Effect of Body Mass Index Towards Duration of Controlled Ovarian Hyperstimulation in Patients Undergoing *In Vitro* Fertilization

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**Background:** Effect of obesity on response to controlled ovarian hyperstimulation (COH) in assisted reproductive technologies has yielded conflicting results in numerous studies. Obesity may be associated with longer durations and increased amounts of gonadotropin stimulation. **Objective:** To assess the effect of body mass index (BMI) towards duration of COH in patients undergoing *in vitro* fertilization (IVF). **Methods:** Cross-sectional study with data obtained retrospectively among patients undergoing IVF procedure in Yasmin IVF Clinic, Cipto Mangunkusumo General Hospital, Jakarta, Indonesia during 2016. BMI and duration of COH was obtained from medical record. Statistical analysis including comparison and correlation were assessed to reveal significances. **Results:** Two hundred and eighteen subjects were included in the study with mean of age, BMI, and duration of COH were 35.57 (± 4.82) years old, 23.89 (± 3.83) kg/m², and 11.43 (± 2.33) days, respectively. Obese patient were found in 72 subjects (33%). There was no significant difference in duration of COH between obese and non-obese subjects (p = 0.495). Moreover, correlation between BMI and duration of ovarian stimulation revealed no significant association (p = 0.129). **Conclusions:** There was no significant difference in duration of COH between obese and non-obese subjects. BMI was not associated with duration of COH in patients underwent IVF.

**Keywords:** Body Mass Index, Controlled Ovarian Hyperstimulation, Duration of COH.

### 1. INTRODUCTION

Body mass index (BMI) has an impact on a woman’s infertility even tough not a prerequisite. Obesity and extremely low body mass are known to be related to hormonal imbalances or ovulatory dysfunction that may impair fecundity.¹ Studies suggest that one of the prognostic factors in assisted reproduction treatment is BMI.²

Effect of BMI on assisted cycle parameters and outcomes has been investigated recently by many researchers and it has been recommended that patients with abnormal BMI should normalize their BMI before initiating assisted reproduction treatment.² Studies of the effects of obesity on response to ovarian stimulation and outcomes achieved with assisted reproductive technologies (ART) have shown conflicting results. Retrospective analysis of *in vitro* fertilization (IVF) revealed that obesity was associated with longer durations and increased amounts of gonadotropin stimulation, an increased frequency of cycle cancelation for inadequate response, and lower oocyte retrieved in evaluation of 5,019 cycles.³

Data regarding the impact of BMI towards duration of controlled ovarian hyperstimulation for *in vitro* fertilization are scarce especially in Indonesia. Hence, this study will assess the effect of body mass index (BMI) towards duration of controlled ovarian hyperstimulation (COH) in patients undergoing *in vitro* fertilization (IVF).

### 2. MATERIAL AND METHODS

This was cross sectional study of patients underwent *in vitro* fertilization during January to August 2016. We have collected medical records of 218 patients retrospectively and assessed association between BMI and duration of COH in IVF patients. Infertility etiologies in women were varied and consists of polycystic ovarian syndrome (PCOS), endometriosis, poor ovarian response (POR), tubal factor infertility, male factor infertility and unexplained infertility. All patients were stimulated with
antagonist protocol. The decision for stimulation protocol to be used was based on the preference of the treating physician.

The antagonist protocol consisted of daily gonadotrophin (recombinant follicle stimulating hormone/FSH (Gonal F, Serono)) stimulation from day 2 of menstruation followed by daily injections of Cetrotide 0.25 mg (Serono, Switzerland), from the point at which leading follicle reached 14 mm to the day of human chorionic gonadotrophin (HCG) injection. Gonadotrophin dose use was tailored according to antral follicle count, anti-Mullerian hormone level and previous medical and fertility history.

Ovarian response was monitored by vaginal ultrasound measurements of follicular growth and serum estradiol concentration on day six, nine, and ten, starting on the day 5 or 6 of stimulation and the FSH dosage was adjusted accordingly. HCG (Ovidrel, 250 µg; Serono, Italy) was administered when at least two leading follicles measured was 18 mm or more. Ovum pick-up was performed after 36 hours of HCG administration.

Body mass index was calculated based on weight and height measurement in medical record. BMI patients were categorized according to WHO classification for Asia-Pacific population. Duration of controlled ovarian stimulation was also obtained from medical record. All data were analyzed descriptively and analytically with SPSS software for Windows version 22. Normality of data was assessed using Kolmogorov-Smirnov test. Comparison of duration stimulation between obese and non-obese patients was analyzed with T-independent test or Mann-Whitney test. Correlation between BMI and duration of COH was assessed with Pearson correlation test or Spearmen’s rho test based on normality of data.

### RESULTS

From this research, 218 medical records were recruited. Data obtained was age of subjects, weight and height to measure body mass index, cause of infertility and duration of controlled ovarian hyperstimulation. Characteristics of the subjects were displayed in Table I.

According to the characteristics of subjects, most subjects’ age ranged between 35–39 years old, male factor infertility as the most common indication for IVF, and normal BMI. We categorized subjects into obese and non-obese patients with cut-off point of 25 kg/m². We compared duration of COH between two groups as seen in Table II.

There was no difference in duration of controlled ovarian hyperstimulation between obese and non-obese subjects, as stated with $p$-value over 0.05. Furthermore, association between body mass index and duration of controlled ovarian hyperstimulation is shown in Table III.

As seen in Table III, there was no correlation between body mass index and duration of controlled ovarian hyperstimulation ($p > 0.05$).

### DISCUSSION

The aim of this study was to assess the effect of body mass index towards duration of controlled ovarian hyperstimulation (COH) in patients undergoing in vitro fertilization (IVF). Obesity and its response to ovarian stimulation in assisted reproduction technology had conflicting results. But overall, obesity had effect on IVF. Obesity is associated with longer duration and increase in gonadotrophin dose in ovarian stimulation. In addition, obesity also correlate with increased cycle cancelation due to inadequate response and lower number of oocytes obtained.

There are several factors contributing to prediction of ovarian stimulation response. Those factors are antral follicle count (AFC), anti-Mullerian hormone (AMH), level of basal FSH, age, body mass index, menstrual cycle, and history of ovarian surgery.

Previous studies showed that high body mass index was associated with longer duration of ovarian stimulation. Studies conducted by Farhi et al. and Rittenberg et al. showed that longer duration of ovarian stimulation seen in women with BMI more than 25 kg/m² compared to women with BMI less than 25 kg/m². Besides, 5 studies that compared normal BMI with BMI between 25–29.9 kg/m² showed significantly longer duration of COH. The same goes with women with BMI more than 30 kg/m².
In this study, we did not found significant different in duration of COH on obese and non-obese subjects. In addition, there was no correlation between BMI and duration of COH. Those different results may be caused by several factors. In this study, subjects had different etiologies of infertility as well as wide variety of age that may confound the results of this study.

Suggestions for the next study, the research should be conducted by adjusting factors that may confound the results such as infertility causes, AFC, age, and other factors. Hence the bias can be minimalized.

From this study can be concluded that there was no significant difference in duration of controlled ovarian hyperstimulation between obese and non-obese subjects. Body mass index was not associated with duration of controlled ovarian hyperstimulation in patients underwent in vitro fertilization.

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References and Notes

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