

Evaluation of Some Antioxidant Enzymes in Women with Infertility in Reproductive Age

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Abstract

Background: Millions of women worldwide struggle with infertility, and oxidative stress has been linked to the etiology of the condition. Superoxide dismutase (SOD) and catalase (CAT) are examples of antioxidant enzymes that are essential for preventing oxidative damage to cells. **Objectives:** The purpose of this study was to investigate the connection between body weight and antioxidant enzyme activity in infertile women of reproductive age. **Materials and Methods:** A case-control study was conducted involving 40 infertile women and 20 controls (fertile). Body weight and levels of antioxidant enzymes (catalase [CAT], SOD, folate, and total antioxidant status, or TAS) were compared between the two groups. The association between age, body weight, and antioxidant enzyme levels in infertile women was evaluated using correlation analyses. **Results:** Compared to controls, infertile women had significantly lower levels of TAS, CAT, SOD, and folate. Weight was positively correlated with CAT levels and negatively correlated with folate levels in infertile women, whereas age was negatively correlated with folate levels. **Conclusion:** These results imply that antioxidant enzyme activity and folate levels may be viable biomarkers for female infertility, and that weight may contribute to the onset of infertility by affecting these parameters. In conclusion, women who are infertile exhibit reduced levels of antioxidant enzyme activity and folate. It is possible that weight affects these parameters and plays a role in the pathophysiology of infertility.

Keywords: Age, antioxidant enzymes, catalase, infertility, SOD, women

INTRODUCTION

Infertility, which has been staring at people at the point of the sword since the beginning of history, the problem of infertility, has assumed a new color in the present-day world. There has always been some difficulty in conceiving and bearing children among couples in society, but the problem of infertility has only increased in recent past generations which has brought the joy of parenthood into darkness for millions of couples.^[1] This emerging issue has pushed infertility to the forefront and placed it in the limelight of public health debates for the need to be addressed, recognized, and studied.^[2] Here is a brief overview of the current situation as we find it today and as we try to conceive a child, the blockers that have emerged in the twenty-first century to enhance the difficulty. The causes of delayed child-bearing include environmental

factors, consumption of junk foods, and other vices resulting in high cases of infertility among women of reproductive age.^[3] Furthermore, oxidative stress, which is a condition involving an excess of free radicals and lesser amounts of antioxidants, has another major factor that causes reproductive health problems^[4] They can interfere with the basic functioning of cells and DNA and harm fertility both in men and women. The role of emotion in infertility is significant.^[5] To the many women and men out there yearning to be parents, experiencing infertility aches them and torments them with grief and perceived

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social isolation. It must also be stressed that financial considerations, when it comes to the costs of fertility treatments, prove to be yet another major source of stress for the couples in question.^[6] This yet again necessitates that we come up with a holistic approach to infertility and acknowledge the emotional and psychological implications of the condition before accepting futuristic tailored treatment measures for patients who are denied fertility.^[7]

The female reproductive system is a very intricate and delicately balanced biological system that requires stringent regulation of various physiological and biochemical processes.^[8,9] The most important consideration in the reproductive health of a female is how oxidative stress is related to antioxidants in the body.^[10] Resulting of an imbalance, oxidative stress in which reactive oxygen species (ROS) generation overrides the antioxidant defense level can be devastating for reproductive health.^[11] The long-term action of excessive ROS is the destruction of reproductive health due to the impaired quality of the oocytes, disrupted normal patterns of follicular development, and infertility.^[12,13]

ROS can cause oocyte and follicle damage and loss, leading to infertility because it would elevate the miscarriage rate and other reproductive abnormalities.^[14] It can also affect the endometrial lining, resulting in endometriosis and polycystic ovary syndrome, which are major causes of infertility.^[15] Furthermore, ROS and antioxidants are connected to reproductive health. Antioxidants like vitamins C and E, beta-carotene, and polyphenols play a major role in quenching ROS and combating the attacks on the reproductive system due to damage by oxidative stress.^[16,17] As such, a well-organized diet with the right choice and combination of antioxidants can ameliorate hazardous oxidative stress effects on reproductive health.^[18] However, other lifestyle aspects about cigarette smoking, alcohol intake, and recreational use of drugs may lead to oxidative stress directly and thereby impact reproductive health adversely.

Environmental pollutants, such as pesticides and heavy metals, bring about oxidative stresses and have been observed to be significantly harmful to female fertility.^[19] The balance between oxidative stress and antioxidants in reproduction is very delicate; therefore, it forms the basis upon which understanding the interaction between the two becomes necessary in the prevention and treatment of infertility. It means that recognizing the relevance of this balance and taking steps to offset oxidative stress in the female population will minimize their risks of reproductive complications.

Concerning the connection between antioxidant enzymes and the weight of women with infertility of reproductive age, it can be stated that the problem is rather ambiguous and has a multifactorial character. Scholars have

established that the antioxidant status is altered in women with infertility, and they have reduced antioxidant enzyme activity, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase GPx.^[20] This imbalance can result in a state of oxidative stress, and this has been known to affect negatively the overall reproductive status of an individual or couple.^[21] In addition, other research works have observed that women with infertility have a bigger body mass index than those without, a factor that increases oxidative stress and decreases antioxidant enzymes.^[22] This implies that weight could influence the occurrence of infertility through effects on antioxidant enzymes and oxidation stress. Also, it should be noted that antioxidant enzyme levels and their connection to weight in women with infertility depend on diet, way of life, and hormonal disorders.^[23] For example, daily consumption of fruits, vegetables, and whole grain products will increase the antioxidant enzymes while foods that are processed and foods with high sugar content will reduce the levels of antioxidant enzymes in the body. Likewise, managing the levels of exercise and indulging in healthy habits can also decrease the impact of oxidative stress and unleash the efficiency of antioxidant enzymes.^[23] Hormonal imbalance, for instance, polycystic ovary syndrome, can also affect the antioxidant enzymes and thus lead to infertility.

Consequently, this work shows that the relationship between antioxidant enzymes and women with infertility of reproductive age and weight is not simply the composition of antioxidant enzymes in women of reproductive age with infertility but is more complex and multifaceted.

MATERIALS AND METHODS

Design of experimental

In this study, a case-to-control strategy was used to assess putative biomarkers of female infertility. We recruited two distinct groups: Cohort 1 composed of 20 samples of possibly reproductive-age women, without any known fertility problems, and the case group composed of 40 infertile women. Thus, we sought to compare the demographic and biometric profiles of the large population of these samples and to identify major disparities that they could potentially signify with respect to infertility. These insights could then be examined to reach out for other relevant biomarkers and help clinics diagnose infertility at an earlier stage of a clinic to provide proper treatment plans.

Examining biomarkers associated with infertility in women

Age was recorded for each participant, and weight was measured to assess body composition. Blood samples were drawn to measure the levels of several factors: First, SOD and CAT, which are enzymes that help protect against oxidative stress, were measured according to

Gusti *et al.*^[24] Second, total antioxidant status (TAS) was measured, which reflects the overall antioxidant capacity of the blood. Third, folate levels were also measured, as folate is a B vitamin, that is, important for reproduction.

Antioxidant enzyme examination in case and control

We collected data on the levels of SOD, CAT, TAS, and folate in both the control and case groups. The levels of particular antioxidant enzymes were compared between the two groups of women in the study: a control group that was not infertile and a case group that was infertile, using the Mann–Whitney *U* test.

Relationship between women's age and infertility with antioxidant enzymes

The study collected data on the age of women with infertility and their levels of SOD, CAT, TAS, and folate. Using Pearson correlation analysis, we aimed to investigate the potential relationship between age and the levels of different antioxidant enzymes in women experiencing infertility. The age of each female was determined by asking all the females in the experiment from both groups, excluding females whose age was not in the reproductive age.

Weight influences antioxidant enzyme levels in infertile women

This study examined the potential link between weight and antioxidant enzymes in women with infertility. Weight (kg) was measured by “A smart digital scale to know body weight and fat, with an LED screen and a mobile application, multi-color” alongside the levels of SOD, CAT, TAS, and folate. Pearson correlation analysis was used to assess the strength and direction of any linear correlation between weight and each of these antioxidant enzyme levels.

Statistical analysis

Using Statistical Package for the Social Sciences (SPSS) version 26.0 (SPSS, IBM Company, Chicago, IL 60606, USA), we compared the average values of each parameter between the control and case groups using statistical tests. This aids in determining statistically significant variations between women who are fertile and those who are not. The study utilized the Mann–Whitney *U* test to compare the levels of specific antioxidant enzymes between two groups of women. The Mann–Whitney *U* test is a non-parametric statistical test commonly used to compare the medians of two independent groups when the data is not normally distributed. Utilizing the statistical technique known as Pearson correlation, we examined the relationship between each antioxidant enzyme level and age and weight. The results of this analysis can be used to assess the strength and nature of the relationship, as well as whether it is positive (growing together) or negative (opposites).

Ethical approval

The Declaration of Helsinki served as a framework for all research. Patients gave us verbal and written consent before obtaining samples from them. A local ethics committee accepted the study methodology, subject data, and permission form in Document 11/2023 (April 22, 2023).

RESULTS

Examining biomarkers associated with infertility in women

When examining the profiles of 20 control and 40 case subjects experiencing infertility, notable differences emerged. The average age in the control group stood at 31.6 years (± 7.741), closely mirroring the case group's average age of 31.7 years (± 7.261). However, a significant contrast emerged in weight, with the control group averaging 45.4 kg (± 8.999) compared to the case group's notably higher average of 64.05 kg (± 7.524). The average SOD level was 4.43 (± 1.105) in the control group, contrasting with the lower average of 3.67 (± 0.967) in the case group. Similarly, CAT levels averaged 16.21 (± 2.390) in the control group versus 14.91 (± 3.581) in the case group. Notably, TAS levels were markedly higher in the control group, averaging 18.81 (± 5.578), whereas the case group displayed a significantly lower average of 11.67 (± 2.913). Lastly, folate levels also exhibited a divergence between the two groups, with the control group averaging 2.57 (± 0.514) compared to the case group's lower average of 1.65 (± 0.535). These findings underscore the potential significance of these biomarkers in understanding and addressing infertility issues among women [Table 1].

Antioxidant enzyme examination in case and control

Table 2 demonstrates infertile women show decreased antioxidant enzyme activity in their bodies. The test's *P* values were used to determine how significant the differences that were observed were. There is a statistically significant difference between the groups when the *P* value is less than 0.05. Significant variations in SOD, TAS, and folate levels were observed between the case and control groups, suggesting a possible

Table 1: Distribution of studied sample by their characteristics

Factors	Control (<i>n</i> = 20)	Case (<i>n</i> = 40)
Age (years)	31.6 \pm 7.741	31.7 \pm 7.261
Weight	45.4 \pm 8.999	64.05 \pm 7.524
SOD (0.75–24 ng/mL)	4.43 \pm 1.105	3.67 \pm 0.967
Catalase (10–40 ng/mL)	16.21 \pm 2.390	14.91 \pm 3.581
TAS (10–320 ng/mL)	18.81 \pm 5.578	11.67 \pm 2.913
Folate (2.5–20 ng/mL)	2.57 \pm 0.514	1.65 \pm 0.535

SOD: superoxide dismutase, TAS: total antioxidant status

Table 2: Statistical differences in antioxidant enzymes between case and control

Variable	Groups	No.	Mean rank	Sum of ranks	cz	Sig.
SOD (0.75–24 ng/mL)	Control	20	38.18	763.50	246.500	0.016
	Case	40	26.66	1066.50		
Catalase (10–40 ng/mL)	Control	20	35.10	702.00	308.000	0.149
	Case	40	28.20	1128.00		
TAS (10–320 ng/mL)	Control	20	46.50	930.00	80.000	0.001
	Case	40	22.50	900.00		
Folate (2.5–20 ng/mL)	Control	20	45.63	912.50	97.500	0.001
	Case	40	22.94	917.50		

cz = Mann–Whitney test, No. = number, sig. = significant level at 0.05. The Mann–Whitney U test revealed noteworthy disparities in SOD ($P = 0.016$), TAS ($P = 0.001$), and folate ($P = 0.001$) levels between women classified as controls (without infertility) and cases (experiencing infertility)

Table 3: Association between antioxidant enzymes and infertility women's age

Correlation statistics	1	2	3	4	5
1. Age/years	1				
2. SOD (0.75–24 ng/mL)	−0.088	1			
3. Catalase (10–40 ng/mL)	0.189	0.174	1		
4. TAS (10–320 ng/mL)	0.248	0.121	0.206	1	
5. Folate (2.5–20 ng/mL)	−0.280*	0.245	0.135	−0.060	1

*Correlation is significant at the 0.01 level (two-tailed). The findings reveal a negative correlation between infertility women's age and their folate levels ($r = -0.280$; $P < 0.005$)

Table 4: Association between antioxidant enzymes and infertility women's weight

Correlation statistics	1	2	3	4	5
1. Weight/kg	1	0.022	0.305	−0.029	−0.366*
2. SOD (0.75–24 ng/mL)	0.022	1	0.174	0.121	0.245
3. Catalase (10–40 ng/mL)	0.305*	0.174	1	0.206	0.135
4. TAS (10–320 ng/mL)	−0.029	0.121	0.206	1	−0.060
5. Folate (2.5–20 ng/mL)	−0.366*	0.245	0.135	−0.060	1

*Correlation is significant at the 0.05 level (two-tailed). The findings reveal a positive correlation between infertility women's weight and their catalase levels ($r = 0.305$; $P < 0.005$) and negative correlation with folate levels ($r = -0.366$; $P < 0.005$)

connection between reduced antioxidant enzyme activity and infertility.

Relationship between women's age and infertility with antioxidant enzymes

The strength and direction of a linear relationship can be determined by the correlation coefficient (r). A negative r value indicates a negative correlation, which means that the level of the enzyme decreases with advancing age. The statistical significance of the correlation can be determined by the P value. A P value of less than 0.05 indicates a significant correlation. The results showed a significant inverse relationship between age and folate levels ($r = -0.280$; $P < 0.005$), suggesting that infertile women may experience a decline in folate levels as they age [Table 3].

Weight influences antioxidant enzyme levels in infertile women

The findings showed a strong positive correlation ($r = 0.305$; $P < 0.005$) between weight and CAT levels,

indicating that infertile women who are heavier have higher CAT activity. On the other hand, a noteworthy inverse relationship was found between weight and folate levels ($r = -0.366$; $P < 0.005$), indicating that individuals in this population with higher weight may also have lower folate levels. The linear relationship's strength and direction are determined by the correlation coefficient (r). When the weight increases and the enzyme level increases as well, this is indicated by a positive correlation with a positive r value. A negative r value denotes a negative correlation, meaning that the enzyme level falls as weight rises. The correlation's statistical significance can be ascertained with the aid of the P value. A significant correlation is indicated by a P value of less than 0.05 [Table 4].

DISCUSSION

Till now, infertility is one of the most common reproductive health disorders among women at the child-bearing age, affecting over 180 million women globally; both physiological and biochemical processes like oxidative stress remain key factors affecting the health of

women^[25] ROS, which are free radicals, when they exceed the body's natural scavenging ability the condition referred to as oxidative stress has been linked with infertility.^[14] Antioxidant enzymes SOD and CAT help in alleviation of oxidative stress, by eliminating the free radicals.^[26] Thus, current research suggests that female infertility may be closely associated with antioxidant enzyme activity. Thus, the further investigation of the role of antioxidant enzyme levels in female idiopathic infertility by comparing them to women with normal infertility in the reproductive age and understanding how levels of antioxidant enzymes are affected by body weight remains uncertain.

The current research work focused on the profiling of biomarkers associated with infertility in women. In this study, the results highlight some significant differences between the control and case groups, which denote the possible role these biomarkers could play in understanding and alleviation of issues related to infertility. In that regard, it was found that the control and case groups showed a rather homologous mean age: the control group averaged an age of 31.6 and the case group around 31.7 years. In contrast, large deviations existed in weight, wherein the control group had an average of 45.4 kg, while that of the case group was 64.05 kg. This large deviation in weight could be indicative that there is probably a relationship between obesity and infertility since other studies have also postulated a relationship between the two. The levels of SOD, CAT, and TAS were different in both groups. The mean levels of SOD, CAT, and TAS in the control group were 4.43 ± 1.105 , 16.21 ± 2.390 , and 18.81 ± 5.578 , respectively, compared to that in the case group. Results were in agreement with the suggestion that infertility could be caused by a state of oxidative stress, since SOD as well as other enzymes, such as CAT, are known to reduce the effects of oxidative stress.^[26-28] Moreover, it was found that the folate levels were significantly lower in the case as compared to the control. This is supported by the available literature, which suggests that a folate deficiency could contribute to infertility in women.^[29,30] These results raise the potential significance of these biomarkers in defining and treating infertility in women. Based on the significant differences observed in antioxidant enzyme activity, TAS, and folate levels, the study suggests that these factors might be potential biomarkers associated with infertility in women.

The results of the study on antioxidant enzyme activities in cases of infertile women, as compared to those in women without infertility—controls—reveal differences in a variety of key enzymes. Reduced activities of SOD, TAS, and folate were found in infertile women, compared to the control group in this study. The difference was statistically significant, as evidenced by the Mann–Whitney U test with *P* values of 0.016, 0.001, and 0.001 for SOD, TAS, and folate, respectively. The results suggest that there may be a connection between reduced activity of antioxidant

enzymes and infertility in women. The diminished activity of SOD, TAS, and folate in infertile women can lead to important pathophysiological correlations for infertility.^[31] SOD, for example, plays a very important role in the scavenging of free radicals and thus maintains the balance between the pro-oxidants with the antioxidants present in the body. Decreased SOD activity can contribute to increased oxidative stress, which has already been linked to infertility in many studies.^[21,32,33] In this regard, TAS and folate are powerful antioxidants that ensure protection against cellular damage arising from the action of free radicals. Hence, decreased levels of these enzymes will contribute to the incidence of oxidative stress and, hence, infertility.^[34] These findings support the idea that antioxidant enzyme activity may be an important factor in the development of infertility.

The results of the study indicate that there is an inverse significant relationship between the age of infertile women and their folate levels, which is statistically significant with a correlation coefficient $r = -0.280$, with *P* value less than 0.005. Therefore, it indicates a decrease in folate levels with respect to an increase in age among infertile women.^[35] There is a negative correlation between age and folate levels; hence, at an increased age, the folate levels in infertile women are decreased.^[29] This is an important observation in view of the role that folic acid can play in maintaining reproductive health and fertility. This decline in folate levels with age may add to the risk of infertility with advancing age among women.^[36] This study accentuates the need to consider the age effect on circulating folate concentration in infertile women. The data interpreted from this study may indicate that older infertile women may need supplementation of folate to have a better chance of conceiving and, hence, improve their reproductive outcomes. Nevertheless, additional studies are needed to establish this relationship and to determine the optimal circulating folate levels for women with different infertility causes and ages.

This study examined the relationship between infertile women's weight and levels of antioxidant enzymes, and the results showed a complex interaction between these variables. According to our research, there is a positive relationship between CAT activity and weight, meaning that infertile women who weigh more typically have higher levels of the enzyme. On the other hand, a negative correlation between weight and folate levels was noted, indicating that in this population, higher weight may be linked to lower folate levels. It is interesting to note the positive correlation between CAT levels and weight. An essential antioxidant enzyme called CAT shields cells from ROS-induced oxidative damage.^[37] Although more research is needed to determine the precise mechanisms underlying this correlation, a number of possibilities exist. Higher body weight is frequently linked to higher oxidative

stress and ROS production, especially when combined with metabolic disorders like obesity. To counteract the increased oxidative damage, this might cause a compensatory rise in CAT activity.^[38] Hormone levels are known to be impacted by weight fluctuations, and hormone levels can then affect the activity of antioxidant enzymes. For instance, some research has indicated that the hormone estrogen, which is impacted by weight, affects the expression of CAT. Notable is also the negative relationship found between folate levels and weight. Folate is a vital nutrient for healthy reproduction that is involved in cell growth and division. Previous research has linked lower levels of folate to infertility.^[39] The reason for this negative correlation could be that people who weigh more may not eat as healthily or as diversely, which could result in consuming less folate. Increased metabolic demand may be linked to higher weight, which could result in higher folate utilization and lower levels of circulation.^[39] These results emphasize how critical it is to help infertile women manage their weight. Changes in antioxidant enzyme activity and folate levels associated with weight may be a factor in infertility. Future studies should examine the causal relationships among infertile women's weight, antioxidant enzyme activity, and folate levels while taking hormonal profiles, genetic predisposition, and metabolic health into account.

CONCLUSION

In conclusion, the study concluded that infertile women had lower levels of SOD, CAT, TAS, and folate than control groups. The weight of the infertile women correlated positively with CAT and negatively with folate, despite the fact that their age and folate levels were negatively correlated. These findings imply that antioxidant enzyme activity and folate levels may be useful biomarkers of female infertility, and that weight may influence these parameters and contribute to the pathophysiology of infertility. Therefore, more research is required to comprehend the temporal patterns of associations among infertile women regarding weight, antioxidant enzyme activity, and folate levels, as well as to consider targeted interventions aimed at enhancing reproductive outcomes.

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Conflicts of interest

There are no conflicts of interest.

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