

ETIOLOGY OF MALE INFERTILITY IN JAKARTA

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ABSTRACT

Objective: The etiology and risk factors of male infertility in huge Indonesian population has not yet been defined. This study was aim to evaluate the distribution and pattern of male infertility in Jakarta. **Material & Methods:** Retrospective study of Infertility database of Cipto Mangunkusumo Referral Hospital Jakarta, Bunda Hospital Jakarta, and ASRI Hospital Jakarta from 2005 until 2015 were analyzed using SPSS ver. 20. Patients' characteristic and demography were stated. **Results:** There were 1062 patients with most of them suffered from primary infertility of their first time-marriage. Average age of husband, wife, and duration of marriage were 36.63 ± 7.10 , 32.32 ± 4.92 , and 5.7 ± 4.18 years old respectively. Smoking habit was recorded in 25% of patients while exposure and occupational hazard were only found in less than 2% of them. Coital problems occurred in 17% of patients with 30% of them did not have routine sexual intercourse per week. Physical examination revealed that more than 70% of them had varicocele while USG Doppler of scrotum found varicocele in less than 50%. Only 5.13% of patients had normal sperm analysis, mostly azoospermia. Hormonal abnormality occurred in more than 30% patients, varied in testosterone, FSH, and LH level. **Conclusion:** Male infertility was mostly caused by abnormal sperm characteristics followed by abnormal hormonal analysis. Exposure and occupational hazard did not play a big role in male infertility. Future study in risk factors of abnormal sperm characteristics could be done.

Keywords: Infertility, male, etiology, Jakarta, azoospermia.

ABSTRAK

Tujuan: Etiologi dan faktor risiko infertilitas pria pada penduduk Indonesia dalam jumlah besar belum diketahui. Penelitian ini bertujuan untuk mengevaluasi distribusi dan pola infertilitas pria di Jakarta. **Bahan & cara:** Penelitian retrospektif didapatkan dari data base infertilitas di RSUPN Cipto Mangunkusumo Jakarta, RS Bunda Jakarta, dan RS ASRI Jakarta, dari tahun 2005 sampai 2015 dianalisis dengan menggunakan SPSS ver. 20. Pasien demografi dan karakteristik dicatat dan ditampilkan. **Hasil:** Terdapat 1.062 pasien dengan sebagian besar dari mereka menderita infertilitas primer. Rerata usia suami, istri, dan durasi pernikahan adalah 36.63 ± 7.10 , 32.32 ± 4.92 , dan 5.7 ± 4.18 tahun pada masing-masing variabel. Kebiasaan merokok tercatat pada 25% dari pasien, sementara paparan dan risiko pekerjaan hanya ditemukan pada 2% pasien. Masalah dalam berhubungan seksual terjadi pada 17% pasien dengan 30% dari mereka tidak melakukan hubungan seksual rutin per minggu. Pemeriksaan fisik menunjukkan bahwa lebih dari 70% dari mereka memiliki varikokel sementara konfirmasi USG Doppler skrotum hanya ditemukan kurang dari 50% pasien. Hanya 5.13% dari pasien memiliki analisis sperma normal, dengan sebagian besar pasien menderita azoospermia. Kelainan hormonal terjadi di lebih dari 30% pasien, bervariasi antara masalah testosteron, FSH, dan LH. **Simpulan:** Infertilitas pria kebanyakan disebabkan oleh karakteristik sperma yang abnormal diikuti dengan analisis hormonal yang abnormal. Paparan dan risiko pekerjaan tidak memainkan peran besar dalam infertilitas pria. Penelitian pada masa depan dalam faktor risiko karakteristik sperma yang abnormal bisa dilakukan.

Kata kunci: Infertilitas, pria, etiologi, Jakarta, azoospermia.

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INTRODUCTION

Infertility is a condition in which there is a failure to achieve and maintain successful pregnancy

during 12 months of regular sexual intercourse without any protection that could prevent pregnancy.^{1,2} The prevalence of infertility is different in every country which are related to local risk

factors In North America region, infertility is around 11.5-15.7% while in Europe is around 16.7%.^{3,4} In Asia itself, prevalence of infertility almost hit 9% of total productive couple.⁵ Wordwidely, infertility is account for 10% of total population.⁶ Average age of male with primary infertility is 32 years old while in secondary infertility is around 34 years old.⁴

Infertility could cause various problems including personal, interpersonal, social, as well as religion issue. These problems could lead into guilty feeling, loss, and failure.² Around 5% of couples with infertility problems suffered from divorce in the future.⁵ Thus, knowing the cause of infertility will be very helpfull in order to choose appropriate medication and treatment to handle the issue.

Today paradigm of infertility already different compared to previous years. In the past time, infertility problems were associated only to female or wife's side. This point of view already dramatically changes. Nowadays, people are openly accepted that infertility could be caused in both side of couple. Based on report released by World Health Organization, half of infertility issue are caused by male factor while previous studies showed that around 30-45% of infertility were caused by male factors.⁷⁻⁹ Infertility caused by male factors are mainly discussed in urology, while female factors are discussed in obstetric and gynaecology. However, almost 50% of male infertility are idiopathic.¹⁰

There are around 8% of reproductive men are seeking for medical treament for their infertility issue.¹¹ The way to diagnose etiology of male infertility including history taking, physical examination, and supporting examination.¹⁰ Most common supporting examination performed in male patient with infertility problem are sperm analysis, hormonal status, and radio-imaging.¹²

OBJECTIVE

The etiology and risk factors of male infertility in huge Indonesian population has not yet been defined. This study was to evaluate the distribution and pattern of male infertility in Jakarta.

MATERIAL & METHODS

Descriptive-retrospective study of patients with infertility problem whom came Urology Polyclinic in Cipto Mangunkusumo Referral Hospital or Bunda Hospital were recorded from

2005 to 2015. Patients' biodata including age, type of infertility (primary of secondary infertility), duration of infertility, exposure and occupational hazard, lifestyle related male infertility, history of previous disease, history of medication, history of surgical intervention, sexual behaviour, age of spouse, and spouse's health status.

Occupational hazard including chemical exposure, electromagnetic, kitchen stove, machined, etc. Lifestyle related male infertility are smoking habit, alcohol, sauna, hot bathing, tight pants, and frequently place laptop in tight. History of previous disease are diabetes mellitus, tuberculosis, mumps, venereal disease, liver disease, orchitis, epidymitis, gonorrhea, cystitis, prostatitis, varicocele, and cryptorchismus.

History of medication including cimetidine, sulfasalazine, chemotherapy, steroid, marijuana, radiation, etc. History of surgical intervention including herniotomy, cryptorchismus, urogenital trauma surgery, testicular torsion, pelvical trauma, etc. Information of sexual behaviours including erectal dysfunction, penetration problem, ejaculation issue, frequency of coital per week, and use of lubricant during sexual intercourse. Physical examination including testicular volume and morphology, patency of vas deferens, morphology of epididymis, and occurence of varicocele. Supporting examination were sperm analysis, DNA fragmentation index, hormonal analysis, and ultrasonography (USG) Doppler of scrotum.

Semen analysis used in this study was based on World Health Organization (WHO)⁶ sperm classification 2010. Concentration $> 15 \times 10^6$ per ml, progressive motility $> 40\%$, normal morphology $> 4\%$ were classified as normal sperm result.¹³ Hormonal analysis were mostly done in Cipto Mangunkusumo Referral Hospital and Prodia Laboratorium. All data were described using SPSS ver. 20.

RESULTS

Total patients whom came to either Urology Polyclinic in Cipto Mangunkusumo Referral Hospital Jakarta, Bunda Hospital Jakarta, or ASRI Hospital Jakarta from 2005 to 2015 were 1064 patients. The average age of patients was 36 years old (18-67 years old) while 32 years old (18-51 years old) for their spouse. Most of them (90.7%) were in their first time-marriage with average duration of marriage was 5.7 ± 4.18 years old and they were

never have offspring. Regarding spouse's reproductive health status, most of them were healthy with just 4.4% of them suffered from cyst in their reproductive organ, followed by abnormal ovum, myoma, and fallopian tube problem.

Table 1. Patients' and spouse' characteristics.

	Mean (years)	Std.Deviation
Patients' Age	36.63	± 7.10
Spouse's Age	32.32	± 4.92
Duration of Marriage	5.7	± 4.18

Table 2. Spouse's health status.

Spouse's Health Status	N	%
Cyst in Reproductive Organ	47	4.4
Abnormal Ovum	23	2.2
Myoma	21	2.0
Fallopian Tube Problem	18	1.7
Poly Cystic Ovarian Syndrome	17	1.6
Polip in Reproductive Organ	13	1.2
Hormonal Imbalance	9	.8
Endometriosis	8	.8
Uterus Problem	7	.7
Misscariage	3	.3

Risk factor of male infertility caused by exposure and occupation were recorded in less than 2% of patients while lifestyle and behaviour such as smoking habit was recorded in around 25% of patients. Combination of smoking habit and alcoholism was the second most frequent risk factor

with more than 6% of patients. Erectile dysfunction and difficulty to penetrate were recorded in 7.1% while ejaculation problem occurred in more than 10% of patients. None of patient used lubricant during their sexual intercourse, but supprisingly one-third of them did not have routine sexual intercourse (no sexual intercourse per week). More than 59% of patient had sexual intercourse less than 2 times per week. More than 2% of patients said that they were ever had varicocele previously. Liver disease as an underlying risk factor of male infertility was observed in 4.6% followed by diabetes mellitus for 1.8% of patients.

Supporting examination were done in most of the patients. Some patient did not performed some specific examination because they were referred by other physician, not directly come to our polyclinic. Supporting examination in determing the etiology of infertility were sperm analysis, DNA fragmentation Index analysis, Hormonal Examination such as Testosterone, FSH, and LH. Other supporting examination was USG Doppler. Sperm analysis and hormonal examination were mostly examined in Cipto Mangunkusumo Referral Hospital and Prodia Laboratorium while DNA fragmentation index analysis only in Cipto Mangunkusumo Referral Hospital. USG Doppler was performed by urologist or radiologist.

From 740 patients whom underwent physical examination, more than half of them had bilateral varicocele, with just 28.51% did not suffer from varicocele. USG Doppler was done in 819 patients. It was differed from patients whom underwent physical examination because some

Table 3. Lifestyle-risk factors of male infertility.

Risk Factor	N	%
Alcohol	18	1.7
Alcohol + Sauna + Hot Bathing	2	0.2
Hot Bathing	2	0.2
Smoking	263	24.8
Smoking + Alcohol	73	6.9
Smoking + Alcohol + Hot Bathing	2	0.2
Smoking + Alcohol + Sauna	4	0.4
Smoking + Alcohol + Sauna + Hot Bathing	3	0.3
Smoking + Hot Bathing	5	0.5
Smoking + Sauna	4	0.4
Smoking + Sauna + Hot Bathing	2	0.2
Sauna	3	0.3
Sauna + Hot Bathing	3	0.3
Any Risk Factors Denied	678	63.8

patients already done USG Doppler of scrotum before they came to our clinic. From USG Doppler of scrotum, 51.04% of them did not have varicocele and 33.94% of them suffered from bilateral varicocele. However, 26.3% of patients whom had varicocele on physical examination were confirmed by USG Doppler scrotum examination. Less than 5% of patients who had normal physical examination were have normal USG Doppler examination for varicocele.

Table 4. Diagnosis of varicocele based on physical examination and USG Doppler scrotum.

	Physical Examination		USG Doppler	
	N	%	N	%
Bilateral	414	55.95	278	33.94
Right only	9	1.22	14	1.71
Left only	106	14.32	109	13.31
Normal	211	28.51	418	51.04
Total	740	100	819	100

From sperm analysis, only 5.13% of them had normal results. Almost half of patient whom underwent sperm analysis had azoospermia (46.21%) followed by oligoasthenozoospermia (10.88%) and oligoasthenoteratozoospermia (8.31%). In 65 patients, 50% of them had poor DNA fragmentation index criteria.

From those who had hormonal analysis, 30.11% of them had abnormal hormonal results. Abnormal hormonal results were categorized as abnormal result either in testosterone, FSH, and/or LH serum level. Most of testosterone results were normal, with just 17.83% and 3.57% were low and high respectively.

Table 7. Classification of hormonal analysis in infertile men.

	N	%
Abnormal hormonal examination	196	30.11
Normal	455	69.89
Total	651	100

Note: abnormal hormonal examination is defined as abnormality either in testosterone, FSH, and/or LH serum level.

Table 5. Varicocele based on physical examination confirmed by USG Doppler.

	N	%
Physical Examination + USG were normal	35	3.3
Varicocele on Physical Examination with Normal USG Examination	4	0.4
Varicocele on Physical Examination and USG Examination	279	26.3
Normal Physical Examination with Varicocele on USG Examination	44	4.1

Table 6 . Sperm analysis.

Sperm Analysis Classification	N = 818	%
Normozoospermia	42	5.13
Single Sperm Criteria Abnormality		
Asthenozoospermia	52	6.36
Azoospermia	378	46.21
Cryptozoospermia	46	5.62
Oligozoospermia	43	5.13
Teratozoospermia	14	1.71
Severeoligozoospermia	63	7.70
Double Sperm Criteria Abnormality		
Oligoasthenozoospermia	89	10.88
Oligoteratozoospermia	10	1.22
Teratoasthenozoospermia	14	1.71
Three Sperm Criteria Abnormality		
Oligoasthenoteratozoospermia	68	8.31

Table 8. Testosterone, FSH, and LH serum level in infertile men.

	Testosterone		FSH		LH	
	N	%	N	%	N	%
Normal	485	45.7	426	40.1	404	38.0
Rendah	110	10.4	9	0.8	12	1.1
Tinggi	22	2.1	189	17.8	113	10.6
Total	617	100	624	100	529	100

DISCUSSION

In this study, there were 1064 male with infertility issue. Patients's age was $36.63 \text{ y.o} \pm 7.10$ while spouse's age was $32.32 \text{ y.o} \pm 4.92$. Patient mean age was not really different compared to studies done in Italy and Iran with mean age of 33 years old.^{14,15} Spouse's age in our study was older compared to study done in Israel, Italy, and Iran which were 29.6, 28.5, and 29 years old respectively.^{8,14,15} The differences in term of spouse's age might be caused by lack of information of infertility in Indonesia. Indonesia just only has 20 government regulated fertility clinics.¹⁶ Thus, they were late in order to seek medical assistance while then related to duration of infertility before the seek for treatment. In our study the duration of infertility was longer compared to other studies. Our patients had mean duration of infertility before they were seeking for treatment was 5.7 years old while in Italy and Israel, it just around 2 years.^{8,14} In Western Siberia, duration of infertility before they seek for treatment was even shorter.⁴

This study showed that more than 90% patients were suffered from primary infertility. This result was quite high compared with study done in Iran with less than 80% of patients was suffered from primary infertility.¹⁵ Spouse health status of fallopian tube problems were observed in 1.7% of partner while in other study was 13.8%.⁸

In this study we found that patients suffered from varicocele (diagnosed by physical examination and confirmed by USG Doppler of scrotum) was around 26.3%. Our results was higher compared to other study done by Miyaoka et al but lower compared to Chandra et al (26.3% vs 21.9% vs 35%).^{17,18} Our study showed that hormonal problem was observed in more than 30% of patients. It was significantly higher compared to other study. Doddy et al showed that hormonal problems was observed in 2% while Miyaoka et al 2.3%.^{17,18}

Regarding sperm analysis, our study showed that more than 90% of patients had abnormal sperm analysis. This result almost twice the result of previous studies with semen issue occurred in 50.5% and 45.7% of patients.^{4,15} Azoospermia was the most common abnormal sperm analysis result with 46.21% of patients suffered from it. This result was 5 times higher compared to study done in Siberia.⁴

Behaviour and lifestyle could lead to low count of sperma, or even no sperma et al.¹⁹ Smoking habit was the biggest prevalence of behavioural risk factor related to infertility with one fourth of our subjects were smoker. This result was 10 times higher compared to study done by Hamid et al.²⁰ This discrepancy could be explained based on national prevalence of smoking habit. In Indonesia, 64.9% of male population aged more than 15 were smoker while in Iran its only around 15% of male population.^{21,22}

CONCLUSION

Male infertility was mostly caused by abnormal sperm characteristics followed by abnormal hormonal analysis. Exposure and occupational hazard did not play a big role in male infertility. Future study in risk factors of abnormal sperm characteristics could be done.

REFERENCES

1. Definitions of infertility and recurrent pregnancy loss: A committee opinion. *Fertil Steril*. 2013; 99(1):63.
2. Rutstein SO, Shah IH. Infecundity, infertility, and childlessness in developing countries. *DHS Comparative Reports 9*. DHS Comp Reports. 2004; 9: 13-50. Available from: <http://www.who.int/reproductivehealth/topics/infertility/DHS-CR9.pdf?ua=1>.
3. Bushnik T, Cook JL, Yuzpe AA, Tough S, Collins J. Estimating the prevalence of infertility in Canada. 2012; 27(3): 738-46. Available from: <http://humrep>.

- oxfordjournals.org/content/early/2012/01/17/humrep.der465.full.pdf+html.
4. Philippov OS, Radionchenko AA, Bolotova VP, Voronovskaya NI, Potemkina TV. Estimation of the prevalence and causes of infertility in Western Siberia. *Bull World Health Organ.* 1998; 76(2): 183-7. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2305650/pdf/bullwho00002-0079.pdf>.
5. Che Y, Cleland J. Infertility in Shanghai: prevalence, treatment seeking and impact. *J Obstet Gynaecol.* 2002; 22(6): 643-8.
6. Coulson C, Lambert Pa, Watt EM, Desai KM. Population study of causes, treatment and outcome of infertility. *Br Med J.* 1985; 291(December): 1693-7. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1418755/pdf/bmjcred00478-0029.pdf>.
7. Quan Q, Li TJ, Ding XP, Wei J, Li LX, Fu L. Infertility caused by male partners with genetic defects in Sichuan Province of China. 2013; 12(4): 6512-20. Available from: <http://www.geneticsmr.com/year2013/vol12-4/pdf/gmr2493.pdf>.
8. Farhi J, Ben-Haroush A. Distribution of causes of infertility in patients attending primary fertility clinics in Israel. *Isr Med Assoc J.* 2011; 13(January): 51-4. Available from: <http://www.ima.org.il/Files/Upload/IMAJ/0/38/19450.pdf>.
9. Al-Moushaly a. Considerations on male infertility in genital infections with Chlamydia Trachomatis (CT). *J Med Life [Internet].* 2013; 6(3): 283-6. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3786487/pdf/JMedLife-06-283.pdf>.
10. Iammarrone E, Balet R, Lower aM, Gillott C, Grudzinkas JG. Male infertility. *Best Pract Res Clin Obstet Gynaecol.* 2003; 17(2): 211-29. Available from: <http://www.sciencedirect.com/science/article/pii/S1521693402001475>.
11. Miyaoka R, Esteves SC. A Critical Appraisal on the Role of Varicocele in Male Infertility. 2012; 2012: 4-5. Available from: <http://www.hindawi.com/journals/au/2012/597495/>.
12. Sabarre K-A, Khan Z, Whitten AN, Remes O, Phillips KP. A qualitative study of Ottawa university students' awareness, knowledge and perceptions of infertility, infertility risk factors and assisted reproductive technologies (ART). *Reprod Health [Internet].* Reproductive Health. 2013; 10(1): 41. Available from: http://www.pubmedcentral.nih.gov/article/render.fcgi?artid=3751831&tool=pmcentrez&render_type=abstract.
13. Reference values and semen nomenclature. Examination and processing of human semen. 5th Ed. Switzerland: World Health Organization; 2010. p. 224. Available from: http://apps.who.int/iris/bitstream10665/44261/1/9789241547789_eng.pdf.
14. Grasso M, Lania C, Blanco S, Confalonieri S, Grasso AAC. Efficacy of spermatic vein ligation in patients affected by high grade left varicocele. 2014; 40(1): 62-6. Available from: http://brazjurol.com.br/January_february_2014/Grasso_062_066.htm.
15. Malekshah AK, Moghaddam AE, Moslemizadeh N, Peivandi S, Barzegarnejad A, Musanejad N, et al. Infertility in Mazandaran province - North of Iran: An etiological study. *Iran J Reprod Med.* 2011; 9(1): 21-4. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4212141/pdf/ijrm-9-021.pdf>.
16. Bennett LR, Wiweko B, Hinting A, Adnyana IP, Pangestu M. Indonesian infertility patients' health seeking behaviour and patterns of access to biomedical infertility care: an interviewer administered survey conducted in three clinics. *Reprod Health [Internet].* Reproductive Health; 2012; 9(1): 24. Available from: <http://www.reproductive-health-journal.com/content/pdf/1742-4755-9-24.pdf>.
17. Esteves SC, Miyaoka R, Agarwal A. An update on the clinical assessment of the infertile male. *Clinics (Sao Paulo).* 2011; 66(4): 691-700. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3093801/pdf/cln-66-04-691.pdf>.
18. Chandra A, Martinez GM, Mosher WD, Abma JC, Jones J. Fertility, family planning, and reproductive health of U.S. women: data from the 2002 National Survey of Family Growth. *Vital Health Stat* 23; 2005. p. 1-160. Available from: http://www.cdc.gov/nchs/data/series/sr_23/sr23_025.pdf.
19. Thomas WE. Drug and Sperm. *Br Med J (Clin Res Ed).* 1982; 284(March): 1266-7. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1496805/pdf/bmjcred00602-0056a.pdf>.
20. Delavar M, Haydari F, Mahdinejad N, Abedi S, Shafi H, Esmaeilzadeh S. Prevalence of varicocele among primary and secondary infertile men: Association with occupation, smoking and drinking alcohol. *N Am J Med Sci [Internet].* 2014; 6(10): 532. Available from: <http://www.najms.org/text.asp?2014/6/10/532/143285>.
21. Penelitian B, Pengembangan dan Riset Kesehatan Dasar; 2013.
22. Nazary AA, Ahmadi F, Vaismoradi M, Kaviani K, Arezomandi M, Faghihzadeh S. Smoking among male medical sciences students in Semnan, Islamic Republic of Iran. *East Mediterr Heal J.* 2010; 16(2): 156-61.