Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate

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ORIGINAL ARTICLE

Primary infertility of male and female factors, polycystic ovary syndrome and oligoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia

ABSTRACT

Introduction: Indonesia is a country with a large agricultural and industry, known to utilize various types of pesticides, as well as several other industries with uncontrolled pollution levels, distributed across the nation. In addition, numerous studies have stated the adverse effects of chemicals substances used in daily life and industrial waste, on the health of living things, including humans. The purpose of this study was to determine the infertility characteristic in the agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

Methods: The study was conducted retrospectively on medical records. This study therefore to determine the infertility characteristics based on sperm analysis, the etiology of the causes of infertility in female, and the diagnosis of infertility. Data collection obtained from the medical records of patients in the Infertile Poly of RSIA Mitra Bunda Amanda Karawang, Karawang Regency, West Java Province, Indonesia.

Result: The results showed infertility was most prevalent in male aged 30-40 years (55.79%) and female below 30 years (61.05%). Furthermore, the most prevalent educational qualification possessed by the male and female (33.68% and 36.84%, respectively) was discovered to be high school diploma. In terms of occupation, majority of the male (56.84%) were laborers, while the female were mostly housewives (36.84%). Meanwhile, olygoasthenoteratozoospermia was the most analyzed sperm type (33.68%), and polycistic ovary syndrome was the most common etiology of infertility in female (26.32%). The most prevalent diagnosis was primary infertility factors, male and female (45.26%).

Conclusion: Primary infertility of male and female factors, polycystic ovary syndrome and olygoasthenoteratozoospermia dominate the infertile population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

Keywords: pollutans, sperm analysis, infertility, Oligoasthenoteratozoospermia, polycistic ovary syndrome.

INTRODUCTION

Pollutants are harmful to human health and damage the environment. Pollutants in the human environment have various effects that are detrimental to health to cause disease.[1] The character of disease risk due to exposure to multi-pollutants can be determined using an "environmental risk score".[2] Environmental pollutants with estrogenic effects generally have biological effects in women, as do pollutants with anti-androgenic effects that affect male fertility.[3]

Pollutants from agricultural and industrial activities can pollute the air, water and soil. Of course, pollutants can move places. Pollutants in the air can move to water and land or vice versa. Directly or indirectly, pollutants can cause human health problems. Air pollution can occur because it contains particles with aerodynamic diameters below 10 and 2.5 μm (PM10 and PM2.5). Apart from that, it can also contain NO, NO2, NOx and SO2. It has been proven that air pollutants cause endocrine disorders and hormonal disturbances. Women who are exposed to high concentrations of air pollutants, namely PM 2.5, NO, NO2, NOx and SO2, have a high risk of developing polycystic ovary syndrome.[4] Beside that, it has been shown that particles less than 0.3 μm in diameter can dominate the acute effects of particulate air pollution resulting in cardiac autonomic dysfunction.[5] Furthermore, it was reported that PM interferes with energy metabolism thereby disrupting the endocrine glands and becoming a risk for cardiovascular disease.[6] In this regard, we have reported a case of aortic enlargement on cadaveric heart and great vessels dimensions.[7] Becuase that, studies are still needed on the effect of pollutants on aortic enlargement. This is important because cardiovascular disease as a risk factor has been shown to have a strong correlation with a history of infertility in women of childbearing age and menopause.[8] Moreover, chemicals that are frequently used in the textile industry are believed to produce persistent organic pollutants (POPs). These chemicals include dichlorodiphenyltrichloroethane (DDT), dichlorodiphenyldichloroethylene (p, p´-DDE) and polychlorinated biphenyls (PCBs). POP is a stable lipophilic compound found in the environment. These pollutants are difficult to break down, are insoluble in water, and can accumulate in the human body. Furthermore, pollutants in the body can cause human health problems.[9] How are people living in agricultural and industrial areas exposed to pollutants?.

Of course, people living in the area are exposed of various pollutants from agricultural and industrial activities. One proof that agricultural and industri activities in Karawang Regency, West Java Province, Indonesia have an impact on the environment can be seen in the water quality of the Citarum river. The Citarum River is a large and long river in West Java that crosses Karawang Regency. It has been reported that the water in the Citarum river is of poor quality, making it unsuitable for drinking. This fact illustrates that the water in the Citarum river contains high pollutants.[10] It should be noted that 18 sub-districts in Karawang Regency are crossed by the downstream segment of the Citarum River. Furthermore, it is shown that the high pollutant load of COD, BOD, phosphate and nitrate in the downstream section of the Citarum river. The high pollutant load found in the downstream of the Citarum river is caused by excess waste from domestic, agricultural and industrial activities.[11]

Epidemiological studies show that pollutants affect animal and human life. It has been shown that air pollution play a role in infertility. Factory waste is a disruptive endocrine hormone able to damage the body's endocrine system, through various mechanisms.[12] Moreover that pollutants cause disruption of spermatogenesis leading to decreased reproductive capacity in exposed populations.[13] The results of previous studies show specifically the effect of environmental lead pollution on blood lead and sex hormone levels in the electronic waste disposal area.[14] Previous studies have also shown that pollution affects chromosomes, thereby affecting infertility and sex hormone levels.[15] Infertility is still a problem for many married couples. It was also stated that the average age of childbearing in women was increasing.[16] Moreover that infertility in Indonesia occurs in about 10-15% of couples of childbearing age.[17]

Based on the data submitted by the researchers, it is necessary to conduct a study on the characteristics of infertile communities living in agricultural and industrial areas. The purpose of this study was to determine the characteristics of infertility in the agricultural and industrial areas. The infertility characteristics include the results of sperm analysis, the etiology of the causes of infertility in female, and the diagnosis of infertility in the agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia.

METHODS

This research is a retrospective study with descriptive analysis. This research is part of a research project on the characteristics of infertility in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia in 2015-2020.

The research material is secondary data obtained from the medical records of patients. The study was conducted from June to November 2019 in the Infertile Poly of RSIA Mitra Bunda Amanda Karawang, Karawang Regency, West Java Province, Indonesia. Collection of medical record data used from January 1^{st} to December $31^{st,}$ 2015. The individuals whose data were used in this study all live in Karawang Regency, West Java, Indonesia.

RESULTS

The map of the research location in Karawang Regency, West Java Province, Indonesia is presented in Figure 1.

Figure 1. The map of the research location in Karawang Regency, West Java Province, Indonesia.

Source: https://www.google.com/maps/place/Karawang+Regency,+West+Java/@-6.2647322,107.0835336,10z/data=!3m1!4b1!4m5!3m4!1s0x2e69775e79e70e01:0x301576d14feb9e0!8m2!3d-6.3227303!4d107.3375791

Age distribution of research Subjects presented in Table 1.

Table 1. Age distribution of Research Subjects

Age	N (190 Subjects)	%
Male	95	
<30 years	35	36.84%
30–40 years	53	55.79%
>40 years	7	7.37%
Female	95	
<30 years	58	61.05%
30–40 years	35	36.84%
>40 years	2	2.11%

Based on the Table 1, showed infertility was most prevalent in male between 30 and 40 years (55.79%), followed by the age group below 30 years (36.84%) and above 40 years (7.37%). Meanwhile, in the female, infertility was most prevalent in the age group below 30 years (61.05%), followed female aged 30-40 years (36.84%), and above 40 years (2.11%).

Educational qualification of research Subjects presented in Table 2.

Table 2. Educational qualification of Research Subjects

Age	N (190 Subjects)	%
Male	95	
Junior High School	20	21.05%
High School	32	33.68%
Academy	25	26.32%
Bachelor	18	18.95%
Female	95	
Junior High School	30	31.58%

High School	35	36.84%
Academy	22	23.16%
Bachelor	8	8.42%

According to Table 2, the most common educational qualification possessed by the male education is high school diploma (33.68%), followed by academy (26.32%), junior high school (21.05%), and bachelor (18.95%) degrees. Similarly, the most prevalent educational qualification possessed by the female was high school diploma (36.84%), followed by junior high school (31.58%), academy (23.16%), and bachelor (8.42%) degrees.

Characteristics of research Subjects based on occupation presented in Table 3.

Table 3. Characteristics of Research Subjects Based on Occupation

Age	N (190 Subjects)	%
Male	95	
Laborer	21	22.11%
Factory Employees	54	56.84%
Entrepreneur	28	29.47%
Civil servants	12	12.63%
Female	95	
Laborer	12	12.63%
Factory Employees	22	23.16%
Entrepreneur	18	18.95%
Civil servants	12	12.63%
Housewife	35	36.84%

Based on Table 3, infertility was discovered to be most prevalent in factory employees (56.84%), followed by entrepreneurs (29.47%), laborers (22.11%), and civil servant male (12.63%), in terms of occupation. Meanwhile in the female, infertility cases were most prevalent in housewives (36.84%), followed by factory employees (23.16%), laborers (12.63%), and civil servants (12.63%).

Infertility diagnosis based on the research Subjects presented in Table 4.

Table 4. Infertility diagnosis based on the research Subjects

Diagnosis	(N=95 couples)	%
Primary Infertility ex Male Factor	30	31.58%
Primary Infertility of Male and Female Factors	43	45.26%
Primary Infertility ex Female factor	18	18.95%
Secondary Infertility	4	4.21%

Based on the Table 6 shows the most common infertility diagnosis was primary infertility male and female factor (45.26%), followed by primary infertility ex male factor (31.58%), primary infertility ex female factor (18.95%), and secondary infertility (4.21%).

The etiology of infertility in the female research Subjects presented in Table 5.

Table 5. The Etiology of Infertility in the Female Research Subjects

Etiology	N (95 Subjects)	%
Tubal Factor	19	20.0%
PCOS	25	26.32%
Myoma	16	16.84%
Endometriosis	20	21.05%
Ovulation	15	15.79%

Abbreviations: PCOS=polycystic ovary syndrome

According to Table 5, the etiology of infertility in female was discovered to be majorly due to polycystic ovary syndrome (PCOS) 26.32%, followed by endometriosis 21.05%, tubal factors 20.0%, myoma 16.84%, and ovulation 15.79%.

Sperm analysis of research Subjects presented in Table 6.

Table 6. Sperm Analysis of Research Subjects

Age	**N (95 Subjects)**	**%**
Normospermia	4	4.21%
Oligospermia	6	6.32%
Asthenospremia	4	4.21%
Teratospermia	7	7.37%
Oligoasthenospremia	20	21.05%
Oligoteratozoospremia	22	23.16%
Oligoasthenoteratozoospermia	32	33.68%

Based on the Table 6, shows that oligoasthenoteratozoospermia being the most prevalent sperm type (33.68%), followed by oligoteratozoospremia (23.16%), oligoasthenospremia (21.05%), teratospermia (7.37%), oligospermia (6. 32%), normospermia (4.23%), and asthenospremia (4.23%).

DISCUSSION

This study showed that infertility is most prevalent in male between 30 and 40 years (55.79), and female below 30 years (61.05%). Ordinarily, these age groups ought to be rather reproductive, however, on the contrary, these are the groups with the most infertility problems. Meanwhile, the highest educational qualification possessed by the male and female, is High School diploma (33.68% and 36.84%, respectively). This is a possible early indication of another harmful impact of the factories in work environments and around residences. It has been reported that demographic factors such as gender, education, income and geographic location influence the prevalence of infertility in infertile Chinese men and women.[18] In addition, the general levels of education, knowledge, and socioeconomic development within the region, are currently low. Consequently, many people are ignorant, or forced to live near factories and to utilize polluted water sources. In terms of occupation, the male were mostly laborers (56.84%), while the female were majorly housewives (36.84%). The occupation of laborers is a possible cause of infertility, especially in cases of exposure to heat and direct contact with heat sources, often encountered in manufacture of metal rim, tires, steel plates, zinc, machine operators, motorcycle body frames, forklifts, and other products. This exposure of male reproductive organs to heat is possibly associated with reduction in sperm quality. This can occur because high temperatures cause an increase in testicular metabolism so that sperm is damaged.[19]

Pollution has detrimental effects on health, not only by direct inhalation of pollutants, but also through other means of exposure, including ingesting contaminated water or contact with skin. One easy example is carbon monoxide as a pollutant from industrial activities. In humans, carbon monoxide poisoning affects the cardiovascular, neurological, and affective systems.[20] The most common health effects are respiratory infections. However, pollutants affect all body systems, including reproduction. The exact pathophysiology of pollutant effect on ovaries is not currently known. However, pollutants are known to bind to hemoglobin during blood circulation, and cause toxicity, upon entering body organs.[21] We already know that agricultural and industrial activities produce pollutants as a by-product. Therefore the negative effects of pollutants on the population must be avoided. In addition, The government has long established of technical guidelines for industrial estates (Pedoman Teknis Kawasan Industri).[22]

Based on the diagnosis of infertility, the results of this study showed that the main factor of male and female infertility has the biggest role compared with the other factors (Table 4). We already know that various hormones play a role in the reproductive process, including gonadotrophin-releasing hormone (GnRH), follicle stimulating hormone (FSH), lutheinizing hormone (LH), estrogen, progesterone, testosterone, and inhibin. It has been proven that estrogen plays a role in the reproductive system of women and men. Apart from that, estrogen also plays a role in the neuroendocrine, skeletal, vascular and immune systems. Therefore, estrogen has implications for infertility and other diseases.[23] Therefore, exogenous estrogenic compounds have the potential to interfere with the reproductive system. In this regard, the effects of diethylstilbestrol (DES) and methoxychlor (MXC) have been investigated on the peripubertal period in female rhesus monkeys. The results of these studies indicate that DES had a striking effect on adolescent maturation and MXC also altered development during this period. The pattern of effects across agents and doses may be based on specifics of estrogenic action.[24] On the other hand, it has also been proven that xenoestrogen involved in the decrease in the number and quality of human sperm, consequently contributing to a decrease in fertility and decline in the proportion of male births. Xenoestrogens have also been shown to increase the occurrence of abnormalities in the male reproductive tract. Moreover, it has also been shown that xenoestrogens play a role in increasing spontaneous abortion.[25]

It has been stated that primary infertility is associated with protein that bind with sex hormone. In humans, there are proteins that bind with sex hormones in the circulatory system and in the testes. The protein that binds with sex hormones in the circulating system is called sex hormone binding globulin (SHBG). Proteins that bind to sex hormones in the testes are called androgen binding protein (ABP). SHBG in the circulatory system has a function to bind sex steroid hormones and mediate the work of these hormones to target cells outside the testes, while ABP functions to mediate the action of sex steroid hormones in the testes.[26] It is shown that the distribution of SHBG concentrations is broad based on age and body mass index (BMI) values in primary infertile men. From these two variables, it turns out that the relationship between BMI and a decrease in SHBG levels is stronger than the relationship between age and increased levels of SHBG.[27] The other study showed that the levels of SHBG, total testosterone, free testosterone and percent of free testosterone have a negative correlation with age, but the insulin and free testosterone index do not correlate with age. The rate of decrease in SHBG levels per decade in healthy Indonesian men was 8.19%, while the decrease of total testosterone levels per decade in healthy Indonesian men was 9.8%.[28] The results of previous studies show that low total testosterone levels can increase fasting blood glucose levels in adult men, but SHBG levels do not predict fasting blood glucose levels.[29] Although it has been stated that SHBG levels are influenced by many factors, including genetic factors such as the genetic polymorphism of SHBG.[30]

With regard to primary infertility, research has been carried out to reduce SHBG levels in postmenopausal women, namely by isoflavone supplementation.[31] We recommend that this method be implemented in women of childbearing age to increase fertility. In addition, women of childbearing age in industrial areas also need special attention to BMI, especially those less than 18.5 kg/m^2. We recommend that women of childbearing age in these areas have a normal BMI. We need to present this matter because our results show that women of reproductive age with a BMI <18.5 kg/m^2 and having a heterozygous variant SHBG genotype (W/v) is undernutrition. Moreover, it has also been shown that women of childbearing age with a BMI <18.5 kg/m^2 and having the heterozygous variant SHBG genotype (W/v) have the lower of protein, fat and carbohydrate intake.[32] It has been stated that abnormalities in protein metabolism in cells are caused by gene mutations. Disorders of protein metabolism in cells cause various forms of organ abnormalities, thus resulting in congenital abnormalities[33] and morphological variations.[34] Therefore it is necessary to improve nutrition for repoductive women in agricultural and industrial areas such as in Karawang Regency, West Java Province, Indonesia. Various natural ingredients can be used as a source of protein. Proteins that are sourced from natural materials can be developed to meet protein intake. Moreover, it has also been shown that proteins from natural ingredients contain several enzymes that have the potential for therapy.[35] All the results of the above studies which reveal the role of SHBG in the reproductive system of both men and women clarify the relationship between SHBG and primary infertility. Apart from hormones and SHBG which can affect primary infertility, of course, it is necessary to discuss pollutants that have an effect on populations in agricultural and industrial areas.

Based on the etiology of infertility in female subjects in this study indicates that PCOS ranks top, that is 26.32% of the total subjects. PCOS are potentially valuable indicators of cultural, environmental, and genetic factors that may contribute to excess risk in certain regions of the world. It has been proven that the prevalence of PCOS is determined by region and race/ethnicity.[36] The results of a study in the US showed that the prevalence of PCOS in the southern region was 47.5%, in the central region 23.0%, while in the western region it was 18.7% and in the northeast region 10.3%.[37] In addition, it has also been stated that genetic and environmental (lifestyle) factors are associated with the pathophysiology of PCOS after prenatal exposure to androgens.[38] Moreover it has been shown that environmental toxins, dietary diet, obesity and geographical variations are associated with PCOS.[39] Besides these pollutants, bisphenol A {2, 2,-bis (4-hydroxyphenyl) propane=BPA)} is made by combining acetone and phenol. BPA is used in food packaging and in general as an industrial ingredient. BPA exposure to humans can be through the inhalation, skin and digestive tract. BPA has weak estrogenic, antiandrogenic and antithyroid activity, although it can accumulate in various tissues of the human body. It has been reported that BPA affects metabolism and the reproductive system in humans. It is more detailed that BPA decreases male and female fertility.[40] In more detail, it shows the impact of 2,2-bis 4-hydroxyphenyl propane (BPA) as a water and soil pollutant with the incidence of PCOS.[41] The results of previous studies showed that the women with PCOS had higher blood levels of BPA than the control group.[42] With the high percentage of primary infertility in this study, research on various types of pollutants in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia should be conducted.

Oligoasthenoteratozoospermia in this study reached 33.68% of the population (N=95 subjects). The results of this study are different with study results in India. The results of a study in India showed that 3.8% of 105 men with fertility problems experienced oligoasthenoteratozoospermia.[43] We suspect that the high prevalence of oligoasthenoteratozoospermia in the group of infertile men in this study is related to environmental pollutants. It has been explained previously that high pollutant loads are found in the downstream part of the Citarum river which crosses Karawang Regency. Our statement is in accordance with the results of research which states that significant positive correlation between seminal total PCB level and the percentage of single-stranded DNA in sperm.[9]

CONCLUSION

Primary infertility of male and female factors, polycystic ovary syndrome and olygoasthenoteratozoospermia dominate the population in agricultural and industrial areas in Karawang Regency, West Java Province, Indonesia. Therefore, it requires supervision and protection from the government, society, factory owners, and related health workers. This is intended to overcome the impact of pollutants that threaten the health of residents who live and work in agricultural and industrial areas in Karawang district, West Java Province, Indonesia. Of course, this is also applied in the other agricultural and industrial areas in Indonesia.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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AUTHORS CONTRIBUTIONS

Conceptualization: AG, RW, DD. Data acquisition: AG, DD, HGW and DK. Data analysis or interpretation: AG, RW, HJE, HGW, DK and DT. Drafting of the manuscript: AG, RW and MLEP. Critical revision of the manuscript: DD, HJE, HGW and DT. Approval of the final version of the manuscript: all authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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