



Original Research

Relationship Between Body Mass Index and Male Infertility at Kasih Ibu General Hospital Denpasar

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Abstract

Infertility is the inability of a couple to achieve pregnancy after 12 months of regular sexual intercourse without protection. Infertility can also occur in men. The causes of male infertility are multifactorial, one of which is obesity. Obesity status in the Asian population is defined as a body mass index of 25 kg/m² or higher. This study aims to determine the relationship between obesity with body mass index measurement and male infertility. This type of research is an analytical cross-sectional study. This research was located at the Kasih Ibu General Hospital Denpasar. Purposive sampling was chosen as the sampling technique. The samples were 50 male patients aged 25-45 years with chief complaints related to infertility, reproductive system disorders, and sexual dysfunction who checked themselves at the Kasih Ibu General Hospital Denpasar between January and December 2020. The Pearson Chi-Square test was used to analyze the data. The results were 26 subjects (52%) with BMI \geq 25 kg/m² (obese) and 24 subjects (48%) with BMI < 25 kg/m² (non-obese). About 28 subjects (56%) were infertile, and 22 subjects (44%) were fertile. This study found that body mass index was significantly associated with infertility in male patients at Kasih Ibu General Hospital Denpasar. Obese men had a 2,308 higher risk of infertility than men who were not obese ($p = 0.002$, $RR = 2.308$ (CI95% 1.262-4.220)). The study showed a significant relationship between body mass index and the event of male infertility.

1. Introduction

One of the developing countries with a large population is Indonesia. Fertility is one of the components that affect the population of a nation. However, not all couples are aware of the importance of reproductive health before marriage, so most couples check themselves to health facilities if problems related to infertility are encountered. A couple unable to achieve pregnancy after 12 months of regular sexual intercourse without protection is known as infertility.¹ Two types of infertility are primary infertility if there has never been a pregnancy and secondary infertility if there has been a previous pregnancy.²

In 2010, World Health Organization (WHO) estimated that around 8-10% of couples in the world experienced infertility, which means 50-80 million couples (1 in 7 couples) experienced infertility.³ About 10-15% of the 39.8 million couples experienced infertility in Indonesia, and around 4-6 million couples need treatment to get children.⁴ Based on the causes, infertility can occur due to female factors around 40%, male factors around 40%, and a combination of male and female factors around 30%.⁵ Infertility in men can be caused by urogenital disorders, malignancy, infection, increased scrotal temperature, endocrine disorders, genetic disorders, and immunological factors.⁶ Other risk factors such as lifestyle like smoking, alcohol consumption, and obesity can impact fertility.¹

Anamnesis, physical examination, and semen analysis must be carried out to establish the diagnosis of infertile patients. Semen analysis is an essential laboratory test that provides information about the condition of germ cells, epididymis and accessory glands.²⁰ The components assessed in the semen analysis include volume, concentration, motility, morphology, and vitality.¹²

The excessive accumulation of fat in the body can be defined as obesity. One of the parameters that can be used in determining obesity is body mass index (BMI). Body mass index can be calculated from the division of body weight with height squared in kg/m^2 .⁷

Based on the WHO classification for the Asian population, $\text{BMI} \geq 25 \text{ kg}/\text{m}^2$ is classified as obesity.⁸ In 2013, the prevalence of obesity among men in Indonesia was 15.4%.⁹ In 2018, the prevalence of obesity in men in Indonesia was 14.5%, and the prevalence in Bali was higher than the national one was 20.3%.¹⁰

Based on research conducted by Ahsan in Palu City in 2012 with a total sample of 140 men consisting of 70 infertile men and 70 fertile men. It was found that 62.9% of obese subjects

experienced infertility. While subjects who were not obese, as much as 61.4% did not experience infertility. From the bivariate analysis, it was found that a significant association between body mass index and infertility in men was indicated by a p-value of 0.04.¹¹

Data and research in Indonesia regarding the association between body mass index and infertility in men is very limited. This study aims to determine whether obesity with body mass index measurement is associated with infertility in men. The research was conducted in Indonesia and specifically in Bali to provide information and education regarding the importance of maintaining a normal weight to prevent obesity, which is a risk factor for infertility. Kasih Ibu General Hospital Denpasar was chosen to conduct this research because the Kasih Ibu General Hospital Denpasar is a private hospital that has an andrology clinic with many patients. Therefore, it is necessary to research the relationship between obesity with body mass index measurement and male infertility at Kasih Ibu General Hospital Denpasar.

2. Methods

The study design for this study is cross-sectional. This research was located at the Kasih Ibu General Hospital Denpasar between January and December 2020. Ethical approval for this research has been received from the Research Ethics Commission of Sanglah Hospital Denpasar with the letter number 365/UN14.2.2.VII.14/LT/2021. The total number of subjects used in this study was 50 people. Research data could be seen from the medical record of patients. The data consisted of body mass index as the independent variable, male infertility as the dependent variable, age, smoking and alcohol consumption history, and medical history as confounding variables.

In this study, the sampling technique chosen was purposive sampling. The inclusion criteria included men aged 25-45 years who were married and lived with their wives and came voluntarily with chief complaints related to infertility, reproductive system disorders, and sexual dysfunction at the Kasih Ibu General Hospital Denpasar from January to December 2020. Subjects who came voluntarily to the hospital diagnosed with primary and secondary infertility were included in the infertile group. Infertility is the inability of a couple to achieve pregnancy after 12 months of regular sexual intercourse without protection. There are two types of infertility such as primary and secondary infertility.¹ Primary

infertility is the condition when there has never been a pregnancy, whereas secondary infertility is the condition when there has been a previous pregnancy.² Fertile is defined as the ability of a couple to establish a clinical pregnancy.²¹ So, subjects who came voluntarily to the hospital with other chief complaints such as reproductive system disorders and sexual dysfunction were included in the fertile group. Exclusion criteria included incomplete data from patient medical records, which did not include the variables studied.

Body mass index is classified based on the Asia-Pacific perspective redefining obesity and its treatment by World Health Organization (WHO) Western Pacific Region, 2000. Body mass index can be divided into five groups, namely underweight ($<18.5 \text{ kg/m}^2$), normal ($18.5\text{--}23 \text{ kg/m}^2$), overweight ($23\text{--}25 \text{ kg/m}^2$), obesity level I ($25\text{--}30 \text{ kg/m}^2$), and obesity level II ($\geq 30 \text{ kg/m}^2$).²² Smoking can be grouped according to its intensity, namely never, mild (<10 cigarettes/day), and severe (≥ 10 cigarettes/day).²³ Alcohol consumption can also be divided into three groups, namely never, mild (≤ 4 cups/day), and severe (>4 cups/day).²⁴ Medical history which consists of varicocele, spermatocele, mumps, hypertension, diabetes mellitus, sexually transmitted infection, undescended testis, erectile dysfunction, scrotal hernia, Peyronie's disease, and microtestis.

The last is semen analysis results based on the 6th edition of World Health Organization (WHO) laboratory manual for the examination and processing of human semen, 2021. There are several results of semen analysis, namely teratozoospermia, oligoasthenozoospermia, oligoteratozoospermia, asthenoteratozoospermia, oligoasthenoteratozoospermia, severe oligoasthenoteratozoospermia, azoospermia, cryptozoospermia, and normozoospermia.

Univariate analysis was presented in tabular form to obtain data on the frequency distribution and proportion of independent, dependent, and confounding variables. Bivariate analysis was presented to determine the association between body mass index and infertility in men using the Pearson Chi-Square test. Processing and analyzing data with the Statistical Package for the Social Science (SPSS) for Windows version 26.0.

3. Results

In this study, the following results are:

Table 1. Distribution of Subject Characteristics

Variable	Frequency	Percentage (%)
Domicile		
Denpasar	24	48
Other Cities in Bali	26	52
Occupation		
Government Employees	6	12
Private Employees	34	68
Entrepreneur	10	20
Age (Years)		
25-35	32	64
36-45	18	36
Length of Marriage (Years)		
1-3	31	62
4-9	12	24
10	7	14
Diagnosis		
Primary Infertility	23	46
Secondary Infertility	5	10
Fertile	22	44

Table 1 describes the distribution of subject characteristics based on domicile, occupation, age, length of the marriage, and diagnosis. Most of the patients who lived in other cities in Bali were 26 subjects (52%). The majority of patients' occupations are private employees were 34 subjects (68%) and followed by entrepreneurs, as many as ten subjects (20%). The data is dominated by patients aged 25-35 years were 32 subjects (64%), while 18 subjects aged 36-45 years. From all of the samples, the average age was 33.3 years. Most patients with a length of marriage of 1-3 years were 31 subjects (62%), and the least data for the length of marriage of more than ten years were seven subjects. About 28 subjects (56%) were experiencing infertility. Of most patients who experienced primary infertility were 23 subjects, while five subjects experienced secondary infertility.

Table 2. Subject Distribution of Male Infertility Based on Body Mass Index

Body Mass Index (kg/m²)	Infertile n (%)	Fertile n (%)	Total n (%)
Underweight	0 (0)	1 (100)	1 (100)
Normal	5 (38)	8 (62)	13 (100)
Overweight	3 (30)	7 (70)	10 (100)
Obesity Level I	13 (76)	4 (24)	17 (100)
Obesity Level II (≥ 30 kg/m ²)	7 (78)	2 (22)	9 (100)
Total	28 (56)	22 (44)	50 (100)

Table 2 describes the distribution of subjects by body mass index. Most patients with obesity level I was 17 subjects (34%). The least data for the underweight patient was one subject. From the total sample, the average body mass index was 26,3 kg/m². In addition, patients with obesity level I and obesity level II were more likely to experience infertility, as many as 13 subjects (76%) and 7 subjects (78%). Meanwhile, more fertile patients had normal weight, as many as 8 subjects (62%).

Table 3. Distribution of Subjects Based on Smoking and Alcohol Consumption

Variable	Frequency	Percentage (%)
Smoking		
Never	31	62
Mild (<10 cigarettes/day)	3	6
Severe (≥ 10 cigarettes/day)	16	32
Alcohol Consumption		
Never	26	52
Mild (≤ 4 cups/day)	14	28
Severe (>4 cups/day)	10	20

Table 3 presents the distribution of the subjects based on smoking and alcohol consumption. In this study, most of the patients did not smoke 31 subjects (62%). Patients with a smoking habit were more often found with severe intensity (≥ 10 cigarettes/day), as many as 16 subjects.

Table 5. Distribution of Subjects Based on Semen Analysis Results

Semen Analysis Results	Frequency	Percentage (%)
Teratozoospermia	13	26
Oligoasthenozoospermia	1	2
Oligoteratozoospermia	1	2
Asthenoteratozoospermia	13	26
Oligoasthenoteratozoospermia	9	18
Severe oligoasthenoteratozoospermia	5	10

Most patients stated that they had never consumed alcohol, were 26 subjects (52%). Patients who consumed alcohol were more often found with mild intensity (≤ 4 cups/day), as many as 14 subjects.

Table 4. Distribution of Subjects Based on Medical History

Medical History	Frequency	Percentage (%)
Varicocele	27	54
Spermatocele	7	14
Mumps	4	8
Hypertension	2	4
Diabetes Mellitus	1	2
Sexually Transmitted Infection	1	2
Undescended Testis	1	2
Erectile Dysfunction	2	4
Scrotal Hernia	1	2
Peyronie's Disease	1	2
Microtestis	1	2

Table 4 presents the distribution of subjects based on medical history. Most of the patients had a history of varicocele, as many as 27 subjects (54%). It is followed by spermatocele were seven subjects, and mumps in four subjects.

Azoospermia	6	12
Cryptozoospermia	1	2
Normozoospermia	1	2

Table 5 shows that the most results of semen analysis were teratozoospermia, which was 13 subjects (26%), and asthenoteratozoospermia which was 13 subjects (26%) out of a total of 50 subjects.

In the second place, there was oligoasthenoteratozoospermia in as many as 9 subjects or 18%. This was followed by azoospermia of 6 subjects or 12%.

Table 6. Bivariate Analysis of Body Mass Index with Male Infertility

Body Mass Index (kg/m ²)	Infertile		Fertile		Total		<i>P</i>
	<i>n</i>	(%)	<i>n</i>	(%)	<i>n</i>	(%)	
Obese	20	(77)	6	(23)	26	(100)	0.002
Non-Obese	8	(33)	16	(67)	24	(100)	
Total	28	(56)	22	(44)	50	(100)	

Table 6 describes the results of the analysis of the association between body mass index and infertility in men. It was found that infertility was more common in obese patients (BMI ≥ 25 kg/m²) in as many as 20 subjects (77%). In comparison, fertile patients were found with non-obese (BMI < 25 kg/m²) were 16 subjects (67%). Based on the Pearson Chi-Square test, it was found that the association between body mass index and infertility in men was indicated by a *p*-value of 0.002. The relative risk (RR) in this study was 2.308 (CI95% 1.262-4.220). It means that obese men have a 2.308 times higher risk of experiencing infertility than non-obese men.

4. Discussion

Patients who checked themselves to the andrology doctor at Kasih Ibu General Hospital Denpasar had chief complaints related to infertility, disorders of the reproductive system, and sexual disorders. More than half of the subjects came from outside Denpasar. The majority of the subjects worked as private employees. In addition, it was also found that most of the patients had been married for 1-3 years, which means that the patient's awareness of fertility problems was relatively high, especially at the beginning of a marriage.

The aging phase is divided into three stages, namely the subclinical phase (25-35 years), the transition phase (35-45 years), and the clinical phase (> 45 years). Between 45-50 years, it is estimated that there will be a decrease in the quality of spermatogenesis due to degenerative changes in the testicular blood vessels, resulting in a decrease in the effect of testosterone.¹² Therefore in this study, patients over 45 years were excluded to reduce the possibility of infertility due to aging factors.

Most of the patients were aged 25-35 years, with an average age was 33.3 years. This result is similar to the research in Palu city, with most of the samples aged 26-35 years.¹¹ This study found that the type of infertility experienced by most of the patients was primary infertility. The research conducted at Sanglah Hospital and Puri Bunda Hospital Denpasar found similar results that more patients were experiencing primary infertility than secondary infertility.^{12,13}

Semen examination can be interpreted by the WHO's standards.²⁰ The most semen analysis results in the study were teratozoospermia and asthenoteratozoospermia, followed by oligoasthenoteratozoospermia, and in the third place is azoospermia. One of the risk factors that cause male infertility is obesity.¹ Obesity can be known from the measurement of body mass index (BMI), which is a measure of body fat based on the prevailing height and weight.⁸ Based on the analysis with the Pearson Chi-Square test, it was found that the association between body mass index and infertility in men. This result is similar to the research by Ahsan in Palu City that found a significant association between obesity and infertility in men.¹¹ Likewise, research by Rehman in Pakistan shows that there was a significant relationship between obesity and infertility in men.¹⁴ Research conducted by Hodeeb in Egypt also found a significant relationship between obesity and abnormal semen analysis in infertile men.¹⁵

Adipose tissue in obese men causes excessive aromatase activity, which converts testosterone to estradiol. High estradiol levels affect the hypothalamic-pituitary-gonadal (HPG) pathway, causing a decrease in GnRH followed by a decrease in anterior pituitary activity that secretes FSH and LH. Low FSH levels will decrease the activity of

Sertoli cells in secreting inhibin B, which leads to disruption of spermatogenesis. Low inhibin B also causes seminiferous tubular dysfunction. In addition, low LH levels cause a decrease in the hormone testosterone. So that obese men get an image of unbalanced sexual hormone levels due to high levels of estradiol and low testosterone.^{16,17}

Most of the fat-soluble toxins will accumulate in adipose tissue if around the scrotum will directly impact spermatogenesis in the testes.¹⁸ Furthermore, reactive oxygen species (ROS) can cause severe oxidative stress and significant cell damage in the body because they are very unstable and reactive molecules. ROS impacts spermatogenesis abnormalities by causing DNA damage, deformity of spermatozoa, and damage to the plasma membrane in spermatozoa. In addition, ROS can also impair spermatozoa function and motility by disrupting the mitochondrial genome.¹⁸

White adipose tissue plays a role in producing leptin. One of the receptors for the hormone leptin is in the neurons of the hypothalamus. Suppose the condition of hyperleptinemia lasts for a long time. In that case, it can cause leptin resistance so that leptin will be difficult to work on its receptors so that GnRH secretion will decrease and cause FSH and LH secretion to decrease. The result is a decrease in testosterone levels and impaired spermatogenesis.¹⁷ In addition, the distribution of fat in the upper thigh, suprapubic, and scrotum also causes the testicular temperature to increase. Spermatogenesis can run optimally in a temperature range of 34°C to 35°C. If the testicular temperature increases, it will interfere with spermatogenesis and steroidogenesis in the testes, reduce spermatozoa motility, damage spermatozoa DNA, and increase spermatozoa oxidative stress.¹⁹

In this study, the relative risk (RR) was 2,308 (CI95% 1.262-4.220). This relative risk indicates that obese men have a 2.308 times higher risk of experiencing infertility than non-obese men. Multifactorial causes can cause male infertility, so there are other risk factors apart from obesity. Male infertility can also be affected by medical history, smoking, and alcohol consumption.¹ Cigarette contains harmful substances that cause damage to the morphology of spermatozoa and also affect the quality of semen. Alcohol can impact Leydig cell function so that testosterone synthesis is reduced and the basement membrane is damaged.² In this study, more than half of the sample also admitted that they never smoked and consumed alcohol. From the previous medical history, most of the patients had a varicocele. However, this study focuses on the association between obesity as measured by the body mass index and infertility in men, so other risk factors like medical history,

history of smoking, and alcohol consumption were used as confounding variables.

Suggestions from the author are for further research with a large sample and research sites in several hospitals to make it more accurate in the broader population. Further research is also suggested to examine semen analysis as an initial laboratory test to determine spermatozoa's volume, concentration, motility, morphology, and vitality.²⁰ In addition, testosterone and estradiol levels can also be checked, while the generalization to other risk factors that can cause male infertility can also be carried out.

5. Conclusion

The conclusion obtained from this study is a significant relationship between obesity with body mass index measurement and the event of male infertility. Obesity can contribute to being one of the risk factors for infertility in men. The author suggests for further research should generalize to other risk factors that can cause male infertility.

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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 final manuscript.

Conflict of Interest

The authors state there is no conflict of interest.

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