The influence of age, body mass index, waist-to-hip ratio and anti-Mullerian hormone level on clinical pregnancy rates in ART

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ABSTRACT

The aim of this study was to estimate the influence of age, body mass index, waist-to-hip ratio and anti-Mullerian hormone levels on clinical pregnancies in assisted reproduction technologies (ART). We used the database of the fertility clinic both the in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) units. A total of 1134 treatment cycles from 2013 through 2015 were analyzed. We evaluated clinical pregnancy rate in terms of age, body mass index, waist-to-hip ratio, anti-Mullerian hormone level. The clinical pregnancy rate was 39.9%. The live birth rate was 25.5%. Women who conceived where statistically significantly younger and had lower body mass index. No statistical differences across pregnancy groups were found for waist-to-hip ratio, and anti-Mullerian hormone levels. Low AMH levels do not influence pregnancy rates in younger patients (<36 years).

Introduction

One in six couples worldwide experience some form of infertility problem at least once during their reproductive lifetime. The current prevalence of infertility lasting for at least 12 months is estimated to be ~9% worldwide for women aged 20–44 years. Around 1.6 million ART cycles are now performed each year worldwide, with an estimated 400,000 babies born. (www.eshre.eu)

Of infertility cases, 20–30% are explained by male factor infertility, 20–35% by female factor infertility, and 25–40% of cases are because of a problem in both partners. In 10–20%, no clear cause is found. Infertility is also associated with lifestyle factors such as smoking, body weight and stress. According to ESHRE statistics, increasing age in the female partner is one of the most common explanations today (www.eshre.eu).

Excess body weight and obesity are associated with alterations in the reproductive system in women. Several studies show that obesity adversely affects the outcome of in vitro fertilization (IVF) [1–3]. Although there are some controversies. Sneed et al. [4] conducted a study which demonstrated that the effect of body mass index (BMI) on IVF success appeared to be related to age. At younger ages, a higher BMI had a pronounced negative influence on pregnancy rate, but this effect was attenuated as age increased [4].

Anti-Mullerian hormone (AMH) has a regulative function in the activation of folliculogenesis and an influence on atresia of the follicles. It is considered one of the markers for the ovarian reserve. We know that a correlation exists between AMH levels and oocyte retrieval numbers, antral follicle count, pregnancy rates and birth rates. The role of AMH as an efficient prognostic factor in determining the probability of pregnancy has been largely discussed [5–8]. Revelli et al. [9] calculated that in women with very low circulating AMH level the probability of pregnancy was significantly affected by age.

The aim of this study was to investigate the influence of age, BMI, waist-to-hip ratio and AMH levels on the IVF treatment outcomes (as expressed by pregnancy rates).

Material and methods

We used the database of our fertility clinic on fresh IVF and ICSI treatment cycles from year 2013 through 2015. A total of 1134 fresh IVF/ICSI cycles were analyzed. Embryo transfer was performed in 1032 cycles. The indications for treatment were as follows: mechanical factor infertility (272 cases 24%), male infertility (409 cases 36.1%), idiopathic infertility (239 cases 21%), endometriosis (147 cases 13%), anovulation (47 cases 4.1%) and others (20 cases 1.8%). The clinical pregnancy rate was 39.9%. The live birth rate was 25.5%. The rate of multiple pregnancies was 17.6%. Controlled ovarian hyperstimulation was achieved using gonadotropins follitropin alfa (rFSH, recombinant follicle stimulating hormone) (Gonal-F, Serono, Geneva, Switzerland) and gonadotropin hormone antagonist (Cetrotide 0, 25 mg per day). GnRH antagonist was administered when the leading follicle reached >14 mm. We used the short antagonist protocol. rFSH was started daily on either the third, fourth, or fifth day of the following menstrual cycle. Only clinical pregnancies were evaluated. A single serum β-hCG measurement was performed 12 days after embryo transfer procedure. If serum hCG was >40 IU/l, indicating pregnancy, the luteal support (Crinone 8% one applicator per day vaginally until the eighth week of gestation) was continued until the ultrasound scans.
pregnancy was confirmed when an intrauterine gestational sac with fetal heartbeat was detected during transvaginal ultrasound examination.

**Oocyte pick up and IVF**

Follicular fluids (FF) containing oocyte–cumulus complexes were recovered by Single Lumen Follicle Aspiration Needle (Genetics, Charleroi Gosselies, Belgium) on Day 0, at 36 h after hCG administration. Oocyte collection was carried out using a stereomicroscope with a warm operating area (37°C). Collected oocytes were washed twice in flushing medium (Medicult, Jyllinge, Denmark) and then transferred into IVF medium (Medicult) until the insemination. IVF or intracytoplasmic sperm injection (ICSI) procedure was used, depending on infertility indication.

**Fertilization rate and embryo grading**

Fertilization determination was performed on the second day (16–18 h after insemination) under an inverted microscope (Olympus IX-70, Nagano, Japan). Zygotes were transferred into fresh medium and cultivated until embryo transfer procedure. According to morphological criteria, the best quality embryos were transferred into uterus on the second or third day. Surplus embryos were frozen.

**Results**

**Age**

The mean age of all women was 33.4 ± 4.48 years. Women who conceived were statistically significantly (p < .001) younger (mean age 32.68 ± 4.06 years) than those who did not get pregnant (mean age 33.82 ± 4.68 years). We divided all women into three age groups: 775 (68.3%) women were ≤35 years old; 268 (23.6%) were 36–40 years old and 91 (8%) women were >40 years old.

The clinical pregnancy rates were: 44.4% (344/775) for women ≤35; 34.7% (93/268) for women 36–40 years old and 16.5% (15/91) for women >40 years old (p < .001). The live birth rates were: 30.8% (239/775) for women ≤35; 18.3% (49/268) for women 36–40 years old and 1.1% (1/76) for women >40 years old (p < .001).

**BMI**

We evaluated body mass index of 1133 women. The mean BMI was 23.2 ± 3.95. Women who conceived had statistically significantly (p < .001) lower BMI (mean BMI 22.37 ± 3.27) than those who did not get pregnant (mean BMI 23.75 ± 4.25). All women were divided to four groups according to BMI: 43 (3.8%) were underweight (BMI >18.5); 809 (71.3%) had normal weight (BMI between 18.5 and 24.9); 206 (18.2%) were overweight (BMI between 25 and 29.9) and 75 (6.6%) were obese (BMI >30). The clinical pregnancy rates were: 44.2% (19/43) for underweight women; 44.7% (362/809) for women who had normal weight; 27.2% (56/206) for overweight women and 18.7% (14/75) for obese women (p < .001). The live birth rates were: 30.23% (13/43) for underweight women; 29.42% (238/809) for women who had normal weight; 14.08% (29/206) for overweight women and 10.67% (8/75) for obese women (p < .001).

We also calculated clinical pregnancy rate depending on age and BMI. For women who were ≤35 years old the clinical pregnancy rates were: 43.8% (14/32) for underweight women; 49.1% (287/584) for women who had normal weight; 28% (33/118) for overweight women and 22.5% (9/40) for obese women (p < .001). The live birth rates were: 32.38% (11/32) for underweight women; 34.76% (203/584) for women who had normal weight; 16.1% (19/118) for overweight women and 12.5% (5/40) for obese women (p < .001). For women who were 36–40 years old, the clinical pregnancy rates were: 37.5% (3/8) for underweight women; 37.4% (64/171) for women who had normal weight; 33.8% (22/65) for overweight women and 16.7% (4/24) for obese women not significant (ns). The live birth rates were: 12.5% (1/8) for underweight women; 20.47% (35/171) for women who had normal weight; 15.38% (10/65) for overweight women and 12.5% (3/24) for obese women (ns). For women who were >40 years old, the clinical pregnancy rates were: 66.7% (2/3) for overweight women; 20.4% (11/54) for women who had normal weight; 4.3% (1/23) for overweight women and 9.1% (1/11) for obese women (p = .03). The live birth rates were: 33.33% (1/3) for overweight women; 0% (0/54) for women who had normal weight; 0% (0/23) for overweight women and 0% (0/11) for obese women (ns).

**Waist-to-hip ratio**

We measured waist-to-hip ratio of 597 women. All women were divided to four groups according to waist-to-hip ratio: 171 (28.6%) had an excellent WTH ratio (<0.75); 150 (25.1%) had a good WTH ratio (0.75–0.79); 160 (26.8%) had an average WTH ratio (0.80–0.86) and 116 (19.4%) were at risk (WTH ratio ≥0.86). The clinical pregnancy rates were: 41.5% (71/171) for the excellent WTH ratio group; 39.3% (59/150) for a good WTH ratio group; 40% (64/160) for the average WTH ratio group and 31.9% (37/116) for at risk WTH ratio group (ns). The live birth rates were: 25.73% (44/171) for the excellent WTH ratio group; 27.33% (41/150) for a good WTH ratio group; 23.13% (37/160) for the average WTH ratio group and 17.24% (20/116) for at risk WTH ratio group (ns).

**AMH**

AMH levels were evaluated in 316 women. Women were divided to three groups according to AMH levels: 47 (14.9%) had low levels of AMH (AMH <1 μg/L); 230 (72.8%) had normal levels of AMH (AMH between 1 and 7 μg/L) and 39 (12.3%) had high levels of AMH (AMH >7 μg/L). The clinical pregnancy rates were: 29.8% (14/47) for low AMH group; 41.7% (96/230) for normal AMH group and 41% (16/39) for high AMH group (ns). The live birth rates were: 17.02% (8/47) for low AMH group; 27.83% (64/230) for normal AMH group and 33.33% (13/39) for high AMH group (ns).

We also evaluated clinical pregnancy rate depending on age and AMH level. For women who were <35 years old the clinical pregnancy rates were: 52.9% (9/17) for low AMH group; 51% (74/145) for normal AMH group and 45.5% (15/33) for high AMH group (ns). The live birth rates were: 47.06% (8/17) for low AMH group; 36.55% (53/145) for normal AMH group and 36.36% (12/33) for high AMH group (ns). For women who were 36–40 years old, the clinical pregnancy rates were: 27.8% (5/18) for low AMH group; 30.2% (19/63) for normal AMH group and 16.7% (1/6) for high AMH group (ns). The live birth rates were: 0% (0/18) for low AMH group; 17.46% (11/63) for normal AMH group and 16.7% (1/6) for high AMH group (ns). For women who were >40 years old, the clinical pregnancy rates were: 0%
(0/12) for low AMH group; 13.6% (3/22) for normal AMH group and no women had high AMH (ns). The live birth rates were: 0% (0/12) for low AMH group and 13.6% (3/22) for normal AMH group.

Discussion
As we can see the main and most important predictor of IVF outcome is woman’s age and the best results are achieved in women under 35 years of age. European Society of Human Reproduction and Embryology Capri Workshop Group issued a press release stating that it is important to acknowledge the role of time to pregnancy but at the same time it is very important to not over treat [10]. The availability of validated dynamic models based on real-life data that could predict both natural and ART-mediated conceptions may be of benefit. They could facilitate patients’ counseling and could optimize the chances of success without exposing patients to unnecessary, expensive and demanding treatments [10].

According to our results, BMI did have an influence on clinical pregnancy rates and it was not affected by age. Espinos et al. [11] suggested that weight loss results in a significantly increased cumulative live birth rate. However, not all studies find significant correlation between BMI and clinical pregnancy rate, recommending that BMI should not be a basis for IVF treatment denial [12].

We did not find significant difference between AMH group’s clinical pregnancy rates, but this might be due to quite low numbers of women in low and high AMH groups. However, we did find that in young women (≤35 years old) the clinical pregnancy rate was not affected and remained quite high in all AMH groups. This finding is supported by other studies [5,6] suggesting that AMH levels should only be monitored in women above 36 years of age.

Conclusions
Women who conceived where statistically significantly younger and had lower BMI. No statistical differences across pregnancy groups were found for waist-to-hip ratio, and AMH levels. Low AMH levels do not influence pregnancy rates in younger patients (<36 years).

Disclosure statement
No potential conflict of interest was reported by the authors.

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