

Impact of Oxidative Stress on Reproductive Hormones in Fertile and Non-Fertile Females

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Abstract: *The reproduction in human is a very complex process which includes appropriate working of both male as well female reproductive system and the various hormones of the system. Free radicals are involved in many metabolic disorders such as hypertension, diabetes, cancer, Chronic obstructive pulmonary disorders, kidney the disorders, rheumatoid arthritis, atherosclerosis, asthma. Increased free radicals in the body cause oxidative stress. Oxidative stress also impacts the reproduction. This study is designed to study the effect of oxidative stress on the female reproductive hormones. To achieve this aim 500 married female of reproductive age 25-35 yrs having no history of any metabolic disorder were included in the study. Thus the level of the oxidative stress marker MDA and the reproductive hormone i.e. estradiol, progesterone and follicle stimulating hormone (FSH) (during different phases of ovulation by) were measured ELISA method. The level of the three hormones was measured during follicular phase, mid leutal phase and leutal phase. In the study, the level of the three hormones in different phases of ovulation was found to be significantly ($p > 0.0001$) increased in fertile group in comparison to the infertile group. On the other hand the MDA was found to be decreased ($p > 0.0001$) in the infertile group in comparison to the fertile group. Thus with this study it may be concluded that the oxidative stress impacts the female reproductive system and may be the reason of pathophysiology of infertility in the females.*

Keywords: Infertility, oxidative stress, reproductive hormones, melondialdehyde.

1. Introduction

Oxidative stress is very common condition, which occurs when the increasing amount of the free radicals produced during different metabolic activities of the human body is not controlled by the antioxidants. This further enhances the production of many more free radicals causing a cascade of chain reaction and severe disease state in the body. Many studies suggest that oxidative stress is involved in the pathophysiology of many diseases including cancer, diabetes, pulmonary disorders, neurodegenerative disorders, infertility etc.

It is very essential to maintain the appropriate hormonal balance in body for the proper functioning of the body. This is case of reproduction also stands true. The proper functioning of menstrual cycle of the female reproductive system is totally dependent on the cycle dependent changes in the level of hormones like estrogen, progesterone and FSH in the body which may also impacts on the oxidative stress in the system such as increased level of progesterone, indirectly indicates ovulation. The oxidative stress level may also be influences by the life style as well as envoi mental factors that may also cause variation in the hormone level. Many studies suggest that oxidative stress influences the sperm concentration in men (Appasamy.M *et.al* 2007)

2. Literature Survey

Many literature surveyed highlight the role of free radicals or oxidative stress to be involved in a lot of pathologic condition in the humans including gastrointestinal

inflammatory disorders, HIV, Sickle cell disease, Neurogenrative disorders. On the other hand it has also been involved in the alteration in pregnancy related complications such as preeclampsia, endometriosis, recurrent abortions. The free radicals also interrupt in the procedures of IVF. Oxidative stress also affects the sperms and damages the DNA of the sperm.

3. Methodology

The blood sample of infertile and fertile married females having child bearing age (25-35yrs) without any metabolic disorder (known from the history of the patient) from different gynecologist clinical hospitals and infertility centers of Allahabad were collected. The present study was carried out by collecting venous blood sample (5ml) of fertile and non fertile selected married females in Allahabad. Collection of blood sample was done thrice according to the days of their menstrual cycle for both fertile and infertile selected married females to analyze the level of the hormones during different phases of menstruation i.e.

5th -12th day of menstrual cycle for follicular phase of hormonal analysis.

12th -14th day of menstrual cycle for mid leutal phase of hormonal analysis.

15th -28th day of menstrual cycle for leutal phase of hormonal analysis.

The Hormone values were measured for the two groups of married females

1.Group I: 250 fertile married females having children.(Fertile group)

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2.Group II: 250 infertile married females not having children.(Infertile group)

The level of Melondialdehyde was determined by procedure described by Santos (1978). The hormones were analysed by using ELISA method on poly system PR-601 machine.

4. Result and Discussion

Table 1 shows the increased level of MDA found in the infertile group in comparison to the fertile group i.e increase oxidative stress in the infertile group. The MDA level was found to be statistically significant ($p > 000.1$). Age wise the groups were similar but the level of the hormones were statistically ($p > 000.1$) significantly different. Lipid peroxidation measured as MDA content is considered to be indicator of oxidative damage from stress (Yasar *et.al.*, 2008). As Melondialdehyde is known to be a oxidative stress marker and is only formed in the lipid peroxidation. The test result is supported by results Of (Bhaskar *et.al.*, 2008, Jaiswar 2006)

Table 1: Mean± SD and p value significance of oxidative stress marker of group I (Infertile female) group II (Fertile female)

S. No	Parameters	Group I	Group II	t-test
1	MDA	.85±.0603	3.00±0.295	126.111

Table 2: Mean± SD of Estrogen, progesterone and FSH hormone in follicular phases of menstrual cycle

	Group I	Group II	t test
Estrodiol	109.27±16.853	42.24±13.556	49.0021
Progesterone	1.3±.2598	0.42±.2474	38.7845
FSH	8.48±1.29	4.45±.944	39.8620

The level of estrogen, progesterone and FSH hormone was found to be increased in all the phases of ovulation in the fertile group in comparison to the infertile group. The level of estrodiol, progesterone and FSH is shown in **table 2**.

In the follicular phase the estrodiol hormone level in the group I (109.27±16.853 Pg/ml) was increased in comparison to group II (42.24±13.556).

In the follicular phase the progesterone hormone level in the group I (1.3±.2598 ng/ml) was increased in comparison to group II (0.42±.2474 ng/ml). FSH hormone in the follicular phase was found to be decreased in the group II (4.45±.944 mIU/ml) as compared to the group I (8.48±1.29 mIU/ml) and showed significant difference

Table 3: Mean± SD of Estrogen, progesterone and FSH hormone in Mid luteal phases of menstrual cycle

	Group I	Group II	t test
Estrodiol	290.6±53.55	101.3±38.76	45.2775
Progesterone	20±3.43	7.8±2.0	67.3477
FSH	27±2.79	11.7±3.174	57.2454

The mid luteal level of the estrodiol, progesterone and FSH is displayed in **table 3**. The level of estrodiol hormone was found to be decreased in the group I (290.6±53.55

Pg/ml) as compared to the group II (101.3±38.76 Pg/ml). The level of progesterone hormone was found to be decreased in the group I (20±3.43 ng/ml) as compared to the group II (7.8±2.0 ng/ml) in mid cycle phase. The decrease level of FSH hormone was also found in the mid cycle phase of ovulation with increased seen in the group I (27±2.79 mIU/ml) as compared to group II (11.7±3.174 mIU/ml).

The level of the three hormone estrogen progesterone and FSH in luteal phase is shown in **table 4**. The level of estrodiol hormone in the luteal phase was found to be increased in the group I (198.2±6.663 Pg/ml) as compared to group II (71.82±6.607 Pg/ml). the level of progesterone hormone in the luteal phase was found to be increased in the group I (24.7±3.23 ng/ml) as compared to group II (7.8±2.3 ng/ml). Similarly the FSH was also found decreased in the luteal phase of ovulation in the group II (8.1±1.286 mIU/ml) in comparison to the group I (4±1.459 mIU/ml)

Table 4: Mean± SD of Estrogen, progesterone and FSH hormone in luteal phases of menstrual cycle

	Group I	Group II	t test
Estrodiol	198.2±6.663	71.82±6.607	212.9554
Progesterone	24.7±3.23	7.8±2.3	48.5830
FSH	4±1.459	8.1±1.286	33.3323

The results showed significant increase in the level of hormones of fertile group in comparison to the infertile group. Thus it can be easily understood that increase in the oxidative stress reduces the level of the reproductive hormone which may cause infertility. The possible reason for this decrease found in the infertile group in the estrogens and progesterone hormone level in the three phase of ovulation may be because both these hormones are produced from the ovary ie estrogens from the follicle and progesterone from the corpus luteum whereas FSH from the pituitary gland which stimulates ovary to develop and mature follicle. Many studies done earlier have shown that the increased level of reactive oxygen species play a critical role in the folliculogenesis as well as corpus lutea function such as **Das and Chowdhury 1999** concluded in their study that vitamin E deficiency during aging is associated with the decrease body weight and decrease levels of sex hormone in mouse model. Ageing on the other hand is also associated with the oxidative stress. Phase wise hormonal study is not done earlier thus support of the results is not possible. A study done by **luck and Zhao 1993** says that ascorbic acid which also possess an antioxidant property is required for the corpus lutea collagen formation.

Al-Katib, et al., 2013 found that progesterone concentration was found increased significantly with the effect of vitamin C in second period as compared with control group in fertile and infertile women only and the effect of vitamin C supplementation on serum estrogens that is increased significantly in first period and second period as compared with control group in both fertile and unmarried women. A significant increase on the endometrial thickness in both first period and second period was seen as compared with control group for both

fertile and infertile women after the supplementation of Vitamin C.

Murdoch (1998) investigated the antioxidant properties of estrogen in lutea and follicular tissue in pig exposed to hydrogen peroxide in vitro, in which high doses of estrogen (≥ 40 pg/ml) protected against apoptosis, suggesting that ovarian estrogen (E₂) function as reactive oxygen species scavenger during pregnancy mediated luteal rescue and folliculogenesis.

ROS are increased in the corpus luteum during regression phase (**Riley and Behrman, 1991, Shimamura et.al, 1995**) and inhibit progesterone production in rats (**Behrman and Aten, 1991, Kodaman et.al, 1994, Behrman and Preston, 1989**) suggesting the involvement of ROS in corpus luteum regression (**Kato et.al, 1997**). The presence of endometrial tissue in the extra-uterine location is the characteristic of endometriosis, a benign but estrogen dependent gynaecological disorder. Although benign, the disease leaves many affected females infertile. (**Giudice L.C. and Kao L.C. 2004**). Thus it can be easily understood that the antioxidants are important for the proper functioning of the reproductive system as well but the presence of oxidative stress in the infertile group strongly indicates that the decreased level of antioxidant in the infertile group may impact on the hormonal level in the body.

5. Conclusion

The results of the present study clearly indicate that the levels of the hormones i.e. estrogen, progesterone and FSH are statistically found to be decreased in the infertile group as well as the level of MDA is found to be increased in the infertile group. Thus it may be concluded that the increase in the oxidative stress impacts on the female reproduction and may also lead to infertility. Thus to counter the oxidative stress, the protective attempt i.e. antioxidant supplementation included in the diet may be very beneficial for the body.

6. Future Scope

With the results of this study it may be easily understood that increased oxidative stress impacts on the fertility of the male as well as female. Thus involving the antioxidants in the diet is beneficial for protection. In future adding the level of oxidative stress measurement may be in the infertile females may help the gynaecologist to find out the cause of infertility and involving the various antioxidants in the diet with other medical help may be useful to overcome with infertility.

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