Biopsychosocial Factors Associated with the Occurrence of Female Infertility

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ABSTRACT

Background: Infertility is not a disease that needs to be worried. However, it becomes a serious problem for certain people such as causing divorce. Infertility in women can be affected by Polycystic Ovary Syndrome (PCOS), Body Mass Index (BMI), lifestyle, age, occupation, stress, metabolic disorder, endometriosis, and uterine myoma. This study aimed to determine the factors associated with female infertility.
Subjects and Method: This was an analytic observational study with a case control design. This study was conducted at Dr. Moewardi hospital, Surakarta, Central Java, from May to July 2019. A sample of 200 women was selected by fixed disease sampling. The dependent variable was infertility. The independent variables were PCOS, BMI, lifestyle, age, occupation, stress, metabolic disorder, endometriosis, and uterine myoma. The data were collected by questionnaire and medical record. The study was analyzed by a multiple logistic regression.
Results: Female infertility was affected by age ≥35 years (OR= 9.05; 95% CI= 2.61 to 31.39; p= 0.001), occupation (OR= 8.29; 95% CI= 2.25 to 30.48; p= 0.001), BMI ≥25 (OR= 8.16; 95% CI= 2.44 to 27.29; p=0.001), PCOS (OR=117.34; 95% CI=10.31 to 1334.83; p <0.001), endometriosis (OR= 5.01; 95% CI= 1.17 to 21.38; p=0.029), uterine myoma (OR=6.59; 95% CI= 1.76 to 24.67; p= 0.005), and metabolic disorder (OR= 15.39; 95% CI= 4.02 to 58.84; p<0.001).
Conclusion: Female fertility is affected by age ≥35 years, occupation, BMI ≥25, PCOS, endometriosis, uterine myoma, and metabolic disorder.

Keywords: female infertility, PCOS, endometriosis

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BACKGROUND

A family is incomplete without the presence of a child. A child brings together the harmony of a family. The presence of a child is very important for the family. However, not all families get offspring naturally. Infertility is not considered a disease that needs to be worried, but it can be a serious problem for certain people and also causes a divorce (Vita-health, 2007). According to the National Commission on Violence Against Women (2016), in 2015, Indonesia had802 cases of divorce which were caused by infertility.

World Health Organization (2013) states there are 48.5 million couples in the world having infertility problem. The occurrence of infertility in developing countries is high. It reaches 30%. However, the occurrence of infertility in developed countries is only 5-8%. The infertility level in Indonesia is 21.3% out of the total population of reproductive age. It can be assumed that 2 out of 10 couples of reproductive age are infertile. The high level of infertility is assumed to increase with changes on existing demographic patterns.

Infertility is the failure of a couple to get pregnant within 1 year or more of a marriage, after having sexual intercourse regularly without using any contraception method (Prawirohardjo, 2011). Infertility can be caused by men and women. The percentage of factors that can cause male infertility is 30-40%, while from female is 60-70% (Manuaba, 2010). The level of female infertility in Indonesia reached 15% or around 6 million Indonesian women experiencing infertility (Indonesia Demographic and Health Survey, 2012). Female infertility is caused by age, occupation, stress level, BMI, abnormalities of the reproductive organ, comorbidity lifestyle, ovulation disorders (PCOS), tubal disorders, and uterine disorders (Oktarina et al., 2014; Indarwati et al., 2017; Hestiantoro et al., 2013).

There are several factors affecting the risks of female infertility. According to Santoso et al. (2014), 75% of female infertility are caused by PCOS. PCOS (Polycystic Ovary Syndrome) is associated with ovulation disorders in a woman of reproductive age. The absence of ovulation for 35 days to 6 months reduces the chance of sperm meeting with the ovum; therefore, it causes infertility (SListina et al., 2016).

Infertility is also caused by nutritional status. BMI (Body Mass Index) is used to assess a person's nutritional status. Abnormal nutritional status will affect on the delayed fertilization (Ahsan et al., 2012). The obesity rate in Indonesia has increased from year to year by 10.5% in 2007 and 21% in 2018. Chronic energy deficiency in women of reproductive age is also quite high, which is 14.5% (Ministry of Health, 2018).

Nutritional status can affect a person's immunity, thus making her/him susceptible to disease. The most common non-infectious diseases in infertility women are endometriosis (25.6%) and uterine myoma. After removing the disease, the scar tissue will appear, thus inhibiting fertilization (Oktarina et al., 2014).

Another factor that affect female infertility is age. If a woman is still in the reproductive period and having regular menstruation, pregnancy is likely to occur. Increasing age will reduce a woman's ability to get pregnant (Saraswati, 2015). In addition, the risky jobs increase the incidence of female infertility. There are several occupations that related to exposures to dangerous substancesfor female fertility. The substances that have been identified and can affect fertility are heat, X-ray radiation, metals, and pesticides (Hestiantoro et al., 2013). Jobs with high workloads can increase stress level to depression. The prevalence of depression in Indonesia is 6.1% and 9% of them have medical treatment (Ministry of Health, 2018). Stress is a condition where there is a pressure on someone can lead to various reactions. One of the effects of stress is affecting body functions, including the reproductive system. If it happens to women, it will affect the female fertility (Indarwati et al., 2017).

Several studies related to infertility have been carried out. However, various complex causative factors make the incidence of infertility in Indonesia still high. Therefore, the further study on the analysis of risk factors for female infertility is needed. This study aimed to analyze the risk factors associated with the occurrence of female infertility.

SUBJECTS AND METHOD

a. Study Design

This was an analytic observational study with a case control design. The study was conducted at Dr. Moewardi Hospital from May to July 2019.

b. Population and Sample

The case population in this study was all infertile female patients at Dr. Moewardi Hospital. The control population was all fertile female patients at Dr. Moewardi Hospital. A sample of 200 female was selected by fixed disease sampling.

c. Study Variables

The dependent variable was female infertility. The independent variables were age, occupation, BMI, PCOS, endometriosis, uterine myoma, and metabolic disorder.

d. Operational Definition of variables

Female infertility was a failure of a woman who has never been pregnant or has ever been pregnant to get another pregnancy after at least 12 months of sexual intercourse regularly without using any contraception. The data were collected by medical record. The measurement scale was categorical.

Polycystic Ovary Syndrome (PCOS) wasa group of symptoms of chronic ovulation disorders, hyper-androgenemia, and polycystic ovary morphological features experienced by women of reproductive age. It could interfere with fertility. The data were collected by medical record. The measurement scale was categorical.

Body Mass Index (BMI) was one of the methods used to measure a person's nutritional status by comparing weight and height. The measurement scale was continous and transformed into dichotomous.

Life style was a person's lifestyle that was expressed in her activities, interests, and opinions. The examples were smoking habits, alcohol consumption, balanced diet, exercise, rest patterns, drugs consumption. The data were collected by questionnaire. The measurement scale was continous and transformed into dichotomous.

Age was the time duration since birth to the study was carried out in units of years. The data were collected by questionnaire. The measurement scale was continous and transformed into dichotomous.

Occupation was the main activity that was carried out everyday. The data were collected by questionnaire. The data were collected by medical record. The measurement scale was categorical.

Stress was a mental disorder faced by a person due to pressure. The data were collected by the Perceived Stress Scale questionnaire. The measurement scale was continous and transformed into dichotomous.

Metabolic disorder was a metabolic disease suffered by women who experienced natural inability to get pregnant, such as diabetes, hypertension, and heart disease. The data were collected by medical record. The measurement scale was categorical.

Endometriosis was the growth of glands and endometrial stroma that still had function outside the uterine cavity and the myometrium. The data were collected by medical record. The measurement scale was categorical.

Uterine myoma was a benign and solid uterine muscle tumor that grew in the uterus. The data were collected by medical record. The measurement scale was categorical.

e. Study Instrument

The data were collected by the researcher using primary data from questionnaires for the age and occupation variables. BMI data collection was carried out with height and weight measurement. Height was measured by measuring height. Weight was measured by a scale. Other variables were collected by medical records.

f. Data Analysis

Univariate analysis aimed to describe the characteristics of each variable. Continuous data were described in n, Mean, SD, Min, and Max. Categorical data were described

in n and percentage (%). Bivariate analysis in this study was conducted to determine the correlation between female infertility and independent variables using the chi-square test. Multivariate data analysis used multiple logistic regression analysis.

g. Research Ethics

The research ethics in this study included the approval sheet, anonymity, confidentiality, and research ethics. The ethical eligibility in this study was from the Health Research Ethics Committee of Dr. Moewardi Hospital number: 493/IV/HREC/-2019.

RESULTS

1. Sample Characteristic

Table 1 shows the frequency distribution of age, lifestyle, stress, and BMI variables in continuous data. The age of 200 study subjects had a mean by 32.04, SD by 6.08, lowest age by 17 years, and highest age by 50 years. BMI in 200 study subjects had a mean by 23.94, SD by 3.73, lowest BMI by 17.2 and highest BMI by 36.2

The frequency distribution of study variables with categorical data is presented in Table 2. Female who were in the reproductive age (<35 years) were 70.5%, who worked were 54%, who had normal BMI were 70.5%, who were diagnosed as infertile as a case group were 25% and as fertile as a control group were 75%. The study subjects who had Polycystic Ovary Syndrome were 11.5%, had endometriosis were 13%, had uterine myoma were 13%, and had metabolic disorder were 17%.

Table 1. The frequency distribution of the continous data variables

Variables	n	Mean	SD	Min	Max
Usia (tahun)	200	32.0	6.1	17.0	50.0
IMT	200	23.9	3.7	17.2	36.2

Table 2.The frequency distribution of the categorical data variables

Characteristic	Frequency	Percentage (%)
Age		
< 35 years	141	70.5
≥ 35 years	59	29.5
Occupation		
Unemployed	92	46
Employee	108	54
Body Mass Index		
18.5 - 25	141	70.5
<18.5 or≥25	59	29.5
Infertility		
No	150	75
Yes	50	25
Polycystic Ovary Syndrome		
No	177	88.5
Yes	23	11.5
Endometriosis		
No	174	87
Yes	26	13
Uterine Myoma		
No	174	87
Yes	26	13
Metabolic disorder		
No	166	83
Yes	34	17

2. Bivariate Analysis

Table 3 shows the result of a bivariate analysis of various factors related to infertility. Female infertility was significantly affected by age ≥35 years (OR=4.88; p<0.001), occupation (OR=8.03; p<0.001), unhealthy lifestyle (OR=2.92; p=0.001), high stress (OR=2.17; p=0.034), BMI ≥ 25 (OR=7.10; p <0.001), PCOS (OR=117.07; p<0.001), endometriosis (OR=2.53; p=0.029), uterine myoma (OR= 3.70; p= 0.002), and metabolic disorder (OR= 15.60; p <0.001).

3. Multivariate Analysis

Table 4 shows the result of multivariate analysis of various factors related to infertility. Women aged ≥35 years had a greater risk for having infertility (OR=9.05; 95% CI=2.61 to 31.39; p=0.001). Women who worked had a greater risk for having infertility than women who did not work (OR= 8.29; 95% CI= 2.25 to 30.48; p= 0.001). Women with BMI of ≥25 had a greater risk for having infertility than BMI of 18.5 to 25 (OR= 8.16; 95% CI=2.44 to 27.29; p= 0.001).

Women with PCOS had a greater risk for having infertility than those without PCOS (OR= 117.34; 95% CI= 10.31 to 1334.83; p<0.001). Women who had endometriosis were at greater risk for having infertility than those who did not have endometriosis (OR = 5.01; 95% CI=1.17 to 21.38; p=0.029). Women who had uterine myoma were at greater risk for having infertility than those who did not have uterine myoma (OR= 6.59; 95% CI= 1.76 to 24.67; p=0.005). Women who had metabolic disorder were at greater risk for having infertility than those who did not have metabolic disorder (OR=15.39; 95% CI=4.02 to 58.84; p<0.001).

Table 3. The result of the bivariate analysis of the risk factors of female infertility

Independent Variables	Infertility				Total		OR	p
	Fertile		Infertile					
	N	%	n	%	n	%		
Age								
< 35 years	119	84.4	22	15.6	141	100	4.88	<0.001
≥ 35 years	31	52.5	28	47.5	59	100		
Occupation								
Unemployed	85	92.4	7	7.6	92	100	8.03	<0.001
Employee	65	60.2	43	39.8	108	100		
Body Mass Index								
18.5 - 25	122	86.5	19	13.5	141	100	7.10	<0.001
<18.5 or≥25	28	47.4	31	52.5	59	100		
Infertility								
No	149	84.2	28	15.8	177	100	117.07	<0.001
Yes	1	4.3	22	51.9	23	100		
Polycystic Ovary Syndrome								
No	135	77.6	39	22.4	174	100	2.53	0.029
Yes	15	57.7	11	42.3	26	100		
Endometriosis								
No	137	78.7	37	21.3	174	100	3.70	0.002
Yes	13	50	13	50	26	100		
Uterine Myoma								
No	141	84.9	25	15.1	166	100	15.60	<0.001
Yes	9	26.5	25	73.5	34	100		

Table 4.The result of the analysis of multiple logistic regression of the risk factors of female infertility

Independent Variables	OR	95% CI		p
		Lower limit	Upper limit	
Age (≥35 years)	9.05	2.61	31.39	0.001
Occupation (Yes)	8.29	2.25	30.48	0.001
BMI (≥25)	8.16	2.44	27.29	0.001
PCOS (Yes)	117.34	10.31	1334.83	<0.001
Endometriosis (Yes)	5.01	1.17	21.38	0.029
Uterine myoma (Yes)	6.59	1.76	24.67	0.005
Metabolic disorder (Yes)	15.39	4.02	58.84	<0.001
N observation = 200				
Log likelihood = -44.23				

DISCUSSION

1. The effect of age on female infertility

Based on the result of the analysis, age had a significant effect on female infertility. The age of ≥35 years increased the risk of infertility in women.

According to Deyhoul et al., (2017), the risk of infertility increases with age. A woman at the age of >30 has a greater risk of pregnancy failure. It is in line with a study conducted by Crawford et al., (2015). The fecundity or ability to get pregnant decreases with age. Women who have never been pregnant have a lower chance of achieving pregnancy. The fecundity decreases significantly at the end of 30 years of age and at the early age of 40 years. The probability of infertility increases from 10% to 20% at age>35 years and to 45% at the early age of 40 years (Steiner et al., 2016)

2. The effect of occupation on female infertility

Based on the result of the analysis, occupation affected female infertility. Women who worked were at a greater risk for having infertility than women who did not work.

Some occupations that involve exposures to dangerous substancescan increase the risk of infertility. The substances that have been identified and can affect fertility are heat, X-ray radiation, metals, and pesticides. Occupations that can increase the risk of female infertility are paramedics, office workers, and farmers (Hestiantoro et al., 2013). According to Fernandez et al. (2016), working with a shift work system causes menstrual disorders and the risk factor of miscarriage.

3. The effect of BMI on female infertility

Based on the result of the analysis of the study data, BMI had a significant effect on female infertility. BMI ≥25 increased the risk of infertility in women.

This study is in line with the study result conducted by Fontana et al. (2016) that abnormal BMI such as undernutrition, overnutrition, and obesity affect fertility in women. It is related to changes in metabolism in the reproductive system. Fatty acids, carbohydrates, and proteins have their ways of working. If the intake is not balanced quantitatively or qualitatively, it can damage the homeostatic metabolism and fertility in women.

4. The effect of Polycystic Ovary Syndrome on female infertility

Infertility was significantly affected by Polycystic Ovary Syndrome (PCOS). PCOS increased the risk of infertility in women.

PCOS is a group of symptoms of chronic ovulation disorders, hyper-andro-

genemia, and polycystic ovary morphological features (Heffner, 2010). According to Wang et al. (2019), the presence of perfluorododecanoic acid in plasma increases the risk of infertility in women with PCOS. According to Wang et al. (2017) in another study, PCOS can also cause infertility due to an-ovulation in PCOS sufferers. Therefore, the fertilization cannot occur. An-ovulation in women with PCOS is a result of hormonal disorders in the body (Heffner et al., 2010).

5. The effect of endometriosis on female infertility

Based on the result of the study analysis, endometriosis had a significant effect on female infertility. Endometriosis increased the risk of infertility in women.

The result of this study is in line with a study conducted by Zhou et al. (2018) that patients with endometriosis have 3 times greater risk for having infertility than those who do not have endometriosis. Concentration of Perfluorobutane Sulfonic Acid (PFBS) in plasma on the endometriosis increases the risk of female infertility (Wang et al., 2017). Endometriosis can also cause ovulation disorders; thus decreasing the ability to get pregnant (Conto et al., 2017). In addition, female infertility is also caused by scar tissue due to surgical removal of endometriosis (Hart, 2019).

6. The effect of uterine myoma on female infertility

Uterine myoma was significantly affected on female infertility. Uterine myoma increased the risk of infertility in women.

This study is in line with a study by Lisiecki et al. (2017) that uterine myoma with a large size and proportion can increase uterine stretching. This stretching causes contractility in the uterus. It has implications for the implantation disorders of fertilization. As a result, uterine myoma becomes one of the risk factors associated with the occurrence of female infertility.

7. The effect of metabolic disorder on female fertility

Metabolic disorders affected female infertility. Metabolic disorders increased the risk of infertility in women.

Infertility is associated with cardiovascular disease due to metabolic dysfunction in the body (Hanson et al., 2017). Thyroid dysfunction is also associated with reproductive disorders. 1 out of 8 women with hypothyroidism experience infertility. The thyroid antibodies in patients with hypothyroidism cause difficulty of getting pregnant, implantation failure, and risk of miscarriage (Hart, 2019).

AUTHOR CONTRIBUTION

Suci Arsita Sariis the main researcher who plays a role in collecting and processing the data of the study. Uki Retno Budihastuti examined the conceptual framework and methodology of the study. Eti Poncorini Pamungkasari gave the suggestion related to the discussion.

FUNDING AND SPONSORSHIP

This study used independent fund by the main researcher.

CONFLICT OF INTEREST

There is no conflict of interest.

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