



eISSN: 2281-7824

<https://www.pagepressjournals.org/index.php/hls/index>

**Publisher's Disclaimer.** E-publishing ahead of print is increasingly important for the rapid dissemination of science. The **Early Access** service lets users access peer-reviewed articles well before print / regular issue publication, significantly reducing the time it takes for critical findings to reach the research community.

These articles are searchable and citable by their DOI (Digital Object Identifier).

The **Healthcare in Low-resource Settings** is, therefore, e-publishing PDF files of an early version of manuscripts that undergone a regular peer review and have been accepted for publication, but have not been through the typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear on a regular issue of the journal.

E-publishing of this PDF file has been approved by the authors.

Healthc Low-resour S 2024 [Online ahead of print]

*To cite this Article:*

Safitri YI, Rahayu EP, Rizki LK, et al. **Analysis of determinants of infertility among women at *in vitro* fertilization clinic in Surabaya.** *Healthc Low-resour S* doi: 10.4081/hls.2024.11985

 ©The Author(s), 2024

Licensee [PAGEPress](#), Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

## **Analysis of determinants of infertility among women at *in vitro* fertilization clinic in Surabaya**

Yati Isnaini Safitri,<sup>1</sup> Esty Puji Rahayu,<sup>1</sup> Lailatul Khusnul Rizki,<sup>1</sup> Siska Nurul Abidah,<sup>1</sup> Ima Nadatien<sup>2</sup>

<sup>1</sup>Department of Midwifery, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya; <sup>2</sup>Department of Nursing, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, Indonesia

**Correspondence:** Yati Isnaini Safitri, Department of Midwifery, Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya, Surabaya, Indonesia.

E-mail: [yati@unusa.ac.id](mailto:yati@unusa.ac.id)

**Key words:** abdominal surgery; BMI; endometriosis; infertility; PCOS.

**Contributions:** YIS, data curation; YIS, EPR, LKR, conceptualization, validation, writing – original draft; YIS, LKR, formal analysis; EPR, IN, investigation; IN, resources; YIS, EPR, LKR, SNA, methodology; YIS, SNA, visualization and writing. All the authors participated in the review and editing and approved the final version to be published.

**Conflict of interest:** the authors declare no potential conflict of interest.

**Funding:** this study was fully funded by the Institute of Research and Community Services (LPPM), Universitas Nahdlatul Ulama Surabaya with contract number: 570.206/UNUSA-LPPM/Adm-I/IV/2023.

**Ethics approval and consent to participate:** the research procedure received an ethical letter from the Health Research Ethics Committee at Nahdlatul Ulama University, Surabaya No. 0274/EC/KEPK/UNUSA/2023. During the research, the researcher paid attention to the ethical principles of information to consent, respect for human rights, beneficence, and non-maleficence.

**Availability of data and materials:** all data generated or analyzed during this study are included in this published article.

**Informed consent:** written informed consent was obtained for anonymized patient information to be published in this article.

**Acknowledgments:** we would like to thank Prof. Dr. Ir. Achmad Jazidie, M. Eng, as Chancellor of Universitas Nahdlatul Ulama Surabaya. Dr. Khamida, S. Kep. Ns., M. Kep as Dean of the Faculty of Nursing and Midwifery, Universitas Nahdlatul Ulama Surabaya. Nanik Handayani, S. Kep. Ns., M. Kes as Chair of the Midwife Professional Education Study Program. Achmad Syafiuddin S. Si., M. Phil., PHD as Chair of the Research Institutions and Community Service of Universitas Nahdlatul Ulama Surabaya. Dr. Amang Surya SpOG. as Leader of ASHA IVF Surabaya PHC Hospital. Intan Kusuma Hadie, and Endang Larasati as research enumerators. UNUSA academic community and all respondents who participated in this study. Also, we would like to acknowledge the contribution of the mentoring program conducted by the Research Centre of Excellence in Advancing Community Health, Surabaya, Indonesia.

## **Abstract**

In social life and global health, infertility is common. History of abdominal surgery, body mass index (BMI), endometriosis, menstrual history, and polycystic ovarian syndrome (PCOS) have not been fully explained as female infertility factors. This study examined infertility causes at **ASHA** *in vitro* fertilization Primasatya Husada Citra (PHC) Hospital Surabaya. This quantitative study was cross-sectional. In May-July 2023, 82 childbearing-age women with infertility issues visited the hospital and completed questionnaires. Description and analysis were performed using the Wilcoxon rank test to evaluate menstrual history, BMI, PCOS, endometriosis, and abdominal surgery history in relation to infertility. Infertility was statistically associated with abdominal surgery history ( $P=0.008$ ), BMI ( $P=0.000$ ), endometriosis diagnosis ( $P=0.000$ ), and PCOS ( $P=0.000$ ). Women with abdominal surgery, endometriosis, and PCOS had significant infertility. Women's infertility can be caused by ovulation disorders, tubal and pelvic disorders, or uterine disorders, but one-third of cases are unexplained. Infertility treatment may benefit from addressing abdominal surgery history, BMI, endometriosis, and PCOS. Early intervention and targeted care based on these determinants may improve fertility outcomes and reduce unexplained infertility.

## **Introduction**

Infertility significantly impacts the psychology of married couples, causing feelings of depression, worry, and guilt. It also affects their social lives, making them reluctant to engage with others, yet it does not deter them from maintaining their household.<sup>1,2</sup> The incidence of primary infertility is 62%, while secondary infertility, defined as the inability to have or maintain a pregnancy, stands at 38%.<sup>2</sup> Research shows that 10-15% of the 39.8 million couples in Indonesia experience infertility, with 4-6 million couples requiring treatment to conceive.<sup>3</sup> Basic health research data from 2018 indicates a rise in overweight (13.6%) and obesity (21.8%) among adults, correlating with a 31% increase in central obesity in those over 15 years old.<sup>4</sup> The stress related to infertility negatively affects the quality of life, with family coherence mediating this stress impact.<sup>5</sup>

Infertility necessitates medical attention and treatment and is a significant life event affecting personal, relational, and social dimensions.<sup>6</sup> It reveals intense stress and psychological vulnerability, sometimes leading to decreased marital satisfaction and family estrangement.<sup>7</sup> Causes of female infertility are classified into ovulation disorders [*e.g.*, polycystic ovarian syndrome (PCOS), menstrual cycle disorders, primary ovarian insufficiency], tubal and pelvic disorders, and uterine disorders (*e.g.*, submucous myoma, endometrial polyps, leiomyomas, Asherman's syndrome).<sup>8,9</sup> Factors contributing to infertility include occupational factors (*e.g.*, shift work, stress, radiation, chemicals), lifestyle factors (*e.g.*, age, nutrition, exercise, obesity, psychological stress, smoking, alcohol consumption), and environmental pollution.<sup>10-13</sup> Smoking and alcohol consumption also significantly impact male reproduction.<sup>7,14,15</sup>

Hormonal changes due to PCOS, such as increased luteinizing hormones and progesterone levels, are linked with higher body mass index (BMI), increasing the risk of PCOS.<sup>16</sup> Despite its status as a global health issue, research has not fully explained determinants of infertility like menstrual history, BMI, PCOS, endometriosis, and history of abdominal surgery. This study aimed to analyze the determinant factors causing infertility at **ASHA** *in vitro* fertilization (IVF) Primasatya Husada Citra (PHC) Hospital Surabaya.

## **Materials and Methods**

### ***Research design***

The research design employed was a quantitative descriptive study with a cross-sectional approach. This research aimed to analyze the determinant factors causing infertility (menstrual history, BMI, PCOS, endometriosis, history of abdominal surgery) at ASHA IVF at PHC Hospital Surabaya.

### ***Study participants***

The sample consisted of all new patients of childbearing age (17-49 years) who experienced infertility problems. These patients were visited from May to July 2023, totaling 82 respondents selected using a simple random sampling technique. The respondents were women of childbearing age with infertility problems, and their names were medically registered at the ASHA IVF PHC Hospital. Data was obtained directly through interviews and questionnaires diagnosing the causes of infertility experienced by respondents.

### ***Variable, instrument and data collection***

Independent variables included factors influencing infertility (history of abdominal surgery, BMI, endometriosis, menstrual history, PCOS). The dependent variable was the infertility rate. The research instrument was a questionnaire developed by the authors containing questions on general data (age, height, weight to determine BMI, categorized as underweight, normal, overweight, and obesity) and specific data (menstrual history measured as regular or irregular, PCOS, uterine endometriosis, history of abdominal surgery, and diagnosis of the cause of infertility). This data was obtained from secondary sources such as medical resumes. Data tabulation and analysis were conducted after collection.

### ***Data analysis***

The analysis aimed to determine the determinant factors (menstrual history, BMI, PCOS, endometriosis, history of abdominal surgery) causing infertility at ASHA IVF PHC Surabaya Hospital using the Wilcoxon rank test ( $P < 0.05$ ).

### ***Ethical clearance***

The research procedure received an ethical approval letter from the Health Research Ethics Committee at Nahdlatul Ulama University, Surabaya (No. 0274/EC/KEPK/UNUSA/2023). During the research, the researcher adhered to ethical principles including informed consent, respect for human rights, beneficence, and non-maleficence.

### **Results**

There were 82 respondents in this research, selected using the simple random sampling method. Table 1 shows that the characteristics of women in this study according to age reveal that the majority (59.8%) were in early adulthood (26-35 years). Regarding the history of abdominal surgery, the majority (54.9%) had no history of abdominal surgery. Based on the menstrual cycle, the majority (76.8%) of women had regular cycles. According to complaints of menstrual pain, almost a third of

the respondents (29.3%) experienced mild pain. Respondent characteristics based on BMI results showed that most women (53.7%) had a normal BMI. The diagnosis results indicated that some female respondents (26.8%) had endometriosis and others (20.7%) had PCOS.

Based on the Wilcoxon signed-rank test results in Table 2, several factors influence infertility, including a history of abdominal surgery ( $P=0.008$ ), BMI ( $P=0.000$ ), a diagnosis of endometriosis ( $P=0.000$ ), and a diagnosis of PCOS ( $P=0.000$ ). In contrast, factors that do not affect infertility are the menstrual cycle ( $P=0.286$ ) and the level of menstrual pain ( $P=0.166$ ).

## Discussion

Most respondents fall within the early adulthood age range (26-35 years), comprising 49 individuals (59.8%). Age significantly influences both male and female fertility, with women's age being the primary determinant of conception and healthy pregnancies. While infertility can stem from various factors, it often involves contributions from both partners. Multivariate regression analysis has identified women's age, duration of marriage, and socioeconomic status as predictive factors for reduced reproductive opportunities in cases of secondary infertility.<sup>17</sup> The incidence of infertility increases with age, particularly due to diminished egg quality in older women.<sup>18</sup> Research by Dewi *et al.* revealed that a significant portion of couples seeking fertility treatments had husbands over 35 years old and wives aged 20-35 years, highlighting the importance of female age in fertility treatments. Several factors, including the woman's age, significantly influence the success of IVF procedures.<sup>19</sup>

Respondent characteristics based on BMI results showed that the majority of women (53.7%) had a normal BMI. Dag and Dilbaz highlighted the association between overweight and obesity in women of reproductive age and anovulatory infertility.<sup>10</sup> In America, approximately 25% of cases of anovulatory infertility are attributed to being overweight. BMI serves as a straightforward tool for monitoring adult nutritional status, particularly in relation to being underweight or overweight.<sup>20</sup> BMI is calculated by dividing a person's weight in kilograms by their height in meters squared ( $\text{kg}/\text{m}^2$ ). However, the relative risk of anovulation increases significantly in women with BMI values of 24-31  $\text{kg}/\text{m}^2$  and  $>32 \text{ kg}/\text{m}^2$  compared to women with normal weight.<sup>21</sup> Obesity induces three changes that disrupt normal ovulation, which can be corrected through weight loss. Despite having a normal BMI, women still face the risk of primary and secondary infertility, indicating the influence of factors beyond BMI on infertility.<sup>21,22</sup>

Women diagnosed with endometriosis in this study exhibit a significant association with infertility, as indicated by a P-value of 0.000. Endometriosis, a prevalent condition among women of childbearing age in this study, involves the abnormal growth of endometrial glands and stroma outside

the uterus, often forming what is known as a chocolate cyst in the ovaries.<sup>23</sup> Symptoms may vary, with women experiencing severe pelvic pain even in mild cases, while those with severe endometriosis may exhibit milder symptoms such as dysmenorrhea and dyspareunia.<sup>24</sup> Other symptoms include abnormal uterine bleeding and infertility, both primary and secondary. Internal examinations may reveal small lumps in the sacro uterine ligament and a retroflexed uterus or adnexa that are difficult to move. Endometriosis, traditionally defined as the presence of endometrial tissue outside the uterus, has been recognized as a painful condition often requiring surgical intervention.<sup>25</sup> This study found that 26.8% of respondents were diagnosed with endometriosis, which significantly impacts fertility, with 30-50% of affected women experiencing infertility. Untreated endometriosis reduces the likelihood of conception compared to the general population, and even mild cases are associated with decreased pregnancy rates compared to unexplained fertility<sup>24</sup>. Studies on IVF suggest that advanced endometriosis is linked to poor ovarian reserve, low oocyte and embryo quality, and compromised implantation rates.<sup>26,27</sup>

Women diagnosed with PCOS account for 20.7% of all respondents in this study. This finding is consistent with research conducted by Riska Mareta in 2018,<sup>28</sup> which highlighted the significant relationship between PCOS and infertility. Mareta's research concluded that individuals with PCOS face an 8.5 times greater risk of experiencing infertility. PCOS, one of the most common endocrine abnormalities among women of reproductive age, manifests as a collection of symptoms and signs including hyperandrogenism and anovulation resulting from disorders of the endocrine system.<sup>29,30</sup> This condition affects approximately 5-10% of women of reproductive age, often without primary diseases in the pituitary or adrenal glands. PCOS is closely associated with chronic inflammatory processes, with sufferers often exhibiting high levels of visceral fat due to insulin resistance mechanisms.<sup>28,31</sup>

## **Conclusions**

This study reveals several factors that significantly impact infertility, including a history of abdominal surgery, BMI, a diagnosis of endometriosis, and PCOS. Conversely, menstrual cycle factors and menstrual pain levels were found to have no effect on infertility. It is recommended that healthcare professionals increase education about infertility within the community to enhance public awareness. Additionally, society should prioritize factors such as age at marriage, nutritional status, and lifestyle choices to mitigate the incidence of infertility.

## **References**

1. Bahar F, Zalika P, Lestari SW, et al. Male infertility as a bad news: A review. J Glob Pharma

Technol 2019;11:109-14.

2. Alhassan A, Ziblim AR, Muntaka S. A survey on depression among infertile women in Ghana. *BMC Womens Health* 2014;14:42.
3. Novrika B. Hubungan mekanisme koping dengan tingkat kecemasan pada pasangan infertil di RSIA Annisa Jambi tahun 2015. *Ris Inf Kesehat* 2018;6:184.
4. Kemenkes RI, Kementrian Kesehatan Republik Indonesia. Hasil Riset Kesehatan Dasar Tahun 2018;1689-99.
5. Ngai F-W, Loke AY. Relationships between infertility-related stress, family sense of coherence and quality of life of couples with infertility. *Hum Fertil* 2022;25:540-7.
6. Bhattacharjee NV, Schumacher AE, Aali A, et al. Global fertility in 204 countries and territories, 1950–2021, with forecasts to 2100: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. *Lancet* 2024;403:2057-99.
7. Ferreira M, Antunes L, Duarte J, Chaves C. Influence of infertility and fertility adjustment on marital satisfaction. *Procedia Soc Behav Sci* 2015;171:96-103.
8. Fritz MA, Speroff L. Female infertility. In: *Clinical Gynecologic Endocrinology and Infertility*. 8<sup>th</sup> ed. Wolters Kluwer Health; 2011.
9. Santoso B, Rahmawati NY, Sa'adi A, et al. Elevated peritoneal soluble endoglin and GDF-15 in infertile women with severe endometriosis and pelvic adhesion. *J Reprod Immunol* 2021;146.
10. Dağ ZÖ, Dilbaz B. Impact of obesity on infertility in women. *J Turkish Ger Gynecol Assoc* 2015;16:111-7.
11. de Angelis C, Nardone A, Garifalos F, et al. Smoke, alcohol and drug addiction and female fertility. *Reprod Biol Endocrinol* 2020;18:21.
12. Sirait BI, Reviani N, Udjung GIVW. Factors affecting infertility in women of reproductive age in the IVF programme. *Int J Trop Dis Heal* 2023;44:65-75.
13. Zhu L, Zhou B, Zhu X, et al. Association between body mass index and female infertility in the united states: data from national health and nutrition examination survey 2013-2018. *Int J Gen Med* 2022;15:1821-31.
14. Finelli R, Mottola F, Agarwal A. Impact of alcohol consumption on male fertility potential: a narrative review. *Int J Environ Res Public Health* 2021;19.
15. Kovac JR, Khanna A, Lipshultz LI. The effects of cigarette smoking on male fertility. *Postgrad Med* 2015;127:338-41.
16. Hashemi AH, Mozdarani H, Mozdarani S. The relationship between hormones level and body mass index with insertion and deletion (D/I) polymorphism of ACE gene in infertile patients



with polycystic ovary syndrome. *Bali Med J* 2017;6:90-6.

17. Benksim A, Elkhoudri N, Addi RA, et al. Difference between primary and secondary infertility in Morocco: frequencies and associated factors. *Int J Fertil Steril* 2018;12:142-6.
18. Igarashi H, Takahashi T, Nagase S. Oocyte aging underlies female reproductive aging: biological mechanisms and therapeutic strategies. *Reprod Med Biol* 2015;14:159-69.
19. Dewi NLPMC, Lindayani IK, Rahyani NKY, Suindri NN. Gambaran Faktor-Faktor Penyebab Infertilitas Dan Tingkat Keberhasilan Program Bayi Tabung Yang Diikuti Oleh Pasangan Usia Subur. *J Ilm Kebidanan (J Midwifery)* 2022;10:1-8.
20. Piyakong D, Apiratanawong S, Suasing C. Insights from leaders on effectively addressing overweight and obesity in the Thai community. *J Ners* 2023;18:117-23.
21. Handini A, Mirfat M. Hubungan Usia dan Obesitas dengan Infertilitas pada pasien di Rumah Sakit Kepresidenan RSPAD Gatot Soebroto. *Maj Kesehat Pharmamedika* 2018;9:33.
22. Vembu R, Devi MN, Nallepalli SR, et al. Impact of body mass index on the prevalence of metabolic syndrome among infertile south Indian women. *Int J Infertil Fetal Med* 2020;10:42-5.
23. Wiyono T, Dwiningsih SR, Widjiati W. The impact of endometriosis on intracellular calcium levels, cyclic dependent kinase 1 (Cdk1) expression, and cyclin b expression in post-ovulation oocytes of mice model. *J Reprod Infertil* 2023;24:232-9.
24. Kim M-R, Chapron C, Römer T, et al. Clinical Diagnosis and Early Medical Management for Endometriosis: Consensus from Asian Expert Group. *Healthcare* 2022;10.
25. Hendarto H. *Endometriosis Dari Aspek teori sampai penanganan klinis*. Airlangga University Press; 2015.
26. Rahmawati NY, Ahsan F, Santoso B, et al. Role of TNF superfamily members lymphotoxin- $\alpha$ , sCD40L, and TNF- $\alpha$  in endometriosis-related infertility. *J Endometr Pelvic Pain Disord* 2024;0.
27. Macer ML, Taylor HS. Endometriosis and infertility: a review of the pathogenesis and treatment of endometriosis-associated infertility. *Obstet Gynecol Clin North Am* 2012;39:535-49.
28. Mareta R, Amran R, Larasati V. Hubungan polycystic ovary syndrome (PCOS) dengan infertilitas di praktik swasta dokter obstetri ginekologi Palembang. *Maj Kedokt Sriwij* 2018;50:85-91.
29. Rachmawati DA, Sa'adi A, Utomo B, Tunjungseto A. Relationship between angiopoietin-like-protein-2 levels and anti-mullerian hormone levels in polycystic ovary syndrome of reproductive age. *Bali Med J* 2023;12:861-5.

30. Santoso B, Rusnaldi, Widjiati. Effect of alpha lipoic acid on polycystic ovary syndrome with insulin resistance. *Indian J Forensic Med Toxicol* 2020;14:1015-20.
31. Calcaterra V, Verduci E, Cena H, et al. Polycystic ovary syndrome in insulin-resistant adolescents with obesity: the role of nutrition therapy and food supplements as a strategy to protect fertility. *Nutrients* 2021;13.

**Table 1. Distribution of respondents by characteristics (N=82).**

Characteristics	Data distribution	
	Frequency	%
<b>Age group</b>		
Late teens (17-25 years)	1	1.2
Early adulthood (26-35 years)	49	59.8
Late adult (36-45 years)	31	37.8
Early elderly (46-55 years)	1	1.2
<b>History of abdominal surgery</b>		
Has a history of abdominal surgery	37	45.1
No history of abdominal surgery	45	54.9
<b>Menstrual cycle</b>		
Regular	63	76.8
Irregular	19	23.2
<b>Menstrual pain</b>		
No pain	21	25.6
Light	24	29.3
Currently	14	17.1
Heavy	23	28.0
<b>BMI</b>		
Less	2	2.4
Normal	44	53.7
Overweight	23	28.0
Obesity	13	15.9
<b>Diagnosis</b>		
Endometriosis	22	26.8
Uterine myoma	5	6.1
PCOS	17	20.7
POF	5	6.1
Endometrial polyp	8	9.8
Adenomyosis	3	3.7
Tuba non-paten	6	7.3
Obesity	1	1.2

Hydrosalpinx	4	4.9
An explanation	10	12.2
Uterus bicornis	1	1.2

BMI; body mass index; PCOS, polycystic ovarian syndrome; POF, premature ovarian failure.

**Table 2. Statistical test result.**

Statistical test <sup>a</sup>					
	Infertile – history of abdominal surgery	Infertile – menstrual cycle	Infertile - BMI	Infertile - diagnosis	Infertile – menstrual pain levels
	-2.661 <sup>b</sup>	-1.067 <sup>c</sup>	-7.057 <sup>b</sup>	-6.611 <sup>b</sup>	-1.384 <sup>b</sup>
P-value	0.008	0.286	0.000	0.000	0.166

BMI; body mass index; <sup>a</sup>Wilcoxon signed ranks test; <sup>b</sup>based on positive ranks; <sup>c</sup>based on negative ranks.