IABJ. Volume 3 No 1. June 2022
Available online at https://e-journal.unair.ac.id/iabj

e-ISSN: 2746-4474
DOI=10.20473/iabj.v3i1.35875

INDONESIAN ANDROLOGY AND BIOMEDICAL JOURNAL

Original Research

Relationship Between the Age of Female Partner and the Intrauterine Insemination Success in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar

Alycia Madeleine [1], Yukhi Kurniawan[2], I Gusti Ngurah Pramesemara[2]

[1] Medical Program, Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia
[2] Department of Andrology and Sexology, Faculty of Medicine, Universitas Udayana, Denpasar, Indonesia

OPEN ACCESS

ARTICLE INFO

Received: December 27, 2021
Accepted: June 09, 2022
Published: June 30, 2022

*) Corresponding author:
E-mail:
alyciamadeline@gmail.com

Keywords:
Age
Intrauterine Insemination
Infertility
Pregnancy

Abstract

Infertility is the inability of couples who have regular sexual intercourse without using protection to achieve pregnancy within one year. The prevalence of infertility was 21.3% in Indonesia. Intrauterine Insemination (IUI) is an assisted reproductive technology chosen by infertile couples to have children. Various factors influence the success of IUI. One factor that influences the success of IUI is the female partner's age. To determine the relationship between the age of female partners and the success of IUI. This study is descriptive-analytical research with the Cross-Sectional method using secondary data obtained from medical records of patients who underwent IUI procedures from January to March 2020 at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar. Total research subjects are 31 patients with an average age of 32 years. Positive pregnancies in female partners aged 25-35 years are 8 patients (33,3%) and female partners aged 35-40 are 1 patient (14.3%). Most patients had secondary infertility with a duration of 1-3 years. There is no relation between the increasing age of female partners and the decreasing success of IUI at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar (p=0,329). But female partners aged 25-35 years tended to have a positive pregnancy 2,333 times higher than female partners aged 35-40 years (RR=2,333; CI 95%: 0,349-15,612)..

Cite this as: Madeleine A, Kurniawan Y, Pramesemara IGN. Relationship Between the Age of Female Partner and the Intrauterine Insemination Success in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar. Indonesian Andrology and Biomedical Journal. 2022 June 30;3(1):7-12. DOI: https://doi.org/10.20473/iabj.v3i1.35875

1. Introduction

Infertility is the inability of couples who have sexual intercourse without using protection to achieve pregnancy within one year regularly.[1] While the prevalence of infertility in Asia was reported at 30.8% and 21.3% in Indonesia.[2] High infertility rates encourage couples who have difficulty conceiving children to seek another alternative procedure. One of the alternatives is Intrauterine Insemination (IUI). IUI is the first-line choice for couples with infertility problems as an alternative to having children. The usage of Intrauterine Insemination was chosen because the price is more affordable compared to other Assisted Reproductive Technologies. However, many factors affect the success rate of IUI.[3]

The female partner's age is a factor that significantly influences the success of IUI. The results showed that the highest pregnancy ratio was in women under 30 years of age. The decline in the pregnancy rate in women is associated with the use of IUI in women aged 35 years and over which is known to be lower than women under 35 years.[4]

A study by Govindarajan on the impact of increasing the age of a female partner on IUI pregnancy rates found pregnancy rates for women aged 25-30 by 18%, ages 30-35 by 15%, and ages 35-40 years by 13%.[5] The decrease in the success rate of IUI in middle-aged women is related to ovarian aging, which causes an increase in the levels of Follicle Stimulating Hormone (FSH)[6] and a decrease in Anti Mullerian hormone (AMH) which causes a decrease in oocyte quality with age.[7]

Based on the description stated above and the limitations of related literature sources in Bali, the author is interested in conducting research to determine the relationship of the female partner's age to the success of Intrauterine Insemination in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar, Bali.

This study is a Cross-Sectional study that was conducted from May to September 2021. Ethical Clearance was acquired from the Faculty of Medicine, Universitas Udayana Ethics Committee with letter number 1321/UN14.2.2.VII.14/LT/2021. The data used is secondary data, the medical record of the patients who perform IUI procedures in the Reproductive Service Unit (WIN) Rumah Sakit Ibu dan Anak (RSIA) Puri Bunda Denpasar.

The data was collected using purposive sampling. Inclusion criteria were female patients aged 25-45 years, married, diagnosed with infertility (either primary or secondary), undergoing Intrauterine Insemination procedures from January to March 2020. In sampling, data regarding ovarian stimulation and sperm preparation unavailable. Also, because the study focused only on the effect of the female partner's age on the success of IUI, the researcher did not include this data. Data in medical records containing complete research variables. The data listed in the medical record are the medical record number, the age of the female partner, the duration of infertility, the type of infertility, the number of IUI cycles, smoking history, history of drinking alcohol, history of having children, and IUI results. Sampling was done indirectly by the author, where the sample was given by the staff of RSIA Puri Bunda Denpasar. The authors obtained a total sample of 31 medical records of patients who underwent IUI procedures from January to March 2020 at the RSIA Puri Bunda Denpasar that met the inclusion criteria.

The data collected was processed and analyzed univariate and bivariate to see the description of the IUI pregnancy rate as well as the relationship between the increasing age of the female partner and the decrease in IUI success with Chi-Square test using the Statistical Package for the Social Science (SPSS) for Mac ver.22.

2. Result

Table 1. Characteristics of Research Subjects

Variable		Frequency (n=31)	Persentase (%)
Age	25-35 Years	24	77,4%
	35-40 Years	7	22,6%
Average Age	32 Years		
Origin	Badung	5	16,1%
	Buleleng	2	6,5%
	Denpasar	18	58,1%
	Gianyar	4	12,9%
	Outside Bali	2	6,5%
Occupation	Private Employees	15	48,4%
	Government Employees	4	12,9%

	Housewife	8	25,8%
	Entrepreneur	4	12,9%
Duration of Marriage	1-5 Years	14	45,2%
	6-10 Years	10	32,3%
	>10 Years	7	22,6%
Average Duration of Marriage	7 Years		
Types of Infertility	Primary Infertility	9	29,0%
	Secondary Infertility	22	71,0%
Infertile Duration	1-3 Years	16	51,6%
	4-5 Years	9	29,0%
	>5 Years	6	19,4%
Average Infertility Duration	4 Years		
Number of IUI cycles	1 Cycle	25	80,6%
	2 Cycle	6	19,4%
Pregnancy	Positive Pregnancy	9	29,0%
	Negative Pregnancy	22	71,0%

From table 1, it can be seen that the characteristics of research subjects according to the age of the female partner, origin, occupation, duration of the marriage, type of infertility, duration of infertility, number of IUI cycles, and pregnancy outcomes. The author divides the age of female partners in the medical record into two groups, namely the age of women 25-35 years and 35-40 years. The average age of the female partners in this study was 32 years. The division of the age of 25-35 years and 35-40 years was chosen because several studies reported that the decline in the pregnancy ratio began at the age of more than 35 years, and also the age of the youngest sample is 26 years old. The were divided into 2 groups so that the effect of age on the success of IUI is more visible, between ages above 35 years and under 35 years.

The study showed that seven patients had a positive pregnancy based on the results of Beta-hCG >25 mIU/ml and 2 people who had a positive urine pregnancy test. This study showed that 29.0% had a positive pregnancy with the IUI procedure. Based on the data obtained, 24 female patients (77.4%) aged 25-35 years and 7 female patients (22.6%) aged 35-40 years underwent the IUI procedure. More than half of the subjects resided in Denpasar (58.1%). The most significant percentage of the type of work on the subject in the medical record is a private employee (48.4%) and followed by housewives (25.8%). The majority of patients were married for 1-5 years (45.2%), experienced secondary infertility (71.0%), with a duration of infertility of 1-3 years (51.6%), and did one IUI cycle (80.6%). Most infertile patients need at least two years after marriage to seek health services.

Table 2. Distribution of Samples by Type of Infertility and Pregnancy

Variables		Pregnancy		Total (n)
		Positive Pregnancy (%)	Negative Pregnancy (%)	
Types of Infertility	Primary	2 (22,2%)	7 (77,8%)	9
	Secondary	7 (31,8%)	15 (68,2%)	22
Total		9 (29,0%)	22 (71,0%)	31

Table 2 shows that 22 patients (71.0%) had secondary infertility and 9 patients (29.0%) had primary infertility.

Positive pregnancies were higher in secondary infertility (31.8%) compared to primary infertility, while negative pregnancies were higher in primary infertility (77.8%).

Table 3. Distribution of Samples Based on Duration of Infertility and Pregnancy

Variables		Pregnancy		Total (n)
		Positive Pregnancy (%)	Negative Pregnancy (%)	
Infertility Duration	1-3 Years	4 (25%)	12 (75%)	16
	4-5 Years	5 (55,6%)	4 (44,4%)	9
	>5 Years	0 (0%)	6 (100%)	6
Total		9 (29,0%)	22 (71,0%)	31

As can be seen in Table 3 above, there are 16 patients (51.6%) with an infertility duration of 1-3 years achieved a positive pregnancy of 25%, and from 9 patients with an infertility duration of 4-5 years, 55.6% were found to have a positive pregnancy. Positive pregnancies were only found in infertile durations of 1-5 years, whereas for patients with infertile durations >5 years, found no pregnancy.

Table 4. Distribution of Samples Based on Number of IUI Cycles and Pregnancy

Variables		Pregnancy		Total (n)
		Positive Pregnancy (%)	Negative Pregnancy (%)	
Number of IUI Cycles	1 Cycle	9 (36%)	16 (64%)	25
	2 Cycle	0 (0%)	6 (100%)	6
Total		9 (29,0%)	22 (71,0%)	31

Table 4 indicates that the majority of patients who underwent 1 IUI cycle were 25 patients (80.6%) and positive pregnancies were only found in patients with 1 IUI cycle as many as 9 patients (36%). No positive pregnancy was found in patients who did 2 IUI cycles.

Table 5. Intrauterine Insemination Pregnancy Outcomes Based on the Female Partner Age

Variables		Pregnancy		Total (n)	RR	(p)
		Positive Pregnancy (%)	Negative Pregnancy (%)			
Age of Female Partner	25-35 Years	8 (33,3%)	16 (66,7%)	24	2,333	0.329
	35-40 Years	1 (14,3%)	6 (85,7%)	7		
Total		9 (29,0%)	22 (71,0%)	31		

From table 5, it can be concluded that the IUI success is based on the female partner group. Eight patients (33.3%) aged 25-35 years had a positive pregnancy, while 16 patients (66.7%) had a negative pregnancy. The positive pregnancy rate is lower in women aged 35-40 years. Only 1 (14.3%) of the seven women had a positive pregnancy. Based on the results of the Chi-Square correlation test. The relationship between the age of the female partner and the success of IUI got a significance value (p-value) of 0.329, which exceeds the value of 0.05. This shows that the results of the data obtained in Table 5 are insignificant so it can be interpreted that there is no relationship between the age of the female partner and the success of Intrauterine Insemination at RSIA Puri Bunda Denpasar.

Calculation of the Relative Risk (RR) regarding the relationship between the female partner's age on the success of IUI got a figure of 2,333 (95% CI 0.349-15,612). These results mean that female partners aged 25-35 years can experience a positive pregnancy 2,333 or 2 times higher than the age of the female partner of 35-40 years.

3. Discussion

Analysis of the data obtained in this study found that there was no relationship between the female partner's age and the success of IUI at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar

(p=0.329). The total number of positive pregnancies was 29.0%. However, it was observed that the pregnancy rate was lower in the age group of the female partners 35-40 years. Positive pregnancies in the age group of female partners 25-35 years were 33.3%, while 14.3% were of female partners 35-40 years with positive pregnancies.

The results of this study were similar to the results of a study in 2016 where the survey found a decrease in pregnancy rates in women aged >35 years, but the results obtained were not significant (p=0.212). The decline in pregnancy rates could be seen at the age above 30 years. The age group 31-35 had a pregnancy rate of 15%, while in the age group 35-40 years, the pregnancy rate decreased to 13.4%. The results of the study that were not significant between the age of the female partner on the success of the IUI might occur due to the small number of samples and not randomized so that the decrease in IUI success at the age of the female partner of 35- 40 years was not seen. Possible errors in data input could affect the results of this study. Lack of data on other factors that influence the decline in IUI success other than the age of the female partner that did not included in this study. Also, the decrease in efficacy might occur due to poor oocyte quality, decreased endometrial receptivity, a higher chance of chromosomal abnormalities, ovarian aging, and reproductive tract diseases.[8] Research by Atasever in 2016 found no significant correlation between a woman's age and the success rate of pregnancy at IUI (p=0.462).[9] Research by Vichinsartvichai in 2015 also found a decrease in clinical pregnancy rates that was not significant (p=0.124). There was a significant decrease in the clinical pregnancy rate at >40 years of age. The study found clinical pregnancy rates in the <35 years, 35-40 years, and >40 years age groups of 18.5%, 12.8%, and 3.6%, respectively.[10]

The age group of the female partner of 25-35 years had a 2,333 or 2 times greater chance of having a positive pregnancy than the age group of the female partner of 35-40 years (RR=2,333; 95% CI: 0.349-15,612). Research conducted by Ashrafi found an Odds Ratio of 2.1, which means that women aged <40 years have a 2.1 times greater chance of having a pregnancy with the IUI procedure.[11] So, when viewed from descriptive statistics and calculations of Relative Risk, found that a decrease in the ratio of pregnancies in the 35-40 years age group and the 25-35 years old female partner group has a greater chance of experiencing clinical pregnancy with IUI.

The Increasing age of the female partners causes a decrease in female fertility, which can be caused by decreased egg quality,[12] reduced ovarian reserves, and increased aneuploid follicles.[13] As the female partner's age increased, the AMH decreased and FSH increased. AMH is a hormone that functions as an ovarian reserve marker that shows the number of follicles in the ovaries and helps follicle growth.[14] As the age of the female partner increases, ovarian aging occurs, which is seen at low AMH levels, resulting in a decrease in the number of follicles and disrupting the growth of follicles in the ovaries, which causes fertilization rates and the possibility of getting pregnant to decrease.[7]

The FSH hormone functions to stimulate the growth of egg cells in the ovaries.[6] Inhibin B secretion decreases with age, contributing to an increase in serum FSH levels because inhibin B suppresses FSH release.[15] An increase in FSH will make egg production decrease and harm oocyte development so that a low egg count makes it difficult for older women to get pregnant. Therefore, a decrease in AMH levels and an increase in FSH levels can lead to a decrease in the chances of successful pregnancy with IUI.[6,7]

In addition to the factors described above, there are other factors, such as the thickness of the endometrium and the quality of the follicles which are assessed by looking at the diameter of the follicles that also affect the success of IUI pregnancy but are not included in this study. Several studies found a significantly higher pregnancy rate at endometrial thickness >7 mm. The correlation between endometrial thickness and pregnancy rate is still unclear. It should not be used as an exclusion criteria in IUI.[17,20] Yavuz found that the number of follicles in 3 increased fertility thereby increasing the possibility of pregnancy. More follicles development can improve the quality of the endometrium and the fertilization chances.[20] The patient's dominant follicle measuring 14-22 mm has a positive pregnancy outcome.[21,22] Two studies have shown higher pregnancy rates in Gonadotropins in the IUI.[23,24] Based on WHO guidelines, currently sperm count is considered normal if the sperm count is more than 15 million sperm with a normal sperm morphology of more than 5%, and 40% sperm motility is good to fertilize an egg.[1] Intrauterine Insemination is effective when initial sperm motility is 30%, and a total motile sperm count after washing of 5 million or more is associated with high pregnancy rates. [24,25]

The results of the pregnancy ratio in this research (29,0%) are high because Schorsch research shows that the ratio of IUI pregnancies after insemination is 5-15% with the number of research samples greater than 1000 samples.[26] The high pregnancy ratio may also occur because most

of the subjects are of 25-35 years and suffer from secondary infertility. In addition, in data collection, there can be bias due to the sample being given by the staff of RSIA Puri Bunda so that the sample is not taken directly and randomized which could have led to the possibility that more samples were given to the successful IUI procedure than to the failed IUI procedure thereby increasing the pregnancy rate in this study.

4. Conclusion

There was no significant relationship between the female partner's age and Intrauterine Insemination's succes in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar. However, based on the results of descriptive statistics, there was a decrease in the pregnancy ratio at the age of a female partner of 35-40 years. It can see from this study that positive pregnancies from IUI are 29.0%. The age of the female partner of 25-35 years had a positive pregnancy of 33.3% and the age of the female partner of 35-40 years experienced a positive pregnancy of 14.3%. Another factor that influences the success of IUI is the early cycle of IUI and the duration of infertility <5 years have a higher pregnancy ratio. Positive pregnancies in patients with secondary infertility are higher than in those with primary infertility. The Relative risk is 2,333 (95% CI 0.349-15,612), which means that the age of a female partner 25-35 years has a 2.333 times higher chance of having a positive pregnancy than the age of a female partner 35-40 years.

Further studies are needed to conduct a more comprehensive study by taking into account other factors from both men and women, such as endometrial thickness, follicle quality, sperm motility, and the addition of ovarian stimulation that could affect the success of IUI. Extending the duration of the study and increasing the number of samples can also be done to increase the precision of the study.

Acknowledgement

We would like to thank Universitas Udayana for the support for this article.

Authors' Contributions

All authors have contributed to the final manuscript. The contribution of each author as follow: collected the data, drafted the manuscript and designed the figures, devised the main conceptual ideas and critical revision of the article. All authors discussed the results and contributed to the finalmanuscript.

Conflict Of Interest

The authors state there is no conflict of interest.

Funding Information

This work does not receive any funding.

References

1. WHO. Infertility Definitions and Terminology. Human Reproduction Programme. World Health Organization; 2021. p. 1.
2. Soebijanto S. Konsensus Penanganan Infertilitas. Konsensus penanganan infertil. 2013.
3. Guan H, Tang H, Pan L, Song H, Tang L. Pregnancy Predictors in Unexplained Infertility After Intrauterine Insemination. Vol. 50, Journal of Gynecology Obstetrics and Human Reproduction. Elsevier Masson; 2021. p. 102071.
4. Patel AP, Patel MS, Shah SR, Jani SK. Predictive Factors For Pregnancy After Intrauterine Insemination: A Retrospective Study of Factors Affecting Outcome. J SAFOG. 2016;8(2):140–144.
5. Govindarajan M, Mallikarjunan S, Ahmed HR, Lakshmanan N, Silambuchelvi D, Sujatha M, et al. Retrospective Study of Factors Affecting Intrauterine Insemination Pregnancy Outcome: The Impact of Male Habits and Working Environment. J Hum Reprod Sci. 2017;10(2):114.
6. Dua M, Malik S, Prakash V, Bhatia V. ART Outcome in Young Women With Premature Ovarian Aging. J Midlife Health. 2013;4(4):230.
7. Revelli, A. et al. IVF Results in Patients with Very Low Serum AMH are Significantly Affected by Chronological Age, Journal of Assisted Reproduction and Genetics. Springer, 2016. 33(5):603–609.
8. K. J, Abraham S, Nambiar D. Factors Affecting Success of Intrauterine Insemination: A 3 Year Prospective Study. Int J Reprod Contraception, Obstet Gynecol. 2016;5(4):1077–1083.
9. Atasever M, Kalem MN, Hatırnaz Ş, Hatırnaz E, Kalem Z, Kalaylıoğlu Z. Factors Affecting Clinical Pregnancy Rates After IUI for The Treatment of Unexplained Infertility and Mild Male Subfertility. J Turkish Ger Gynecol Assoc. 2016;17(3):134–138.
10. Vichinsartvichai P, Siriphadung S, Traipak K, Promrungrueng P, Manolertthewan C,

Ratchanon S. The Influence of Women Age and Successfulness of Intrauterine Insemination (IUI) Cycles. J Med Assoc Thai. 2015;98(9):833–838.
11. Ashrafi M, Rashidi M, Ghasemi A, Arabipoor A, Daghighi S, Pourasghari P, et al. The Role of Infertility Etiology in Success Rate of Intrauterine Insemination Cycles: An Evaluation of Predictive Factors for Pregnancy Rate. Int J Fertil Steril. 2013;7(2):100–107.
12. Hoshino, Y. Updating The Markers for Oocyte Quality Evaluation: Intracellular Temperature as A New Index, Reproductive Medicine and Biology. Wiley-Blackwell, 2018. pp. 434–441.
13. Crawford NM, Steiner AZ. Age-related infertility. Vol. 42, Obstetrics and Gynecology Clinics of North America. Obstet Gynecol Clin North Am; 2015. p. 15–25.
14. Kini S, Li HWR, Morrell D, Pickering S, Thong KJ. Anti-Mullerian Hormone and Cumulative Pregnancy Outcome In In-Vitro Fertilization. J Assist Reprod Genet. 2010;27(8):449–456.
15. Wang S, Zhang Y, Mensah V, Huber WJ, Huang YT, Alvero R. Discordant Anti-Müllerian Hormone (AMH) and Follicle Stimulating Hormone (FSH) among Women Undergoing In Vitro Fertilization (IVF): Which One ss The Better Predictor For Live Birth?, Journal of Ovarian Research. J Ovarian Res, 2018. 11(1).
16. Jeon YE, Jung JA, Kim HY, Seo SK, Cho SH, Choi YS, et al. Predictive Factors for Pregnancy During The First Four Intrauterine Insemination Cycles Using Gonadotropin. Gynecol Endocrinol. 2013;29(9):834–838.
17. Weiss NS, Van Vliet MN, Limpens J, Hompes PGA, Lambalk CB, Mochtar MH, et al. Endometrial Thickness in Women Undergoing Iui With Ovarian Stimulation. How Thick is Too Thin? A Systematic Review and Meta-Analysis. Vol. 32, Human Reproduction. Oxford Academic; 2017. p. 1009–1018.
19. Liu Y, Ye XY, Chan C. The Association Between Endometrial Thickness and Pregnancy Outcome in Gonadotropin-Stimulated Intrauterine Insemination Cycles. Reprod Biol Endocrinol. 2019;17(1):1–8.
20. Yavuz A, Demirci O, Sözen H, Uludoğan M. Predictive Factors Influencing Pregnancy Rates After Intrauterine Insemination. Iran J Reprod Med. 2013;11(3):227–234.
21. Panda B, Mohapatra L, Sahu MC, Padhy RN. Success in Pregnancy Through Intrauterine Insemination at First Cycle In 300 Infertile Couples: An Analysis. J Obstet Gynecol India. 2014;64(2):134–142.
22. Diamond MP, Legro RS, Coutifaris C, Alvero R, Robinson RD, Casson P, et al. Letrozole, Gonadotropin, or Clomiphene for Unexplained Infertility. N Engl J Med. 2015;373(13):1230–1240.
23. Rachmiawaty A, Djuwantono T, Sasotya RMS. Analisis Faktor yang Mempengaruhi Keberhasilan Kehamilan pada Inseminasi Intrauterin. Indones J Obstet Gynecol Sci. 2018;1(1):24–30.
24. Dorjpurev U, Kuwahara A, Yano Y, Taniguchi T, Yamamoto Y, Suto A, et al. Effect of Semen Characteristics on Pregnancy Rate Following Intrauterine Insemination. J Med Investig. 2011;58(1–2):127–133.
25. Allow AK, Abdulmogny SSM, Maryam B, Ghafouri KN, Fakhrildin M-B, Muhamad, et al. The Relationship between Duration of Infertility and Intrauterine Insemination: A Multi-Centers Study. J Clin Dev Biol. 2016;1(3):1–7.
26. Schorsch M, Gomez R, Hahn T, Hoelscher-Obermaier J, Seufert R, Skala C. Success Rate of Inseminations Dependent on Maternal Age? An Analysis of 4246 Insemination Cycles. Geburtshilfe Frauenheilkd. 2013;73(8):808–811.