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IMPACT OF OXIDATIVE STRESS AND ANTIOXIDANT ENZYME ON FERTILITY

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ABSTRACT

Infertility is common health problem and is experienced by many couples now a day. Many studies suggest that oxidative stress is a cause of a range of many pathologic disorders including cancer, cardiovascular disorders, neurogenrative disorders and many of the other thus this study is design to find the effect of oxidative stress on fertility in the females. To achieve this aim 500 married female were included for this study in which 250 were fertile and 250 infertile married females of reproductive age 25-35 yrs having no history of any metabolic disorder. The level of oxidative stress marker Melondialdehyde (MDA) and three antioxidant enzyme catalase (CAT), ceruloplasmin and superoxide dimutase (SOD) were measured. The results of MDA showed a significant ($p>0.0001$) increase in the MDA level and significant ($p>0.0001$) decrease in the catalase, ceruloplasmin and SOD in the infertile group when compared to the fertile group. The correlative study between the superoxide and Melondialdehyde indicated ($r=-0.53$, $p<0.05$) a significant negative correlation, similarly a significant negative correlation was found among Melondialdehyde and catalase ($r=-0.29$, $p<0.05$) as well as in between Melondialdehyde and ceruloplasmin ($r=0.20$, $p<0.05$).These results suggest that oxidative stress is related with the pathophysiology of fertility in the females.

KEY WORDS: **Infertility, Oxidative stress, Melondialdehyde, Antioxidant enzyme.**

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INTRODUCTION

Oxidative stress is a consequence of an imbalance between the productions of ROS and the ability of the biological system to detoxify the reactive intermediates or easily repair the resulting damage [1]. Oxidative stress occurs when the production of ROS increases or when the levels of antioxidants decrease [2]. All forms of life maintain a reducing environment within their cells. Normal cellular aerobic metabolism also results in the generation of ROS. Minimal levels of ROS act through signaling pathways, which is necessary for the normal physiological functions in the female reproductive tract. [3]These free radicals are generated in the normal cellular metabolism. Oxidative stress can cause tissue injury or even cell death which can occur essentially by two mechanism, necrosis and apoptosis. [4]. Oxidative stress also effects the human fertilization and can induce apoptosis which can further result in failure in implantation, fragmentation of the embryo or can cause abortions. Many of the unsuccessful reproductive performance such as infertility, miscarriage and preeclampsia are found to be related to adverse health effects of oxidative stress oxidative stress[5]. Successful pregnancy is a combination of a long list of complex biological steps like, ovulation, production of competent sperm and oocyte in the reproductive tract, proper fertilization, successful transportation of the conceptus to the uterus and implantation of the embryo etc. Disruption in one or more of these complex biological steps can lead to infertility [6]. In the fallopian tubes, damaging effect to an embryo may be induces by oxidative stress. The imbalance of the ROS and antioxidants in the reproductive tract can cause defect in the endometrium which facilitates embryo implantation and development.

MATERIALS AND METHODS

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 The present study was carried out by collecting venous blood sample 5ml of fertile and non fertile selected married females in Allahabad and were divided in two groups 1.Group I: 250 fertile married females having children.(Fertile group) 2.Group II: 250 infertile married females not having children.(Infertile group).

The level of Melondialdehyde was determined by procedure described by Satoh [7] Catalase (CAT) activity was determined by the Brannan [8] method, SOD by Mishra and Fridovich [9] method.

RESULTS AND DISCUSSION

During this study it was found there was significant difference in the MDA mean values of the two groups with increase in the group II (3.00±0.295 nmol/ml) as compared to the group I (0.85±.0603 nmol/ml). The results showed significant increment in the MDA value of infertile group which strongly indicates the lipid peroxidation and denotes presence of oxidative stress in the infertile females.

Table 3.1
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	P.Value Significance	t-test
1	MDA	85±.0603	3.00±0.295	Statistically significant (>0.0001)	**126.111**

S: Significant, NS: Non Significant
MDA (nmol/ml):0.5-2.0

Table 3.2
Mean± SD and p value significance of antioxidant enzymes for group I (fertile female) group II (Infertile female)

S.No	Parameters	Group I	Group II	P.Value Significance	t-test
1.	Ceruloplasmin	32.08±1.152	19.367±0.970	Statistically significant (>0.0001)	133.4738
2.	Superoxide dimutase	10.47±0.831	17.0±0.679	Statistically significant (>0.0001)	62.6192
3.	Catalase	7.3±1.024	3.5±0.484	Statistically significant (>0.0001)	16.4760

Lipid peroxidation measured as MDA content is considered to be indicator of oxidative damage from stress. [10] As Melondialdehyde is known to be a oxidative stress marker and is only formed in the lipid peroxidation. The test result was supported by results of [11, 12].The level of antioxidant enzyme was found significantly (p > 000.1) increased in the fertile group in comparison to the infertile group as shown in table 3.2.

The table shows the increase in the group I (32.08±1.152 unit /mg/protein) when compared with the group II (19.367±0.970 unit /mg/protein) (p value > .000.1 highly significant). Significant difference in the serum ceruloplasmin mean values of the two groups with increase in the group II (17.0±0.679 unit /mg/protein) as compared to group I (10.47±0.831 unit /mg/protein). The catalase was found to be increased in

the group I (7.3±1.024 unit/mg protein) as compared to group II (3.5±0.484 unit/mg protein) . The results indicate that the antioxidant enzymes were lower in the group II in comparison to group I ie low level of defense against oxidative stress was found in the infertile group. The results showed significant increment in the activity of serum ceruloplasmin value of infertile group thus the lower amount of the antioxidant enzyme is found in the infertile group.

Correlation between MDA and Antioxidant enzymes in infertile females

The result for the correlative study of oxidative stress marker and antioxidant enzyme is displayed in table 4.3. The correlative study between the superoxide and melondialdehyde indicated ($r=-0.53$, $p<0.05$) a significant negative correlation, similarly a significant negative correlation was found among Melondialdehyde and catalase ($r=-0.29$, $p<0.05$) as well as in between Melondialdehyde and ceruloplasmin ($r=-0.20$, $p<0.05$).This results of correlation study as found to be negatively correlated itself indicates that the MDA and antioxidant enzymes are inversely correlated i.e increase in one parameter leads to decrease in the other and vice versa.

Table 4.3

Correlation factors of serum Melondialdehyde with the antioxidant enzymes i.e. superoxide dismutase (SOD), catalase, ceruloplasmin in infertile women

	Parameters	r value	p. value	Significance level
MDA Verses Antioxidant enzymes	SOD	-0.53	<0.00001	Significant at p<0.05
	Catalase	-0.29	<0.00001	Significant at p<0.05
	Ceruloplasmin	-0.20	0.00148	Significant at p<0.05

DISCUSSION

The infinite normal healthy process in both men and women counts for a successful pregnancy. Any disturbance in any of these process or system in men or women disruption to this interactive system, whether in a man or woman, can result in an inability to have a biological child is called infertility[13]. Oxidative stress can effects the various processes such as ovulation, fertilization, embryo development implantation in females [14] Thus, OS is considered as a cause of female infertility. Many literatures highlights the role of OS in the physiological functions in female reproduction and also in disease states such as pre-eclampsia [15,16] hydatidiform mole [17], free radical-induced birth defects [18], polycystic ovarian disease and other situations such as abortions [19].The results in support with the study done by [20] indicate that the infertile women have decreased level of antioxidant enzyme GST and CAT. The results are also well supported with study done by [12] Successful pregnancy is a combination of a long list of complex biological steps like, ovulation, production of competent sperm and oocyte in the reproductive tract, proper fertilization, successful transportation of the conceptus to the uterus and implantation of the embryo etc. Disruption in one or more of these complex biological step can lead to infertility [21].ROS plays a role during pregnancy [22] and normal parturition [23] and in initiation of preterm labor [24]. Oxidative stress can also cause preeclampsia by disrupting the body's vasodilatation signalling process, allowing maternal blood pressure to rise, and disrupting placental blood flow [25]. OS plays a critical role in the process of ovulation by inducing apoptosis of leutal cells within the ovary, which perturbs the area in and around ova and granulosa cells that could potentially decrease oocyte and embryo viability

CONCLUSION

With the results observed in this study it may be concluded that oxidative stress, adversely effect the female reproduction and may also lead to infertility. As ROS are naturally made up by the human body and is a part of normal healthy metabolic activity but an increased amount of ROS burdens immensely and affects the fertility rate of the females. Thus to counter the ROS, the protective attempt i.e. antioxidants supplementation in the diet may be very beneficial for the body.

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