Research Article

Some clinical & biochemical predictors of Ovulation in infertile women induced with Clomiphene citrate

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Abstract
Introduction: Numerous studies have been carried out to establish the best factors predictive of in vitro fertilization (IVF) success. **Patients & Methods:** This study is a prospective cohort observational study. All women with anovulatory infertility who were scheduled to have ovulation induction with CC were approached. **Results:** This table showed that study included 70 patients, they were classified according to AFC, AMH and day 2 FSH Level. these 2 groups were group A included 23 patients with poor ovarian reserve group B included 47 patients with good ovarian reserve. **Discussion:** Numerous studies have been carried out to establish the best factors predictive of in vitro fertilization (IVF) success. **Summary:** In the present study, we used clinical, biochemical and radiological tests for the assessment of ovarian reserve and thereby prediction of successful outcome of ovulation induction amongst our registered patients.
Keywords: IVF, Vitro fertilization

Introduction
Numerous studies have been carried out to establish the best factors predictive of in vitro fertilization (IVF) success (Sharif et al., 2005 and LaMarca et al., 2012).

Some studies have reported that increasing maternal age correlates with a decrease in the probability of natural conception and of successful infertility treatment (Akande et al., 2008).
Increasing follicle-stimulating hormone (FSH) and decreasing anti-Müllerian hormone (AMH), which are associated with a decrease in ovarian reserve, are also associated with a decrease in IVF success (Chuang et al., 2003).

Approximately 20–150 early growing follicles, 0.05–2.00mm in diameter, are present in the ovaries of women aged 25–40 years and are, therefore, too small to be accurately identified using conventional imaging techniques. Levels of anti-mullerian hormone (AMH) may provide a means of estimating the number of early growing follicles (Visser et al., 2006). Anti-mullerian hormone is expressed by the granulose cells of growing follicles (Visser et al., 2006), and serum AMH levels correlate with the number of antral follicles (deVet et al., 2002).

Whether the AMH level also correlates with antral follicles<2 mm in diameter remains to be established (Broekmans F, et al., 2008).

Anti-mullerian hormone (AMH) is produced by the granulosa cells of the recruited follicles until they become sensitive to FSH (Velde and Pearson, 2002).

AMH has been identified as a regulator of the recruitment process, which prevents the depletion of all primordial follicles at once (Themmen, 2005).

As AMH is produced by small follicles whose numbers reflect the primordial pool, concentrations decline with age in adult women (van Rooij, et al. 2005) The fall in AMH as the ovarian reserve declines has been documented in large populations of women.(Nelson, et al. 2011) This has led to the investigation into whether AMH can be used as a predictor of remaining reproductive lifespan and age at the menopause (Sowers, et al., 2008; Tehrani, et al., 2009) AMH becomes undetectable some 5 years before the final menstrual period.

Aim of the Work
This study aims to evaluate age, body mass

index, antral follicle count, follicle-stimulating hormone, anti-mullerian hormone, and as predictive factors of ovulation in infertile women under induction of ovulation by using clomiphene citrate.

Patients & Methods

This study is a prospective cohort observational study. All women with anovulatory infertility who were scheduled to have ovulation induction with CC were approached.

Subject selection:

The inclusion criteria for the study were:
Age: 18-39 years.
BMI ≤ 35
Infertility due to anovulation.
Proven patency of at least one fallopian tube (for women receiving ovulation induction).
The exclusion criteria were:
Age > 40 years old.
Current or recent hormonal treatment (within 3 months).
Presence of ovarian masses.
History of previous ovarian surgery.
Polycystic ovary.
Endometriosis
Absence of any of the inclusion criteria.
Mental incapacity to give informed consent.
Inability to understand verbal or written information.

Subject recruitment and screening:

The study patients were recruited from those attending the infertility clinic at Minia Maternity University Hospital, and assisted conception unit at Minia University,Minia, Egypt. The initial screening tests were all part of the routine work up of anovular infertile patients i.e. is not a part of theresearch. Other causes of anovulation were excluded by thyroid function tests and measurement of serum prolactin level. Patients with marked hperandrogenaemia were screened for congenital adrenal hyperplasia (by measuring serum concentration of 17α hydroxyl-progesterone) and Cushing syndrome (by measuring urinary free cortisone). Tubal patency in patients undergoing ovulation induction was assessed by hysterosaplingogram (HSG). Semen analyses of the male partners were assessed according to WHO criteria. Two tests with 2-3 months apart were required to define an abnormal semen analysis.

Results

This table showed that study included 70 patients, they were classified according to AFC, AMH and day 2 FSH Level. these 2 groups were group A included 23 patients with poor ovarian reserve group B included 47 patients with good ovarian reserve.

Table: Relation between poor reserve group and good reserve group as regard AFC, FSH, AMH.

	Group A (n=23) poor reserve	Group B (n=47) good reserve	P value
AFC	3.65 ± 0.64	6.02 ± 1.48	< 0.001*
FSH	8.85 ± 2.72	6.69 ± 2.43	0.001*
AMH	2.08 ± 1.47	3.95 ± 2.71	< 0.001*

This table shows a statistically significance difference between group A poor reserve and group B good reserve as regard AFC, FSH, AMH.

Discussion

Numerous studies have been carried out to establish the best factors predictive of in vitro fertilization (IVF) success (Sharif et al., 2005 and LaMarca et al., 2012).

Some studies have reported that increasing maternal age correlates with a decrease in the probability of natural conception and of successful infertility treatment (Akande et al., 2008).

Increasing follicle-stimulating hormone (FSH) and decreasing anti-Müllerian hormone (AMH), which are associated with a decrease in ovarian reserve, are also associated with a decrease in IVF success (Chuang et al., 2003).

Anti-mullerian hormone (AMH) is produced by the granulosa cells of the recruited follicles until they become sensitive to FSH (Velde and Pearson, 2002).

AMH has been identified as a regulator of the recruitment process, which prevents the depletion of all primordial follicles at once (Themmen, 2005).

Body mass index (BMI) remains a controversial factor with studies showing conflicting results (McCormick et al., 2008).

The mean age of infertile females was 25.28 ± 4.93 years. Mean FSH level in these 70 infertile women was 7.4 ± 2.71 mIU/ml, with a range of 2.4-12 mIU/ml. The mean AMH level on day 2 was 3.33 ± 2.52 ng/ml, with a range of 0.01-12.68 ng/ml. Although AMH and FSH are not directly dependent on each other, there was a significant inverse relationship between serum AMH concentrations and serum FSH concentration ($r = -0.410$, $P < 0.001$) was taken on day 2 of menstrual cycle. This correlation is shown in. The presumed linkage in the relationship between baseline FSH and AMH is that both hormones are indicators of ovarian reserve. Baseline FSH level increases in infertility and our study also shows mean FSH level is 7.4 ± 2.71mIU/ml, which is on the higher side. Determinations of FSH, however, are characterized by many difficulties. One quite obvious problem is the inconvenience of a required blood draw on the day 2 or 3 of menses. The second issue of concern is the degree of cycle-to-cycle fluctuation in baseline FSH levels, at least partially caused by the dependency of FSH levels on the negative feedback from E2 levels (Iverson et al, 2011). Anti-Mullerian hormone does not exhibit these difficulties.It is relatively stable throughout the cycle (La Marca et al, 2006; Hehenkamp et al, 2006; La Marca et al, 2007). and therefore can be drawn at random. This makes serum AMH a more reliable test, as it is not constrained to a time frame for measurement. It is also said not to be affected by other hormonal variations, including the use of oral contraceptives (Streuli et al., 2008; Somunkiran et al., 2007).

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