

Impact of subfertility

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Faiza Alam

*Clinical Academia, Pengiran Anak Puteri Rashidah Sa'adatul Bolkiah Institute of Health Science,
Universiti Brunei Darussalam, Bandar Seri Begawan, Brunei*

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Impact of subfertility

Irrespective of the society, culture, class, division, and educational status of an individual, subfertility affects both the male and the female. Both have an equal sense of the debarment; nevertheless, it has been observed that for various reasons in different cultures, females are stigmatized for being responsible for this condition. Influence of infertility has resulted in the aggravation of medical, social, psychological, and economic burdens of developing countries.¹ Infertile couples receive discriminative treatment from society, especially from friends and relatives. Our culture imposes social pressure more on newly married women in this context, especially to have sons. The debarment places infertile women in a lonely place shadowed by pain, agony, sorrow, and empathy.² Various losses faced by infertile couples may include loss of health, self-esteem, self-assurance, parental identity, personal control, genetic legacy, grand-parenting relationship, trust in religion, optimism in the future, sexual identity, and childbearing and child-rearing experience in the long list of deprivations for the infertile couples.² Commonly, infertile females of the Third World countries feel profound self-reproach and embarrassment for this condition. Generally, the impact of infertility can broadly be characterized into physical, social, psychological, and economic factors.

Effect on the marital relationship

A number of infertile females regret to accept that during their struggle with subfertility, their relationship with their husbands has been negatively affected. Stress-related alteration of the hypothalamic–pituitary–adrenal (HPA) axis influences the human pituitary ovarian (HPO) axis, which results in the modified sexual behavior along with changes in the luteinizing hormone-releasing hormone and luteinizing hormone levels. Increased levels of cortisol and proopiomelanocortin (POMC) reduce the synthesis of sex hormones accounting for the changes in the HPA and HPO axis, which along with other hormones affects the release of oxytocin. Oxytocin is also involved in the maintenance of social and sexual life. Evidence shows that adequate levels of oxytocin keep the mood and sexual drive of a female elevated; however, it modulates the transport of the sperm within the female genital tract.

Many a times the psychological irritability going on within the woman's mind, the burden of treatment, its schedule, and the finances involved in this process make the marriage stressful. It has been observed that some men are against the infertility investigation and treatments as; (i) they are petrified of being responsible for the cause (male infertility), a big taboo on manhood!, (ii) it comes with financial burden (especially for the rural dwellers), (iii) they do not want to miss the chance of second marriage, (iv) they are unaware of the treatment success rate and its impact, (v) they are too busy to actually feel the debarment, and (vi) they believe it collides with their social and religious beliefs. In some scenarios, the man demands child but females are either: (i) not willing for the treatment and (ii) too career-oriented and feel that an additional responsibility of becoming pregnant and bearing a child might hinder their success. Whatever the reason, subfertility leads to arguments and eventually affects the marital relationship.

Psychological effects

The feeling of losing their “womanhood” renders the women not to be considered as a “woman” if they do not have a child. A newlywed female faces a great social pressure, to conceive on as soon as possible basis, which becomes a psychological burden eventually. The negative attitude of the family members and questioning behavior regarding this issue pushes the female to have intense emotions such as rage, profound sorrow, resentment, responsibility, seclusion, and desperation.

Three kinds of relationships have been observed in relation to subfertility and psychological factors: (i) psychological factors resulting in subfertility, (ii) subfertility leading to psychological issues, and (iii) existence of a reciprocal relationship between the two. Depression and anxiety are persistent finding in infertile females to an extent that many women have reported about an attempt to suicide. Although infertility generates a state of depression and anxiety in a couple, psychological factors have their own influence on the reproductive abilities of both partners. Depression directly affects the HPO axis, elevates the prolactin levels, and disturbs the thyroid functions. All these three changes have their impacts on fertility.

Impact of treatment

Where couples are being challenged mentally by their subfertility, fertility treatment itself is associated with high levels of depression and anxiety. The sense of uncertainty and anxiety in females at different levels of treatment or failed trials of in vitro fertilization (IVF) and ICSI increase the depression. First-time participants have lesser anxiety and depression when compared with the women undergoing repeated attempts. The result of these treatments can bless the couple with a gift for a lifetime or can add to their disturbed mental status.

The persistent stressful condition causes increased cortisol secretion by activating corticotrophin axis. Cortisol being a stress hormone belongs to the glucocorticoid family and its release is a response to a stressful condition, which in turn effects the mechanisms like gluconeogenesis, mobilization of amino acid, and cellular immunity. The HPA axis has been recognized to bring about the changes in the reproductive system in response to stress. This psychobiological pathway reacts to stress at the central level that results the secretion of corticotrophic-releasing hormone (CRH), pituitary-secreted adrenocorticotrophic hormone, and consequently cortisol from the adrenals.³ CRH-induced POMC derivatives from the pituitary regulate the hypothalamic–gonadal axis while cortisol also inhibits the axis.

Additively it also suppresses the reproductive hormones by disturbing HPO axis at the hypothalamic level, by causing the inhibition of GnRH release.⁴ This suppression of GnRH involves protein–protein interaction of the DNA-bound Oct1 transcription factor.⁵ Furthermore, the cortisol also plays a role in regulating normal physiological mechanisms within the ovary, primarily by changing the expression of the two isoforms of 11 β -HSD. Through the follicular maturation phase, the levels of active glucocorticoids are controlled by the dehydrogenase activity of 11 β -HSD, while during ovulation, the 11 β -HSD surges the levels of active glucocorticoids, which induces inflammation concomitant with oocyte rupture. Furthermore, regulation of steroid production, oocyte maturation, conservation, and deterioration of the corpora lutea are also some of the functions. It is evident that an optimum level of cortisol is required for ovulation. Interestingly, cortisol also regulates the mitochondrial function by altering its activity. Thus, it is not surprising to have oxidative stress developed in the presence of cortisol.⁶ Oxidative stress not only leads to mitochondrial dysfunction but also results in other systemic changes.

Stress also stimulates the release of tumor necrotic factor (TNF) and natural killer cell activity. TNF induces ovarian cell apoptosis; however, NK cells' activity has been noted to be high in unexplained cases of miscarriages and subfertility.

Authors conclude with the existence of ties between stress and fertility treatment outcomes. Poor outcome of assisted reproductive treatment (ART) such as IVF has been reported due to adverse cardiovascular activity owing to stress. Females waiting for ART have been known to have four times higher levels of depression and anxiety as compared to the women without fertility problems. The level of stress is noted to start after 6 months and accelerates after one to one and a half years of subfertility and is found highest in the group with subfertility lasting for 2–3 years. However,

women experiencing subfertility for 6 years seem to get accustomed to their condition and somewhat accept their debarment.

Psychotherapy and group support sessions are practiced along with the infertility treatment plan. It reduces stress and has proved to increase the pregnancy rates, but this data is still controversial. Gentle touch like massage between the partners encourages the release of oxytocin in females and is an appreciated way of stress reduction.

Socioeconomic burden

Socially, the female is considered fortunate and high-class if she is childbearing. Despite strong financial and educational status of a female, in many societies, subfertile females are not allowed to participate in a number of family and childbearing rituals. In short, the honor of being treated equally as a fertile female is seized.⁷ They are being questioned in every gathering by the fertile females and given tips for how to conceive. It becomes like a taunt or insult for the female and this creates rift initially between the couple that may lead to physical abuse and later with the family, which is usually a mental harassment. As a consequence, the female demands for a separate living, extending to affect the society financially and morally, at large.

In other cases, where the legacy or inheritance is concerned, the men are forced to marry another woman, for the sake of bearing a next of kin for extension of the family. In such a case, the infertile female either suffers the burden of another woman or is agonized by a divorce to add to the incidence of unsuccessful marriages in a said society. Conclusively, this barrenness becomes a curse for the female.

The European Society of Human Reproduction and Embryology through their Task Force in Developing Countries and Infertility is employed to recognize infertility as a magnitude public health dispute. This Task Force is actively spreading awareness of causes and impact of subfertility in Third World countries and is creating the appropriate facilities required for treatments, counseling, and other services and to outsource to the poor resource societies suffering from infecundity. This struggle becomes very laborious as it is encountered by social, financial, religious, and ethnical constraints.

Systemic effects

Emotional stress has recently been linked to oxidative stress. During stress, the body experiences some level of sympathetic activity, which might increase the respiratory oxygen intake, leading to a turnover of free radicals. Increased levels of adrenaline and reduced levels of glutathione reductase in such a scenario also aids in occurrence of oxidative stress. While some authors agree upon the vulnerability of the brain to the oxidative stress as it consumes a large percentage of oxygen as compared to its size. Once the oxygen-derived metabolites rise, they damage the cellular structures

and lipid constitution of the cell membrane, including the neurons and the reproductive tissues. If not countered, OS can give rise to several diseases, inclusive of chronic and degenerative diseases, and can speed up both bodily aging and acute pathologies like trauma and stroke.

In animal model experiments, it has been evident that the glutathione reductase and glyoxalase's antioxidant activity is enhanced in anxious and depressed mice. In a very recent study conducted by Faiza et al., SIRT1 levels have been found to be reduced owing to the genetic mutation, resulting in a probable decline in the antioxidant counterbalance activity against the oxidants. This mutation affects the mitochondrial antioxidant action even in the granulosa cells and causing maturation failure of the oocytes. Increased levels of ROS along with anxiety and depression predisposes to conditions like inflammation and recurrent infections.

The hyperthyroidism, obesity, increased age, and mutations can prompt oxidative stress. The existence of free radicals is capable of causing reproductive disorders, cardiovascular, and metabolic disorders including diabetes and cancers.

Alterations in immune mechanisms secondary to stress and depression also have adverse effects on the reproductive physiology. However, studies are warranted to differentiate the direct effects of depression or anxiety on reproductive outcomes from the influence of behaviors.

Obesity and hypertension are common features of PCOs, while ROS levels are found elevated in the females with unexplained infertility.

During oxidative stress when an excess of hydroxyl radical and peroxy nitrite are produced, they cause intense lipid peroxidation, thus detrimental to the cell membranes and lipoproteins. Lipid peroxidation is a rather rapidly spreading chain reaction and affects a large number of lipid constituting molecules. This destruction leads to the formation of malondialdehyde and conjugated diene compound, which are known as cytotoxic and mutagenic agents.⁸ Proteins may be affected too by undergoing conformational modifications. They may lose their functional properties as well as the enzymatic capabilities. Likewise, DNA is also prone to "stress-related lesions" in the presence of oxidative stress and 8-oxo-2'-deoxyguanosine (8-OHdG) formation is the most common consequence of pernicious DNA mutation.⁹ Furthermore, oxidative stress impairs the CpG island methylation, which is a key player of the gene promoter region, causing epigenetic changes.

Counseling

Subfertility and psychological stress have a very deep relationship with great complexity. Counseling plays a crucial and supportive role in the management of subfertility. Psychological stress experienced by the couples going ART, especially IVF should be acknowledged and should be talked out to release the stress by counseling. Counseling encompasses a professional rapport between an eligible counselor and a patient, who may be a distinct, a couple, or a group of people. A formal agreement is explained and is understood by both parties. Health-care workers and researchers

working in infertility clinics offer emotional care and show empathy with couples as a part of their professional role, but it is necessary to recognize this by means of counseling services within their current roles.

The HFEA Code of Practice (HFEA 2008) recognizes three distinctive types of counseling, all of which must be unmistakably discriminated from the informative conversation.

Implication counseling focuses on enabling the infertile couple/person to comprehend the consequences of artificial reproductive treatments and subsequent arrangements for themselves, their relatives including the child born consequentially, or whoever affected by the donation or treatment.

Support counseling focuses on giving emotional support to the clients at times of particular stress, for example, when there is a failure to achieve a pregnancy. This may occur at any stage before, during, and after donation or treatment.

Therapeutic counseling focuses on helping people handle the implication of subfertility and its treatment, to find possible solutions for the hardships that these might be caused, and to alter their anticipations so as to cope with the outcome of such treatment methods.

In case of genetic causes, genetic counseling is the best and efficient tool for making a better choice of cost-effective treatment for better pregnancy outcomes. A lot of options of treatment and “oocyte donation” along with “egg-sharing scheme” can be discussed.

Counseling can be helpful, but researchers have not found it to be a predictor of a positive outcome of ART. Studies suggest that couples do not take counseling very open-heartedly. Many gave feedback that they could attend such sessions if they were free of charge. Where ART is an expensive choice of treatment, counseling adds to the overheads.

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