

Research Article

## Anti Müllerian Hormone as a Predictor of Metabolic Syndrome in Polycystic Ovary Syndrome

### *Hormon Anti Mülleri sebagai Prediktor Sindrom Ovarium Polikistik Metabolik*

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#### Abstract

**Objective:** To evaluate whether Anti Müllerian Hormone (AMH) can be used as a predictor of metabolic syndrome in Polycystic Ovarian Syndrome (PCOS).

**Methods:** This cross-sectional study was conducted in Yasmin Clinic, Dr. Cipto Mangunkusumo General Hospital Jakarta between June and December 2012. Forty-one patients diagnosed with PCOS based on Rotterdam Criteria were enrolled. Secondary were was taken from medical record.

**Results:** A total of 22 subjects were involved in this study. Mean AMH level in the metabolic syndrome group is compared to the non-metabolic syndrome group ( $10.72 \pm 6.23$  ng/ml vs  $7.97 \pm 4.50$  ng/ml,  $p=0.12$ ). AMH was strongly associated with HDL, triglyceride and insulin resistance (r-value of -0.29, 0.23, and 0.21 respectively,  $p < 0.05$ ).

**Conclusion:** AMH can be used as a predictor of metabolic syndrome in PCOS.

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**Keywords:** anti müllerian hormone, metabolic syndrome, polycystic ovarian syndrome

#### Abstrak

**Tujuan:** Untuk mengevaluasi apakah Anti Müllerian Hormone (AMH) dapat dijadikan prediktor untuk sindroma metabolik pada pasien Sindroma Ovarium Polikistik (SOPK).

**Metode:** Studi ini merupakan studi potong lintang yang dilakukan di Klinik Yasmin Rumah Sakit Dr. Cipto Mangunkusumo Jakarta pada bulan Juni hingga Desember 2012. Empat puluh satu persen pasien didiagnosis SOPK berdasarkan kriteria Rotterdam. Data sekunder didapatkan dari rekam medis.

**Hasil:** Pada studi ini terdapat 22 pasien yang mengalami sindroma metabolik. Nilai rerata kadar AMH pada pasien SOPK dengan sindroma metabolik ditemukan lebih tinggi dibandingkan dengan pasien tanpa sindroma metabolik ( $10,72 \pm 6,23$  ng/ml vs  $7,97 \pm 4,50$  ng/ml,  $p=0,12$ ). Hasil penelitian ini juga menunjukkan bahwa AMH berhubungan dengan HDL, trigliserida, dan resistensi insulin dengan nilai r -0,29, 0,23, dan 0,21 ( $p < 0,05$ ).

**Kesimpulan:** AMH dapat menjadi salah satu parameter untuk memprediksi sindrom metabolik pada pasien SOPK.

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**Kata kunci:** anti müllerian hormone, sindroma metabolik, sindroma ovarium polikistik

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#### INTRODUCTION

Anti Müllerian Hormone (AMH), also known as Mullerian inhibiting substance, is a member of the transforming growth factor  $\beta$  family of growth and differentiation factors. AMH is known to have an essential role in folliculogenesis. AMH inhibits the growth of primordial follicles, and inhibits the sensitivity of antral follicles to follicle-stimulating hormone (FSH) during cyclical recruitment. Thus, AMH is believed to play an important role in the regulation of the ovarian follicular growth. In addition, AMH is widely used as an ovarian reserve marker.<sup>1,2</sup> To date, the raise of AMH level found in polycystic ovarian syndrome (PCOS) is

believed due to increased expression of the promoter gene. In addition, its level increases up to two to three times compared to normal women worldwide.<sup>3,4</sup> In addition, the more severe PCOS phenotype one person has, the higher level of plasma AMH is detected.<sup>4,5</sup>

PCOS is one of the diseases frequently found in reproductive aged women. It affects both endocrine and metabolic system. In fact, 46% women with PCOS has shown association in the development of metabolic syndrome in later life ( $p < 0.0001$ ).<sup>6</sup> A study in Korea surprisingly demonstrated that young women with PCOS (mean age of 26.5 years old) had a three-fold

increased risk of developing metabolic syndrome compared to normal population.<sup>7</sup> However, due to many panels of examinations should performed to diagnose metabolic syndrome and not all patients present with the same characteristics, sometimes the diagnosis of metabolic syndrome is disregarded.

Currently, the relationship between level of AMH with the risk of cardiovascular event, particularly metabolic syndrome, remains unknown. Several studies suggested that the disturbance in lipid profile in patient with PCOS was not associated with body mass index.<sup>8</sup> However, Skalba et al found that AMH was significantly associated with total cholesterol, LDL and HDL.<sup>9</sup> Legro et al found that numerous PCOS patients with metabolic syndrome were under diagnosed, which may lead to inadequate therapy.<sup>10</sup> Therefore, a panel of examination that can predict the risk of cardiovascular event in PCOS is needed to be carried out, therefore clinicians will be able give adequate treatment to patients with PCOS.

## METHOD

A cross sectional study design was used. The inclusion criteria were women of reproductive age (15-45 years) who met the diagnostic criteria for PCOS based on Rotterdam 2003 in Yasmin Clinic, Dr. Cipto Mangunkusumo General Hospital during the period of June to December 2012 and agreed to participating in the research. Patient who consumed hormonal therapy or uses insulin-sensitizing agents within three months before, and had done ovarian drilling was being excluded. The patient would be diagnosed as having PCOS according to the Rotterdam consensus,<sup>11</sup> which

were the finding of 2 out of the 3 following criterias; oligo-and/or an ovulation, hyper androgenism, defined as hirsutism (Ferriman-Gallwey score > 8), or minor signs including acne, seborrhea, and/or testosterone > 3 nmol/l and/or androstenedione > 12 nmol/l, and criteria for polycystic ovary by ultrasound examination (minimum of 12 follicles with 2-9 mm diameter in each ovary, and/or increasing ovarian volume with a minimum size 10 mm<sup>3</sup>).

According to the American Heart Association,<sup>12</sup> metabolic syndrome is diagnosed when someone fulfill three among five diagnose criteria which are blood pressure  $\geq$  130/85 mmHg, triglyceride  $\geq$  150 mg/dl, fasting blood glucose  $\geq$  100 mg/dl, HDL-C < 50 mg/dl, and waist circumference  $\geq$  80 cm (Asian women).

Secondary data derived medical records were used to obtain the data of the subjects including AMH levels and all panels to diagnose metabolic syndrome: blood pressure, triglyceride, HDL-C, fasting blood glucose, and waist circumference.

Data were processed using Windows SPSS version 11.0. Results were presented as mean  $\pm$  SD. Relationship between each variable to AMH level was analyzed with independent t-test, p-value of < 0.05 would be considered statistically significant.

## RESULT

Using the Rotterdam criteria, 41 subjects were diagnosed with PCOS. Among these patients, twenty-two subjects were confirmed to have metabolic syndrome while nineteen had normal metabolic profile. Characteristics of the subjects in the study are presented in Table 1.

**Table 1.** Baseline Characteristics of the Subjects

	Metabolic syndrome (n=22)	Non metabolic syndrome (n=19)	p
Age (years)	30.14 $\pm$ 2.88	31.11 $\pm$ 3.43	0.33
BMI (kg/m <sup>2</sup> )	29.62 $\pm$ 4.62	26.89 $\pm$ 4.11	0.05
Waist circumference (cm)	91.80 $\pm$ 9.72	87.00 $\pm$ 7.19	0.08
Fasting blood Glucose (mg/dl)	102.45 $\pm$ 29.45	89.16 $\pm$ 6.64	0.06
HDL (mg/dl)	42.36 $\pm$ 6.99	48.68 $\pm$ 11.93	0.04
Triglyceride (mg/dl)	195.27 $\pm$ 10.41	101.26 $\pm$ 4.69	0.001
AMH (ng/ml)	10.72 $\pm$ 6.23	7.97 $\pm$ 4.50	0.12

Mean age between patients who had metabolic syndrome was younger than non metabolic syndrome ( $30.14 \pm 2.88$  vs  $31.11 \pm 3.43$ ). Significant results in the metabolic syndrome group were found in HDL level ( $42.36 \pm 6.99$  vs  $48.68 \pm 11.93$ ,  $p = 0.04$ ) and triglyceride ( $195.27 \pm 10.41$  vs  $101.26 \pm 4.69$ ,  $p < 0.001$ ). Despite no significant association was found, the level of AMH was higher in the metabolic syndrome group compared to the non - metabolic syndrome group ( $10.72 \pm 6.23$  vs  $7.97 \pm 4.50$ ,  $p = 0.12$ ).

Independent t-test was performed to determine the association of AMH between each of variable of metabolic syndrome. Variables such as BMI, waist circumference and fasting blood glucose were not significantly associated with AMH, whereas both HDL and triglyceride were significantly associated with AMH ( $p < 0.05$  [Table 2]).

**Table 2.** p-value of AMH as Predictor of each Variable of Metabolic Syndrome

	AMH p-value
BMI	0.05
Waist circumference	0.08
Fasting blood glucose	0.06
HDL	0.04
Triglyceride	0.01

## DISCUSSION

We found no significant difference between metabolic syndrome and non metabolic syndrome in PCOS. Moreover, metabolic syndrome can be seen as early as 30 years old. This finding is consistent a previous study conducted Park which demonstrated that young PCOS Korean women with mean age of 26.5 years old were three times at risk in developing metabolic syndrome in later life.<sup>7</sup>

In this study, AMH was higher in the PCOS group. This is consistent with previous studies.<sup>3,4</sup> In addition, the metabolic syndrome population had higher AMH levels compared to the non-metabolic syndrome group. ( $10.72 \pm 6.23$  vs  $7.97 \pm 4.50$ , respectively). Despite the non-significant difference ( $p=0.12$ ), 25% difference in clinical view might be considered as a significant finding.

Numerous studies found that increased plasma AMH level was significantly correlated with body weight.<sup>13,14</sup> However, we found no significant association between BMI and AMH level ( $p=0.05$ ), which is consistent with a previous study conducted by Skalba et al.<sup>13</sup>

To date, there is a new finding that AMH can replaced one of the criteria diagnosis of Rotterdam, such as polycystic ovarian morphology. Wiweko et al found that AMH was proven to be significant predictor of PCOS (cutoff value = 4.19ng/ml).<sup>4</sup> More over, AMH can be used of predictor of therapeutic response in PCOS.<sup>15</sup> AMH was found to have significant association with fasting insulin, glucose, in women with or without PCOS. However, this study did not demonstrate significant association between fasting blood glucose with level of AMH ( $p = 0.06$ ).

It is well known that metabolic syndrome is related to the development of cardiovascular risk in later life. PCOS is not only disease of reproductive system but also a disease of metabolic. 46% women with PCOS suffer from metabolic syndrome.<sup>6,8</sup> In addition, PCOS was associated with the development of dyslipidemia in obese women due to the increment of androgen level which may lead to atherosclerosis.<sup>10,16</sup> We found that AMH was significantly associated with HDL and triglyceride, which is in line with a previous study conducted by Skalba et al. Based on these findings, we suggest that AMH can be used as potential predictor of metabolic syndrome in PCOS. Our limitations include limited sample size. Further studies are required to make the result more useful, to treat PCOS more holistically.

## CONCLUSIONS

AMH level is associated with two markers of metabolic syndrome, triglyceride and HDL. This study demonstrates that AMH might be used as a potential predictor of metabolic syndrome in PCOS. Thus clinician can be aware and treat it as early as it can to prevent women with PCOS from developing cardiovascular event.

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