (64.7)	265 (79.3)	135 (80.8)	0.001**
Ongoing pregnancy per started Cycle (%)	12.5	23.4	30.5	0.001**
Ongoing pregnancy per transfer (%)	19.3	29.4	37.8	0.01**
Miscarriages (%)	26.1	19.6	20.6	0.8**
Frozen embryos (%)	19.1	40.4	56.9	<0.001**

*Fisher exact test, ** Chi square

IVF outcomes for Patients < 35 years of age, Univariate and multivariate analysis

Age group	< 35 years N=211				
AMH percentile (ng/dl)	< 25 ^{eme} (≤ 0.99)	25-75 ^{eme} (1.0-2.33)	> 75 ^{eme} (≥ 2.34)	p Brute*	p Ajusté*
Ongoing pregnancy per started Cycle (%)	23.2	39.6	46.3	0.03*	
Frozen embryos, (%)	37.5	59.4	66.7	0.01*	
Implantation rate, Mean (SD)	0.26 (0.42)	0.45 (0.49)	0.50 (0.46)	0.05**	0.04**
Multivariate analysis	OR (IC95%)	Reference	OR (IC95%)		
Ongoing pregnancy per started Cycle	0.46 (0.22-0.96)	1	1.31 (0.67-2.56)		
Frozen embryos	0.41 (0.21-0.80)	1	1.37 (0.68-2.73)		

** ANOVA adjusted on age and total dose of gonadotropins, * Chi square, * Fisher exact test, ** Kruskal Wallis

CONCLUSIONS

AMH plays a major role in ART. It allows not only the quantification of the ovarian reserve, but also the prediction to an eventual ovarian response to the stimulation [1-4].

In addition, our results suggest that **AMH is a reliable biomarker of oocyte quality.**

Patients with AMH<0.47ng/ml should be advised before starting a stimulated IVF cycle, of the poorer prognosis compared to our reference population (25-75th percentile), independently of their age, total exogenous FSH dosage and number of eggs retrieved. We emphasize that same results were noted in patients under 35 years of age with an AMH below 1ng/ml.

AMH could enable a more individualised embryo transfer policy based on oocyte quality. Therefore, Double Embryo Transfer (eDET) should be evaluated for this young cohort with anticipated poorer prognosis in a future randomized control trial.

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