

**How to Cite:**

Salman, F. S., Al-Qadhi, H. I., & Alkareem, B. A. (2022). N-acetyl-cysteine effect on total antioxidant capacity in Iraqi men with oligoasthenoteratozoospermia. *International Journal of Health Sciences*, 6(S3), 2360–2365. <https://doi.org/10.53730/ijhs.v6nS3.6034>

## **N-acetyl-cysteine effect on total antioxidant capacity in Iraqi men with oligoasthenoteratozoospermia**

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**Abstract**---The aim of this prospective study is to evaluate the effect of using N-acetyl cysteine (600mg/day) for 3 consecutive months on the serum level of total antioxidant capacity of Iraqi males with idiopathic infertility. This study was performed at infertile center of ALKUT hospital during the period from October 2021 to March 2022 .A total 45 patients with idiopathic oligoasthenoteratozoospermia were received N-acetyl cysteine (NAC) for 12 weeks, their total antioxidant capacity (TAC) was measured at the baseline and after 12 weeks. The results showed that TAC levels were significantly higher ( $0.61 \pm 0.02$  vs.  $0.86 \pm 0.02$  ;  $LSD = 0.10$  ) which confirmed that NAC has positive effect in increasing the level of antioxidant capacity in infertile men and thus decreasing the reactive oxygen species ROS and restore the oxidant balance level resulting in better spermatogenesis and sperm function.

**Keywords**---N-acetyl cysteine, TAC, male infertility.

## Introduction

Infertility is defined as the inability of infertile couples to become pregnant after at least one year of unprotected intercourse, with male factors accounting for roughly half of the documented instances <sup>(1)</sup>. Testicular dysfunction or reproductive tract obstruction are considered secondary to infertility <sup>(2)</sup>. Several reasons of male factor infertility have been identified, however the actual cause in the majority of cases is unknown <sup>(3)</sup>. OS (oxidative stress) is a condition marked by an imbalance between increased cell destruction caused by oxygen and oxygen-dependent free radicals known as reactive oxygen species (ROS) and scavenger antioxidant mechanism over abundance reactive species or repairing the subsequent injuries <sup>(4,5)</sup>. Reactive oxygen species (ROS), also known as free radicals, cause oxidative stress and have a high reactive capacity; ROS could be both endogenous and exogenous. This may result in spermatogenesis problems and infertility in men <sup>(6)</sup>.

ROS play a major role in cell signaling and homoeostasis, they are created in minute amounts by sperm cells and have beneficial functional effects such as initiating sperm capacitation which is an important process to obtain fertilizing facility, regulating sperm maturation, and enhancing cellular signaling pathways <sup>(7,8,9)</sup>. When the sperm cells' natural defense mechanisms fail to heal the damage, an imbalance between reactive oxygen species (ROS) and total antioxidant capacity (TAC) develops <sup>(10)</sup>. However, increased levels of ROS may have negative impacts on sperm function, resulting in infertility. Oxidative stress is a significant factor of the aetiology of male infertility and a primary cause of sperm cell damage <sup>(11)</sup>. An increased level may have negative consequences on sperm Deoxyribonucleic acid (DNA), which causes lipid peroxidation and decreased sperm motility, eventually leading to an increased risk of male factor infertility and birth abnormalities in offspring <sup>(5,9,10,11,12)</sup>.

The body uses dietary and endogenously produced antioxidants to bring the system back to homeostasis, when ROS levels approach a pathological level <sup>(13)</sup>. N-acetyl cysteine (commonly known as NAC) is a precursor to the amino acid L-cysteine and, the antioxidant glutathione (GSH) <sup>(14)</sup>. It is a potent antioxidant agent that, due to its characteristics, can improve both male and female infertility <sup>(15)</sup>. Keeping this in mind, the present study was designed with the aim to evaluate the total antioxidant capacity of infertile males before and after using N acetyl cysteine.

## Study design

This prospective study was conducted at Al-Kut governorate, from November 2021 to April 2022.

## Methods

A total 45 infertile men (20-45) years old for at least one year and diagnosed as idiopathic oligoasthenoteratozoospermia according to world health organization (WHO) classification were referred to Center of Infertility in Al-Kut hospital were subjected to this study. The control group include 20 apparently healthy fertile

volunteers with normal seminal parameters according to WHO (2010). Those patients were admitted to hospital for further investigations, monitoring, and treatment. They have normal female partner, not alcoholics, not suffering from any other serious systemic illnesses like diabetes mellitus, cardiac diseases, renal diseases and hepatic diseases, and didn't have any hormonal disturbances, so as not to interfere with the result of measured parameters and the outcome of the study.

### **Assessment of serum total antioxidant capacity before and after treatment with NAC**

Total Antioxidant Capacity (T-AOC) was measured using Colorimetric Assay Kit (ABTS, Chemical method, mybiosource, USA).

### **Result**

As shown in( table 1) TAC levels were significantly higher ( $0.61 \pm 0.02$  vs.  $0.86 \pm 0.02$  ;  $LSD = 0.10$  ) after treatment with NAC(Asist plus,bilim®) for 3 consecutive months (600mg per day).

Table 1

The effect of treatment with NAC on TAC in idiopathic infertile men compare to pre NAC treatment and control group, Means with a different letter in the same column are significantly different ( $P < 0.05$ )

| GROUPS        | TAC              |
|---------------|------------------|
| Control n=20  | $0.92 \pm 0.06a$ |
| Pre NAC n=45  | $0.61 \pm 0.02b$ |
| Post NAC n=45 | $0.86 \pm 0.02a$ |
| LSD           | 0.10             |

Figure 1 shows the sensitivity (the probability that a test will indicate 'disease' among those with the disease) is (95.6%), Specificity (the fraction of those without the disease who will have a negative test result) is (92.9%) and criterion  $\leq 0.77$ . Worthy to mention that the test with high sensitivity and low specificity means the test has few false negatives (failed test) and many false positives (passed test) respectively.

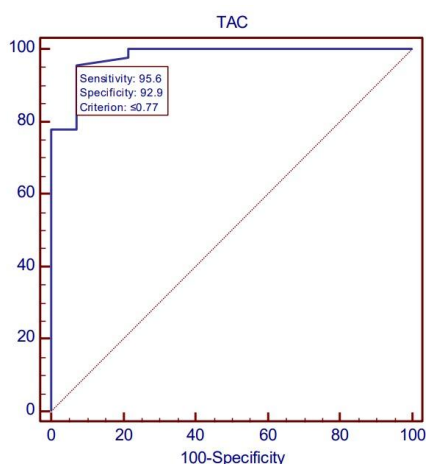


Figure 1. Sensitivity, specificity and criterion values

## Discussion

The elimination of hydroperoxides by glutathione peroxidases and conjugation processes catalyzed by glutathione- S-transferases are examples of cellular defense against oxidative stress <sup>(16)</sup>; as a result, glutathione is fundamental for the body's antioxidant defense system. Glutathione depletion occurs under oxidative stress and can be restored with NAC supplementation. NAC, on the other hand, directly faces free radicals, particularly ROS, and keeps them by donating an electron from its capacity layer via a sulphur group from its chemical composition <sup>(17)</sup>. NAC's antioxidant action in vivo can be attributed to at least three separate pathways, including:

- It has a direct antioxidant impact on specific oxidant species.
- An indirect antioxidant impact due to NAC's capacity to operate as a precursor of Cys, a building block and rate-limiting step in glutathione formation, with GSH being a well-known direct antioxidant and a substrate of multiple antioxidant enzymes.
- A disulphide-breaking effect and the ability to restore thiol pools, that modulate the redox state <sup>(18)</sup>.

## Conclusion

The results approved the positive effect of NAC in increasing the level of antioxidant capacity in infertile men (figure 2) and thus decreasing the ROS and restore the oxidant balance level resulting in better spermatogenesis and sperm function.

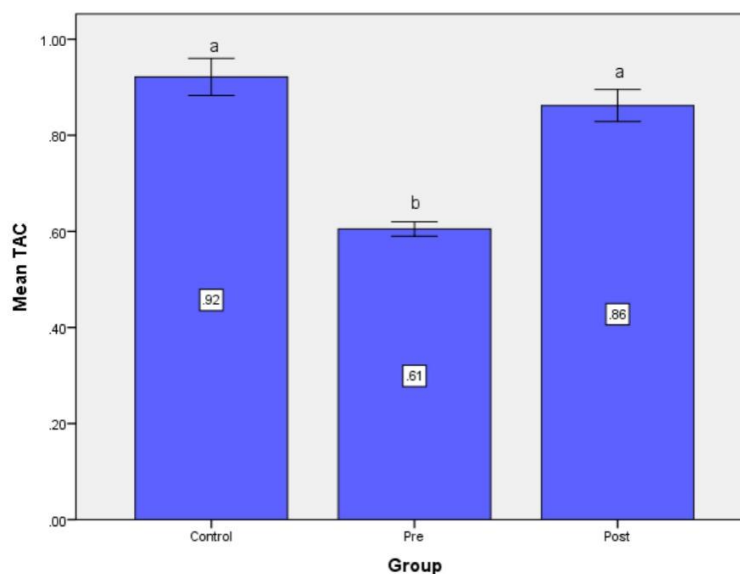


Figure 2. Mean of TAC in control ,pre and post NAC treatment

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