International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 335-340 www.ijprajournal.com ISSN: 2456-4494

Antioxidants and Idiopathic Male Infertility: Their Impact on Sperm Quality Parameters and Pregnancy Rates

Dr. Lokesh. K, Dr. Borus Purushothaman, Dr. Yashmi Agwina Xavier, Veerammal, Dr. Suman Sharma
Dr. Borus Andro Lab And Research Center, Chennai

Date of Submission: 10-09-2024 Date of Acceptance: 20-09-2024

ABSTRACT:
The effect of antioxidants on sperm quality parameters and pregnancy rates in idiopathic male infertility has been a subject of interest in recent reproductive medicine research. Idiopathic male infertility refers to cases where the cause of infertility is unknown despite standard investigations. Oxidative stress has been identified as a potential contributing factor to male infertility. It happens when the body's levels of antioxidants and reactive oxygen species (ROS) are out of equilibrium. Elevated ROS levels can damage sperm by affecting their DNA, membranes, and motility, ultimately compromising fertility. Since antioxidants neutralize ROS, they have been proposed as a treatment to improve sperm function in cases of idiopathic infertility.
Keywords: antioxidants, sperm quality parameters, idiopathic male infertility, pregnancy rate.

I. INTRODUCTION

Infertility affects approximately 15% of couples worldwide; male factors are estimated to be present in about 50% of cases, and 20% of cases have common contributing female factors **[1-3]**. Despite significant advancements in our understanding of the causes of male infertility, idiopathic male infertility remains a difficult condition to diagnose and treat because, unlike unexplained male infertility (UMI) with normal sperm parameters, patients diagnosed with idiopathic male infertility have altered sperm characteristics without a known cause. The cause of female factor infertility must be ruled out **[4-6]**.

The overwhelming body of research indic ates that oxidative stress (OS), which is defined as an imbalance between reactive oxygen species (RO S) and protective antioxidants, is a major factor in t he etiology of male infertility**[7,9].** OS can result in abnormal sperm parameters and high levels of sper m deoxyribonucleic acid fragmentation**[8].** A conce pt known as "male oxidative stress infertility" (MO SI) has recently been proposed, highlighting the fac t that sperm ROS levels are elevated in 30–80% of infertile men, affecting approximately 37.2 million men. Antioxidants may therefore be used to counteract high OS in the treatment of infertility**[10,11,12].** Oral antioxidants have been shown to benefit sperm in a number of trials**[13,14].** Supplementation like Exogenous L-carnitine , L-carnitine+Lcoenzyme-Q10, zinc, selenium, w-3 fatty acid, acetylcarnitine, vitamins C and E have a beneficial effect on sperm parameters**[15,16,17].**

ANTIOXIDANTS AND SPERM QUALITY PARAMETERS

Antioxidants play a significant role in improving sperm quality parameters, particularly by combating oxidative stress, which is known to negatively affect male fertility. Oxidative stress arises from an imbalance between reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants**[18].** Elevated ROS levels can damage sperm cells, leading to decreased motility, abnormal morphology, DNA fragmentation, and reduced overall fertility potential**[19,20].**

Key Sperm Quality Parameters Affected by Antioxidants:

1] Sperm Motility:

Antioxidants, such as Vitamin C, Vitamin E, Coenzyme Q10, and selenium, help protect sperm from oxidative damage, improving their mobility. Poor motility reduces the sperm's ability to swim toward the egg for fertilization.

2] Sperm Count:

A higher concentration of antioxidants can protect the testicular environment from ROS-induced damage, helping to preserve or enhance sperm production. Selenium and zinc are particularly known to support spermatogenesis.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 335-340 www.ijprajournal.com ISSN: 2456-4494

3] Sperm Morphology:

Oxidative stress can lead to abnormal sperm shapes, which may hinder the sperm's ability to fertilize an egg. Antioxidants like folic acid and zinc can help maintain normal sperm morphology.

4] Sperm DNA Integrity:

ROS can cause DNA fragmentation in sperm cells, reducing fertility. Antioxidants like Vitamin C, Vitamin E, and glutathione can protect sperm DNA from oxidative damage, improving genetic integrity.

5] Semen Volume:

Some studies suggest that antioxidants, particularly zinc and selenium, may support the production of seminal fluid, potentially increasing semen volume**[21-25].**

Common Antioxidants for Sperm Health:

- **Vitamin C:** Reduces oxidative damage to sperm and improves DNA integrity.
- **Vitamin E:** Sperm membranes are being protected from oxidative damage.
- **Coenzyme Q10:** Enhances mitochondrial function, leading to improved motility.
- **Zinc:** Essential for spermatogenesis and hormone regulation.
- **Selenium:** Protects sperm from oxidative stress, crucial for motility and DNA protection.
- **L-carnitine:** Enhances sperm motility by providing energy to sperm cells**[1,2,3].**

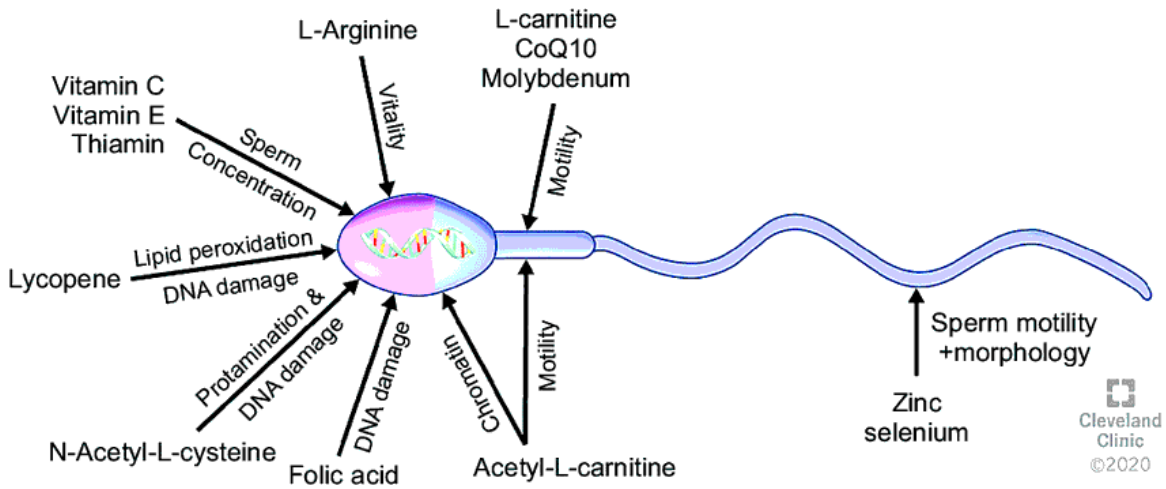

Fig. 1. Antioxidant site of action

THE EFFECT OF ANTIOXIDANTS ON PREGNANCY RATES FOR IDIOPATHIC MALE INFERTILITY

Antioxidants have been increasingly explored as a treatment option for idiopathic male infertility, which is infertility with no identifiable cause after standard testing. One of the key reasons behind their use is the ability of antioxidants to combat oxidative stress, a condition often linked to impaired sperm function even when no obvious cause of infertility is found. Oxidative stress can result in sperm DNA fragmentation, reduced motility, and other factors that affect fertility**[27-29].**

Impact of Antioxidants on Pregnancy Rates

1. Oxidative Stress and Sperm Function

Men with idiopathic infertility often have elevated levels of reactive oxygen species (ROS) in their seminal fluid, which negatively impacts sperm quality. This can reduce the likelihood of successful fertilization and pregnancy. Antioxidants work by neutralizing ROS, thereby reducing oxidative stress and protecting sperm from damage.

2. Improvements in Sperm Parameters

While improvements in sperm quality (motility, count, morphology, and DNA integrity) are often noted with antioxidant use, the relationship between these improvements and

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 335-340 www.ijprajournal.com ISSN: 2456-4494

actual pregnancy rates is complex. Sperm quality improvements, however, can increase the chances of conception, either naturally or via assisted reproductive technologies (ART) such as in vitro fertilization (IVF) or intrauterine insemination (IUI).

3. Clinical Evidence on Pregnancy Rates

Several studies have investigated the effect of antioxidant supplementation on pregnancy rates in men with idiopathic infertility:

- **Systematic Reviews and Meta-Analyses**:

Multiple meta-analyses have shown that antioxidant supplementation may increase pregnancy rates in couples where the male partner has idiopathic infertility. For example, a 2011 Cochrane review found that antioxidant treatment in men was associated with improved pregnancy and live birth rates, though the quality of the evidence varied.

- **Randomized Controlled Trials (RCTs)**:

Some RCTs have demonstrated that antioxidant supplements like Vitamin C, Vitamin E, Coenzyme Q10, selenium, and zinc are associated with higher pregnancy rates, both in natural conception and ART settings. For example:

- **Coenzyme Q10** supplementation has been linked to improved sperm motility and an increase in spontaneous pregnancy rates in certain cases of idiopathic infertility.
- **Vitamin E** supplementation has been found to improve pregnancy rates by enhancing sperm function, particularly when combined with other antioxidants like selenium and zinc.

- **Natural Conception vs. Assisted Reproductive Techniques**:

In natural conception, improvements in sperm quality from antioxidants may translate into better pregnancy outcomes. However, when used in conjunction with ART, antioxidants may improve outcomes such as embryo quality, fertilization rates, and implantation success, thereby increasing pregnancy rates.

4. Antioxidants Commonly Used for Idiopathic Infertility

- **Vitamin C and Vitamin E**: These vitamins work together to reduce oxidative damage to sperm DNA and membranes, with evidence suggesting they enhance natural conception rates.
- **Coenzyme Q10**: Known for improving sperm motility and energy production, it has been associated with higher pregnancy rates.
- **Zinc and Selenium**: Both minerals play crucial roles in sperm production and function, and some studies show they contribute to better outcomes in fertility treatments.
- **L-carnitine**: Promotes sperm energy metabolism, and research suggests it may improve pregnancy rates by enhancing sperm motility.

5. Limitations and Considerations

Not all studies show conclusive evidence for a significant increase in live birth rates, though many do report improvements in sperm parameters. The ideal types and combinations of antioxidants, dosages, and durations of treatment vary, and more research is needed to establish standardized protocols. Antioxidant supplementation may not be effective for all men with idiopathic infertility, especially if there are other underlying factors contributing to infertility that have not been identified **[30-42].**

II. CONCLUSION

Antioxidants show promising results in improving pregnancy rates in men with idiopathic infertility, particularly through their positive effects on sperm quality and the reduction of oxidative stress. While evidence supports their use in increasing both natural conception and success rates with assisted reproductive techniques, more large-scale, high-quality studies are needed to fully understand the best treatment protocols and to confirm their efficacy across diverse populations. Research supports the positive effect of antioxidants on sperm quality parameters such as motility, morphology, count, and DNA integrity. These improvements, in turn, are associated with increased pregnancy rates, particularly in men with idiopathic infertility.

REFERENCE:

[1]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr. Yashmi Agwina Xavier, Veerammal, Dr. Suman Sharma, The Impact of Oxidative Stress in Male Infertility; Dr. Borus Andro Lan and Research Center, Chennai, 2024. Volume 9, Issue 5 Sep - Oct 2024, pp: 177-185.

[2]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr. Harini. V, veerammal, Dr. Suman sharma, Antioxidant Supplementation and Duration of Antioxidant in Male Infertility

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 5 Sep - Oct 2024, pp: 335-340 www.ijprajournal.com ISSN: 2456-4494

– A Systemic Review; Dr. Borus Andro Lan and Research Center, Chennai, 2024.
[3]. Dr. Lokesh. K, Dr. Borus Purushothaman, Dr. Harini. V, veerammal, Dr. Suman sharma, A Comprehensive Approach and Critical Evaluation of Clinical Practice Guidelines for Sperm DNA Fragmentation; Dr. Borus Andro Lan and Research Center, Chennai, 2024. Volume 9, Issue 3 May-June 2024, pp: 844-848.
[4]. Hussein TM, Eldabah N, Zayed HA. Assessment of Serum Vitamin D Level and Seminal Vitamin D Receptor Gene Methylation in a Sample of Egyptian Men With Idiopathic Infertility. Andrologia (2021) 53:e14172. doi: 10.1111/ and.14172
[5]. Kokubu D, Ooba R, Abe Y, Ishizaki H, Yoshida S, Asano A, et al. Angelica Keiskei (Ashitaba) Powder and its Functional Compound Xanthoangelol Prevent Heat Stress-Induced Impairment in Sperm Density and Quality in Mouse Testes. J Reprod Dev (2019) 65:139–46. doi: 10.1262/jrd.2018-141
[6]. Illiano E, Trama F, Zucchi A, Iannitti RG, Fioretti B, Costantini E. Resveratrol-Based Multivitamin Supplement Increases Sperm Concentration and Motility in Idiopathic Male Infertility: A Pilot Clinical Study. J Clin Med (2020) 9:4017. doi: 10.3390/jcm9124017
[7]. Agarwal A, Parekh N. Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practice Guidelines for Management of Idiopathic Male Infertility. World J Mens Health (2019) 37:296–312. doi: 10.5534/ wjmh.190055
[8]. Ko EY, Siddiqi K, Brannigan RE, Sabanegh ESJr. Empirical Medical Therapy for Idiopathic Male Infertility: A Survey of the American Urological Association. J Urol (2012) 187:973–8. doi: 10.1016/j.juro.2011.10.137
[9]. Russo A, Troncoso N, Sanchez F, Garbarino JA, Vanella A. Propolis Protects Human Spermatozoa From DNA Damage Caused by Benzo[a]Pyrene and Exogenous Reactive Oxygen Species. Life Sci (2006) 78:1401–6. doi: 10.1016/ j.lfs.2004.10.085
[10]. Adeoye O, Olawumi J, Opeyemi A, Christiania O. Review on the Role of Glutathione on Oxidative Stress and Infertility. JBRA Assist Reprod (2018) 22:61–6. doi: 10.5935/1518-0557.20180003
[11]. Kumar N, Singh AK. Reactive Oxygen Species in Seminal Plasma as a Cause of Male Infertility. J Gynecol Obstet Hum Reprod (2018) 47:565–72. doi: 10.1016/j.jogoh.2018.06.008
[12]. Majzoub A, Agarwal A, Esteves SC. Antioxidants for Elevated Sperm DNA Fragmentation: A Mini Review. Transl Androl Urol (2017) 6:S649–s53. doi: 10.21037/tau.2017.07.09
[13]. Arafa M, Agarwal A. Efficacy of Antioxidant Supplementation on Conventional and Advanced Sperm Function Tests in Patients With Idiopathic Male Infertility. Antioxid (Basel) (2020) 9:219. doi: 10.3390/ antiox9030219
[14]. Omar MI, Pal RP, Kelly BD, Bruins HM, Yuan Y, Diemer T, et al. Benefits of Empiric Nutritional and Medical Therapy for Semen Parameters and Pregnancy and Live Birth Rates in Couples With Idiopathic Infertility: A Systematic Review and Meta-Analysis. Eur Urol (2019) 75:615–25. doi: 10.1016/j.eururo.2018.12.022
[15]. NohS, GoA,KimDB,ParkM,JeonHW,KimB.Role ofAntioxidant Natural Products in Management of Infertility: A Review of Their Medicinal Potential. Antioxid (Basel) (2020) 9:957. doi: 10.3390/antiox9100957
[16]. Ali M, Martinez M, Parekh N. Are Antioxidants a Viable Treatment Option for Male Infertility? Andrologia (2020) 53:e13644. doi: 10.1111/and.13644
[17]. Song F, Loke YK, Walsh T, Glenny AM, Eastwood AJ, Altman DG. Methodological Problems in the Use of Indirect Comparisons for Evaluating Healthcare Interventions: Survey of Published Systematic Reviews. Bmj (2009) 338:b1147. doi: 10.1136/bmj.b1147
[18]. Buhling K, Schumacher A, Eulenburg CZ, Laakmann E. Influence of Oral Vitamin and Mineral Supplementation on Male Infertility: A Meta-Analysis and Systematic Review. Reprod BioMed

Online (2019) 39:269–79. doi: 10.1016/j.rbmo.2019.03.099

[19]. Safarinejad MR, Safarinejad S. The Roles of Omega-3 and Omega-6 Fatty Acids in Idiopathic Male Infertility. Asian J Androl (2012) 14:514–5. doi: 10.1038/aja.2012.46

[20]. Agarwal A, Nallella KP, Allamaneni SS, Said TM. Role of Antioxidants in Treatment of Male Infertility: An Overview of the Literature. Reprod BioMed Online (2004) 8:616–27. doi: 10.1016/s1472-6483(10)61641-0

[21]. Agarwal A, Mulgund A, Hamada A, Chyatte MR, A unique view on male infertility around the globe, Reprod Biol Endocrinol, 2015,13,37.

[22]. Agarwal A, Parekh N, Panner Selvam MK, Henkel R, Shah R, Homa ST, et al. Male oxidative stress infertility (MOSI), proposed terminology and clinical practice guidelines for management of idiopathic male infertility, World J Mens Health, 2019,37,296 312.

[23]. Hamada A, Esteves SC, Nizza M, Agarwal A. Unexplained male infertility, diagnosis and management, Int Braz J Urol, 2012,38,576-94.

[24]. Leisegang K, Henkel R. Oxidative stress, relevance, evaluation, and management. In, Rizk B, Agarwal A, Sabanegh ES, Male infertility in reproductive medicine, diagnosis and management, Boca Raton, 2019, 119-28

[25]. Cardoso JP, Cocuzza M, Elterman D. Optimizing male fertility, oxidative stress and the use of antioxidants, World J Urol, 2019,37,1029-34.

[26]. Kuchakulla M, Soni Y, Patel P, Parekh N, Ramasamy R. A systematic review and evidence based analysis of ingredients in popular male fertility supplements, Urology 2020,136,133-41.

[27]. Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. Cochrane Database Syst Rev, 2011,1, 120-125

[28]. Showell MG, Mackenzie-Proctor R, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility, Cochrane Database Syst Rev, 2014,12,1-10

[29]. Majzoub A, Agarwal A. Systematic review of antioxidant types and doses in male infertility, benefits on semen parameters, advanced sperm function, assisted reproduction and live-birth rate, Arab J Urol 2018,16,113-24.

[30]. Smits RM, Mackenzie-Proctor R, Yazdani A, Stankiewicz MT, Jordan V, Showell MG. Antioxidants for male subfertility. Cochrane Database Syst Rev 2019,3, 213 - 220

[31]. Adewoyin M, Ibrahim M, Roszaman R, Isa MLM, Alewi NAM, Rafa AAA, et al. Male infertility, the effect of natural antioxidants and phytocompounds on seminal oxidative stress. Diseases 2017,5,9.

[32]. Keskes-Ammar L, Feki-Chakroun N, Rebai T, Sahnoun Z, Ghozzi H, Hammami S, et al. Sperm oxidative stress and the effect of an oral vitamin E and selenium supplement on semen quality in infertile men, Arch Androl, 2003,49,83-94.

[33]. Ménézo YJ, Hazout A, Panteix G, Robert F, Rollet J, CohenBacrie P, et al. Antioxidants to reduce sperm DNA fragmentation, an unexpected adverse effect. Reprod Biomed Online, 2007,14,418-21.

[34]. Henkel R, Sandhu IS, Agarwal A. The excessive use of antioxidant therapy, a possible cause of male infertility? Andrologia 2019,51,31-62.

[35]. Panner Selvam MK, Agarwal A, Henkel R, Finelli R, Robert KA, Iovine C, et al. The effect of oxidative and reductive stress on semen parameters and functions of physiologically normal human spermatozoa. Free Radic Biol Med, 2020,152,375-85.

[36]. Arafa M, Agarwal A, Majzoub A, Panner Selvam MK, Baskaran S, Henkel R, et al. Efficacy of antioxidant supplementation on conventional and advanced sperm function tests in patients with idiopathic male infertility. Antioxidants (Basel) 2020,9,219.

[37]. Tremellen K, Miari G, Froiland D, Thompson J. A randomised control trial examining the effect of an antioxidant (Menevit) on pregnancy outcome during IVF-ICSI treatment, Aust N Z J Obstet Gynaecol, 2007,47,216-21.

[38]. Tunc O, Thompson J, Tremellen K. Improvement in sperm DNA quality using

an oral antioxidant therapy. Reprod Biomed Online,2009,18,761-8.

[39]. Shukla KK, Mahdi AA, Ahmad MK, Jaiswar SP, Shankwar SN, Tiwari SC. Mucuna pruriens reduces stress and improves the quality of semen in infertile 25 men, Evid Based Complement Alternat Med, 2010,7,137-44.

[40]. Bejarano I, Monllor F, Marchena AM, Ortiz A, Lozano G, Jiménez MI, et al. Exogenous melatonin supplementation prevents oxidative stress-evoked DNA damage in human spermatozoa, J Pineal Res, 2014,57,333-9.

[41]. Moslemi MK, Tavanbakhsh S. Selenium-vitamin E supplementation in infertile men, effects on semen parameters and pregnancy rate. Int J Gen Med 2011,4,99-104.

[42]. Ajayi R, Okhowat J, Spitzer D, Schechinger B, Zech NH. Impact of antioxidative supplementation on semen quality according to MSOME criteria. JBRA Assist Reprod, 2013,17,27-31.