

Risk factors for endocrine diseases in human reproduction causes of infertility (a literature review)

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ARTICLE INFO

Article history:

Received Feb 24, 2023

Revised Mar 8, 2023

Accepted Mar 14, 2023

Keywords:

Endocrine
Infertility

ABSTRACT

According to WHO, 50-80 million people in the world suffer from infertility. The most common cause of infertility in women with non-ovulatory disorders is due to polycystic ovary syndrome (PCOS) of 66.2% and ovulation disorders of 57.6%. Meanwhile, the cause of male infertility is vascular disorders including varicocele of 49.4% and according to semen analysis the most common causes are azoospermia of 56.4%, oligosperma 24.5%. The purpose of this research is to look for risk factors for endocrine diseases that commonly occur and to treat the disease using Assisted Reproductive Technology (ART) solutions. This research is a Systematic Literature Review (SLR) with the PRISMA method. The keywords used to search the article are endocrine and infertility. Google Scholar and PubMed are journal databases used to conduct a literature search and the search results found 5 relevant articles. In conclusion, the risk factors for endocrine diseases that cause infertility are body weight, calorie intake in women, gender, age, nutritional status and obesity, alcohol consumption, marijuana consumption, age > 35 years, risky work, stress levels, abnormal BMI and organ abnormalities. reproduction. The recommendation is that it is hoped that the government will be able to facilitate the community with easy access to health services, especially infertility treatment services that are cheap and of good quality for the welfare of its people.

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INTRODUCTION

Infertility has been identified by WHO (World Health Organization) as a global public health problem and is an important gynecological complication experienced by married couples who have been married for one year, have regular intercourse without using contraception. (Moridi et al., 2019). Factors that affect couples in the decision-making process in their treatment are the cause of infertility itself, the age of the woman, the duration of infertility and the number of cycles of treatment carried out previously. Counseling of the highest quality offered to couples along with diagnostic tests should be properly selected and effective treatments such as conservative

pharmacological methods (drugs), surgery (endoscopy) and assisted reproductive systems (ART), with the hope of developing ART into future infertility treatments. front(Szamatowicz & Szamatowicz, 2020). According to the latest WHO statistics, around 50-80 million people worldwide suffer from infertility, male factor is responsible for around 20-30% of all cases.(Babakhanzadeh et al., 2022).

The most common causes of female infertility include non-ovulatory disorders due to polycystic ovary syndrome (PCOS) in 66.2% and ovulation disorders in 57.6%. Meanwhile, the cause of male infertility is vascular disorders including varicocele of 49.4% and according to semen analysis the most common causes are azoospermia of 56.4%, oligosperma 24.5%. In women with PCOS, hormone levels including androgens and testosterone increase due to high levels of luteinizing hormone (LH) and low levels of follicular stimulating hormone (FSH), so that the follicles in these individuals are prevented from producing mature eggs. Furthermore, PCOS increases the risk of insulin resistance, along with type 2 diabetes,(Moridi et al., 2019).

Evaluation of infertility can be done by exploring the medical history of the husband and wife, which in men is the duration of infertility, history of surgery and medical illness, use of drugs and alcohol, or whether there is sexual dysfunction (impotence). While the evaluation of women involves gynecological history, surgical history, menstrual history, number and results of previous pregnancies. Semen analysis is an attempt to determine the diagnosis and level of male fertility, whereas in women it is done by assessing ovulation (number of antral follicles), hormone levels (progesterone, estradiol, prolactin, FSH, LH, TSH, AMH etc.) as well as several examination procedures such as a patency test. tubes and uterus i.e. Hysterosalpingogram (HSG), Diagnostic hysteroscopy, Diagnostic laparoscopy with or without chromotubation(Szamatowicz & Szamatowicz, 2020).

A decrease in the fertility rate is characterized by a decrease in physiological potential (fecundity) as indicated by several markers such as increased demand for infertility treatment, high prevalence of polycystic ovary syndrome, poor semen quality and decreased serum progesterone in men, as well as related to other factors including obesity, poor nutrition. inadequate and exposure to environmental pollutants such as endocrine disrupting chemicals(Rotella et al., 2020). Many factors that can cause infertility in humans have been studied, several diseases caused by endocrine disorders in the human reproductive system in women for example polycystic ovary syndrome (PCOS) are characterized by hyperandrogenism, oligo-anovulation, polycystic ovary morphology while in men with analytical procedures Semen can detect the quality and quantity of sperm owned by the husband.

Assisted reproductive technology (ART) has progressed since 1927 by successfully identifying gonadotropins for the first time, which have now increased individualization. This care is a central aspect of all assisted reproductive medical consultation and care. Pure gonadotropin products are now available in pen injection devices that are injected subcutaneously, resulting in increased ease of use and more precise dose selection and adaptation. Work on preparing these new preparations is continuing, with the aim of still developing orally active FSH agonists and antagonists(Lunenfeld et al., 2019). World report of the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) on a global statistical census of data collected reviewing the use, effectiveness and safety of ART, number of ART clinics, procedures and outcomes related to IVF, ICSI, oocyte donation (OD), embryo transfer freezing (FET), pre-implantation genetic testing (PGT) and intra-uterine insemination (IUI) both with partners/husbands and with sperm donors which account for two-thirds of the world's ART activity which is experiencing changes in ART technology and practice making analysis and interpretation of data be challenging(de Mouzon et al., 2020).

The aim of this research is to look for risk factors for endocrine diseases (disorders) and the management of diseases related to the human reproductive system that cause infertility in men and women, which is currently a global health problem in the world, especially in couples of childbearing

age by adjusting to developments in medical science. and increasingly advanced health technology, namely assisted reproductive technology (ART) solutions.

RESEARCH METHOD

This literature review only focuses on the independent variables. Research will focus on tracing various types of diseases related to reproductive disorders due to human endocrine disorders and on infertility and its management medically and with Assisted Reproductive Technology. Inclusion criteria in the form of the full text of relevant articles and research case studies are located in Indonesia. The selected articles go through a screening process through the Google Scholar database, PubMed, and are then reviewed by reading the entire text, especially in the results section to look for variables that affect infertility in men and women. This literature review uses the PRISMA method with an analytical research design. The data collection technique is to review article information by searching it with the help of the internet in order to strengthen the argumentation of this article. This study uses three journal databases, namely Google Scholar, and PubMed. And using the Mendeley application as a reference manager, starting with opening the Mendeley application, on the Mendeley desktop, click help, then click Mendeley website.

Type in the relevant article title, then click search. Meanwhile, in the Google Scholar and PubMed databases, all you have to do is type the relevant article title and search for it. The criteria set by the researcher are that the article must be relevant to the topic, complete text and related to diseases or disorders of the human reproductive endocrine system that affect infertility and the risk factors that affect it and the research is located in Indonesia. Then the publication year range is 2016-2022. A literature search was carried out using keywords, namely endocrine and infertility. Each article is reviewed first, then the relevant articles are downloaded, then copy and paste into one file on the laptop. From the search results found 30 articles that are considered relevant. Then from this number it was re-selected and determined 5 articles which were considered to have inclusion criteria. All data is filtered and collected manually. The results of this literature review were compiled through a process of reviewing selected articles and referring to research objectives. The author searched for articles using three data bases, namely PubMed and Google Scholar, and managed to identify 30 articles, then conducted a selection of similarity, obtained 15, then screened titles and abstracts obtained 10 relevant articles, after assessing feasibility, obtained 9 articles. In accordance with inclusion, namely to determine endocrine diseases and risk factors that cause human infertility, 9 articles were obtained. The literature obtained was synthesized using the narrative method by grouping extracted data similar to the results measured to answer the research objectives.

RESULTS AND DISCUSSIONS

This literature review was compiled through a process of reviewing selected articles and referring to research objectives. The keywords entered were: Endocrine and Infertility. The author searched for articles using two data bases, namely PubMed and Google Scholar, and managed to identify 50 articles, then carried out a similarity selection to get 30, then screened titles and abstracts to get 10 relevant articles, after assessing feasibility, 9 articles were obtained. In accordance with inclusion, namely to determine risk factors for human endocrine diseases that cause infertility and those related to their management in ART, there were 8 articles. The literature obtained was synthesized using the narrative method by grouping extracted data similar to the results measured to answer the research objectives.

The results of research articles that match the inclusion criteria are combined in a table which includes the name and year of research, journal name, research title, variables studied, study design, research sample, statistical methods, results of statistical analysis, research results, research conclusions, and suggestions made presented in table 1 below:

Table 1. Summary of research articles on risk factors that affect endocrine diseases that cause human infertility.

No	Name and year of research	Journal name	Types of research	The variables studied	Study Design	Research sample	Statistical Method	Research Conclusion
1	Anisya V ¹ , Graharti R ² 2019	LPPM - UNILA-IR	Literature Review	Heavy body weight, caloric intake in PCOS women.	-	Scientific articles	-	Calorie restriction can cause androgen levels to drop and restore normal menstrual cycles.
2	Leni Amelia ¹ Soraya Rahmanis a ² , 2019	JIMKI	Literature Review	Semen abnormalities	-	Scientific articles	-	Men with abnormal semen parameters or other known risk factors for infertility should undergo urological evaluation
3	Mareta R ¹ , Amran ² , Larasati V ³ , 2018	Sriwijaya Medical Magazine	analytic observational	PCOS and Infertility	Cross-sectional	249 subjects	Bivariate analysis, chi square test	There is a very significant relationship between PCOS/PCOS and infertility. People who experience PCOS/PCOS are 8.572 times more likely to experience infertility than people who do not experience PCOS.
4	Saftarina F ¹ , Nur I ² , Putri W ³ , 2016	Medical Journal of Lampung University	Literature Review	Polycystic ovary syndrome/PCOS, androgens in the blood, oligoovulation or anovulation,	-	Scientific articles	-	The relationship between polycystic ovary syndrome and infertility can be attributed to the presence of ovulation disorders in an individual with polycystic ovary syndrome, thereby reducing the possibility of meeting between sperm and ovum.
5	Denni Hermartin ¹ , Nazri Adlani Siregar ² , 2021	Jabar Ghafur university research science journal	analytic observational	Gender, age, nutritional status, smoking habits, alcohol consumption, and marijuana	Cross-sectional	18 patients with primary infertility	Univariate analysis	Research shows that infertility is caused (55.6%) by gender, (61.1%) by age, (38.9%) by nutritional status, (61.1%) by smoking habits, (61, 1%) by the factor of consuming

				consumption.				alcohol, and (94.4%) by the factor of consuming marijuana
6	Agustina EE ¹ , Isnaeni S ² , 2022	JORNAL L BIDAN PRADA	Analytical /survey descriptive	Obesity and stress	Cross- sectional	Nullipara at the Baturaden II Health Center in Banyumas	Univariate analysis, Chi square.	There is a significant relationship between obesity and stress with infertility in nulliparas
7	Zetira Z ¹ , Fakhrudin H ² , 2019	Medical Journal of Lampung University	Literature Review	PCOS Syndrome and Metformin	-	Scientific articles	-	Metformin as an oral biguanide insulin-sensitizing agent can reduce hepatic glucose production, reduce glucose in the intestine, peripheral glucose, absorption by muscles and liver. Today metformin has become an established treatment for women with PCOS
8	Indarwati I1, Retno Hastuti B2, Lanti Y Dewi R3, 2017.	Journal of Maternal and Child Health (2017), 2(2):150- 161 https://doi.org/10.26911/thejmh.2017.02.02.06	observational analytics	Infertility is influenced by factors: Age > 35 years, risky work, stress levels, abnormal BMI and abnormalities of the reproductive organs,	Case Control	The research subjects in the case group were women who experienced infertility at the Sekar Clinic at RSUD dr. Moewardi , Surakarta according to the inclusion criteria. The research subjects for the control group were women who were not infertile at the ob-gyn polyclinic	Univariate, Bivariate and logistic regression analysis	Female infertility is related to factors of age > 35 years, occupation, stress level, BMI and abnormalities of the reproductive organs.

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Discussion

According to Veny Anisya et al, polycystic ovary syndrome (PCOS) is caused by insulin resistance and excessive body weight which is related to androgen hormones, so weight loss efforts are needed to reduce central fat which aims to reduce insulin resistance and reduce the amount of androgen hormone, it is recommended to limit calories, exercise regularly, calculate carbohydrate intake, consume high protein, avoid red meat and calorie-dense snacks and eat lots of fruits and vegetables so that menstruation becomes normal (Anisya et al., 2019). According to Leni Amelia, et al evaluation of infertile men should be done by a urologist and include a complete reproductive and medical history (frequency and duration of coitus, duration of infertility and previous fertility, childhood diseases and history of development, drugs, systemic diseases (eg, diabetes mellitus and upper respiratory disease) and previous surgeries (eg, hernia repair), physical examination, and at least two semen analyzes ideally at least one week apart sexual history including sexually transmitted infections, and exposure to toxins from heat, chemicals, and radiation, including smoking and family history of allergies and assisted reproductive techniques (ART) can be performed such as sperm collection from the testis or epididymis and then combined with in vitro fertilization (FIV) / intracytoplasmic sperm injection (ICSI) can be used. Other options including artificial insemination or donor adoption may be taken if corrective treatment is not available (Leni Amelia, 2019).

According to research by Riska Mareta, et al in private practice of obstetricians and obstetricians, there were 89.6% who had PCOS and 10.4% who did not have PCOS experienced infertility and there was a very significant relationship between polycystic ovary syndrome (PCOS) and infertility ($p = 0.000$) and it was concluded that PCOS sufferers were 8.572 times more likely to experience infertility (Mareta et al., 2018). Fitri Saftarina et al, stated in their article that polycystic ovary syndrome (PCOS) can increase the risk factors for infertility. The link between polycystic ovary syndrome and increased risk factors for infertility is found in ovulatory cycle disorders that occur in this syndrome. (Saftarina et al., 2016). Research by Denni Hermartin, et al on FACTORS AFFECTING PRIMARY INFERTILITY IN THE REPRODUCTIVE PERIOD IN GUNUNG TUA HOSPITAL showed that infertility was caused (55.6%) by gender, (61.1%) by age, (38.9%)) by nutritional status factors, (61.1%) by smoking habits, (61.1%) by consuming alcohol, and (94.4%) by consuming marijuana (Denni Hermartin (1), 2021).

Research by Ely Eko Agustina et al on THE RELATIONSHIP OF OBESITY AND STRESS WITH INFERTILITY IN NULLIPARAS The results showed that there was a significant relationship between obesity and stress with infertility in nulliparas. (Agustina & Isnaeni, nd). Zihan Zetira et al's study on the Effect of Metformin on Infertility Women with Polycystic Ovary Syndrome where the result is that there is some evidence suggesting that metformin has an effect on inducing ovulation, increasing aspects of the metabolic syndrome, increasing menstrual cycles, decreasing circulating androgen levels and decreasing levels of Anti- Mullerian Hormone (AMH) and Plasminogen Activator Inhibitor (PAI). The metabolic benefits of metformin are by increasing the body's metabolism, if the body's metabolism increases there will be weight loss, maternal weight has a very large effect on natural conception and can affect the possibility of getting pregnant and having a healthy pregnancy (Zetira et al., 2019). Research by Ika Indarwati et al. The results of the study concluded that female infertility is affected by age ≥ 35 years, risky work, high stress levels, abnormal body mass index, and abnormalities of the reproductive organs. (Indarwati et al., 2017).

The development of advances in reproductive endocrinology technology can be seen from the discovery of more advanced ways to preserve female fertility, namely by activating human

primordial follicles which at birth function as a reserve for future fertility. However, excessive induction of these primordial follicles can lead to the development of premature ovarian insufficiency (POI). (McGlacken-Byrne & Conway, 2021). Ovarian stimulation in a gonadotropin-releasing hormone (GnRH) antagonist protocol with the use of a GnRH agonist for late oocyte maturation is a cutting-edge treatment in high-responding patients that is expected to significantly reduce the risk of developing ovarian hyperstimulation syndrome (OHSS). (Daniel A. Dumesic¹, Luis R. Hoyos¹, Gregorio D. Chazenbalk¹ & Vasantha Padmanabhan², 2021). The development of methods and strategies for maintaining fertility in patients with cancer, including pharmacological protection of the ovaries against gonadotoxic compounds used as anti-cancer drugs with gonadotropin-releasing hormone (GnRH) agonists, is the only pharmacological way of chemotherapy. (Fisch & Abir, 2018).

CONCLUSION

Based on the results and discussion, it can be concluded that the risk factors for someone to be diagnosed with infertility include weight, calorie intake in women, gender, age, nutritional status and obesity, alcohol consumption, marijuana consumption, age > 35 years, risky work, stress levels, abnormal BMI and abnormalities of the reproductive organs. Most diseases of infertility related to human reproductive endocrine, for example Polycystic Ovary Syndrome (PCOS) which is closely related to ovulation disorders or anovulation and semen abnormalities from infertility in men currently have a solution with advances in medical technology, namely Assisted Reproductive Technology (ART).

ACKNOWLEDGEMENTS

I would like to thank all those who have helped me compile this article, especially my family, friends, and lecturers who have supported me so that I can finish this article on time.

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