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Original Research

Sperm Agglutination in Infertile Men and The Success Rate of Intrauterine Insemination in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar

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Abstract

Every human being, especially a married couple, wants children. Obstacles to obtaining children are called infertility. One of the Assisted Reproductive Technology (ART) procedures used for treating infertility is intrauterine insemination (IUI), a non-invasive procedure with affordable costs. The success of IUI is influenced by many factors, one of which is sperm agglutination. This study determined the relationship between sperm agglutination and the success rate of the IUI procedure. The study is a descriptive-analytic study with a cross-sectional approach. The sample collection technique uses non-probability. The data used were medical records of male patients diagnosed with infertility, aged 25-45 years, and undergoing IUI procedures at the Rumah Sakit Ibu dan Anak Puri Bunda Denpasar from January to July 2022. Of the 91 samples obtained, 9 people experienced sperm agglutination (9,9%), and 82 people did not experience sperm agglutination (90,1%). The success rate of the IUI procedure was 29 couples (31,9%), 1 person (11,1%) experiencing sperm agglutination, and 28 people (34,1%) not experiencing sperm agglutination. Fisher's Exact test carried out has obtained a result (p=0.263). And the value of the odds ratio (OR) obtained=0.241). This study concluded that there is no significant relationship between sperm agglutination in infertile men and the success rate of the IUI procedure. The value of OR showed sperm agglutination is not included in the factors that affect the success rate of IUI.

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1. Introduction

Every human being, especially a married couple, wants children to continue their offspring, but not all couples can experience this. The inability of a married couple to have offspring after frequent sexual intercourse and the absence of protection after one year is called infertility.[1] In 2012, World Health Organization (WHO) also revealed a change from a demographic pattern in developing countries in 20 last years. This demographic change causes the incidence of infertility to have a percentage of 30%.[2] In Indonesia, infertility caused by male factors has a percentage of around 40%.[3]

The state of infertility in men can be detected using laboratory tests, and the test is semen analysis. Semen analysis is a sperm examination of male semen fluids that is performed to determine disorders of sperm by macroscopic and microscopic examination.[4] One of the microscopic parameters in assessing semen analysis is sperm agglutination.[5]

Sperm agglutination is a state of motile sperm that attach to another.[6] The prevalence of men with sperm agglutination is 12.1%.[7] The occurrence of sperm agglutination will cause a decrease in sperm quality, which will affect the fertilization process. This is because sperm agglutination can cause limited sperm motility.[8]

In couples who experience infertility, the management of technology-based infertility can be done to help the occurrence of pregnancy. Management of technology-based infertility is referred to as Assisted Reproductive Technology (ART). Types of ART that can be an option for infertility couples, such as Intrauterine Insemination (IUI), In Vitro Fertilization (IVF), and In Vitro Fertilization with Intracytoplasmic Sperm Injection (ICSI) procedure.[9]

Intrauterine Insemination (IUI) is an ART procedure carried out by placing quality sperm into the uterine cavity when ovulation occurs. IUI is the first-line therapy technology-based management for infertility couples whose costs are affordable, and the level of clinical pregnancy per cycle ranges between 10-20%.[10]

Rumah Sakit Ibu dan Anak (RSIA) Puri Bunda Denpasar is a hospital that provides special services for mothers, children, and those with reproductive problems in both men and women. This hospital has a specific service unit called Wija Insan Nugraha (WIN) Fertility Center. The service unit focuses on providing services to patients who require reproductive services and infertility. RSIA Puri Bunda Denpasar was chosen as the research location because RSIA Puri Bunda Denpasar became one of the referral hospitals to carry out infertility management procedures, which is intrauterine insemination in Bali Province, so the data obtained can be more accurate.

Based on this explanation, it is known that the success rate of clinical pregnancy through the IUI procedure is relatively low, and similar research and literature sources in Bali related to research topics are also lacking. Researchers feel the need to conduct research related to the relationship between factors causing infertility in men, especially sperm agglutination with the success rate of pregnancy through the IUI procedure, and the research location is in the Rumah Sakit Ibu dan Anak Puri Bunda Denpasar.

2. Methods

This is analytical descriptive research with a cross-sectional approach aimed at finding the relationship of sperm agglutination in infertile men with the success rate of intrauterine insemination in the Rumah Sakit Ibu dan Anak Puri Bunda Denpasar. This study was conducted at the Wija Insan Nugraha Fertility Center unit of Rumah Sakit Ibu dan Anak Puri Bunda Denpasar in January-July 2022. The data used was secondary data from patient medical records and the results of semen analysis. This study has been accepted by Komisi Etik Fakultas Kedokteran Universitas Udayana with the letter number 3108/UN14.2.2.VII.14/LT/2022.

The sampling technique in this study was non-probability sampling with the purposive sampling method, which is the process of taking research sampling based on the predetermined criteria, including inclusion and exclusion criteria that were considered to represent the entire population. Inclusion criteria in this study are men aged 25-45 years, married and living with their wife, diagnosed with infertility, undergoing intrauterine insemination procedures from January to July 2022, and having complete medical record data. The diagnosis of sperm agglutination is made by conducting a semen analysis examination. While the exclusive criteria are incomplete medical record data. Based on inclusion and exclusion criteria, the total number of respondents in this study was 91 samples.

The data was collected and analyzed using the SPSS for Windows 10 version 26. Data analysis was carried out with univariate and bivariate analysis. Univariate analysis was carried out to determine the characteristics of each variable,

while bivariate analysis uses the Fisher Exact test to determine the relationship of sperm agglutination with the success rate of IUI and assessment of the risk of sperm agglutination on the success rate of IUI using the assessment of odds ratio.

3. Results

In this study, the following results are:

Table 1. Characteristics of Subjects

Variables	Frequency (n=91)	Percentage (%)
Age (years)		
25-35	55	60,4
36-45	36	39,6
Infertility Type		
Primary	47	51,6
Secondary	44	48,4
Duration of Infertility (years)		
1-4	60	65,9
>4	31	34,1
Smoking History		
Yes	22	24,2
No	69	75,8
Alcohol History		
Yes	1	1,1
No	90	98,9
Domicile		
Denpasar	36	39,6
Outside Denpasar	55	60,4

Table 1 shows the demographic characteristics of the research subjects, including age, infertility type, infertility duration, smoking history, alcohol history, and domicile of research samples. The research sample in the age category of 25-35 years by 55 samples (60.4%) while in the age category of 36-45 years by 36 samples (39.6%). 47 samples (51.6%) experienced primary infertility, and as many as 44 samples (48.4%) experienced secondary infertility. Based on the duration of infertility, samples experienced infertility for 1-4 years by 60 samples (65.9%), while those who experienced infertility >4 years obtained as many as 31 samples (34.1%). In this study, 69 samples (75.8%) did not have a smoking history, while 22 people (24.2%) had a smoking history. On the history of consuming alcohol, as many as 90 samples (98.9%) did not have a history of consuming alcohol, and 1 sample (1.1%) had a history of consuming alcohol. And research samples mostly came from outside Denpasar, as many as 55 samples (60.4%) and 36 samples (39,6%) from Denpasar City.

Table 2. Sample Distribution Based on Sperm Agglutination

Variable	Frequency (n=91)	Percentage (%)
Sperm Agglutination		
Positive	9	9,9
Negative	82	90,1

Table 2 explains the sample distribution with positive sperm agglutination obtained as many as 9 samples (9.9%), while samples with negative sperm agglutination were obtained as many as 82 samples (90.1%).

Table 3 shows the sample distribution based on the success rate of the IUI procedure and obtains the results that the couple carrying out the IUI procedure is mostly unsuccessful. As many as 62 couples (68.1%) were not successful after the IUI procedure was carried out, while 29 couples (31.9%) were pregnant after the IUI procedure was carried out.

Bivariate analysis between sperm agglutination with the success rate of intrauterine insemination is presented in Table 5. From 91 research samples, a higher level of success of the IUI procedure in the sample group with negative sperm agglutination, is 28 samples (34.1%), while the success rate of the procedure IUI in the sample group with positive sperm agglutination obtained 1 sample (11.1%). IUI procedure success is also higher in the sample group with negative sperm agglutination obtained as many as 54 samples (65.9%), while IUI procedures in the sample group with positive sperm agglutination obtained as many as 8 samples (88.9%).

Based on the Fisher's Exact test, it obtained a p-value of 0.263. This indicates that there is no significant relationship between sperm agglutination and the success of the IUI procedure due to the value of P>0.05. And the calculation of the odds ratio (OR) obtained results of 0.241 (CI 95% 0.029-2,025). In this study, it can be concluded that there is no relationship between sperm agglutination with the success rate of intrauterine insemination procedures.

Table 3. Sample Distribution Based on The Success of Intrauterine Insemination

Variable	Frequency (n=91)	Percentage (%)
Success Rate IUI		
Pregnancy Positive	29	31,9
Pregnancy Negative	62	68,1

Table 4. Sperm Agglutination Bivariate Analysis with The Success Rate of Intrauterine Insemination

Sperm Agglutination	Success Rate IUI				Total		p-value	OR (CI95%)
	Pregnancy Positive		Pregnancy Negative					
	n	%	n	%	n	%		
Sperm Agglutination Positive	1	11,1	8	88,9	9	(100,0)		
Sperm Agglutination Negative	28	34,1	54	65,9	82	(100,0)	0,263	0,241 (0,029-2,025)
Total	29	31,9	62	68,1	91	(100,0)		

DISCUSSION

Sperm cells contained in semen fluid will be released by male reproductive organs when having sexual intercourse with their partners. Sperm physiologically must be able to move freely so it can move towards the ovary, and then the sperm can penetrate to the ovum.[11] The quality of sperm indeed determines the success of the penetration process so that the fertilization process can occur. The quality of sperm can be measured by conducting laboratory examinations which is a semen analysis, conducted in both macroscopic and microscopic examinations. The motility of sperm is certainly an important predictor, which is the functional aspect of the sperm itself. In addition, the concentration of sperm in semen fluids per mL, morphology, and sperm viability also need to be considered so that they can find out the success rate of fertilization.[12]

The presence of antisperm antibodies can cause the occurrence of sperm agglutination. However, antisperm antibodies also can not cause agglutination in sperm. Antisperm antibodies can be present in various places and react with different antigens. Male semen fluids have 2 main immunoglobulin classes, IgA and IgG. IgM is rarely found in semen fluid due to the size of the larger size of IgM.[8] Antisperm antibodies that can cause sperm agglutination then can interfere the interaction between sperm cells and ovum cells in the fertilization process, which further indicates infertility in men.[6] Sperm agglutination can also occur due to a history of surgery in the scrotum and E.coli bacterial infection. History of scrotum surgery has a risk of 3.4 times higher to experience sperm agglutination, while the occurrence of infection due to E.coli bacteria can cause the formation of antisperm antibodies that can be seen from increased IgA production.[7,11]

In this study, 9 samples (9.9%) experienced sperm agglutination, while those who did not experience sperm agglutination were 82 samples (90.1%). Other studies conducted by Dhyani *et al* in 2017 obtained the results from 33 research samples, 6 samples (18.2%) experienced sperm agglutination with distribution 1 sample (3.0%) in grade 1 sperm agglutination while 5 samples (15.2%) in grade 2 sperm agglutination.[13]

IUI is one type of non-invasive ART used as a first-line treatment for infertile couples. The success of the IUI procedure is assessed through a pregnancy hormone test such as a beta-HCG test. Before the IUI procedure is carried out, the preparation stage must be completed first. In men, sperm washing is carried out to obtain quality sperm and separate it from other components such as residual ejaculate debris cells. Quality sperm preparation will increase the chances of conception after the IIU procedure is carried out.[14] The most frequently used sperm washing procedures are simple washing, swim-up, and discontinuous density gradient centrifugation. Simple washing is a procedure by diluting the semen sample in a medium, then centrifuging it in order to differentiate motile sperm from other components and quality sperm will be at the bottom.[8,15] The swim-up technique is carried out with culture media in a test tube and during the incubation period, the test tube is tilted at 45^0, quality sperm cells will go to the top layer of the culture media.[16] Discontinuous density gradient centrifugation is a sperm washing procedure in order to obtain sperm cells that are free from other cells by

centrifugation. After the centrifugation process is complete, quality sperm will be in a lower phase due to their high density and good motility.[8,15] This study showed a high success rate of the IUI procedure by 29 couples (31.9%), while 62 couples (68.1%) did not succeed in reaching pregnancy.

Other studies also showed a relatively high level of success procedures is the research conducted by Rachmawaty *et al* in 2018. As many as 25 couples (23.5%) managed to achieve pregnancy, while 75 couples (76.5%) failed to achieve pregnancy.[17] This result shows that the success rate of the IUI procedure in RSIA Puri Bunda Denpasar is higher than the average clinical pregnancy rate.

Fisher Exact test results were conducted to assess the relationship between the independent variable and the dependent variable, obtaining a p-value of 0.263 (p>0.05). The value of the odds ratio (OR) obtained is 0.241 (CI95% 0.029-2.025), so it is concluded that there is no significant statistical relationship between sperm agglutination and IUI success. This can be due to the method of sperm preparation before the IUI procedure that causes only quality sperm that can be used, so the success rate of the IUI procedure becomes higher.

Research conducted by Vij *et al* in 2011 obtained similar results, with a total of 589 samples of the IUI cycle, as many as 55 samples (9.34%) were found agglutination in their sperm. Bivariate analysis shows the results there is no significant relationship between sperm agglutination with the success rate of IUI.[18] Other research conducted by Felemban *et al* obtained a different result. This study obtained the results of the IUI procedure has a relationship with the success rate of pregnancy. In the study, 6 samples (16.2%) were obtained and experienced antisperm antibodies in their sperm with their partners successfully achieved pregnancy after the IUI procedure. The p-value obtained in this study was 0.0046, which showed a significant relationship.[19]

The success of the IIU procedure is not only influenced by 1 factor but is influenced by many factors, both from the internal and external factors of men and women.[20] In this study only focuses on the relationship of sperm agglutination with the success of IUI, so further research is needed in the future regarding the factors that influence the success of IUI. In this study, there was no classification of the severity of sperm agglutination. The type of severity of sperm agglutination is expected to provide a accurate result of the success rate of the IUI procedure, so it needs to be reviewed and controlled in further research.

CONCLUSION

There is no significant relationship between sperm agglutination in infertile men and the IUI procedure success rate (p=0.263). As well as the value of the odds ratio (OR) in this study obtained a result of 0.241 (CI95% 0.029-2,025), which indicates sperm agglutination does not include factors that influence the success of IUI in Rumah Sakit Ibu dan Anak Puri Bunda Denpasar.

Further research is needed with larger samples, more diverse sample characteristics, more diverse research locations, analysis related to external and internal risk factors, and the severity of sperm agglutination that can affect the success rate of IUI procedures.

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Authors' Contributions

All authors contributed to the final manuscript. The first author contributed to collected and processed the data, analyzed and interpreted the data, drafted manuscript, and designing the figures. The second and third authors contributed to planed the main conceptual idea of this research and critically revising this article.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding this article.

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