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FEMALE INFERTILITY: A SYSTEMATIC REVIEW OF THE **LITERATURE**

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ABSTRACT

Due to wars in Iraq, since 1990 and after 2003, the Iraqi environment suffered from acts of profanation. A large number of injuries and deaths were caused by destructive chemicals and radioactive materials. These events resulted in either cancer or infertility. Infertility is one of the medical, social and psychological burdens in Iraqi society. It is defined as "the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Induction of ovulation has remained a milestone in the women treatment anovulatory infertility.

KEYWORDS: Women infertility, gonadotropin.

INTRODUCTION

Infertility according to World Health Organization WHO, is defined as a disease of the reproductive system, by the failure to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.^[1] The inability to become pregnant results in important affecting and profitable tolls, among that artificial nervousness and sadness are more common in infertile couples than infertile couples, also Assisted Reproductive Technologies ART are accessible to care for sterility, but these are pricey. In the last thirty years, Iraq exposed several instability crises causes exasperation in many health problems. One of these problems was the fertility status of many people all over the country. Few studies deal with this health problem in spite of the mental, communal and fiscal proportions of this subject. [2] Infertility can be caused due to many medical disorders, may be due to fallopian tube injury, fertilization and ovulation interference or also hormonal turbulence.^[3] Unable or difficult to conceive is a physically and psychologically painful condition in a female's life.[1]

The Female Reproductive System: The most important organs and structures in the reproductive system is the uterus, it is a vacant muscular organ and pear-shaped organ located between the bladder and lower intestine. It consists of two parts, the cervix and the body; cervix is the uterus lower portion. The os opening is the vessel opening which opens into the vagina and helps the flow out of the menstrual blood from uterus to vagina and leading off the uterus into two fallopian tubes. Next to this is ovary which closes each tube stages. The egg producing organ known as ovary contains 200,000 to 400,000 follicles.^[4]

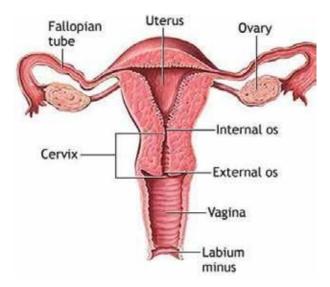


Figure 1: The reproductive system of women.^[4]

Type of Infertility: Infertility may be primary or secondary. Primary infertility refers to couples who have never conceive after a minimum of 1 year of attempting to do so through unprotected intercourse and the live birth absence in non-contraception sexually active woman^[5] whereas, secondary infertility refers to couples who are unable to conceive after one year of unprotected intercourse following previous pregnancy and not using any contraceptives and as the inability to conceive despite exposure to pregnancy for one year (2) years in some epidemiological studies), after having conceived at least once before. [6] Secondary infertility owed to the failure to become pregnant pregnancy failure to a live birth following either a preceding pregnancy or a preceding gift to bear a pregnancy to a live birth.^[7]

Diagnosis of Infertility: Infertility diagnosis is within 1 year failed to conceive and is argued to increase the infertility risk since women about 50% failed to conceive in first year may also

do so in second year. [8]

Female Infertility Causes: Infertility in female may be caused due to variable factors:

Disorders of Ovulation: The (WHO) classifies ovulation disorders into three groups:

Group I: Hypothalamic pituitary failure (hypothalamic amenorrhea or hypogonadotropic and hypogonadism).

Also called as hypogonadotropichypogonadism, may be caused due to failure of hypothalamic pituitary. With these conditions generally women are having amenorrhoea (primary or secondary), also may be known as hypothalamic amenorrhoea, estrogen deficiency and low gonadotrophins levels low gonadotrophins levels are the main characteristics. [9]

Group II: hypothalamic-pituitary-ovarian dysfunction, predominately a product of polycystic ovary syndrome (PCOS). This is the cause of the enormous greater part of ovulation disorder.

Group III: Ovarian failure a result hypo-thalamic cause body mass index (BMI) over 35 (Kg/). BMI will result in irregular menses, amenorrhea, or failure to ovulate and increase in pituitary hormones (FSH and LH) will result in failure to ovulate. [10]

Male Factor: Male infertility is diagnosed when, after testing both partners, reproductive problems have been found in the male.^[11] The first and most common test used to evaluate male infertility is semen analysis. Semen analysis includes a set of descriptive measurements of sperm parameters such as concentration, motility and morphology and some seminal plasma characteristics.^[12] For infertility in males there are six main causes. Abnormal sperm production or function is the first one. Due to repeat infections sperm can be affected, undescended testicles or genetic defects.^[13] Male factor infertility is assessed based on the following values.^[13]

- Underprovided sperm count (less than 10 million per milliliter; volume should be 1 -5 ml. of ejaculate).
- Deficient sperm motility (over 60% should be motile and show purposeful forward movement).
- Poor sperm morphology (more than 50-60% abnormal in form). On the physical examination, testicular abnormalities such as a varicocele or absence of the vas deferens can be detected.

Unexplained Infertility: Unexplained infertility, referring to the failure to conceive of a

couple in whom no definitive cause for infertility can be found, has an incidence of 10-20% in all infertile couples.^[14] Unexplained infertility diagnosis is given when evaluation of standard fertility is normal in both woman and man and it relies upon nature, number and quality of used tests and made conclusions.^[15] The principal treatments for unexplained infertility include expectant observation with timed intercourse and lifestyle changes, clomiphene citrate and intrauterine insemination (IUI), controlled ovarian hyperstimulation (COH) with IUI, and IVF.^[14]

Recurrent Miscarriage: Recurrent miscarriage defined as the loss of three or more consecutive pregnancies affects 1% of couples trying to conceive. It has been estimated that 1-2% of second-trimester pregnancies miscarry before 24 weeks of gestation. Two consecutive miscarriages are experienced by less than 5% of women, and three or more consecutive miscarriages by about 5% women. Subdivision of recurrent miscarriage can be done into primary and secondary recurrent miscarriage, the heterogeneity of this population is potentially reduced. After a positive urinary human chorionic gonadotropin (hCG) a pregnancy loss occurs or a serum β -hCG raised level before histological verification or ultrasound is called as a 'biochemical loss'. Generally it occurs 6 weeks before gestation. Clinical miscarriage term is used when histological evidence or examination of ultrasound has confirmed that an intrauterine pregnancy has existed.

Endometriosis: Endometriosis is an estrogen-dependent chronic inflammatory condition that affects women in their reproductive period and is associated with women infertility and pelvic pain. A chronic condition Endometriosis is characterized by the endometrial tissue growth leaving the uterine cavity, generally in the pelvic cavity, including the endometrial deposits and ovaries, in ovary known as endometriomas. Tubal damage can be due to endometriosis, symptoms also include painful periods, pelvic pain, and during and after intercourse the pain. Endometriosis patients mainly complain of dysmenorrhea, dyspareunia, pelvic pain. The symptoms can affect the patient's mental, social, physical, general, well-being.

Uterine or Cervical with the Fallopian Tubes Causes: Sperm-egg binding, sites are fallopian tubes and normal functioning of them serves natural conception prerequisite. Fallopian tubes obstruction is a common disease and may be main cause of infertility. Inflammation generally causes the obstruction of fallopian tubes and reproductive system infection, generally in infection sources items.^[22] There are several congenital or acquired

uterine disorders, which cause infertility in the females; the acquired uterine abnormalities that are responsible for female infertility include polyps, some types of fibromas, adenomyosis, and some endometrial disorders such as intrauterine adhesions.^[23]

Hormonal Causes of Female Infertility

Ovarian Insufficiency: The average age of menopause is 51, with some women having their last period in their forties and others later in their fifties. A cessation of ovulation prior to the age of 40 is rare and is usually referred to as premature ovarian failure. Primary ovarian defect is premature ovarian failure (POF) described as absent menarche (primary amenorrhea) or ovarian follicles premature depletion before 40 years age (secondary amenorrhea). It is a diverse disorder affecting women of <40 years about approximately 1%, of age 20 1:10,000 women and of age 30 1:1,000 women. With absent pubertal development the most severe forms are present and primary amenorrhea (ovarian dysgenesis 50% cases), whereas post-pubertal onset forms are defined by the menstrual cycles disappearance (secondary amenorrhea) premature follicular depletion associated. [25]

Luteal Phase Deficiency: The luteal phase defect is, by definition, a corpus luteum defective in progesterone production. As indicated by histochemical evidence, in the corpus luteum, estrogen is produced by the luteinized theca cells. The estrogen-producing function of the corpus luteum seems to be unimpaired in this disorder. The clinical manifestations of the defect include infertility and repeated first- trimester abortion.^[26] Hormonal imbalances have been associated with female infertility. The increased or decreased levels of FSH, LH and prolactin hormones may cause infertility.^[27]

Polycystic Ovarian Syndrome: Polycystic Ovarian Syndrome (PCOS) is the most common endocrine disorder affecting women of reproductive age and is closely associated with insulin resistance, metabolic syndrome and future risk of developing diabetes and cardiovascular disease. Anovulatory infertility's PCOS is the major cause, but ovulation failure leaving other factors contributes to impairment in reproductively. Polycystic ovaries generally occur in ovulatory women having unexplained or tubal infertility (with around 50% prevalence) than in the general, (20%) population which is age-matched. This phenomenon considers that circulating hormones abnormalities (such as LH and serum testosterone elevated concentration) which is present in ovulatory women having polycystic ovaries are connected to social group distinctions compromised maturation.

Thyroid Disorders: Both hyper and hypothyroidism may result in menstrual disturbances. The most common manifestation is simple oligomenorrhea (decreased menstrual flow). Anovulatory cycles are very common. Increased bleeding may occur, but is rare in hyperthyroidism. The thyroid is an important endocrine gland and its dysfunctions interfere with numerous aspects of reproduction and pregnancy. In women of reproductive age, thyroid dysfunction can lead to a variety of gynecological disorders ranging from menstrual irregularities to infertility arising from many different pathophysiological mechanisms. Hypothyroidism is a leading cause of difficulty in achieving and maintaining pregnancy. Low thyroid function has a negative impact on reproductive health and is more common than most women realize. It is also linked with menstrual problems and a lack of ovulation in some cases. It can occur spontaneously, develop during or after pregnancy, or after treatment for hyperthyroidism.

External Causes of Female Infertility

Contraception: There is extensive use of contraceptives, generally by young individuals whose years of reproduction commonly lie in front of them. Use of various types of contraceptive varies with marital status reproductive history, race, and age. The return of fertility for women who discontinue oral contraceptives takes longer as compared with women who discontinue other methods of contraception. For contraception there is no perfect method and each method is having advantages and disadvantages balance. Ideal contraceptive characteristic method are: highly cheap; independent of intercourse effective; no side effects or risks; and no regular action is required on the users part; and acceptable to all cultures and religions and having non-contraceptive benefits. [19]

Sterilization: For reversal of contraceptive sterilization in women, in determining whether fertility can be restored, several factors are important: length of tube remaining, tubal site, the surgical method initially used, and surgical skill in restoration. Some form of periodic abstinence is used, suppositories, douche, withdrawal, foam, were also used by women in small percentages.^[40] Female sterilization is a permanent procedure to prevent pregnancy. It works by blocking the fallopian tubes. When women choose have not children.^[29]

Abortion: Abortion means the termination of pregnancy before the fetus reaches viability. Abortion is frequently stated that a high proportion of women who have an induced abortion by dilatation and curettage are subsequently infertile. [29] Individuals without the requisite skills every year performs about 19–20 million abortions or in below minimum

medical standard environments, or both. In developing countries nearly all unsafe abortions (97%) occur.^[22]

Drugs and Environment: Currently, reproductive risks no reliable estimates can be made from environmental factors. Before now, less attention was paid to drug- induced and environmental infertility and sub infertility. However, four health hazards dibromochloropropane, ethylene oxide, ionizing radiation, lead are regulated in part because reproductive system effects. Environmental hazards in general include chemical agents; physical agents such as temperature, altitude, and radiation; and alcohol consumption, smoking, like personal hobbits, use of drugs (both nontherapeutic and therapeutic), and patterns of eating. Drugs affect the fertility. [24]

Diagnosis of Infertility: The most common examination for diagnosis of infertility is [26]:

Couple's history, physical exam, semen analysis, basal body temperature charts and menstrual cycle mapping, hormone assays cervical mucus evaluation, post- immunologic evaluation, endometrial biopsy, coital test hysterosalpingogram, laparoscopy, hysteroscopy, and Hamster-egg penetration assay.

Treatment of Female Infertility: The treatment of infertility can be done with surgery, medicine, assisted reproductive technology, artificial insemination. Many times these treatments are combined. Mostly infertility is treated with surgery or drugs. Specific treatments for infertility are recommended by doctors based on results of test, how long for the pregnancy the couple is trying, both the man and woman age, the partners overall health, and partners preference. [30]

CONCLUSION

This systematic review highlights the existing lack of, and need for, a consensus definition of infertility. It reinforces the case for a reliable and valid survey instrument for measuring infertility and emphasizes the impact of factors, such as age group of women sampled and their cohabitation/marital status, on prevalence rates. While a demographic definition may have its uses in the context of identifying fertility trends in a population, it is not fit for purpose in a clinical setting. In order to identify couples who would benefit from fertility investigations and treatment, we suggest that the definition of infertility should be based on an estimated chance of spontaneous conception that is driven by duration of trying for a pregnancy and the female partner's age.

We are committed to the ethics of scientific research

Conflict of Interest: Nil.

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REFERENCES

- 1. Abdul-Qahar ZH, Omran ZS, Al-Alak MM. Assessment of Thyroid Function in Infertile Iraqi Females. Assessment, 2016; 25.
- 2. Al-Fahham AA. Correlation between oxidative stress and thyroid hormone levels in infertile women. International Journal of Scientific and Research Publications, Dec. 2015: 128.
- 3. Gorthi S, Balen AH, Tang T. Current issues in ovulation induction. The Obstetrician & Gynaecologist, Jul. 1, 2012; 14(3): 188-96.
- 4. Silva CA, Bonfa E, ØStensen M. Maintenance of fertility in patients with rheumatic diseases needing antiinflammatory and immunosuppressive drugs. Arthritis care & research, Dec. 2010; 62(12): 1682-90.
- 5. Brugh 3rd VM, Matschke HM, Lipshultz LI. Male factor infertility. Endocrinology and metabolism clinics of North America, Sep. 2003; 32(3): 689.
- 6. Eraky EM, El-Nasr EM. Risk Factors of Secondary Infertility among Women Attending Outpatient Clinic at Cairo University Hospital; Suggested Guideline.
- 7. No GT. The investigation and treatment of couples with recurrent first-trimester and second-trimester miscarriage, April 2011.
- 8. Mital P, Shefali J, Dinesh J, Bhavesh P, Nandini P, Priti V, Pragya R. Prevalence of different factors responsible for infertility. Research Journal of Recent Sciences _ISSN. 2012; 2277: 2502.
- 9. Sami N, Ali TS. Psycho-social consequences of secondary infertility in Karachi. JPMA. The Journal of the Pakistan Medical Association, 2006; 56(1): 19.
- 10. Gurunath S, Pandian Z, Anderson RA, Bhattacharya S. Defining infertility—a systematic review of prevalence studies. Human reproduction update, Apr. 14, 2011; 17(5): 575-88.
- 11. Jawad AH, Ibrahim SA, Jawad ZH, Hadi DM. A Study of the Correlation of Some Sex Hormone with Obesity in Women with Secondary Infertility. Journal of Al-Nahrain University-Science, 2015; 18(2): 44-9.
- 12. Andrology Australia. 2014. MALE INFERTILITY. First published in May 2004 by Andrology Australia.

- 13. Nazemian, Z. Infertility and Women's Age (Doctoral dissertation). The University of Toronto, 2010; 1-110.
- 14. Quaas A, Dokras A. Diagnosis and treatment of unexplained infertility. Reviews in Obstetrics and Gynecology, 2008; 1(2): 69.
- 15. Matsubayashi, H., Hosaka, T., Izumi, S.I., Suzuki, T. and Makino, T., The emotional distress of infertile women in Japan. *Human Reproduction*, 2001; *16*(5): 966-969.
- 16. Mordan S, Ghorbani R. Dexamethasone in unexplained infertility. Saudi medical journal, Feb. 19, 2009; 1034-6.
- 17. Ricci E, Viganò P, Cipriani S, Chiaffarino F, Bianchi S, Rebonato G, Parazzini F. Physical activity and endometriosis risk in women with infertility or pain: Systematic review and meta- analysis. Medicine, Oct. 2016; (40).
- 18. Murto, T. Folate, Hormones, and Infertility: Different factors affecting IVF pregnancy outcome (Doctoral dissertation, Acta Universitatis Upsaliensis), 2014.
- 19. United States. Congress. Office of Technology Assessment. Infertility, Medical and Social Choices. Congress of the US, Office of Technology Assessment.
- 20. ESHRE Capri Workshop Group. Physiopathological determinants of human infertility. Human Reproduction Update, Sep. 1, 2002; 8(5): 435-47.
- 21. Practice Committee of the American Society for Reproductive Medicine. Multiple gestations associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion. Fertility and Sterility, Apr. 1, 2012; 97(4): 825-34.
- 22. Strathy JH, Molgaard CA, Coulam CB, Melton LJ. Endometriosis and infertility: a laparoscopic study of endometriosis among fertile and infertile women. Fertility and sterility, Dec. 1, 1982; 38(6): 667-72.
- 23. Liu X, Cui H, Chen W, Xuan X, Guo X, Hu Y. Diagnosis and treatment of fallopian tube obstruction: a literature review. Int J Clin Exp Med., Jan. 1, 2017; 10(12): 15950-9.
- 24. Metcalfe NB, Alonso-Alvarez C. Oxidative stress as a life-history constraint: the role of reactive oxygen species in shaping phenotypes from conception to death. Functional Ecology, Oct. 1, 2010; 24(5): 984-96.
- 25. H Sekhon L, Gupta S, Kim Y, Agarwal A. Female infertility and antioxidants. Current Women's Health Reviews, May. 1, 2010; 6(2): 84-95.
- 26. ZRT Laboratory, LLC. FERTILITY PROFILE from American Society for Reproductive Medicine. *Journal of reproduction & infertility*, Jul. 2016; 12(3): 201.
- 27. Miller CS. Possible models for multiple chemical sensitivity: conceptual issues and role

- of the limbic system. Toxicology and Industrial Health, Jul. 1992; 8(4): 181-202.
- 28. Poppe K, Glinoer D, Tournaye H, Devroey P, Schiettecatte J, Haentjens P, Velkeniers B. Thyroid autoimmunity and female infertility. Verhandelingen-Koninklijke Academie voor Geneeskunde van Belgie, 2006; 68(5-6): 357-77.
- 29. Petchesky RP. Abortion and womans choice: the state sexuality and reproductive freedom.
- 30. Delvaux T, Nöstlinger C. Reproductive choice for women and men living with HIV: contraception, abortion and fertility. Reproductive health matters, Jan. 1, 2007; 15(29): 46-66.