Section: Anatomy

Research

EFFECT OF PSYCHOLOGICAL STRESS ON OVARIAN RESERVE IN YOUNG AGED WOMEN

Deepali Vidhale[1], Shabina Anjum[2], Geetanjali Yadgire[3], Anupama Sawal[4], A.D. Bijwe[3], Minoti Pokale[4], Rupa Chhaparwal[5]

[1]Associate Professor, Department of Anatomy, Dr. Panjabrao Deshmukh Alias Memorial Medical College (PDMMC), Amravati, Maharashtra University of Health Sciences (MUHS), Nashik, Maharashtra, India.
[2]Assistant Professor, Department of Anatomy, College of Medicine, Talibah University, Medina, Saudi Arabia.
[3]Assistant Professor, Department of Anatomy, Dr. Panjabrao Deshmukh Alias Memorial Medical College (PDMMC), Amravati, Maharashtra University of Health Sciences (MUHS), Nashik, Maharashtra, India.
[4]Associate Professor, Department of Anatomy, Jawaharlal Nehru Medical College, Sawangi (Meghe), Datta Meghe Institute of Medical Sciences (Deemed University), Nagpur, Maharashtra, India
[5]Professor, Department of Anatomy, SAMC & PGI, Indore, Madhya Pradesh, India

Received : 19/10/2022
Received in revised form : 27/11/2022
Accepted : 11/12/2022

Keywords:
Infecundity, Anxiety, Work pressure, Barrenness, AMH.

Corresponding Author:
Dr. Shabina Anjum,
Email: anjum.shabina37@gmail.com
ORCID: 0000-0003-2078-0537

DOI: 10.47009/jamp.2023.5.1.6

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (1); 17-21

Abstract

Background: To study the effect of psychological stress on ovarian reserve in young aged women. **Materials and Methods:** The study was decided to be conducted on the population from various fertility centres in Amravati District. There were 100 women aged between 18-30 who took part in the study. Patients from Amravati city itself make up half of the study population, while patients from rural regions near Amravati make up the other half. Patients who attended hospitals for fertility-related difficulties were chosen as participants. They were given a questionnaire to complete and counseled about their everyday lives and the elements that cause stress. They were requested to have serum blood cortisol levels, FSH levels, and AMH levels checked on Day 2 of menses, and their answers were noted on the questionnaire. The information gathered was then examined. The patient's prior permission and agreement were obtained with perfect mutual understanding. They were advised by the doctors to maintain a healthy diet and to practice yoga, exercise, and meditation practices in order to reduce their stress levels and after the intervention, we have again asked them to check their hormonal levels in order to interpret that the reduction in stress levels cause some significant changes or not. **Result:** The stress levels of young patients. Levels of serum cortisol in the blood of individuals with a low ovarian reserve. The levels of AMH and FSH in patients with a weak ovarian reserve. High cortisol levels in patients with low ovarian reserve. **Conclusion:** Younger women's AFC was higher and all women's AFC declined more when under psychological stress, arguing that higher levels of stress may improve reproductive readiness in the short term at the expense of hastening the ageing of the reproductive system in the long run. However, because the current study is cross-sectional, the results are just preliminary.

INTRODUCTION

Infertility is identified as critical among almost all cultures and nations, and it affects 10% and 15% of couples of child-bearing age. Due to various factors such as delay of childbirth in women, the development of newer and more successful treatments for infertility treatment, and improved knowledge of available services, the number of couples seeking infertility treatment has radically grown in recent years.[1] This increased use of fertility treatment has put up recognition and created a search into the mental effects of infertility.[2] The relationship between psychiatric illness and infertility has been studied. Studies have also examined the psychological impact of infertility, as well as the long-term effects of invasive infertility therapies on mood and well-being.[3] There is a scarcity of information on successful psychiatric therapies for this population, however, there is some proof to substantiate the use of cognitive methods.[4] Parenthood is one of the most significant

ISSN (O): 2687-5365; ISSN (P): 2753-6556

adjustments in adulthood for both men and women. The tension of being unable to fulfill a dream of having our own child has been linked to emotional sequelae like rage, melancholy, consternation, infecundity, barrenness, unproductiveness, and social isolation. In the context of infertility, couples endure stigma, a sense of loss, and diminished self-esteem. In general, women in infertile marriages experience more distress than their male partners however, when infertility is linked to a male cause, men's retaliation roughly resembles the severity of women's retaliation. Both men and women feel a loss of identity and have strong sentiments of defectiveness and incapacity.[5] Psychological stress caused by bad life events has both undeviating and unintended impacts on the female reproductive system. Negative life experiences might cause the production of cortisol (a stress hormone), which hinders estradiol manufacture from follicular cells, resulting in a decrease in the quality and amount of aspirated oocytes.[6] This can have an inverse impact on progenitive health by altering lifestyle behaviors such as liquor intake, smoking habits, and so on, which leads to the emergence of reactive oxygen species (ROS). It has been observed that alcohol intake and cigarette smoking diminish fertility, presumably owing to an increase in ROS levels, which promotes oxidative stress (OS).[7] Many studies concluded that alcohol intake and smoke intake have reduced fertility because of a rise in reactive oxygen species which leads to an increase in oxidative stress.[8]

Alcohol metabolism includes the synthesis of nicotinamide adenine dinucleotide (NADH). NADH causes the conversion of xanthine dehydrogenase into its oxidase form, which releases superoxide anions and so ROS.[9] Nuptials and mental well-being are often explained by marital assets—communal social, and psychical—as well as relationship steadiness or the absence of stress from breakups.[10] Getting married to a person with hardly any mental health issues may act as a key role in this.

These explanations are pertinent to the psychological well-being of young adults who are into a nuptial to diversified degrees. There are various possible theories for why marriage may benefit or harm young people’s mental imbalance.[10]

Connection steadiness: Marriage is frequently conducted by a sense of bond permanency, and although the moderately exceeded divorce rate in the United State, nuptials are considerably more expediential to continue than other types of partnerships, such as intermarriage.[11] Female partners suffer greatly as a result of infertility in terms of their well-being, conviction, satisfaction, assertiveness, connection, and religious belief, and it is becoming A communal, profitable, psychical, and health burden in emerging nations.[12] Because lack of intimacy may be harmful to one's psychological health, relationship bonding could elucidate the good impacts of nuptial on one's mental well-being. Brown (2000), for example, ascribed cohabitor sadness (as opposed to married persons) to marital instability. Once precariousness was adjudged for in her models, there was no statistically significant difference in depression between married and remarried.[13] Furthermore, single young people who have just broken up have excessive levels of psychical discomfort than those who are in romantic partnerships. Early marriages are, of course, famously turbulent.[10] Their short-term survival, on the other hand, is in some measure high: 77 % of women's young nuptials last for at least 2 years, as do 87 percent of those who started in their early 20s (men’s three-year marital survival rates are 61% for young nuptials and 83 % for nuptials took place in their early twenties). The steadiness in one’s relationship may help delineate the good out-turn of nuptial on young-aged people’s mental well-being, but it would most likely vanquish the negative out-turn.[14]

Stress is typically characterized as a genuine or discerned danger to equipoise that can jeopardize an individual's well-being. To restore homeostasis, organisms engage a complex set of reactions including the endocrinal, neurological, and immune systems, referred to inclusively as stress tension retaliation.[15] The tension feedback prioritizes durability above the least important physical tasks such as development and breeding. The hypothalamic–pituitary–adrenal (HPA) axis, which includes the hypothalamus, pituitary gland, and adrenal glands, controls the body's adaptive response to stress.[16] When the HPA axis is actuated, neurons in the hypothalamic paraventricular nucleus (PVN) release corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP), which invigorates the anterior pituitary to originate and emanate adrenocorticotropic hormone (ACTH). ACTH restores the production and secretion of glucocorticoids, mineralocorticoids, and adrenal androgens, which are generated into the bloodstream from the adrenal cortex. Rising cortisol levels prevent future CRH and ACTH production in a typical endocrine negative feedback loop, allowing the HPA axis to recover to a physiological condition following acute activation.[17] The HPA axis mediates the actions of the hypothalamic–adrenal–gonadal (HPG) axis, which is responsible for the development of the reproductive organs and an organism's reproductive competence, as part of the physiological stress response. The HPG axis regulates the reproductive system by endocrine signaling, which begins with the hypothalamic release of gonadotropin-releasing hormone (GnRH). GnRH induces pituitary gonadotroph cells to synthesize and release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH and LH, in turn, govern oocyte maturity, fertilization, and adrenocortical synthesis in the ovary. Activins, inhibins, and ovarian-produced steroid hormones (estradiol and progesterone) provide feedback to

ISSN (O): 2687-5365; ISSN (P): 2753-6556

control gonadotrophin production. Feedback from activins, inhibins, and ovarian-produced steroid hormones (estradiol and progesterone) regulates gonadotropin synthesis.[18]

Tension signalizing reverberates all levels of the HPG axis. For example, high levels of glucocorticoids have inhibitory consequences on the GnRH neurons, the pituitary gonadotrophs, and the gonads.[19]

Effects on female reproductive organs

The phrase "ovarian reserve" refers to the ovary's capability to produce egg cells proficient in fertilization which results in a healthy and successful pregnancy.[20]

Stress-related glucocorticoid levels have been demonstrated to decrease oocyte competency and hence cause poor ovarian reserve. The ovarian life span has a direct impact on female reproductive function. During a female's reproductive life, the ovary is an anabolically active organ that also acts as a germ cell repository. It is made up of around 0.3 million primordial follicles, each of which contains diplotene-arrested oocytes. In most mammalian species, a surge of pituitary gonadotropins causes steroidogenesis, follicular growth, development, maturation, and ovulation.[21]

Corticosterone exposure caused ovarian epithelial cells to apoptosis, resulting in a reduction in growth element levels and the progesterone to estrogen ratio, as well as an increment in FasL in the fluid obtained from follicles, limiting oocyte production perspective. Glucocorticoids' influence on oocytes has also been examined. The examination linked intra-follicular glucocorticoid levels to ovum development and prosperous fertilization in oocytes retrieved through IVF patients.

Recent depression models have hypothesized that major depressive disorder (MDD) may accelerate biological aging by highlighting connections between depression and cellular aging indicators. However, it is unknown whether depression is connected to components of reproductive biology that underpin ovarian aging in particular.[22] Evidence shows that stress and discomfort (particularly anxiety and depressiveness) lead to infertility. Biological reactions to stress may result in higher proportions of hormones produced due to heavy stress or mental imbalance, which affect granulosa cell activity and limit follicular development, eventually leading to a decrease in the number of oocytes accessible for harvest in IVF cycles. Researchers also discovered that mental imbalance had a favorable relationship with the antral follicular count in younger women, but greater stress levels expedited the age-related decline in AFC in all age groups.[23]

Anti-Müllerian hormone (AMH) is a glycoprotein that is released by the granulosa cells of primary and secondary pre as well as tiny antral follicles that are thought to hinder FSH-dependent oocyte recruitment. As a result, it inhibits oocyte recruitment before maturation.[24] According to the available data, serum Anti -Mullerian Hormone is a valid indicator of the ovarian capability to produce eggs (amount and quality of oocytes), function, and reactivity in ovarian stimulant entente.[25]

Cortisol is one of the hormones that are essential for maintaining blood pressure, blood sugar, metabolism, and adapting to infections and stress. Cortisol is a steroid hormone that is secreted from the cortex of the adrenals and then pushed back into the bloodstream, from where it passes through the body.[26] Depending on the cell to interact with, cortisol has numerous out-turns and its receptors may be present in almost every other cell.[26]

Managing blood sugar levels and hence metabolism, functioning as an anti-inflammatory, impacting memory production, controlled salt, and water equilibration, affecting bp, and aiding fetal development are some of the outcomes. Cortisol is also responsible for activating the processes included in delivering babies among animals.[27] Rodents, birds, and reptiles generate a hormone called corticosterone, which is comparable to this hormone.[26]

Cushing's syndrome is a disorder caused by a hefty amount of cortisol emergence over a lengthy duration. This can be caused by a variety of circumstances, including a tumor that generates ACTH (and hence increases cortisol secretion) or the usage of certain ailments. Among the signs and symptoms are:

- quick gaining of weight primarily in the frontal area of the head, chest, and belly, with thin arms and legs as a contrast
- around as wee as pinkish colored face
- osteoporosis
- skin appears purple and bruised
- High bp
- increased thirst and frequency of urination, also mood fluctuations, such as anxiety, sadness, or irritability muscular tenderness with drastic changes in mood, such as stress, depressiveness, or irritation due to sound, light, etc.[28]

Abundant levels of cortisol over a longer period can bring about a lack of sex drive in males and females, as well as irregular, slightly occurring or hypothetical periods in women (amenorrhoea). Any malfunction with the ductless glands might cause too inferior cortisol emergence. The onset of symptoms is frequently leisure. Fatigue, dizziness, emaciation, muscular fragility, and skin discoloration are all possible symptoms. This is a conclusively lethal condition if not served properly.[29]

Whenever any prodrome of either Cushing’s syndrome or Addison’s disease is surmised, an immediate evaluation by a specialist hormone doctor known as an endocrinologist is essential.[30]

MATERIALS AND METHODS

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The study was decided to be conducted on the population from various fertility centres in Amravati District.

There were 100 women aged between 18-30 who took part in the study.

Patients from Amravati city itself make up half of the study population, while patients from rural regions near Amravati make up the other half. Patients who attended hospitals for fertility-related difficulties were chosen as participants. They were given a questionnaire to complete and counseled about their everyday lives and the elements that cause stress. They were requested to have serum blood cortisol levels, FSH levels, and AMH levels checked on Day 2 of menses, and their answers were noted on the questionnaire.

The information gathered was then examined. The patient's prior permission and agreement were obtained with perfect mutual understanding. They were advised by the doctors to maintain a healthy diet and to practice yoga, exercise, and meditation practices in order to reduce their stress levels and after the intervention, we have again asked them to check their hormonal levels in order to interpret that the reduction in stress levels cause some significant changes or not.

Inclusion Criteria

- Women at a young age.
- Woman with a heavy workload.
- Woman having anxiety or stress issues.

Exclusion Criteria

- Woman with no complaints of stress.
- Women with ages more than 33 years.

Findings

When we evaluated our patients, according to their cortisol levels we got to know about their reproductive health. The patients with abnormal serum cortisol levels seem to have abnormal levels of FSH and LH as well as AMH and this directly affects the oocyte production in their body detrimental to their reproductive health. As we observed, some women are unable to produce oocytes even after stimulating their ovaries and those who are hardly able to produce oocytes do not have good quality and are not considered good for embryo production.

RESULTS

Table 1: The hormone levels of the selected population before intervention

No. of patients	Cortisol levels (mcg/dL)	FSH (m IU/ m L)	LH (mIU/m L)	AMH (ng/mL)
08	21-22	9-12	7-10	1-1.5
10	2.5-4.5	12-14.9	10-12	0.15-0.25
12	22-26	14.9-16	2.5-4.8	1-1.2
15	1-5.2	1-1.8	12-13.5	0.9-1
17	23-25	1.98-2.1	5-8.5	1.1-2
18	3-3.5	2.1-2.4	14-16.5	0.5-0.85
20	25-25.5	17-21.3	17-20.1	0.8-1

Table 2: The hormone levels of the selected population after intervention:

No. of patients	Cortisol levels (mcg/d L)	FSH (m IU/m L)	LH (mIU/m L)	AMH (ng/m L)
08	10-15	4-5	3.9-4.8	1.5-1.8
10	8-11	2.8-3.5	2.6-3.7	2-2.5
12	16-19	1.9-4	2- 4.1	2.5-3.3
15	20-24	5.4-7.1	5.7-7.4	3.8-4
17	18-22	3.5-7.8	3.8-7	3-3.55
18	15-17	7-8.9	7.2-9	1.9-2
20	9-13	7.5-9	9-14.5	3.5-3.95

DISCUSSION

Many studies have been published that reveal the reverberation of mental tension on ovarian reserve in young individuals. By measuring FSH and AMH levels, we can learn about the impact of stress on ovarian reserve. This exemplifies that stress has a direct impact on ovarian reserve by affecting FSH and AMH levels. We may learn that serum blood cortisol levels tested in young aged women indicate Addison's disease, and higher levels indicate Cushing's syndrome, both of which are the leading causes of infertility in females, proving that cortisol levels reduce ovarian reserve.

Filip Szkodziak et Al., conducted a systematic review on Psychological Aspects of Infertility in which they accentuated the obstructive consequences of stress, depression, insomnia, anorexia, bulimia, and addictions have all been shown to have a deleterious impact on female or male fertility.

These illnesses alter the tissue and cellular functions of the anterior pituitary and the immune response, all of which can lead to decreased conception. Considering these links, it's unclear how much mental illness influences fertility and how much infertility influences emotional wellbeing. More study is undoubtedly required to understand the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

precise function of psychological illnesses infertility and its impact to infertility.

Moreover, in order to drastically reduce the number of unexplained infertility diagnoses, a complete approach to the care and prognosis of infertility is required, which includes an examination of the mental state of something like the couple wishing a child.

CONCLUSION

AFC among younger women was higher and there was a higher rate of AFC decline overall, according to the findings of the current study, which concludes. This finding offers preliminary support for the proposed model of reproductive ageing, which contends that stress may encourage the allocation of resources toward greater reproductive readiness by increasing the initial recruitment of dormant primordial follicles into the expanding pool of follicles, improving fertility in the short term at the expense of hastening the depletion of the ovarian reserve in the long run.

REFERENCES

1. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reproductive Biology and Endocrinology. 2015;13(1). doi:10.1186/s12958-015-0032-1
2. Rooney KL, Domar AD. The relationship between stress and infertility. Dialogues Clin Neurosci. 2018;20(1). doi:10.31887/dcns.2018.20.1/klrooney
3. Hasanpoor-Azghdy SB, Simbar M, Vedadhir A. The emotional-psychological consequences of infertility among infertile women seeking treatment: Results of a qualitative study. Iran J Reprod Med. 2014;12(2).
4. Morrison AK. Cognitive behavior therapy for people with schizophrenia. Psychiatry. 2009;6(12).
5. Biaggi A, Conroy S, Pawlby S, Pariante CM. Identifying the women at risk of antenatal anxiety and depression: A systematic review. J Affect Disord. 2016;191. doi:10.1016/j.jad.2015.11.014
6. Moreno-Smith M, Lutgendorf SK, Sood AK. Impact of stress on cancer metastasis. Future Oncology. 2010;6(12). doi:10.2217/fon.10.142
7. Merritt T, Mazela J, Merritt A. Tobacco smoking and its consequences on reproductive health: the impact of a lifestyle choices including cigarette smoke exposure on fertility and birth defects. Przegl Lek. 2013;70(10).
8. Alahmar A. Role of oxidative stress in male infertility: An updated review. J Hum Reprod Sci. 2019;12(1). doi:10.4103/jhrs.JHRS_150_18
9. Zakhari S. Overview: How is alcohol metabolized by the body? Alcohol Research and Health. 2006;29(4).
10. Uecker JE. Marriage and mental health among young adults. J Health Soc Behav. 2012;53(1). doi:10.1177/0022146511419206
11. Hull KE, Meier A, Ortyl T. The Changing Landscape of Love and Marriage. Contexts. 2010;9(2). doi:10.1525/ctx.2010.9.2.32
12. Mahey R, Gupta M, Kandpal S, et al. Fertility awareness and knowledge among Indian women attending an infertility clinic: A cross-sectional study. BMC Womens Health. 2018;18(1). doi:10.1186/s12905-018-0669-y
13. Horn EE, Xu Y, Beam CR, Turkheimer E, Emery RE. Accounting for the physical and mental health benefits of entry into marriage: A genetically informed study of selection and causation. Journal of Family Psychology. 2013;27(1). doi:10.1037/a0029803
14. Oppenheimer VK. Women's Rising Employment and the Future of the Family in Industrial Societies. Popul Dev Rev. 1994;20(2). doi:10.2307/2137521
15. Tsigos C, Kyrou I, Kassi E, Chrousos GP. Stress, Endocrine Physiology and Pathophysiology.; 2000.
16. Smith SM, Vale WW. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues Clin Neurosci. 2006;8(4). doi:10.31887/dcns.2006.8.4/ssmith
17. Herman JP, McKlveen JM, Ghosal S, et al. Regulation of the hypothalamic-pituitary- adrenocortical stress response. Compr Physiol. 2016;6(2). doi:10.1002/cphy.c150015
18. Joseph DN, Whirledge S. Stress and the HPA axis: Balancing homeostasis and fertility. Int J Mol Sci. 2017;18(10). doi:10.3390/ijms18102224
19. Marques P, Skorupskaite K, George JT, Anderson RA. Physiology of GNRH and Gonadotropin Secretion.; 2000.
20. Roudebush WE, Kivens WJ, Mattke JM. Biomarkers of ovarian reserve. Biomark Insights. 2008;2008(3). doi:10.4137/bmi.s537
21. Whirledge S, Cidlowski JA. Glucocorticoids, stress, and fertility. Minerva Endocrinol. 2010;35(2).
22. Yuan HJ, Han X, He N, et al. Glucocorticoids impair oocyte developmental potential by triggering apoptosis of ovarian cells via activating the Fas system. Sci Rep. 2016;6. doi:10.1038/srep24036
23. Palomba S, Daolio J, Romeo S, Battaglia FA, Marci R, la Sala GB. Lifestyle and fertility: the influence of stress and quality of life on female fertility. Reproductive Biology and Endocrinology. 2018;16(1). doi:10.1186/s12958-018-0434-y
24. Almeida FRCL, Costermans NGJ, Soede NM, et al. Presence of anti-Müllerian hormone (AMH) during follicular development in the porcine ovary. PLoS One. 2018;13(7). doi:10.1371/journal.pone.0197894
25. Moolhuijsen LME, Visser JA. Anti-Müllerian Hormone and Ovarian Reserve: Update on Assessing Ovarian Function. Journal of Clinical Endocrinology and Metabolism. 2020;105(11). doi:10.1210/clinem/dgaa513
26. Thau L, Gandhi J, Sharma S. Physiology, Cortisol. StatPearls. 2021;January.
27. Straub RH. Interaction of the endocrine system with inflammation: A function of energy and volume regulation. Arthritis Res Ther. 2014;16(1). doi:10.1186/ar4484
28. Kelsall A, Newell-Price J. Cushing's syndrome. Medicine (United Kingdom). 2021;49(8). doi:10.1016/j.mpmed.2021.05.006
29. Husebye ES, Pearce SH, Krone NP, Kämpe O. Adrenal insufficiency. The Lancet. 2021;397(10274). doi:10.1016/S0140-6736(21)00136-7
30. Sarkar S, Sarkar S, Ghosh S, Bandyopadhyay S. Addison′s disease. Contemp Clin Dent. 2012;3(4). doi:10.4103/0976-237X.107450

ISSN (O): 2687-5365; ISSN (P): 2753-6556