Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Women with clomiphene citrate resistant polycystic ovarian disease: predictors of spontaneous ovulation after laparoscopic ovarian drilling

Wessam M. Abuelghar [a], Hassan A. Bayoumy [a], Mohamed I. Ellaithy [a,*], Marian S. Khalil [b]

[a] Obstetrics and Gynecology Department, Faculty of Medicine, Ain-shams University, Cairo, Egypt
[b] Obstetrics and Gynecology Department, Imbaba Hospital, Cairo, Egypt

A B S T R A C T

Objective: To evaluate the role of different clinical, biochemical and sonographic factors as predictors of spontaneous ovulation after laparoscopic ovarian drilling (LOD) in women with clomiphene citrate resistant polycystic ovarian disease (CCR-PCOD).

Study design: This prospective study recruited 251 infertile women with CCR-PCOD. Several clinical, biochemical and sonographic criteria were tested as possible predictors of spontaneous ovulation after LOD using multivariate analysis.

Results: Women with higher preoperative levels of LH, FSH and/or androstenedione had significantly higher rates of spontaneous ovulation within the first eight weeks after LOD, but only FSH and androstenedione were found to be independent predictors. Other factors including age, BMI, type of infertility, duration of infertility, menstrual pattern, testosterone level, ovarian volume and SHBG were insignificant predictors. Receiver-operating characteristic (ROC) curves derived from FSH, LH, androstenedione, and a logistic regression model showed that the best cut-off values were 4.1 IU/l, 7.8 IU/l, 1.2 ng/ml, and 0.4897, respectively, with sensitivity of 91.18%, 100%, 73.53%, and 88.24% and specificity of 69.57%, 69.57%, 65.22%, and 73.91% for FSH, LH, androstenedione, and logistic regression model respectively. An extended follow up (9 months after LOD) was conducted for the anovulatory and the non-pregnant ovulatory women, who were treated individually according to their clinical situation. Of these women, 53.5% (69/129) got pregnant, resulting in a cumulative pregnancy rate of 48% (82/171). Of these pregnancies, 16/82 (19.5%) were spontaneous while 35.4% (29/82) and 45.1% (37/82) occurred after ovulation induction by CC and gonadotropins, respectively.

Conclusion: This study supports the use of androstenedione, LH and FSH as a simple reliable tool in triaging patients with CCR-PCOD to select the ideal candidates for LOD.

1. Introduction

Around 15–20% of infertile women have ovulatory disorders [1]. Clomiphene citrate (CC) is considered the first-line medical treatment for infertile women with normogonadotrophic anovulation. The next option for women with CC-resistant polycystic ovarian disease (CCR-PCOD) is usually either gonadotrophin therapy or laparoscopic ovarian drilling (LOD) [2]. Both modalities have their own inherent merits and demerits but success rates in terms of pregnancies and live births are comparable [2,3]. In 1984, LOD was first described as an alternative to ovarian wedge resection [4]. There is no well-established mechanism by which LOD leads to induction of ovulation, but it seems to be related to the diminution of androgen production by the ovary [2].

Some retrospective [5–15] and small prospective studies [16–20] have addressed the role of clinical, biochemical and sonographic factors to predict success after LOD, but the findings of these studies were inconclusive and sometimes contradictory. The aim of the current large prospective study was to evaluate the potential value of the different clinical, biochemical and sonographic parameters to predict spontaneous ovulation after LOD in women with CCR-PCOD.

2. Materials and methods

This prospective cohort study was conducted at Ain Shams University Maternity Hospital and included 251 young infertile women with CCR-PCOD scheduled for LOD. PCOD was defined based on the revised 2004 Rotterdam criteria [21], while CCR was defined by the presence of persistent anovulation in spite of taking 150 mg CC/day for 5 days beginning on the second day of the menstrual cycle for a minimum of three and a maximum of six cycles [22]. Women over 35 years old and/or having other infertility factor(s) were excluded from the study. Written

* Corresponding author at: Building 14, Block 14, Alwaha District, Nasr City, Cairo, Egypt. Tel.: +201006873417.
E-mail addresses: drmellisy@hotmail.com, drmellisy@gmail.com (M.I. Ellaithy).

informed consent was obtained from each participant after explaining the study purpose and procedures to all enrolled women. The women who agreed to participate in the study were thoroughly evaluated to ensure fulfillment of the study inclusion and exclusion criteria.

Preoperative serum hormonal concentrations were measured, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, sex hormone binding globulin (SHBG) and androstenedione.

All enrolled women underwent preoperative transvaginal sonography (TVS) to detect PCOD, measure ovarian volume and exclude associated pathology. Ovarian volume was calculated according to the following formula: $4/3\pi xyz$, (x, y and z representing the mean radius of the length, width and thickness of the ovaries).

During laparoscopic visualization of the pelvic organs, other possible causes of infertility were excluded, the diagnosis of polycystic ovaries was confirmed and tubal patency was checked using methylene blue testing. LOD was performed using a unipolar diathermy probe pressed against the ovarian anti-mesenteric surface, performing four punctures on each ovary 4–5 mm apart through the ovarian cortex to a depth of 4–5 mm graduated on the specific needle used for the procedure. A monopolar coagulating electrical current at 30 W power setting was used and the duration of each penetration was ±5 s.

All patients underwent regular postoperative follow-up for 8 weeks. Blood samples were taken from all participants at day 21 of the menstrual cycle, or 8 weeks after LOD if no menstruation occurred, to measure serum progesterone as an indicator of ovulation.
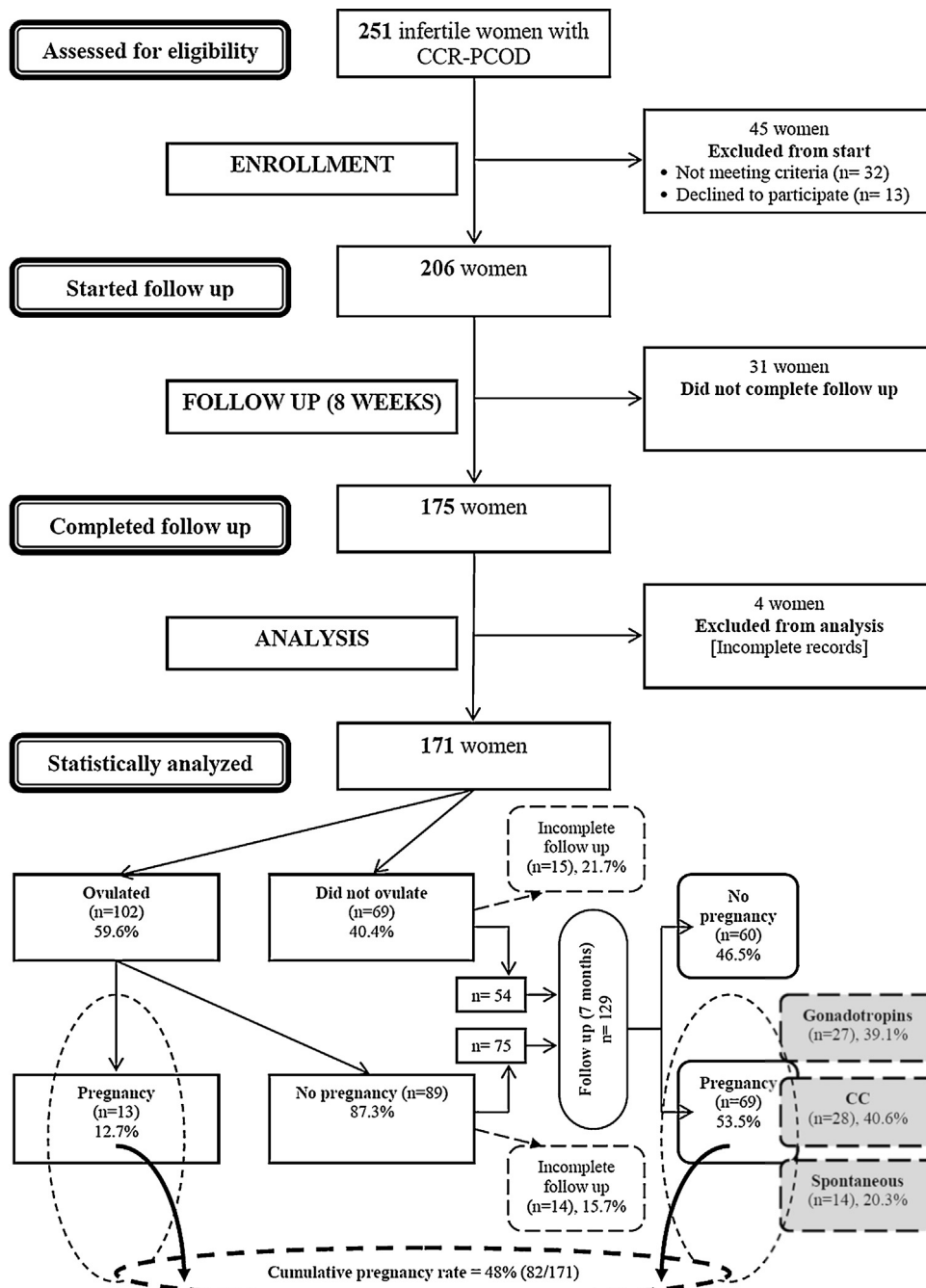

Fig. 1. Participants' flow chart.