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Varicocele in Infertile Male and Intrauterine Insemination Success at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar

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Abstract

Assisted Reproductive Technology (ART), such as intrauterine insemination (IUI), can be an option for infertile couples who are expecting a pregnancy. However, the success of IUI can be influenced by various factors, one of which is varicocele. This study aims to determine the association between varicocele and IUI success. This study is an analytical cross-sectional study using patient medical records. The sample of this study was male patients aged 25-45 years with infertility and undergoing IUI in the period April to June 2021 at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar. The sampling technique used, purposive sampling, was selected based on inclusion and exclusion criteria. Based on the criteria, this study selected 32 samples. From 32 participants, 5 had varicocele (15.6%), and 27 were without varicocele (84.4%). In this study, we found 12 success pregnancy after IUI (37.5%), with 3 participants having varicocele (9.4%) and 9 participants without varicocele (28.1%). The chi-square analysis carried out obtained the results (p>0.05), and the calculation of the relative risk got the result (RR=0.600). This study showed no significant association between varicocele in infertile men and the success of IUI. The RR calculation showed that varicocele was not a risk factor for IUI failure.

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1. Introduction

The number of couples experiencing primary and secondary infertility worldwide is estimated at 186 million people. In Indonesia, 15-25% of couples of fertile age experienced infertility in 2013 and estimated to increase every year.[2] Male factor infertility was found in 50% of cases of infertility.[3]

Advances in Assisted Reproductive Technology (ART), such as intrauterine insemination (IUI), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI), can be helpful for infertile couples who wish to have a pregnancy.[4] The community generally uses IUI because the procedure is easier, cheaper, and less invasive. The success ratio of clinical pregnancy in the IUI technique ranges from 10 to 20%, which can be influenced by male factors such as sperm quality.[5]

Varicocele is a disease that can affect sperm quality and is one of the most common in infertile male patients, with a prevalence of about 15-20% of the normal adult male population, 35% of men with primary infertility, and 70-85% of men with secondary infertility.[7] A study in China showed that the pregnancy rate after the IUI procedure in male partners with grade III varicocele was lower than that in non-varicocele male partners, with a ratio of 4.6%:14.4%.[8] This is in line with the result of a study by Sonmez and Haliloglu. Male partners who underwent varicocelectomy before the IUI procedure had a higher pregnancy rate than male partners without previous varicocele treatment (11.8%:6.3%).[9]

Research on the incidence of varicocele in Indonesia and its relationship to the success of ART is still scarce. Research conducted in other areas in Indonesia shows a high number of varicoceles as a cause of infertility in men and affects the semen quality of male partners.

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Rumah Sakit Ibu dan Anak (RSIA) Puri Bunda Denpasar is a hospital that provides IUI services for infertility patients in Bali, especially Denpasar. RSIA Puri Bunda Denpasar became the researcher's choice as the research location to consider various things. The place of the RSIA Puri Bunda Denpasar, which is easy to reach from the researcher's residence, the ease of data collection, and seeing the various limitations that researchers have regarding time, cost, and so on are among the researchers' considerations in determining RSIA Puri Bunda Denpasar as the research location.

Based on the previously mentioned background, varicocele can affect sperm quality and IUI success. Research on the incidence of varicoceles in Bali, especially in Denpasar, the city with the highest population density in Bali, and its association with IUI success has never been done before. Therefore, it is necessary to conduct a study to determine the association between varicocele in infertile male couples and the success of IUI at one of the ART service centers in Bali, Rumah Sakit Ibu dan Anak Puri Bunda Denpasar.

2. Methods

This analytical cross-sectional study is taken at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar in April-June 2021. Ethical approval has been given by Komisi Etik Fakultas Kedokteran Universitas Udayana with letter number 438/UN14.2.2.VII.14/LT/2021. The sample data were selected from the patient's medical record, including age, infertility diagnosis, duration of infertility, varicocele history, and IUI success.

The sampling technique used the purposive sampling method, which was selected based on inclusion and exclusion criteria. Inclusion criteria included men aged 25-45 years, married and living at home with their wives, diagnosed with infertility (primary and secondary), performed intrauterine insemination at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar, and complete medical record data. The detection and grading of varicoceles are diagnosed by physical examination findings according to Dubin's classification and performed by a physician. In comparison, the exclusion criteria include incomplete medical record data. Based on these criteria, this study selected 32 samples.

The collected data would be processed using the Statistical Package for the Social Science (SPSS) version 26, which would be analyzed univariately and bivariate. Univariate analysis is present to obtain the distribution of sample characteristics. Bivariate analysis was conducted to determine the association between varicocele and IUI success using the Pearson Chi-Square test and calculate the relative risk of IUI failure in the varicocele group.

3. Results

In this study, the following results are:

Table 1. Distribution of Sample Characteristics Based on Age, Diagnosis, and Duration of Infertility

Variable	Frequency n (%)
Age (years)	
25-35	24 (75)
36-45	8 (25)
Diagnosis	
Primary Infertility	16 (50)
Secondary Infertility	16 (50)
Duration of Infertility (years)	
1-5	21 (65.6)
>5	11 (34.4)

Table 2. Participants Characteristics Based on Varicocele Occurrence

Variable	Frequency n (%)
Varicocele History	
Yes	5 (15.6)
No	27 (84.4)
History of varicocelectomy	2 (6.3)
Varicocele grade	
Grade 0	0 (0)
Grade I	2 (6.2)
Grade II	1 (3.1)
Grade III	2 (6.2)

Table 3. IUI Success Distribution

Variable	Frequency n (%)
IUI Result	
Pregnancy	12 (37.5)
Pregnancy negative	20 (62.5)
Pregnancy after IUI	
Varicocele	3 (9.4)
Without varicocele	9 (28.1)
Pregnancy negative after IUI	
Varicocele	2 (6.3)
Without varicocele	18 (56.2)

Table 4. Bivariate Analysis of Varicocele with Intrauterine Insemination Success

Varicocele History	Pregnancy Positive n (%)	Pregnancy Negative n (%)	Total n (%)	p
Varicocele	3 (9.4)	2 (6.3)	5 (15.6)	
Non-varicocele	9 (28.1)	18 (56.3)	27 (84.4)	0.258
Total	12 (37.5)	20 (62.5)	32 (100)	

Table 5. Relative Risk Calculation of Varicocele in IUI Failure

Variable	RR	95% CI	
		Lower Limit	Upper Limit
Varicocele (yes/no)	3.000	0.423	21.297
Pregnancy Positive	1.800	0.737	4.395
Pregnancy Negative	0.600	0.198	1.814

The distribution of sample characteristics based on age, diagnosis, and duration of infertility is shown in table 1. In this study, the age categories of the sample were divided into two, ages 25-35 years by 8 participants (25%) and 36-45 years by 24 participants (75%), and the average age of the patients was 31.8 years. There were 16 participants (50%) with primary infertility patients and 16 participants (50%) with secondary infertility, with a duration of infertility less than five years, as many as 21 participants (65.6%).

Table 2 shows participants that have a history of varicocele as many as 5 participants (15.6%), participants without varicocele are 27 participants (84.4%), and there are 2 participants (6.2%) without varicocele have a history of varicocelectomy. Varicocele is divided into levels based on physical examination, grade 0 (subclinical) to grade III. The highest level of sample varicocele was in grade I varicocele in as many as 2 participants (6.2%), then grade II varicocele in as many as 1 participants (3.1%), and grade III varicocele in as many as 2 participants (6.2%) in. From the total number of participants, no participants had a history of other comorbidities.

Based on the data as shown in table 3, 12 participants were a success (pregnancy) after IUI (37.5%), and 20 participants (62.5%) experienced failure after IUI (negative pregnancy). Of the 12 participants who achieved the success of IUI, 3 participants were with varicocele (9.4%) and nine without varicocele (28.1%). On the other hand, of the 20 participants who failed to achieve success in IUI, 2 participants with varicocele (6.3%), and 18 were without varicocele (56.2%).

Based on the analysis of the association between varicocele and IUI success, shown in table 4, from a total of 32 participants, it was found that the most successful IUI occurred in non-varicocele patients, as many as 9 participants (28.1%). However, the varicocele group showed higher IUI success in 3 participants (9.4%) compared to IUI failure in 2 participants (6.3%). The results of the Pearson Chi-Square test, which concluded as a statistical test, obtained a p-value of 0.258. So, it can conclude that there is no significant association between varicocele and IUI success.

In this study was also carried out to identified relative risk (RR) with the result is 0.600 (CI 95% 0.198-1.814). This result indicated that the varicocele does not include the risk of IUI failure.

4. Discussion

Infertility is categorized into two groups, primary and secondary infertility. Primary male infertility is in men who have never participated in a clinical pregnancy and meet the criteria for infertility. Male secondary infertility occurs in men who meet the criteria for infertility but have previously experienced a clinical pregnancy.[9] Varicocele is one of the diseases that can cause infertility in men. According to Dubin's classification, the severity of varicocele based on physical examination findings is divided into grades 0-III. Grade 0 (subclinical) is not palpable or visible at rest or during the Valsalva maneuver but is visible on scrotal ultrasound. During the Valsalva maneuver, can palpate only Grade 1 (mild), grade II (moderate) is palpable at rest but not visible, and grade III (severe) is palpable and visible through the scrotal skin at rest.[6]

Several sperm washing techniques can be used in carrying out the IUI procedure, including simple wash¸ swim up, and density gradient centrifugation.[10] The simple wash technique was performed by adding 2 ml of culture medium to the semen sample and centrifuging it to separate the seminal plasma. The swim-up technique is performed by placing the sperm under a layer of culture medium in a tube. At the same time, the density gradient centrifugation technique is done by separating sperm cells based on their density.[11] However, from the three techniques, there has been no explicit study on the comparison of pregnancy rates for each technique.[12]

Based on this study, there was no association between varicocele and IUI success (p=0.258). Similar results were also seen based on the RR calculation, which showed that varicocele was not a risk factor for IUI failure. This result may be due to the small number of samples. This study also showed a reasonably high pregnancy rate of 37.5%. These results indicate a success rate for IUI that exceeds the average IUI pregnancy rate of 10-20% per cycle. There are many studies on the significant difference between a woman's age factor on pregnancy rates. This study may be due to the age range of participants, which is dominated by the age group of 25-35 years.[13] However, the success of IUI in the varicocele group was lower than in the non-varicocele group.

The low success of IUI in samples with varicocele may be due to abnormalities in spermatogenesis that are influenced by the incidence of varicocele.[14] Varicoceles can cause several mechanisms, such as oxidative stress due to the formation of reactive oxygen species (ROS), increasing intratesticular pressure, causing decreased blood flow, and resulting in hypoxia and increased temperature in the testes, resulting in damage to sperm cells.[15]

Oxidative stress is one of the factors closely related to sperm cell damage caused by varicocele.[16] xidative stress occurs due to the

release of excessive ROS, resulting in an imbalance between ROS and antioxidant levels. Increased levels of ROS will trigger oxidative stress that can damage germ cells and the basal lamina of the seminiferous tubules, which will then induce apoptosis of sperm cells.[18]

In addition to oxidative stress, a closely related mechanism is scrotal hyperthermia.[19] The process of spermatogenesis is susceptible to temperature changes and takes place optimally at around 36°C in men. Pampiniform plexus dilatation in varicocele causes an increase in testicular blood flow bilaterally and an average scrotal temperature increase of 2.6oC resulting in disruption or a decrease in the process of spermatogenesis.[20]

This study obtained similar results to the study by Li et al. The study showed a non-significant association between varicocele and IUI success (p=440). The study also showed a lower pregnancy rate, especially in grade III varicoceles, by 4.6%, compared to 14.4% in the non-varicocele group. Other previous research by Boman also showed similar results. The study showed IUI success of 10% in the varicocele group and 50% in the non-varicocele group. The chi-square analysis result (p>0.05) showed no significant association between varicocele and IUI success.[21]

Previous research conducted by Daitch also showed similar results. In the sample group that had undergone varicocelectomy, the IUI success rate was 11.9%, and in the group that did not undergo varicocelectomy, the success rate for IUI was only 6.3%. The results of the statistical analysis (p>0.05) showed no statistically significant association between varicocelectomy before IUI and the success rate of IUI.[22]

The success of IUI is not only determined by one factor but also by many other factors in both male and female partners. [23] In this study, the focus of the study was to see the association between varicoceles and the success of IUI, so that external factors of infertility that include the patient's lifestyle, such as a history of drinking alcohol, smoking, and obesity that were not listed in the results of the study could be confounding variables that affect the success of IUI. The relationship between varicocele severity to IUI success rates also didn't analyze due to the small number of participants. In addition, the results of sperm analysis can also provide a clearer picture of the factors that influence the success of IUI. These factors have not been analyzed, so further research is needed.

5. Conclusion

This study showed no significant association between varicocele in infertile men and the success of IUI. The RR value obtained (0.600) also indicates that infertile men with varicocele are not at risk of not achieving pregnancy after undergoing IUI at Rumah Sakit Ibu dan Anak Puri Bunda Denpasar.

Further study is needed with a larger sample size and a longer time so that the study can be more representative of the entire population and include the results of a semen analysis to provide a clearer picture of the association between varicocele and IUI success.

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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.

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