

Path Analysis on the Biopsychosocial Determinants of Infertility among Reproductive Aged Women in Surakarta, Central Java

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ABSTRACT

Background: Infertility is a multidimensional problem. This problem occurs not only because of health problems related to anatomic factors such as problems in the fallopian tubes, ovaries, and endometrium, but also there are more factors such as physiological, genetic, and environmental factors. The purpose of this study was to analyze the factors that influence the incidence of infertility in women.

Subjects and Method: A case control study was conducted at the Gynecology Obstetrics Polyclinic and Sekar Fertility Clinic, Dr. Moewardi hospital, Surakarta, Central Java, from October to November 2019. A sample of 200 women reproductive age was selected by fixed disease sampling. The dependent variable was infertility. The independent variables were age, body mass index (BMI), physical activity, endometriosis, family history, exposure to cigarette smoke, and stress. The data were obtained from medical record and questionnaire. The data were analyzed by path analysis run on Stata 13.

Results: Infertility in women was directly increased with age 35 years ($b= 1.20$; 95% CI= 0.18 to 2.22; $p= 0.021$), BMI <18 or ≥ 25 ($b=$

2.93; 95% CI= 1.95 to 3.91; $p<0.001$), high physical activity ($b= 1.30$; 95% CI= 0.28 to 2.33; $p= 0.013$), endometriosis ($b= 1.17$; 95% CI= 0.20 to 2.13; $p= 0.018$), exposure to cigarette smoke ($b= 1.19$; 95% CI= 0.20 to 2.23; $p= 0.023$), and severe stress ($b= 1.18$; 95% CI= 0.27 to 2.08; $p= 0.011$). Infertility in women was indirectly increased with age, physical activity, and family history of infertile.

Conclusion: Infertility in women is directly increased with age 35 years, BMI <18 or ≥ 25 , high physical activity, endometriosis, exposure to cigarette smoke, and severe stress. Infertility in women is indirectly increased with age, physical activity, and family history of infertile.

Keywords: female infertility, risk factors, path analysis

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BACKGROUND

Infertility is a multidimensional problem with social, economic and cultural implications, which can occur and threatens proportions in countries with strong demographic problems, such as Greece. This prob-

lem occurs not only because of health problems related to anatomic factors such as problems in the fallopian tubes, ovaries, and endometrium, but also many other factors such as physiological, genetic, and environmental factors. Farquhar et al. (2019) states

that the factors that cause infertility in women are ovulation dysfunction, premature ovarian failure (POF) and Primary ovarian insufficiency (POI), the presence of ovarian cysts, abnormalities in the fallopian tubes, pelvis and uterus, and endometriosis. While the risk factors presented by the study are age and lifestyle.

A study by Indarwati (2017) states that the factors that influence the occurrence of infertility in women are age, occupation, stress level, body mass index, and abnormalities of reproductive organs. World Health Organization (WHO) states that infertility is a global health problem faced by about 8-10% of couples. Globally this means that 50-80 million people experience infertility problems.

The Central Statistics Agency (BPS) in 2011 out of a total 237 million people in Indonesia, there were +/- 39.8 million women of childbearing age, but 10-15% of them were declared infertile or sterile and increased to 15-25% of the total number of existing couples (Risquesdas, 2013). The incidence of infertility from female factors is 65%, male factors are 20%, and 15% are other factors and conditions that are still unknown (Oktarina, 2014).

Data of Sekar Fertility Clinic medical records of RSUD DR. Moewardi Surakarta in 2008 reported 979 couples, 2,205 couples in 20-12, and continued to increase to 4,055 couples in 2016 (Retiyansa, 2019). The number of new patients at Sekar Fertility Clinic Dr. Moewardi there were 1,083 infertile couples out of a total number of patients of 3,774 infertile couples. This number is lower compared to the previous year. Of these 74% are female infertility (Setiawan, 2017).

SUBJECTS AND METHOD

1. Study Design

This was an analytic observational study with a case control design. The study was carried

out at the Obstetrics and Gynecology Clinic and Sekar Fertility Clinic, dr. Moewardi hospital, Surakarta, Central Java, from October to November 2019.

2. Population and Sample

A sample of 200 women reproductive age was selected by fixed disease sampling, consisting of 50 infertile women and 150 fertile women.

3. Study Variables

The dependent variable is the incidence of infertility in women. The independent variables are age, body mass index, body activity, endometriosis, family history, exposure to cigarette smoke, and stress.

4. Operational Definition of Variables

Infertility was the inability of a woman to conceive/have children or require a period of more than 1 year to conceive/have children without using contraception. The tool used to collect data was medical record. The measurement scale was categorical, coded 0 for fertile and 1 for infertile.

Age was a unit of time to measure the time of the existence of an object or creature, both living and dead. The age of the study subjects was calculated from the beginning of birth until the time the study was conducted. The data were collected by questionnaire. The measurement scale was continuous and transformed into dichotomous, coded 0 for <35 years and 1 for ≥35 years.

Body mass index was a simple calculation using a person's height and weight to measure a person's body mass. The data were collected by medical record. The measurement scale was continuous and transformed into dichotomous, coded 0 for BMI 18-25 and 1 for BMI <18 or ≥ 25.

Physical activity was any movement carried out by the body and produced by skeletal muscle and requires energy. The data were collected by questionnaire. The measurement scale was continuous and transformed into dichotomous, coded 0 for score <7.9 and 1 for

score ≥ 7.9 .

Endometriosis was a complex disease characterized by inflammation and endometrial bleeding. Pain is caused by endometrial tissue in the pelvic region outside the uterus. The data were collected by medical records. The measurement scale was categorical, coded 0 for no and 1 for yes.

Family history was the presence or absence of a family member (mother or female sibling) who has an infertile history. The data were collected by questionnaire. The measurement scale was categorical, coded 0 for no and 1 for yes.

Exposure to cigarette smoke was exposure to all chemicals from burning cigarettes on smokers and non-smokers. The data were collected by questionnaire. The measurement scale was categorical, coded 0 for not exposed and 1 for exposed.

Stress is a prolonged psychological status that arises to cause negative effects on mood, immune function, and body health. The data were collected by questionnaire. The measurement scale was continuous and trans-

formed into dichotomous, coded 0 for score < 20 and 1 for score ≥ 20 .

5. Data Analysis

Data in this study were processed using univariate analysis, bivariate analysis, and multivariate analysis using path analysis to determine the direct and indirect effects of independent variables on the risk factors of infertility in women.

6. Research Ethic

This study was conducted based on research ethics, namely informed consent, anonymity, confidentiality, and ethical eligibility. Ethics permit in this study was obtained from the Health Research Ethics Commission of dr. Moewardi hospital, Surakarta, Central Java, Indonesia Number 1,066/IX/HREC/2019.

RESULTS

1. Sample Characteristics

Categorical data descriptions describe continuous data. The results of the analysis of the description of categorical data are shown in Table 1.

Table 1. Frequency distribution of continuous research data variables

Variable	n	Mean	SD	Min.	Max.
Age	200	30.1	6.3	19	49
BMI	200	22.5	3.2	16.5	31.1
Stress	200	17.4	9.3	5	38
Physical Activity	200	8.2	1.4	4.6	11.1

2. Univariate analysis

Table 2 shows that the number of study subjects the majority of fertile women aged < 35 years is amounting 146 people (73%). The subjects in this study were the majority had a normal body mass index with 143 people (71.5%) and subjects with an abnormal BMI were 47 people (28.5%). Most of the subjects were not exposed to cigarette smoke amounting to 154 people (77%) and subjects who were exposed to cigarette smoke as many as 46 people (23%). The majority of the subjects did not have a family history of

infertility as many as 150 people (75%) and subjects who had a family history of infertility were as many as 50 people (50%). Subjects who did not have more endometriosis were 148 people (74%) compared to subjects who had a history of endometriosis as many as 52 people (26%). The majority of subjects did high activity as many as 130 people (65%) when compared with subjects who carried out normal activities as many as 70 people (35%). Subjects with normal stress levels more with a total of 130 people (65%) com-

pared with subjects with high stress, as many as 70 people (35%).

Table 2. Frequency distribution of categorical data research variables

Characteristics		Frequency	Percent (%)
Infertility	No	150	75.00
	Yes	50	25.00
Age	<35 years	146	73.00
	≥35 years	54	27.00
BMI	18-25	143	71.50
	<18 or ≥25	57	28.50
Smoke	No	154	77.00
	Yes	46	23.00
Family History	No	150	75.00
	Yes	50	25.00
Endometriosis	No	148	74.00
	Yes	52	26.00
Physical Activity	Score <7.9	70	35.00
	Score ≥7.9	130	65.00
Stress	Normal	130	65.00
	High	70	35.00

Table 3. Results of bivariate analysis of risk factors for infertility in women

Variable	Frequency				Total		OR	P
	Fertile		Infertile		n	%		
	n	%	N	%				
Age								
<35	123	84.2	23	15.8	146	100	5.34	<0.001
>35	27	50.0	27	50.0	54	100		
BMI							15.79	<0.001
Normal (18-25)	129	90.2	14	9.8	143	100		
Not Normal (<18 or >25)	21	36.8	36	63.2	57	100		
Smoke							6.14	<0.001
No	129	83.8	25	16.2	154	100		
Yes	21	45.7	25	54.3	46	100		
Family History							4.40	<0.001
No	124	82.7	26	17.3	150	100		
Yes	26	52.0	24	48.0	50	100		
Endometriosis							2.78	0.003
No	119	80.4	29	19.6	148	100		
Yes	31	59.6	21	40.4	52	100		
Physical Activity							1.06	0.86
Score <7.9	53	75.7	17	24.3	70	100		
Score ≥7.9	97	74.6	33	25.4	130	100		
Stress							2.92	0.001
Normal	107	82.3	23	17.7	130	100		
High	43	61.4	27	38.6	70	100		

3. The result of bivariate analysis

Table 3 shows age (OR= 5.34; p= <0.001), BMI (OR= 15.79; p <0.001), physical activity (OR= 1.06; p= 0.864), endometriosis (OR= 2.78; p= 0.003), family history (OR= 4.40;

p= <0.001), exposure to cigarette smoke (OR= 6.14; p= <0.001), and stress (OR= 2.92; p= 0.001).

4. The result of path analysis

a. Model Specification

This explains the relationship between the variables studied. There are 8 variables calculated in this study, namely infertility, age, body mass index, body activity, endometriosis, family history, exposure to cigarette smoke, and stress.

b. Model Identification

The variables measured include:

- 1) Number of measured variables: 8
- 2) Number of endogenous variables: 3
- 3) Number of exogenous variables: 5

4) Number of parameters: 8

The degree of freedom (df) formula is:

$$df = (\text{number of measured variables} \times (\text{number of measured variables} + 1) / 2) - (\text{endogenous variables} + \text{exogenous variables} + \text{number of parameters})$$

$$= (8 \times (8 + 1) / 2) - (3 + 5 + 8) = 20$$

Path analysis can be done if $df \geq 0$, while in the identification of the model in this path analysis the value of df is 20 which means over identified or path analysis can be used.

Table 4. Results of path analysis on the factors influencing infertility in women

Dependent Variable	Independent Variable	b	(95%) CI		p
			Lower Limit	Upper Limit	
Direct Effects					
Infertility in women	← Age	1.20	0.18	2.22	0.021
	← BMI	2.93	1.95	3.91	<0.001
	← Smoke	1.19	0.16	2.23	0.024
	← Endometriosis	1.17	0.20	2.14	0.018
	← Physical Activity	1.30	0.28	2.33	0.013
	← Stress	1.17	0.72	2.08	0.011
Indirect Effect					
BMI	← Physical Activity	-0.84	-1.47	-0.21	0.009
Endometriosis	← Family History	0.71	0.01	1.41	0.048
	← Age	0.67	-0.02	1.36	0.056
Stress	← Family History	0.74	0.08	1.39	0.028
Physical Activity	← Age	-0.98	-1.62	-0.34	0.003
N observation = 200					
Log likelihood = -543.96					

Several variables have an indirect influence on the incidence of infertility in women, namely physical activity on BMI (b= -0.84; 95% CI= -1.47 to -0.21; p= 0.009), family history of infertility with endometriosis (b= 0.70 ; 95% CI= 0.01 to 1.41; p= 0.048), age with endometriosis (b= 0.67; 95% CI = -0.02 to 1.36; p = 0.056), family history of infertility with stress (b = 0.73; 95% CI = 0.81 to 1.40; p = 0.028), age with physical activity (b= -0.98; 95% CI= -1.62 to -0.34; p= 0.003).

Table 4 shows that there is a direct relationship between the age variable and the incidence of infertility age (b= 1.20; 95% CI= 0.18 to 2.22; p= 0.021), BMI (b= 2.93; 95% CI= 1.95 to 3.91; p<0.001), physical activity (b= 1.20; 95% CI= 0.28 to 2.33; p= 0.013) endometriosis (b= 1.17; 95% CI= 0.20 to 2.13; p= 0.018), cigarette smoke exposure (b= 1.19; 95% CI= 0.16 to 2.23; p= 0.024), and stress (b= 1.18; 95% CI= 0.27 to 2.08; p= 0.011).

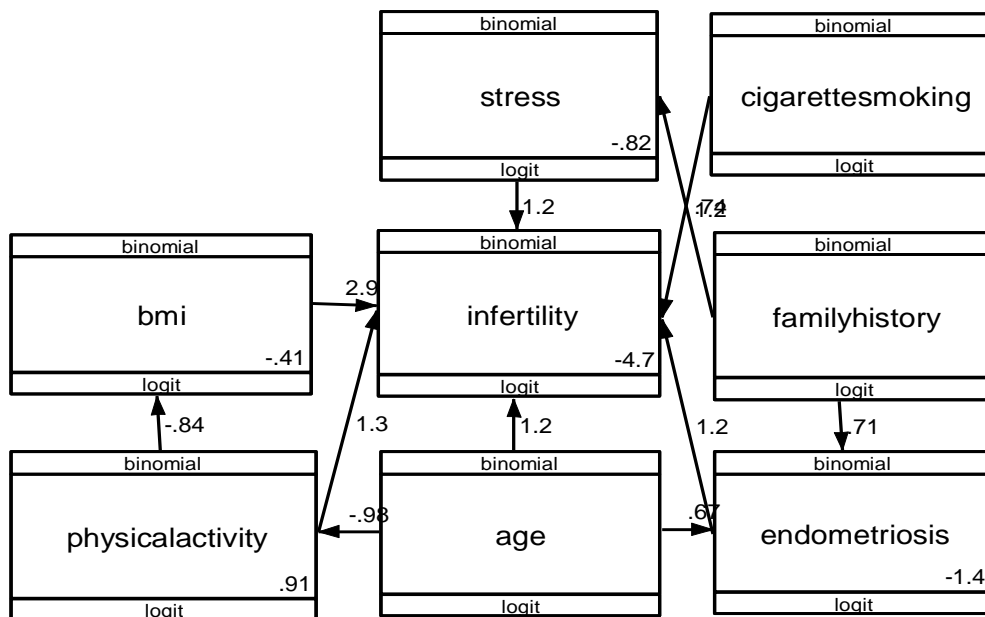


Figure 1. Path Analysis Model with Estimated Values

DISCUSSION

1. The Effect of Body Mass Index on Infertility in Women

Based on the results of the analysis, body mass index has a significant effect on infertility in women directly. Women with an abnormal BMI (<18 or > 25) have a higher risk of experiencing infertility.

This study was in line Cai et al. (2017), which states that BMI is a factor that influence the occurrence of infertility and risky pregnancy. A low BMI can also indicate inadequate intake and energy status, thereby affecting the concentration of gonadotropins, follicular growth and oocyte quality.

Women with more weight experience irregular menstrual cycles twice as common as women with normal body weight. Overweight women are more prone to become infertile compared to women with normal BMI, this is because overweight women have resistance to insulin, hyperinsulinemia, hyperandrogenemia, and increased aromatization of androgens against estrogen in peri-

pheral tissues.

In addition, obesity causes changes in gonadotropin release (GnRH), which is a decrease in sex hormone-binding globulin (SHBG). Growth hormones and growth factor proteins such as insulin, increased levels of leptin and decreased levels of adiponectin (Sanlier and Yorusun, 2018).

The higher the activity carried out, the reduced body mass index. The results of this study are in accordance with a study by Bradbury (2017), which states that high physical activity is related to the average percentage of a person's body fat. The results also showed a relationship between a woman's age and physical activity.

2. The Effect of Age on Infertility in Women

Based on the results of the analysis, age directly affects infertility in women and is statistically significant. Women whose age ≥ 35 years have a greater risk for infertility.

The results of this study are in line with a study by Purwoastuti and Walyani (2015),

female fertility naturally decreases from the age of 35 years due to fewer egg reserves. As women get older, their hormonal become imbalances and it decreased the function of the reproductive organs.

Hormonal imbalances in a woman's body can cause disruption in the menstrual cycle. Increasing age of women makes the hormones in the body become unbalanced. This results in the FSH hormone increasing, the follicular phase getting shorter, while the LH level and duration of the luteal phase do not change, resulting in irregular periods. Increasing age of women makes the number of ovarian follicles decreases.

The decrease in the number of follicles becomes faster when a woman is more than 38 years old. Follicles also become less sensitive to gonadotropin stimulation resulting in decreased female fertility (Indarwati, 2017)

3. The Effects of Physical Activity on Infertility in Women

The results of this study are consistent with a study by Gudmundsdottir et al. (2011), which states there is a relationship between physical activity and menstrual disorders in women. Women with high physical activity experience an increase in cycle length in women \geq 25 years with a higher frequency of LTPA and shortening of the cycle, increased bleeding time and menstrual cycle irregularities, this will affect the fertility of women.

The results also showed a relationship between a woman's age and physical activity. The higher the activity of a woman, the less physical activity is carried out. This is because a person's stamina decreases as he gets older so physical activity is reduced.

4. The Effects of Endometriosis on Infertility in Women

Based on the results of research analyzes, endometriosis significantly influences the incidence of infertility in women. Women who have endometriosis have a higher risk of experiencing infertility.

The results of this study are in line with Prescott et al. (2016) which states that the risk of infertility has doubled in women $<$ 35 years with endometriosis. Endometriosis can interfere with fertility through various pathways, including peritoneal inflammation and endocrine disorders, which then disrupt ovarian function and ultimately reduce the number of oocytes (Tanbo et al., 2017).

The results of the analysis show that family history through endometriosis has an indirect effect on infertility in women. Study by Peterson et al. (2014) states that a family history of infertility increases the likelihood of a diagnosis of endometriosis. Women who have a family history of endometriosis are more likely to have endometriosis.

5. The Effects of Cigarette Smoke Exposure on Infertility in Women

Based on the results of the analysis, exposure to cigarette smoke has a significant effect on the incidence of infertility in women. Women who are often exposed to secondhand smoke have a higher risk of experiencing infertility.

The results of this study are in line with the study by Oboni et al. (2016), which states that women who smoke or are exposed to cigarette smoke are more at risk for infertility or a small number of children compared to women who do not smoke.

Tens of up to thousands of compounds found in cigarette smoke (from active smokers) and side stream smoke (from passive smokers or SHS) are very influential on women's reproductive health. Tobacco poison affects fertility by influencing folliculogenesis, oogenesis, steroid genesis, embryonic transport and implantation, endometrial angiogenesis, uterine blood flow and myometrial growth. Minimum smoke exposure time so that someone can be categorized as passive smokers is 15-60 minutes/day (Dechanet, 2011; Titisari, 2011).

6. The Effects of Stress on Infertility in Women

Based on the results of analyzes, stress has a significant effect on the incidence of infertility in women. Women who have high stress levels have a risk of experiencing infertility.

The results of this study are in line with the study by Hajela et al. (2016), which states that women with a history of depression are twice as likely to experience infertility. The level of stress can have an impact on the number of follicles. When the body responds to stress, the body will produce glucocorticoid hormone, cortisol from the adrenal glands. Cortisol that results from stress can cause follicular numbers to decrease (Setiyono et al., 2015).

Cortisol can also interfere with the pulsation of the GnRH hormone so that it makes the level of the FSH hormone decrease and results in a decreased number of follicles. The analysis shows that family history of stress influences infertility in women indirectly. Study subjects who have a family history of infertile are more at risk of experiencing higher stress than women who have no family history of infertile. Infertility in women is directly increased with age 35 years, BMI <18 or ≥25, high physical activity, endometriosis, exposure to cigarette smoke, and severe stress. Infertility in women is indirectly increased with age, physical activity, and family history of infertile.

AUTHOR CONTRIBUTION

Luthfia Zauma is the main researcher who played a role in conducting study, collecting data, formulating articles, and processing data. Uki Retno Budihastuti played a role in the formulation of the mindset in study. Eti Poncorini Pamungkasari played a role in the formulation of the methods and discussion of results.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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