Relation of recurrent miscarriages with some of fertility hormones

¹Dr. Rehab Jasim Mohammed, ²Asst.Lect. Aseel Ehsan Mahmoud

Department of chemistry, College of Education for Pure Science, University of Karbala, Karbala, Iraq Health and Medical Technical College, Al-Zahraa University for Women, Karbala 56001, Iraq, aseel.ehsan@alzahraa.edu.iq

Abstract: The loss of a pregnancy before the fetus is viable is referred to as a miscarriage. Depending on the data source, this might be considered as being 20 or 24 weeks pregnant. Threatened miscarriage occurs during the first 20 weeks of pregnancy, with pain or without pain. A miscarriage occurs in 10% to 15% of all clinically confirmed pregnancies. Recurrent miscarriages, typically defined as three or more spontaneous miscarriages, affect 1% to 2% of couples. There may never be a cure for recurrent miscarriage for many women and their partners. Pregnancies may now be identified sooner, even if they are going to end in an early miscarriage, thanks to advancements in pregnancy testing and ultrasound technology. These may not have been noticed in the past. Consequently, more women may report losing an early pregnancy. Both couples may experience severe emotional grief if a miscarriage occurs. Initial emotional numbness and denial, anxiety, shock, grief, emptiness, rage, inadequacy, blame, and envy, melancholy, sleep trouble, social isolation, hostility, and marital conflict have all been documented as emotional responses to pregnancy losses.

Keyword: Recurrent miscarriages, Fertility hormones.

Introduction: Recurrent miscarriages are most commonly caused by hormonal imbalances. According to specialists, (infertility and miscarriage) are two examples of reproductive failure that share many of the same causes. The disorders that are connected to both of infertility and miscarriage include PCOS disease, uterine septum, and uterine fibroid, to name just a few. Recurrent miscarriage sufferers are more likely to have infertility ⁽¹⁾. When a female reaches reproductive age, her ovaries begin to secrete the gonadotropins follicle-stimulating hormone and luteinizing hormone, as well as the hormones estrogen and progesterone. These hormones' peak and fall are what control how much are produced and how much are broken down. The uterus' inner layer loses during the menstrual cycle, and the uterus also grows and develops when an egg is laid. This process makes it feasible to get pregnant ⁽²⁾. From the point of view of biology, women should have children when they are between the ages of eighteen and thirty ⁽³⁾. After the age of 30, female fertility starts to decline with fewer pregnancies each cycle and eventual sterility ⁽⁴⁾.

Symptoms of Recurrent Miscarriages: Recurrent miscarriage has different signs and symptoms. Miscarriage may be asymptomatic or bring back the normal signs and symptoms of pregnancy. Threatening or not, miscarriage is associated with pelvic and abdominal pain, vaginal bleeding, fever, vaginal or cervical secretions, tachycardia, and hypotension. Try to estimate the amount of bleeding because heavier than usual menstruation may indicate a miscarriage. The first day of the most recent menstrual cycle and the results of any prior ultrasounds should be used to determine the gestational age and location of the pregnancy. Signs and symptoms of a miscarriage may be seen in patients who experience heavy bleeding. The final step in identifying the most likely reason for the loss is pelvic scan

Recurrent miscarriage risk factor: Recurrent miscarriages are difficult to diagnose and are an extremely stressful that for both spouses and specialists. Pregnancy losses are common, and they happen more commonly in the first than the second trimester. Several variables, such as advanced parent age, smoking, and alcohol use, might result in early pregnancy loss. Other causes were genetic and immunological changes. Genetic changes are sometimes referred to as chromosomal abnormalities in both the afflicted couple and the embryo. The spouse has a genetic test to rule out chromosomal translocations, while the mother is tested for thyroid issues (endocrine), antiphospholipid antibodies (autoimmune), endometrial

ISSN NO: 2771-8840

cancer, and uterine cancer⁽⁶⁾. The likelihood of embryonic chromosomal abnormalities, which are linked to women's age, increases in women who wait until their late 30s or early 40s to become pregnant. Even while maternal age increases the chance of recurrent miscarriage, other factors are more important. With each loss, there is a decreasing probability that the early pregnancy loss was brought on by severe chromosomal abnormalities. The rate of spontaneous abortion rises by two to three times in older women who try to conceive, which also increases the chance of genetic abnormalities ⁽⁷⁾. Obesity increases the chance of miscarriage. The pregnancy and abortion rates are significantly impacted by obesity before conception⁽⁸⁾. Women who have recurrent miscarriage confront more social and familial difficulties than men do since it is often seen as an illness of the female body. Recurrent miscarriages can result in emotional distress, threats to the family, remarriage, separation, and divorce⁽⁹⁾.

LH hormone: LH, a hormone produced by the pituitary gland, activates the corpus luteum and results in ovulation. The ovary secretes progesterone and estrogen throughout the second part of the menstrual cycle⁽¹⁰⁾. Important gonadotropin in the regulation of the reproductive system is luteinizing hormone (LH). By encouraging the production of sex steroids, LH promotes progesterone release during the luteal phase and initiates oocyte maturation⁽¹¹⁾. The hormones LH and FSH, which are normally released on days eight and twelve of a cycle before to ovulation, drive an increase in estradiol (E2) production from the ovaries. Around day 14, progesterone levels increase, whereas estrogen levels rise following ovulation around day 18. the use of hormonal contraception by women. Early in the cycle, progesterone blocks FSH release, delaying the onset of menopause. E2 normally rises, which triggers an increase in LH and prevents ovulation⁽¹²⁾. Pituitary failure may be suggested by disorders including menopause, ovary removal, and premature ovarian syndrome, however rising LH and FSH levels as well as declining gonadal steroid levels may indicate gonadal failure

FSH hormone: is a type of gonadotropin hormone that is produced by the(basophilic cells) of the anterior pituitary gland and is essential for the production of gonadal hormones and the control of the reproductive system⁽¹⁴⁾. The ovarian follicle-stimulating hormone (FSH), where oocytes or egg cells mature ,the ovaries generate estradiol, promotes the growth and development of the ovarian follicles. Based on FSH, maximum FSH is the most accurate measure of ovarian reserve(15). FSH promotes the development of follicular cells, the aromatization of androgens to estrogens, and the expression of LH receptors. LH is also important for follicular development, especially in the latter stages ⁽¹⁶⁾. FSH flows via the circulation to the gonads, where it activates spermatogenesis in males and follicular development in females. The physiology of the reproductive systems of both sexes is clearly impacted by FSH⁽¹⁷⁾. FSH is necessary for development and maturation in females as well as the generation of estradiol. For instance, mono-ovulatory humans. A single kind of egg is produced as a result of FSH's promotion of follicle stimulation, development, selection, and maturity. One developed oocyte is present during the ovulation time⁽¹⁸⁾. As a result, the FSH levels fluctuate. Ovulation happens when the follicular wall bursts and the cumulus-oocyte complex is released ⁽¹⁹⁾.

Estrogen hormone: a steroid hormone that promotes feminine sexual characteristics and is connected to female reproductive systems. In order to have different impacts on the body as a whole, estrogen regulates a range of physiological and pathological processes in both men and women's reproductive system, the immune, endocrine, neurological, skeletal, and cardiovascular systems. As a result, it has been associated with a number of problems, such as polycystic ovarian syndrome, endometriosis, and different malignancies that cause infertility (20). Estrogen's primary effects include promoting female secondary sex traits and preparing the uterus for ovulation and pregnancy. It also possesses endometrial and breast growth-promoting characteristics in addition to vascular advantages including enhancing blood flow and creating new blood vessels(21). Although estrogens are typically considered of as feminine hormones, new research shows that they are crucial for male reproduction(22). In addition, males from birth through adulthood have estrogen receptors found in them (23). High amounts of estrogen stimulate the pituitary, which then produces unexpectedly high quantities of LH and FSH. The LH surge causes the egg to go through its last stages of maturation, which results in ovulation (24).

ISSN NO: 2771-8840

Prolactin hormone: The PRL gene in humans produces the protein known as PRL ⁽²⁵⁾. The pituitary, myometrium, breast, lymphocytes, leucocytes, and prostate in humans all make prolactin ⁽²⁶⁾. During pregnancy, high blood levels of prolactin cause the mammary glands to enlarge and prepare to make milk. The process through which the mammary glands make milk is known as lactation. When a suckling trigger is present, milk production begins when progesterone levels begin to decline toward the end of the pregnancy. Additionally, factors including age, gender, menstrual cycle stage, and pregnancy affect prolactin levels differently. It is necessary to consider the test's circumstances (such as the assay, the patient's condition, etc.) before a prolactin number may be properly interpreted ⁽²⁷⁾. minimal production of gonadotropins, according to specialists, excessive levels of circulating prolactin that interfere with gonadotropin activity at the ovarian level and that affect positive feedback effects at the ovarian level are the two main causes of hypogonadism in women with hyperprolactinemia. Because of the hypothalamus and pituitary's and gonadotropins FSH and LH levels, infertility is caused ⁽²⁸⁾. The most prevalent indicators and symptoms of a persistent rise in prolactin levels in the blood include breast illness, sexual dysfunction, reproductive disorder, anomalies linked to behavioral and emotional changes, immunologic issues, and depression ⁽²⁹⁾.

Progesterone hormone: A kind of steroid hormone is progesterone. The health of the pregnancy depends on this sexual hormone. Progesterone, which is produced by cells of the luteal phase in an unborn woman, is the chemical signal that the ovaries use to transform the endometrial lining of the uterus into a highly secretory tissue that can sustain the fertilized egg (30). During pregnancy, the placenta, adrenal glands, and ovaries all create progesterone. Additionally, Adipose tissue is where it is kept. Women's pre-ovulatory progesterone levels are low during this time of the menstrual cycle. They increase during ovulation and hold their high levels throughout the luteal phase. Progesterone levels typically range from less than 2ng/ml before ovulation to more than 5ng/ml after ovulation seven days before menstruation (31). In ovulation, the egg is expelled from the follicle while being encircled by cumulus cells. The luteal phase, which typically lasts 14 days after ovulation with minimal variation, is caused by the ovary's surviving follicular cells becoming luteinized and producing progesterone. LH is still being produced, which ensures a steady supply of progesterone that helps women get ready for pregnancy and maintains the health of their endometriums. Progesterone are highest during the luteal phase of the cycle. Additionally, the high levels of progesterone prevent any further ovarian follicular expansion during that cycle by limiting the release of FSH and LH⁽³²⁾. Although it helps maintain the endometrium and hence the pregnancy, progesterone is essential before and throughout pregnancy⁽³³⁾.

References

- 1. Cocksedge, K. A., Li, T. C., Saravelos, S. H., & Metwally, M. (2008). A reappraisal of the role of polycystic ovary syndrome in recurrent miscarriage. Reproductive biomedicine online, 17(1), 151-160. 2. Ehterami, A., Khastar, H., Soleimannejad, M., Salehi, M., Nazarnezhad, S., Majidi Ghatar, J., ... & Shariatifar, N. (2021). Bone regeneration in rat using polycaprolactone/gelatin/epinephrine scaffold. Drug Development and Industrial Pharmacy, 47(12), 1915-1923.
- 3. Habbema, J. D. F., Eijkemans, M. J., Leridon, H., & te Velde, E. R. (2015). Realizing a desired family size: when should couples start? Human Reproduction, 30(9), 2215-2221. 4. Garcia, D., Brazal, S., Rodriguez, A., Prat, A., & Vassena, R. (2018). Knowledge of age-related fertility decline in women: A systematic review. European Journal of Obstetrics & Gynecology and Reproductive Biology, 230, 109-118
- 5. Wu, H. L., Marwah, S., Wang, P., Wang, Q. M., & Chen, X. W. (2017). Misoprostol for medical treatment of missed abortion: a systematic review and network meta-analysis. Scientific reports, 7(1), 1-9.
- 6. Dutta, UR, Rajitha, P., Pidugu, VK, & Dalal, AB (2011). Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in the southern region of India: report and review. Journal of assisted reproduction and genetics, 28 (2), 145-149.
- 7. Bulletti, C., Flamigni, C., & Giacomucci, E. (1996). Reproductive failure due to spontaneous abortion and recurrent miscarriage. Human Reproduction Update, 2(2), 118-136.

ISSN NO: 2771-8840

- 8. Metwally, M., Li, T. C., & Ledger, W. L. (2007). The impact of obesity on female reproductive function. Obesity Reviews, 8(6), 515-523.
- 9. Ibrahim, F. M., Al Awar, S. A. A. R., Nayeri, N. D., Al-Jefout, M., Ranjbar, F., & Moghadam, Z. B. (2018). Experiences of Recurrent Pregnancy Loss Through the Perspective of United Arab Emirates Women: A Qualitative Study. International Journal of Women's Health and Reproduction Sciences, 7, 306-312.
- 10. Ortiz-Flores, A. E., Luque-Ramírez, M., & Escobar-Morreale, H. F. (2019). Polycystic ovary syndrome in adult women. Medicina Clínica (English Edition), 152(11), 450-457.
- 11. Baskind, N. E., & Balen, A. H. (2016). Hypothalamic-pituitary, ovarian and adrenal contributions to polycystic ovary syndrome. Best Practice & Research Clinical Obstetrics & Gynaecology, 37, 80-97.
- 12. Hidalgo-Lopez, E., Mueller, K., Harris, T., Aichhorn, M., Sacher, J., & Pletzer, B. (2020). Human menstrual cycle variation in subcortical functional brain connectivity: a multimodal analysis approach. Brain Structure and Function, 225(2), 591-605.
- 13. Abdelmgeed, A., & Ali, T. M. (2018). Sex Hormone Abnormalities in Epileptic Saudi Women. AUMJ, 5(1), 27-34.
- 14. Coss, D., Jacobs, S. B., Bender, C. E., & Mellon, P. L. (2004). A novel AP-1 site is critical for maximal induction of the follicle-stimulating hormone β gene by gonadotropin-releasing hormone. Journal of Biological Chemistry, 279(1), 152-162.
- 15. Gingold, JA, Lee, JA, Whitehouse, MC, Rodriguez-Purata, J., Sandler, B., Grunfeld, L., ... & Copperman, AB (2015). Maximum basal FSH predicts reproductive outcomes better than cycle specific basal FSH levels: waiting for a "better" month conveys limited retrieval benefits.
- 16. Chateau, D., Geiger, JM, Samama, B., & Boehm, N. (1996). Vaginal keratinization during the estrous cycle in rats: a model for evaluating retinoid activity. Skin Pharmacology and Physiology , 9 (1), 9-16 .
- 17. Rastrelli, G., Corona, G., Mannucci, E., & Maggi, M. (2014). Factors affecting spermatogenesis upon gonadotropin-replacement therapy: a meta-analytic study. Andrology , 2 (6), 794-808.
- 18. Andersen, C. Y., Westergaard, L. G., & van Wely, M. (2004). FSH isoform composition of commercial gonadotrophin preparations: a neglected aspect?. Reproductive biomedicine online, 9(2), 231-236.
- 19. Ramasamy, R., Bakırcıoğlu, ME, Cengiz, C., Karaca, E., Scovell, J., Jhangiani, S. N., ... & Lamb, DJ (2015). Whole-exome sequencing identifies novel homozygous mutation in NPAS2 in family with nonobstructive azoospermia. Fertility and sterility , 104 (2), 286-291.
- 20. Callard, G. V., Tarrant, A. M., Novillo, A., Yacci, P., Ciaccia, L., Vajda, S., ... & Cotter, K. A. (2011). Evolutionary origins of the estrogen signaling system: insights from amphioxus. The Journal of steroid biochemistry and molecular biology, 127(3-5), 176-188.
- 21. Coad, J., Pedley, K., & Dunstall, M. (2019). Anatomy and physiology for midwives e-book. Elsevier Health Sciences.
- 22. Hess, R. A. (2003). Estrogen in the adult male reproductive tract: a review. Reproductive Biology and Endocrinology, 1(1), 1-14.
- 23. Bondesson, M., Hao, R., Lin, C. Y., Williams, C., & Gustafsson, J. Å. (2015). Estrogen receptor signaling during vertebrate development. Biochimica et Biophysica Acta (BBA)-Gene Regulatory Mechanisms, 1849(2), 142-151.

ISSN NO: 2771-8840

- 24. Hammond, K. R. (2002). Meniru GI Cambridge guide to infertility management and assisted reproduction. Cambridge, United Kingdom: Cambridge University Press, 2001: 1–276. \$47.95. Fertility and Sterility, 78(2), 445.
- 25. Olooto, W. E., Adeleye, A. O., Amballi, A. A., & Mosuro, A. O. (2012). Pattern of reproductive hormones (follicle stimulating hormone, luteinizing hormone, estradiol, progesterone, and prolactin) levels in infertile women in Sagamu South Western Nigeria. Der Pharmacia Lettre, 4(2), 549-553.
- 26. Gerlo, S., Davis, J. R., Mager, D. L., & Kooijman, R. (2006). Prolactin in man: a tale of two promoters. Bioessays, 28(10), 1051-1055.
- 27. Mortini, P., Nocera, G., Roncelli, F., Losa, M., Formenti, A. M., & Giustina, A. (2020). The optimal numerosity of the referral population of pituitary tumors centers of excellence (PTCOE): A surgical perspective. Reviews in Endocrine and Metabolic Disorders, 21(4), 527-536.
- 28. Isong, I., Okhormhe, Z., Eze-Bassey, I., Okpokam, D., & Usoro, C. (2016). Levels of prolactin, progesterone, estradiol, luteinizing hormone and follicle stimulating hormone in infertile women in Calabar, Nigeria. International Journal of Reproduction, Contraception Obstetrics and Gynecology, 5(3), 804.
- 29. Marrag, I., Hajji, K., Braham, M. Y., Dhifallah, M., & Nasr, M. (2015). Antipsychotics and hyperprolactinemia: prevalence and risk factors. Ann Psychiatry Ment Health, 3(6), 1047.
- 30. Wilcox, A. J. (2010). Fertility and Pregnancy: An Epidemiologic Perspective. Oxford: Oxford University Press.
- 31. EGBAGBA, A.O. (2016). ASSESSMENT OF SERUM, FOLLICLE STIMULATING HORMONE, LUTEINIZING HORMONE, OESTRADIOL, PROGESTERONE, PROLACTIN, AND URINARY FOLLICLE STIMULATING HORMONE AND LUTEINIZING HORMONE IN WOMEN PRESENTING IN WITH BENFERTILITY. Faculty of Pathology.
- 32. Bickerstaff, H., & C. Kenny, L. (2017). Gynaecology by Ten Teachers . CRC Press. 33. Spencer, T. E., Johnson, G. A., Burghardt, R. C., & Bazer, F. W. (2004). Progesterone and placental hormone actions on the uterus: insights from domestic animals. Biology of reproduction, 71(1), 2-10.

ISSN NO: 2771-8840