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Factors Causing Primary Infertility In Couples Of Reproductive Age: Literature Review

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ABSTRACT

Primary infertility, the inability of couples of reproduvtive age to conceive after 12 months of unprotected sexual intercourse, is a complex health problem with multiple causative factors. This literature review aimed to identify and analyze factors associated with primary infertility in couples of reproductive age. The search method was conducted on electronic databases such as PubMed, ScienceDirect, and Google Scholar with the keywords "primary infertility", "infertility factors", "reproductive age couples", and "literature review". The results of the literature review found that primary infertility can be caused by various factors, both from the man (sperm quality disorders, sexual function, reproductive tract infections, chromosomal abnormalities, varicocele, lifestyle), woman (ovulation disorders, fallopian tubes, endometriosis, uterus, hormonal, lifestyle), and partner (age, lifestyle, environment, stress). These factors can be interrelated and result in primary infertility. It can be concluded that primary infertility is a complex and multifactorial health issue. Understanding these factors is important to help couples achieve pregnancy and improve their quality of life.

Keyword : Couples of reproductive age; infertility; infertility factors; primary infertility

INTRODUCTION

Having children is a dream for every married couple. However, not all lucky couples easily achieve it (1). Infertility is defined as the inability of a couple to conceive after 1 year of sexual intercourse without using contraceptives. Primary infertility is infertility experienced by couples who have never been pregnant (2). The problem of infertility can have a major impact on couples who experience it. In addition to medical problems, infertility can also cause economic and psychological problems (3). This is a common problem that affects the couple's mental and emotional health, as well as their quality of life (4)

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Infertility is a global public health problem that occurs both in the world and in Indonesia. About 1 in 7 couples in the world experience infertility. Every year, there are about 2 million new infertile couples. In Indonesia, it is estimated that 1 in 10 couples of childbearing age experience infertility with varying prevalence in each region (5). Previous research obtained data in 2020 as many as 206 (20.15%) women of reproductive age experienced primary infertility and as many as 43 women of childbearing age (20.87%) experienced obesity (4). One type of infertility that is important to note is primary infertility, which is the inability of a couple to conceive since the couple's first marriage. Primary infertility can be caused by various factors, either from the man, the woman, or a combination of both. Understanding the factors that cause primary infertility is essential to help couples achieve their desired pregnancy (6).

The causative factors for primary infertility can be male, female or a combination of both. These factors are complex and involve various aspects, such as biological, lifestyle and environmental factors. Understanding data and information about infertility is important to raise awareness and encourage efforts to prevent and overcome infertility. This effort needs to be done comprehensively and involve various parties, including the government, health workers, and the wider community (7). This literature review aimed to identify and analyze factors associated with primary infertility in couples of reproductive age. The results of this review are expected to provide useful information for couples experiencing primary infertility and for health workers involved in infertility treatment.

METHODS

This literature review was conducted by searching scientific articles relevant to the topic of primary infertility in couples of reproductive age. The data sources used were electronic databases such as PubMed, ScienceDirect, and Google Scholar. The keywords used for the search included “primary infertility”, “infertility factors”, “reproductive age couples”, and “literature review”. The selected articles were then analyzed and synthesized to produce a comprehensive conclusion.

Articles were selected in accordance with the predetermined inclusion criteria, and were carried out systematically based on PRISMA. The inclusion criteria were: 1) articles published in the database in the time span of 2019 to 2024, 2) The scientific literature used is original research articles, 3) Articles are available full text and use English and Indonesian, 4) Studies that discuss infertility in the nursing and health areas, 5) articles are quantitative and qualitative studies. While the exclusion criteria include: 1) articles that are not related to infertility, 2) articles published more than 5 years.

RESULT

The number of articles that the author obtained from searching the data base was 1254 articles obtained from the PubMed, Science Direct, and Google Scholar databases. Furthermore, the author conducted

screening by looking at the suitability of the title and abstract of the article with the topic of this study. From the screening process, the author found 22 articles that were in accordance with the topic raised. Then the author conducted another screening to read the entire content of each selected article. From this process, the author found 12 articles that did not discuss in detail about the factors that cause primary infertility in couples of reproduvtive age. In the end, the total articles that the author used in this study were 10 articles.

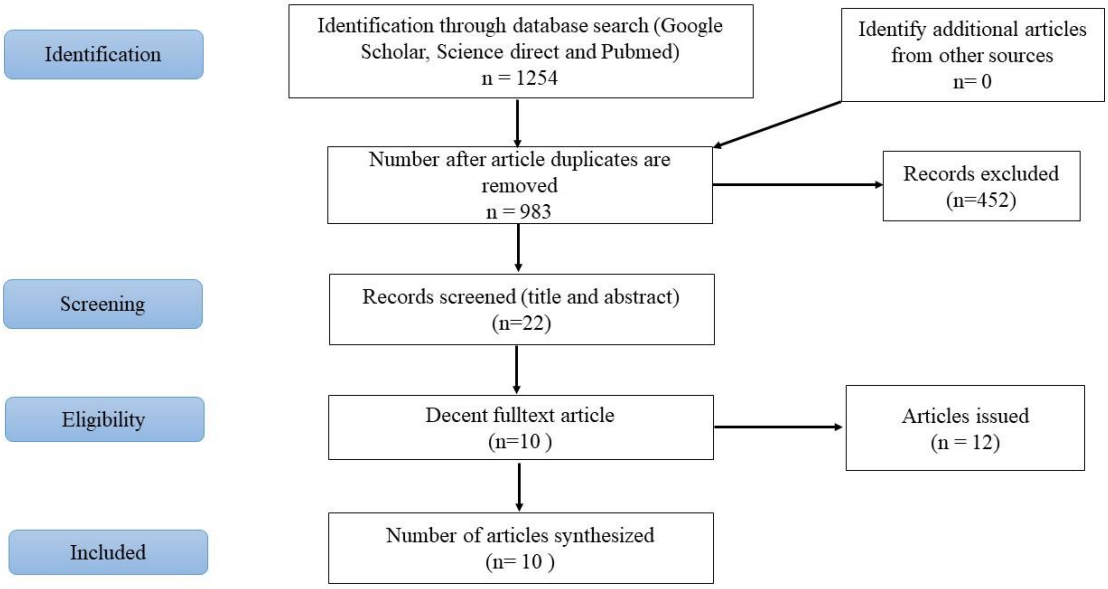

Figure 1. Article Selection Process using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

There are 10 articles that the author gets in this literature review. as for the articles that have been synthesized by the author are shown in table 1 below:

Table 1. Article Search Results

No	Author, Year	Title	Research content	Results
1	Umi Mulyani, Diah Sukarni, Erma Puspita Sari 2021 (8)	Factors Related to Primary Infertility in Couples of Childbearing Age in the Working Area of UPTD Lembak Health Center, Muara Enim Regency in 2021	This study aims to determine the relationship between age, education, occupation, nutritional status, smoking habits, and disease history with primary infertility in couples of childbearing age in the work area of the UPTD Lembak Health Center, Muara Enim Regency in 2021.	The results showed that there was a significant relationship between wife's age, wife's education, husband's job, maternal nutritional status, and husband's smoking habit with primary infertility in couples of childbearing age.
2	Irma Hamdayani Pasaribu,	Factors Affecting the Occurrence of	This study aims to find out the factors related to	The results of the study showed that the factors

No	Author, Year	Title	Research content	Results
	Maria Alia Rahayu, Rina Marlina 2019 (9)	Infertility in Women at Dewi Sri Karawang Hospital	infertility in women at Dewi Sri Krawang Hospital.	related to infertility in women at Dewi Sri Krawang Hospital were occupation, body mass index (BMI), ovulation disorders, tubal and pelvic disorders, and uterine disorders.
3	Ernawati Napitupulu, Isyos Sari Sembiring, Titin Suherni, Elnia Elnia, Rizky Andriani 2023 (10)	Factors Affecting the Occurrence of Primary Infertility in Couples of Childbearing Age at the Pegajahan Health Center, Pegajahan District, Serdang Bedagai Regency in 2023	This study aims to find out the factors related to primary infertility in couples of childbearing age at the Pegajahan Health Center, Pegajahan District, Serdang Bedagai Regency in 2023.	The results showed that there was a significant relationship between the age of the wife, the history of sexually transmitted diseases, and the husband's smoking habit with primary infertility in couples of childbearing age.
4	Shoujing Liang, Yuanhui Chen, Qian Wang, Huanhuan Chen, Chenchen Cui, Xiaohang Xu, Qingwen Zhang, Cuilian Zhang. 2021 (11)	Prevalence and associated factors of infertility among 20–49 year old women in Henan Province, China	This study aims to determine the current prevalence and factors related to infertility in women of childbearing age in Henan Province, China.	The prevalence of infertility in 765 study participants was 24.58%. The prevalence of primary infertility was 6.54%. Age, history of gynecological surgery, and decreased ovarian reserve increase the risk of infertility. Local health authorities and medical personnel need to take a role to reduce high infertility rates and protect women's reproductive health.
5	Nanati Legese, Abera Kenay Tura, Kedir Teji Roba, Henok Demeke 2023 (12)	The prevalence of infertility and factors associated with infertility in Ethiopia: Analysis of Ethiopian Demographic and Health Survey (EDHS)	This study aims to determine the prevalence and factors related to infertility among couples in Ethiopia using data from the Ethiopian Demographic and Health Survey (EDHS) in 2016. This study uses a cross-sectional research design from the data that EDHS in 2016.	The prevalence of infertility in the last 12 months was 24.2%. The vast majority (90.7%) are secondary infertility. In contrast, infertility is less common in women with formal education and a better wealth index. Age over 35, living in the countryside, smoking, and a Body Mass Index (BMI) of <18.5 have a significant association with infertility. Primary infertility was significantly higher in women whose partners drank alcohol and chewed khat (Catha edulis).
6	Sri Winarni,	Risk Factors Of Infertility Cases	This study aims to analyze the occurrence of	The multivariate analysis showed that the variables

No	Author, Year	Title	Research content	Results
	Hanifa M. Denny, Dharminto, Fahmi Arifan, Ari Suwondo, Apoina Kartini, Hardhono Susanto 2021 (13)	Among Shallot Farmers	infertility in men based on the use of pesticides and a diet containing zinc. Researchers measured the use of pesticides, personal protective equipment (PPE), daily clothing practices, hand washing after spraying, and zinc intake.	that had a significant effect were: the risk of infertility was 2.663 times higher in farmers who sprayed more than 3 times a week, the risk of infertility was 0.180 times lower in farmers who sprayed against the wind, and the risk of infertility was 0.346 times lower in farmers who did not respray.
7	Chenfeng Zhu, Li Yan, Chuqing He, Yang Wang, Jiahao Wu, Luting Chen, Jian Zhang. 2022 (14)	Incidence and risk factors of infertility among couples who desire a first and second child in Shanghai, China: a facility-based prospective cohort study	This study aims to evaluate the incidence of infertility and risk factors in couples who intend to have their first and second children. The study was conducted with a prospective cohort from 2013 to 2017 in the pre-pregnancy center of the International Maternal and Child Health Hospital.	The overall incidence rate of infertility is 16.95%, in primary infertility is 19.30%. Primary risk factors for infertility include advanced age (>35 years), abnormal Body Mass Index (BMI), Longer menstrual periods, Endometrial polyps, Polycystic ovary syndrome (PCOS), Salpingostomy, History of mycoplasma.
8	Muji Lestari, Weni Guslia Refi, Maya Dika Dahliana, Tesya Oktavia, Gita Nirmala Sari, 2023 (4)	Obesity is Associated with Primary Infertility in Women of Childbearing Age	This study aims to analyze the relationship between obesity and primary infertility in women of childbearing age. The research method used is quantitative with a cross-sectional approach. The sample used was 840 women of childbearing age who visited the infertility clinic in 2021.	There was a significant relationship between obesity and the incidence of primary infertility in women of childbearing age with a $p <$ value of 0.001. This shows the importance of preventing obesity in women of childbearing age to avoid primary infertility.
9	Qurratul A'yun, Byba Melda, Siti Farida, 2020. (15)	Factor Analysis Infertility Events in Poly Gynekology Hospitals dr.H. Slamet Martodirdjo Pamekasan	This study aims to identify factors that affect the incidence of infertility in infertile couples at the Obstetrics Poly of Dr. H. Islamet Martodirdjo Pamekasan Hospital. The research design used is quantitative with a cross sectional approach. The study was conducted from September 17 to November 23, 2018 with a population of 108 couples and a sample of 85 couples using a simple	Based on logistic regression analysis, it was obtained: physical activity of the wife, nutritional status of the wife, smoking habits of the wife and diet of the wife did not have a significant effect. Meanwhile, the husband's smoking habit has a significant effect. The incidence of infertility in couples of childbearing age is most likely influenced by a combination of physical activity, nutritional status, smoking habits, and diet, as

No	Author, Year	Title	Research content	Results
			random sampling technique.	well as other factors related to the reproductive organs. The most influential factor in infertility in men is smoking habits. This is because cigarette smoke contains chemicals that can damage sperm DNA so that it cannot fertilize eggs, as well as reduce sperm motility so that it inhibits fertilization.
10	Amnah Alghamdi, Nesren Bahnsawy, Keeping the Silence, Amel Dawod Kamel Gouda. 2023. (16)	Assessment Of Prevalence and Risk Factors Of Infertility Among Saudi Women: A Cross Sectional Study	The study aims to identify the types and risk factors for infertility in Saudi women in the city of Riyadh. The research design uses cross sectional. The researcher developed a questionnaire consisting of four parts: demographic data, obstetric and gynecological history, health history, and family history.	The average age of the respondents was 34.03 years ± 1.37 years and half (50.4%) had a BMI categorized as overweight, one-third (33.0%) had primary infertility. The identified causes of infertility include: ovulation disorders (28.9%), fallopian tube adhesion or obstruction (7.4%), and male factors (12.6%). There was a statistically significant relationship between the type of infertility and the age and length of marriage, the method of contraception, the duration of contraceptive use, the cause of infertility, and the type of medication for ovulation induction. Female factors such as ovulation disorders, adhesions or obstruction of the fallopian tubes, uterine fibroids, pelvic inflammatory diseases, endometriosis, urinary tract infections, and male factors are stated as causes of infertility.

DISCUSSION

Infertility, also known as the inability to conceive after 12 months of unprotected intercourse, is a complex problem and can be caused by various factors in both men and women. Primary infertility is a condition in which couples of childbearing age (usually defined as women under the age of 35 years

and men under the age of 40 years) are unable to achieve pregnancy after 12 months of unprotected sexual intercourse. Couples experiencing primary infertility usually do not have specific physical symptoms. The most common symptom is the inability to conceive after 12 months of unprotected sexual intercourse (17)

More than one in five couples in Ethiopia have infertility problems. Factors associated with infertility are both male and female. Based on the search results, there are various factors that cause primary infertility in couples of childbearing age, which can be categorized into several groups, namely male factors, female factors and couple factors (18).

Male factors include sperm quality disorders such as low sperm count, poor sperm motility, abnormal sperm morphology and high sperm DNA fragments. In addition, impaired sexual function such as erectile dysfunction, premature ejaculation and inability to achieve orgasm can hinder fertilization. Infections in the male reproductive organs, such as the epididymis and prostate, can also impair sperm production and quality. Chromosomal abnormalities in men, such as Klinefelter syndrome and Noonan syndrome, can lead to infertility (17,18)

Varicocele, a dilated blood vessel in the scrotum, can also increase testicular temperature and interfere with sperm production. In addition, lifestyle factors such as smoking, excessive alcohol consumption, drug use and obesity can reduce sperm quality and impair male fertility. Infertility is also a problem caused by various factors, both on the part of the woman and the man. Husband's smoking habit was the most influential factor for infertility in this study (15).

Female factors include ovulation disorders such as polycystic ovary syndrome (PCOS), hypothalamic-pituitary-pituitary (HPO) axis dysfunction, and premature ovarian failure (POF), which can cause infertility by interfering with the release of mature eggs. Fallopian tube disorders, such as blocked or damaged fallopian tubes due to infection, endometriosis, or previous surgery can impede the sperm's journey to meet the egg, interfering with fertilization. Another condition in women with infertility is endometriosis, a condition where endometrial tissue grows outside the uterus, which can cause inflammation and interfere with fertility. In addition, uterine disorders such as uterine fibroids, uterine polyps, and congenital malformations can affect embryo implantation and interfere with pregnancy (19).

In women, hormonal disorders such as low progesterone hormone imbalance or high prolactin levels, can disrupt ovulation and menstrual cycles, resulting in infertility. Lifestyle factors such as smoking, excessive alcohol consumption, drug use and obesity can interfere with ovulation and female fertility. Primary infertility is significantly higher in women whose partners chew khat and drink alcohol. Secondary infertility was significantly associated with underweight, obesity, smoking, and age at first delivery. Therefore, action on preventable factors is the most important treatment approach and will improve the health status of the couple in other respects (12).

Partner factors include age, with women's fertility declining with age, especially after the age of 35. The overall infertility rate in Shanghai is similar to other major cities in China. Age is one of the risk factors for both primary and secondary infertility. Marriage at a later age is becoming more common in society. Therefore, the government needs to consider subsidies to encourage childbirth at childbearing age, which can improve fertility rates (14). Unhealthy lifestyles, such as smoking, in both men and women can reduce sperm and egg quality and increase the risk of infertility. Excessive alcohol consumption in both men and women can interfere with hormone production and fertility. Lack of exercise and poor sleep can reduce fertility in couples, and obesity in men and women can increase the risk of infertility.

Environmental factors such as exposure to harmful chemicals like pesticides and heavy metals can damage sperm and eggs and increase the risk of infertility. Radiation and air pollution can reduce sperm quality and increase the risk of infertility. Research showed that the frequency of spraying pesticides in a week is the variable with the highest influence on infertility. Farmers who spray pesticides on shallots more than three times a week have a three times higher risk of infertility. This study shows the importance of using proper PPE and safe practices when applying pesticides to protect male reproductive health. Chronic stress can also impair ovulation and sperm production (13).

Primary infertility is a complex problem caused by various factors. These factors can be interrelated and affect a couple's fertility. A study of Saudi women in Riyadh found risk factors related to infertility, such as maternal age, health problems, and the type of medication used for ovulation induction. The study also identified various factors that contribute to infertility in women. Thus, these findings can help physicians in the diagnosis and management of infertility and increase the chances of a successful pregnancy. Thus, understanding these factors and taking preventive measures can help reduce the problem of infertility in couples of childbearing age (16).

It is important for couples experiencing primary infertility to consult a health professional for proper diagnosis and treatment (18). A physical examination, laboratory tests and other supporting tests are needed to determine the cause of infertility. Treatment of primary infertility depends on the cause (20). In some cases, simple treatments such as lifestyle changes or medications may help. However, in some cases assisted reproductive techniques (ART) such as artificial insemination (IUI) or in vitro fertilization (IVF) are also required to help couples achieve pregnancy (21).

CONCLUSION

Primary infertility is a health problem that can be addressed with a comprehensive approach. Understanding the factors associated with primary infertility is important to help couples achieve pregnancy.

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