

Correlation between menstrual cycle and follicular maturation process in patient with polycystic ovary at Asri Medical Center Yogyakarta, Indonesia

Supriyatningsih^{1,2}, Vivian Resiana¹

¹Obstetrics and Gynecology, Reproductive Health, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta-Indonesia, Indonesia

²Reproductive Clinic, Asri Medical Center, Indonesia

Background To investigate the correlation between menstrual cycle and follicular maturation process in patient with polycystic ovary (PCO) from the prevalence of menstrual cycle abnormalities.

Objective To determine the correlation between menstrual cycle and follicular maturation process in patient with polycystic ovary at Asri Medical Center Yogyakarta, Indonesia.

Methods This study was a retrospective analytical approach with case control study. The study population was female patients in the Department of Obstetrics and Gynecology Asri Medical Center Yogyakarta, Indonesia. While the sample in this study 178 female patients in 2014 at Department of Obstetrics and Gynecology Asri Medical Center that meet the inclusion and exclusion criteria and using total sampling technique. Retrieving data using instruments from medical records. Data were analyzed using chi-square analysis.

Results Patients with oligomenorrhea 2.8 times more at risk of ovarian follicular maturation process disorder than patients who did not experience oligomenorrhea with PCO ($p = 0.003$; OR = 2.8; 95% CI = 1.409 to 5.633).

Conclusion There is a correlation of the menstrual cycle length to the process of maturation of ovarian follicles in patients with PCO at Asri Medical Center. Women who experience menstrual cycle disorders such as oligomenorrhea have a higher risk impaired ovarian follicle maturation process.

Keywords Oligomenorrhea, Menstrual disorders, PCO, Polycystic ovary, Ovarian follicles, Follicular maturation

Introduction

Many women have not aware of Menstrual Disorder that happened to them, until the disorder led to a prominent symptom. The most happens as menstrual disorder is *Oligomenore*. *Oligomenore* is menstrual disorder in the form of a long extension of the menstrual cycle. According to WHO report (2008) about *oligomenore* prevalensi in women around 45%. Bieniasz J *et al.* (2007) found the prevalence of primary *amenorrhea* is 5.3%, 18.4% of secondary *amenorrhea*, *oligomenorrhea* is 50%, *polimenorea* is 10.5%, and the disruption is 15.8%.

Oligomenorea is menstrual disorder cycles attacked 16,7% teenager in Indonesia. (Siegberg dkk,2007).

Prevalence of *Oligomenorea* in Yogyakarta according to Djaswadi (2000) is 36,1%. It is a high number for the prevalence of a disease or a medical disorder. According to the Installation patient data in *obstetrics* and *gynecology* Asri Medical Center (AMC) Yogyakarta in March 2013 until July 2013 there were 22 patients with *oligomenore* and PCO (*Polycystic Ovary*). In August 2013 until December 2013 have 26 patients with PCO, Whereas drastic increasing seen in January 2014 until May 2014 were 53 female patients with PCO.

The incidence rate indicates that more women who have PCO because of irregular menstrual cycle but many women do not realize it.

Irregular menstrual cycles can be caused by a failure of ovarian follicles maturation process. If the failures repeatedly happen, it will increase the factor risk for PCO (*Polycystic Ovary*).

PCO is a disorder of hormonal levels balance and ovulation disorder or the existing of tumor that produces high androgen hormone. Women with PCO will produce high androgen hormone that appearing symptoms such as oily face, obesity, and excessive hair growth, especially on the hands and feet's. Many women are not aware yet about the effects of abnormal ovarian follicle maturation process toward menstrual cycle abnormalities. Therefore, based on this case the researchers interested in studying the relationship of menstrual cycle length towards ovarian follicle maturation process in patients with PCO (*polycystic ovary*) which reviewed from the prevalence of menstrual cycle abnormalities. In the long term, if the problem is not treated well, it will lead to high risk of endometrial cancer. PCO is a hormonal disorder that most often occurs in women with reproductive age.

Menstruation is sexual maturation process for woman (Lee dkk, 2006). Menstruation can also be defined as the process of bleeding from the endometrial that occurs regularly through the vagina as a cleaning process of uterus on blood vessels, glands and cells that are unused due to the absence of fertilization or pregnancy.

Menstruation (menses) or normal periodic uterine bleeding is a physiological function that occurs in female. Basically menstruation is catabolism and occurs under the influence of pituitary and ovarian hormones (Pernoll, 2009).

Menstrual bleeding was blood coming out from uterus healthy women, the duration in 3-6 days, with brownish color, changed the bandage 2-5 times per day, and happens due to decreased levels of progesterone, in a cycle of ovulating (Baziad, 2003). Menstruation occurs when puberty or adolescence that caused by the growth of hormone and the increase of sex hormones that lead to menstruation. Menstruation according to Dorland medical dictionary is a physiological secretions blood and mucosal tissues as well as cyclical through the vagina from the uterus is not pregnant, under the control of hormones and in normal circumstances recur, usually in intervals of about four weeks, except during pregnancy and lactation during the reproductive period (puberty to menopause).

The first menstruation is called *menarche* and *menopause* is the end of menstruation. *Menarche* usually occurs in women aged 8-13 years, while *menopause* usually occurs in women aged 49-50 years.

Follicles are sacs in the ovary that filled fluids (ovarian), where the ovum grows and then released during ovulation or aspiration. Every month the follicle stimulated by hormone called FSH (*follicle stimulating hormonee*) which produces by pituitary gland to release the ovum. Ovary is an important part of normal development and reproductive function of women. Ovaries are a pair of glands almond shaped and sized as in the female reproductive system in which estrogen is produced and ovum are keep. Ovaries are in some ligaments on either side of the uterus.

Each month, approximately 10-20 ovums follicles will grow and there will be a mature ovum cells and the rest will be absorbed into the ovarian tissue. Mature ovums will undergo a process called ovulation. When ovulation of follicles empty is often called the *corpus luteum*. The *corpus luteum* will produce progesterone and hormones essential for pregnancy if fertilization occurs. However, if fertilization does not occur, the corpus luteum will degenerate and the cycle will start again from the beginning.

The follicle can be found in various stages of development, namely primary follicle, secondary and mature follicles (*folikel de Graaf*). Also there are follicles that have degenerated called *follicular atresia*. In the cortex can also be found kinds of corpus, there are *corpus rubrum*, *corpus luteum*, and *corpus albicans*.

Spencer and Brown (2007) stated that in the early stages of the cycle, FSH in sufficient quantities will give a signal to the cells to become mature ovum in the ovaries. The ovum cell present in a small pouch called a follicle. Usually one follicle will mature faster than others. FSH also stimulates the ovaries to produce estrogen. Estrogen accelerates follicular maturation process to form the further development and ensure the lining of the uterus to thicken in preparation for implantation of a fertilized ovum cell. Insistence LH stimulates ovulation process, in which the ovum is released from the mature follicle in the ovary to the fallopian tube. The empty follicle turns yellow is called the *corpus luteum* and begin producing progesterone. Progesterone causes the uterine lining thickens in preparation for implantation of a fertilized ovum or called embryo.

The muscles in the walls of the fallopian tubes contract slowly to stir the ovum. Approximately six days after an ovum is released from the ovary, the ovum cell will reach the uterus. If the ovum has been fertilized by a sperm while still inside of fallopian tube, then the embryo will be implanted in the uterine wall and progesterone levels will remain high, this is the beginning of pregnancy. If the ovum is not fertilized, levels of estrogen and progesterone will decrease, this causes the uterine wall to thicken and the unfertilized ovum cell released during menstruation. The whole process will be repeated.

Desain of the Study

This study is a retrospective analytic correlation with *case control study* approach, because this study is using secondary data of the medical records. This program is used to determine the relationship of menstrual cycle towards on ovarian follicles in patients with PCO (*Polycystic Ovary*).

Population and Sample of the study

1. Population of the study
The population of the study were female patients in *obstetrics and gynecology* installation of Asri Medical Center (AMC) in Yogyakarta

2. Sample of the study
Sample of the study were female patients in *obstetrics and gynecology* installation of Asri Medical Center (AMC) in Yogyakarta that meet the inclusion and exclusion criteria.

1. Inclusion criterias for the subject of the study:
 - Women in productive ages (15-45 years old)
 - Ever or never experienced menstrual cycle disorders such as *oligomenorrhea*
 - Recorded as patients in *obstetrics and gynecology* installation of Asri Medical Center (AMC)
2. Exclusion criterias for the subject of the study:
 - Pregnant Woman.
 - Women who are undergoing treatment to cure other diseases.

Sampling size that used is *total sampling method*.

Result and Discussion

Tabel 4.2 The relationship of *Oligomenorrhea* and Ovarian Follicles Maturation Process

Variables	<i>Oligomenorrhea</i> Positive	<i>Oligomenorrhea</i> Negative	OR	95% CI	p
PFO Positive	98 55,05%	32 17,98%	2,818	1,409-5,633	0,003
PFO Negative	25 14,04%	23 12,92%			

Note:PFO=MaturationDisordersOvarianFollicles

In Table 4.2 shows that PCO patients with *oligomenorrhea* 2,8 times higher risk of ovarian follicle maturation process disorder than PCO patients without *oligomenorrhea*. These results are statistically significant with CI 95%=1,409-5,633. These results are also clinically significant because majority of the sample (55,05%) in the study have *oligomenorrhea* and PCO.

These results also similar to Wibowo’s research (2010), he stated majority PCO respondents in dr. Sardjito Hospital Yogyakarta, 45% of respondents are not impaired maturation of ovarian follicles, 55% of the respondents impaired ovarian follicle maturation process, 97,5% of the respondents have menstrual cycle disorders such as *oligomenorrhea* and 2,48% respondents have not menstrual cycle disorders such as *oligomenorrhea*.

According to Arso (2010) in his research states that there are many factors that influence the occurrence of menstrual cycle disorders and the impaired of ovarian follicles maturation process in patients with PCO, these factors include fiber intake, fat intake, age, and BMI levels of the hormone androgen. Observed from BMI, women with status of overweight is 1.77 times higer risk of experiencing menstrual cycle disorders and impaired maturation of ovarian follicles. These result accordance with the research of Rakhmawati (2012) which states that interference menstrual cycle in women who have overweight, 1.89 times greater than women who had normal BMI.

Table 4.1 Subject Characteristics of the study based on age, marital status, occupations and menstruation period

No	Respondents Characteristics	F	Percentage (%)
1	Ages	15-16 years old	4 2,25
		17-25 years old	68 38,2
		26-35 years old	91 51,12
		36-45 years old	15 8,43
2.	Marital Status	Married	109 61,24
		Unmarried	69 38,76
3.	Occupation	Students	77 43,26
		Civil Servant	67 37,64
		Bussinesman	12 6,74
		Worker	12 6,74
		Other	14 7,87
4.	Menstrual Lenght Period	Normal	55 30,9
		<i>Oligomenorrhea</i>	123 69,1

In table 4.1 shows that most of experienced menstrual cycle disorders and ovarian follicle maturation process disorders are civil servant, student or college student and married patient with risk 0,63 times more likely to suffer menstrual cycle disorders and ovarian follicle maturation process disorders than women unmarried.

Age also being a factor that effected ovarian follicles maturation process and being a sign to review there is menstrual cycle disorders or not. It can be seen in Table 4.1. Range ages between 26 up to 35 years old or early adulthood are the most common menstrual cycle length disorders and ovarian follicle maturation process. Less incidences happened in the age range 15 until 16 years old or early adolescence.

Menstrual cycle disorders such as *oligomenorrhea* and ovarian follicular maturation process disturbance can be caused by hormonal balance disorder include increasment of *luteinizing hormone* (LH) that increased and as the feedback estrogen levels always high so FSH levels cannot reach the top then it activates *theca cells* and producing androgen in the form of *androsteneidon androgen* and *testosterone*. *Hiperandrogen* condotion causes the domination of androgen in the internal environment of follicle so the follicles cannot grow and eventually die. Thus follicular growth stalled so that ovulation does not occur. This situation will affect to the long menstrual cycles that experiences a disruption in the form of *oligomenorrhea*. As previously discussed in Chapter II that the hormone of estrogen is very influential on the length of the menstrual cycle in women, estrogen causes the *proliferation* of endometrial cells. Hormonal disorders in women patients with PCO typically causes ovarian follicles of women shaped into many small size so that the development of each follicle disturb and it

influence menstrual cycle length in the form of *oligomenorrhea*.

Conclusion

Based on the analysis of the relationship between menstrual cycle length towards ovarian follicle maturation process in patients with PCO (*polycystic ovary*) in Asri Medical Center Yogyakarta on May to June 2014 can be concluded that:

1. The duration of the menstruation cycle affect the ovarian follicle maturation process in patients with PCO at Asri Medical Center Yogyakarta ($p=0,003$; $OR=2,8$; 95% ; $CI=1,409$ to $5,633$).
2. Women with menstrual cycle disorders such as *oligomenorrhea* 2,8 times more likely high risk of impaired ovarian follicle maturation process.

Suggestions

Based on the results of research and the limitations of the study, the researchers suggest:

1. For the Doctors Profession
Efforts should be made better for detecting the presence of menstrual cycle disorders that caused by hormonal disorders, especially in patients with *polycystic ovary*.
2. For the Further Researcher
Need to do more research on the relationship of the menstrual cycle length on the process of maturation of ovarian follicles in patients with *polycystic ovary* in other health services.

Bibliography

- Arikunto, S. (2006). *Prosedur penelitian (Suatu Pendekatan Praktik. Edisi Kelima*. Jakarta: Rineka Cipta.
- Arso, A. (2010). *Pengaruh Asupan Serat, Lemak dan Kadar Hormon Androgen terhadap Keberhasilan Perkembangan Folikel pada Pasien PCOS(Polycystic Ovary Syndrome) yang Dilakukan Induksi Ovulasi dengan Kломifen Sitrat*. Yogyakarta : UGM
- Baziad, A. (2003). *Endokrinologi Ginekologi ed. 2*. Jakarta : Media Aesculapius.
- Berek, J.S. (2002). *Novak's Gynecology ed. 13th*. Philadelphia : Lippincott Williams and Wilkins.
- Bieniasz, J., et al. (2007). *Menstrual Pattern and Common Menstrual disorder in Adolescent Girls_ a retrospective Study*. *Endokrynol Diabetol Chor Przemiany Materii Wieku Rozw*, 12(3), 205-10.
- Bobak, L., (2004). *Buku Ajar Keperawatan Maternitas*. Jakarta : EGC.
- Brashers, VL. (2008). *Aplikasi Klinis Patofisiologi : Pemeriksaan & Manajemen ed. 2*. (Alih Bahasa : dr. H. Y. Kuncara). Jakarta : EGC.
- Bringer, J., Lefebvre, P., et al. (1997). *The Confounding Role of Body Habitus in Androgen Excess*. In Azziz, R., Nestler, J.E and Dewally, D. eds *Androgen Excess Disorders in Women*. Philadelphia : Lippincott Raven Publishing, Inc.
- Cakir, M., et al. (2007). *Menstrual Pattern and Common Menstrual Disorder among University Students in Turkey*. *Pediatrics International*, 49(6).
- Camevale, E.M. (2008). *The Mare Model for Follicular Maturation and Reproductive Aging in the Women*. *Theriogenology* 69:23-30.
- Dahlan, S.M. (2005). *Besar Sampel dalam Penelitian Kedokteran dan Kesehatan*. Jakarta : Arkans.
- DeCherney AH, Pernoll ML.(1994). *Current Obstetric & Gynecologic Diagnosis & Treatment. Edisi ke-8*. Lange Medical Book;126-127.
- Depkes. (2009). *Profil Kesehatan Indonesia*. Jakarta.
- Dorland, A.N. (2011). *Kamus Saku Kedokteran Dorland ed. 28*. (Alih Bahasa : dr. Albertus Agung Mahode). Jakarta : EGC.
- Ganong, W.F. (1997). *Buku Ajar Fisiologi Kedokteran* (diterjemahkan oleh Djauhari Widjakusumah, Dewi Irawati, Minartha Siagian, Dangsin Moeloek, dan Brahma U. Pendit). Jakarta: Penerbit Buku Kedokteran EGC.
- Gibbs, R. S. & Kartan, B. Y. (2008). *Danforth's Obstetrics and Gynecology 10th Ed*. USA: Lippincott Williams and Wilkins.
- Guyton, A., Hall,J., (2008). *Buku Ajar Fisiologi Kedokteran*. 11th ed. Jakarta: EGC.
- Hadley, M.E. (2000). *Endocrinology Fifth Edition*. New York: Prentice Hall International Inc.
- Hendrik. (2006). *Problema Haid Tinjauan Syariat Islam*. Solo : Tiga Serangkai.
- Hestiantoro, A., (2011). *Obstetri dan Genekologi, konsep dasar seksio sesarea*. Jakarta: EGC.
- Isselbacher, B.W., et al. (1999). *Harrison Prinsip-Prinsip Ilmu Penyakit Dalam, ed 13 vol 1*. Jakarta : EGC.
- John, G.B., Shidier, M.J. (2010). Kit Signaling via PI3K promotes ovarian follicle maturation but is dispensable for primordial follicle activation. *National Institutes of Health, Dev Biol* 331(2): 292–299.
- Kasdu, D. (2005). *Solusi Problem Wanita Dewasa*. Jakarta : Pustaka Swara.
- Kathryn, M.C. (2006). *Pathophysiology : The Biologic basis for Disease in Adult and Children, ed 5th*. USA : Elseiver Mosby.
- Kusmiran, E. (2011). *Kesehatan Reproduksi Remaja Dan Wanita*. Jakarta: Salemba Medika.
- LaPol, P.S, Lu, J.K.H. (2001). *Effects Aging on Luteinizing Hormon Secretion, Ovulation, and Ovarium Tissue-Type Plasminogen Activator Expression. Experimental Biology and Medicine, vol. 226 :127-132*.
- among adolescent girls in Malaysia: a cross-sectional school survey. *Singapore Med J*;47(10):869-74.
- Lefebvre G, et al. (2005). *Primary dysmenorrhea consensus guideline*. *J Obstet Gynaecol Can*;27(12):1117-30.
- Llewellyn-Jones, D. (2005). *Panduan lengkap Tentang Kesehatan, Kebidanan dan Kandungan : Setiap Wanita*. Jakarta : Delapratasa Puslitbang.
- McLaughlin EA, McIver SC. (2009). Awakening the oocyte: controlling primordial follicle development. *Reproduction*;137:1–11.
- Nelson LM. (2009). Clinical practice. Primary ovarian insufficiency. *N Engl J Med* ;360:606–14.
- Pandidis, D., et al. (2013). Association between menstrual cycle irregularities and endocrine and metabolic characteristics of the Polycystic Ovary syndrome. *European Society of Endocrinology*.
- Pasquali, R., et al. (2012). Weight Control and Its Beneficial Effect in Infertility in Women with Obesity and Polycyclic Ovary Syndrom. *European Society of Human Reproduction and Embriology*.
- Pernoll, R.C., et al. (2009). *BS Obstetri dan Ginekologi*. (Alih Bahasa : dr. Susiani Wijaya). Jakarta : EGC.
- Rakhmawati, A. (2012). *Hubungan Obesitas dengan Kejadian Gangguan Siklus Menstruasi pada Wanita Dewasa Muda*. Semarang : UNDIP.
- Shikanov A, et al. (2009). Interpenetrating fibrin–alginate matrices for in vitro ovarian follicle development. *Biomaterials*;30:5476–85.
- Shikanov, Ariella, et al. (2012). Hydrogel network design using multifunctional macromers to coordinate tissue culture. *National Institutes of Health, Biomaterials* 32(10): 2524–2531.
- Lee LK, et al. (2006). *Menstruation Human Reproduction and Embriology*.
- Speroff L, Fritz MA, penyunting. *Clinical gynecologic andocrinology and fertility. Edisi ke-7*. Philadelphia:Lippincott Williams & Wilkins;2005.h.531- 46.
- Speroff, et al. (1994). *Clinical Gynecologic Endocrinology and Infertility Fifth Edition*. Baltimore: William and Wilkins.
- Wibowo, D. (2010). *Hubungan antara Kadar Malondialdehid (MDA) Plasma dengan Keberhasilan Pematangan Folikel pada Pasien Sindroma Ovarium Polistik (SPOK) yang Dilakukan Induksi Ovulasi dengan Kломifen Sitrat*. Yogyakarta : UGM.