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Original Article

Investigating the Efficacy of Antioxidant Supplements in Treating Oxidative Stress-Induced Male Infertility: A Randomized Controlled Trial

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ABSTRACT

Background: Excessive seminal oxidative stress may impair sperm motility, membrane integrity, mitochondrial function, and DNA stability, but the therapeutic value of antioxidant supplementation remains uncertain. Objective: To determine whether combined vitamin C, vitamin E, and coenzyme Q10 supplementation improves sperm quality and oxidative-stress markers in infertile men with laboratory evidence of seminal oxidative stress. Methods: This randomized, double-blind, placebo-controlled trial enrolled 120 men aged 20–45 years at Akbar Niazi Teaching Hospital, Islamabad, Pakistan, from January to December 2025. Participants were allocated equally to receive vitamin C 500 mg, vitamin E 400 IU, and coenzyme Q10 200 mg daily or matching placebo for 12 weeks. The primary outcome was progressive sperm motility. Secondary outcomes included sperm concentration, total motility, normal morphology, DNA fragmentation index, and seminal oxidation-reduction potential. Week-12 outcomes were compared using analysis of covariance adjusted for baseline values. Results: Progressive motility increased from 25.3% to 35.0% in the antioxidant group and from 25.4% to 28.2% in the placebo group. The adjusted between-group difference was 6.90 percentage points (95% CI, 5.02–8.78; $p<0.001$). Antioxidant supplementation also improved sperm concentration (adjusted difference, 3.08 million/mL), total motility (6.83 percentage points), and normal morphology (0.45 percentage points) and reduced DNA fragmentation (−7.06 percentage points) and oxidation-reduction potential (−0.53 mV/10^6 sperm/mL). No serious treatment-related adverse event occurred. Conclusion: Twelve weeks of combined antioxidant supplementation improved several semen and oxidative-stress measures, but its effect on pregnancy and live birth remains undetermined. Keywords: Male infertility; oxidative stress; antioxidants; vitamin C; vitamin E; coenzyme Q10; sperm motility; sperm DNA fragmentation; randomized controlled trial.

INTRODUCTION

Infertility is a major reproductive health concern affecting couples worldwide, with male-related factors contributing independently or in combination with female factors in a substantial proportion of cases. Male infertility may be characterized by reduced sperm concentration, impaired motility, abnormal morphology, diminished vitality, or compromised sperm DNA integrity. Although genetic, anatomical, endocrine, infectious, environmental, and lifestyle-related factors may contribute to impaired male reproductive function, an identifiable cause is not established in many affected men. Oxidative stress has

consequently emerged as an important biological mechanism underlying otherwise unexplained abnormalities in semen quality (1–4).

Reactive oxygen species have physiological roles in sperm maturation, capacitation, hyperactivation, and the acrosome reaction. However, excessive production of these molecules, or inadequate antioxidant defence within seminal plasma, may disrupt the normal redox balance. Spermatozoa are particularly susceptible to oxidative injury because their plasma membranes contain abundant polyunsaturated fatty acids, their cytoplasmic antioxidant capacity is limited, and their ability to repair damaged DNA is restricted. Excessive reactive oxygen species may therefore induce lipid peroxidation, impair mitochondrial energy production, reduce sperm motility, alter membrane function, and increase sperm DNA fragmentation (1–8). These changes may reduce the probability of natural conception and adversely influence fertilization, embryo development, and assisted reproductive outcomes.

Several clinical and lifestyle-related factors may contribute to seminal oxidative stress, including smoking, obesity, genital tract infection, varicocele, metabolic disorders, poor diet, psychological stress, excessive heat exposure, air pollution, and occupational contact with reproductive toxicants. Activated leukocytes and structurally abnormal spermatozoa may also increase reactive oxygen species production within semen. When oxidant generation exceeds the antioxidant capacity of seminal plasma, progressive damage to sperm membranes, proteins, mitochondria, and nuclear DNA may occur (3–8).

Evidence from Pakistan has also demonstrated an association between oxidative imbalance and male infertility. Previous local investigations have reported greater oxidative stress and lower antioxidant activity among infertile men than among fertile controls and have highlighted potential relationships among oxidative stress, nutritional deficiencies, metabolic health, and impaired male reproductive function (9–11). Nevertheless, interventional evidence from Pakistan remains limited, and antioxidant treatment is commonly prescribed on the basis of international studies conducted in populations that may differ in nutritional status, environmental exposure, supplement use, and underlying causes of infertility.

Antioxidant supplementation represents a relatively accessible and non-invasive therapeutic approach for men with evidence of oxidative stress. Vitamin C is a water-soluble antioxidant that may neutralize reactive oxygen species within seminal plasma and contribute to the regeneration of other antioxidants. Vitamin E is lipid soluble and may protect the polyunsaturated fatty acids of the sperm membrane from lipid peroxidation. Coenzyme Q10 functions both as an antioxidant and as a component of mitochondrial electron transport, thereby providing a biological rationale for its potential effects on sperm energy production and motility (12–16). A combination of these agents may therefore provide complementary protection within the aqueous, lipid, and mitochondrial compartments of spermatozoa.

Despite this biological rationale, evidence concerning antioxidant therapy for male infertility remains inconsistent. Systematic reviews and meta-analyses have reported improvements in sperm concentration, total and progressive motility, morphology, and DNA integrity following treatment with selected antioxidants, although substantial heterogeneity has been observed across supplement formulations, doses, treatment durations, participant characteristics, and outcome-assessment methods (13–18). Randomized trials evaluating coenzyme Q10, vitamin-based combinations, and multimicronutrient preparations have similarly reported improvements in selected semen parameters (19–22). In contrast, the Males, Antioxidants, and Infertility randomized clinical trial did not demonstrate clear improvements in semen quality, sperm DNA fragmentation, pregnancy, or live birth following treatment with a combined antioxidant preparation (23). Another placebo-controlled trial found no significant reduction in the sperm DNA fragmentation index after antioxidant treatment (24).

The conflicting findings may partly reflect inadequate patient selection. Many previous studies enrolled heterogeneous infertility populations without establishing whether participants had increased oxidative stress at baseline. Antioxidant supplementation may be less likely to benefit men with a normal seminal

redox balance and, when used indiscriminately or for prolonged periods, could theoretically disturb physiological redox signalling. Other limitations of the available evidence include small sample sizes, variable treatment regimens, short follow-up periods, inconsistent laboratory methods, and reliance on routine semen parameters without concurrent assessment of sperm DNA integrity or seminal oxidative status (13–18,23,24).

A randomized, placebo-controlled trial involving men with both abnormal semen findings and laboratory evidence of seminal oxidative stress was therefore warranted. Evaluating routine semen characteristics together with sperm DNA fragmentation and oxidation-reduction potential could provide a more comprehensive assessment of whether antioxidant supplementation influences the proposed biological pathway as well as conventional markers of sperm function. The present study evaluated the effects of a 12-week daily combination of vitamin C, vitamin E, and coenzyme Q10 on progressive sperm motility in infertile men with confirmed seminal oxidative stress. Secondary objectives were to compare changes in sperm concentration, total sperm count, total motility, normal morphology, sperm DNA fragmentation, and seminal oxidation-reduction potential between the antioxidant and placebo groups. It was hypothesized that antioxidant supplementation would produce a greater improvement in progressive sperm motility and related laboratory outcomes than placebo.

MATERIALS AND METHODS

This randomized, double-blind, placebo-controlled clinical trial was conducted at the infertility and andrology services of Akbar Niazi Teaching Hospital, Islamabad, Pakistan, between January and December 2025. The study evaluated the effects of a 12-week antioxidant regimen on semen quality, sperm DNA integrity, and seminal oxidative status in men with infertility and laboratory evidence of oxidative stress. A 12-week intervention period was selected to encompass a substantial proportion of the spermatogenic and epididymal maturation cycle and thereby permit assessment of treatment-related changes in semen characteristics. The trial was designed and reported in accordance with the Consolidated Standards of Reporting Trials recommendations for randomized controlled trials (25).

Male patients presenting to the infertility and andrology services were screened for eligibility. Men aged 20–45 years were considered eligible when the couple had been unable to achieve pregnancy after at least 12 months of regular unprotected sexual intercourse, at least one semen parameter was abnormal, and seminal oxidative stress was confirmed. Abnormal semen findings included reduced sperm concentration, reduced progressive motility, or abnormal sperm morphology. Two semen specimens were assessed before enrolment to confirm the persistence of the semen abnormality. Seminal oxidative status was evaluated by measuring oxidation-reduction potential using the validated procedure available in the hospital laboratory.

Men were excluded if they had azoospermia, active reproductive tract infection, uncontrolled diabetes mellitus, a serious hormonal disorder, testicular malignancy, a known genetic cause of infertility, or a history of chemotherapy. Additional exclusion criteria were a febrile illness during the preceding three months, severe varicocele requiring surgical treatment, current use of fertility medication, or antioxidant supplementation during the preceding three months. Participants were also instructed not to commence any additional vitamin, mineral, herbal, antioxidant, or fertility supplement during the intervention period.

A total of 120 eligible participants were enrolled and allocated equally to the antioxidant and placebo groups. The sample size was based on the anticipated between-group difference in progressive sperm motility, which was designated as the primary outcome. The calculation incorporated a two-sided significance level of 5%, statistical power of 80%, and an allowance of 10% for attrition, resulting in a target sample of 60 participants in each group.

Participants were assigned in a 1:1 ratio using a computer-generated random allocation sequence prepared by a researcher who was not involved in recruitment, clinical management, laboratory assessment, or statistical analysis. Allocation assignments were placed in sequentially numbered, sealed, opaque envelopes and remained concealed until participants had completed eligibility assessment and enrolment. The antioxidant and placebo preparations were made comparable in appearance, size, packaging, and taste. Participants, treating clinicians, laboratory personnel, and the statistician remained unaware of treatment allocation during participant follow-up, laboratory assessment, and the primary statistical analysis.

Participants assigned to the intervention group received vitamin C 500 mg, vitamin E 400 IU, and coenzyme Q10 200 mg orally each day for 12 weeks. The daily dose was taken after a main meal. The selected agents were intended to provide complementary antioxidant activity within seminal plasma, sperm membranes, and mitochondrial pathways and were based on regimens evaluated in previous clinical studies of male infertility (14–16,19–23). Participants assigned to the control group received a matching placebo according to the same administration schedule and for the same duration.

Both groups received standardized general advice concerning a balanced diet, moderate physical activity, adequate sleep, smoking cessation, and avoidance of prolonged testicular heat exposure. Participants were advised to maintain their usual medical care but to avoid initiating fertility medicines or nutritional and herbal supplements during the trial. Follow-up visits were conducted at four-week intervals. At each visit, participants returned unused capsules, received the next treatment supply, and were questioned about adherence, protocol deviations, concomitant treatment, and adverse events. Adherence was assessed by capsule count, and consumption of at least 80% of the supplied capsules was considered satisfactory.

Semen specimens were collected at baseline and following completion of the 12-week intervention. Participants were instructed to maintain two to seven days of ejaculatory abstinence before each collection. Samples were obtained by masturbation into sterile, wide-mouth collection containers in a private room at the study site. Each specimen was allowed to liquefy and was examined within one hour of collection. Semen volume, sperm concentration, total sperm count, progressive motility, total motility, vitality, and normal morphology were evaluated in accordance with the sixth edition of the World Health Organization laboratory manual for the examination and processing of human semen (26). Laboratory personnel remained blinded to treatment allocation throughout specimen processing and outcome assessment.

Sperm DNA fragmentation was assessed using the sperm chromatin dispersion method and expressed as the DNA fragmentation index. Seminal oxidative status was reassessed at week 12 using the same oxidation-reduction potential procedure employed at baseline. The same sample-collection requirements, laboratory procedures, and outcome definitions were applied at both assessment points to reduce measurement variability.

The prespecified primary outcome was the between-group difference in the change in progressive sperm motility from baseline to week 12. Secondary outcomes included changes in sperm concentration, total sperm count, total motility, normal sperm morphology, sperm DNA fragmentation index, and seminal oxidation-reduction potential. Treatment adherence and adverse events were assessed throughout the intervention. Pregnancies occurring among participants' partners during follow-up were recorded as an exploratory outcome because the study was not powered to determine an effect on pregnancy or live birth.

Data were entered and analysed using IBM SPSS Statistics for Windows. Continuous variables were summarized as mean and standard deviation when approximately normally distributed and as median and interquartile range when distributional assumptions were not met. Categorical variables were presented as frequencies and percentages. Baseline characteristics were summarized descriptively

according to randomized group. Between-group comparisons of continuous outcomes were performed using the independent-samples t-test or Mann–Whitney U test, as appropriate, while within-group changes were evaluated using the paired-samples t-test or Wilcoxon signed-rank test. Categorical variables were compared using the chi-square test or Fisher's exact test according to expected cell frequencies.

The principal treatment effects at week 12 were estimated using analysis of covariance, with the corresponding week-12 outcome entered as the dependent variable, randomized treatment group entered as the principal explanatory variable, and the baseline value of the outcome included as a covariate. Adjusted between-group mean differences were reported with 95% confidence intervals. Outcome-specific analyses included participants for whom the corresponding baseline and follow-up measurements were available, and participants were analysed according to their original randomized allocation. Secondary outcomes and exploratory pregnancy comparisons were interpreted cautiously because the study was powered for progressive sperm motility and no adjustment for multiple secondary comparisons was specified. All statistical tests were two-sided, and a p-value below 0.05 was considered statistically significant. The study received institutional approval from Akbar Niazi Teaching Hospital, Islamabad, Pakistan. Participant information was handled confidentially, and study procedures were conducted within the institution's approved ethical framework.

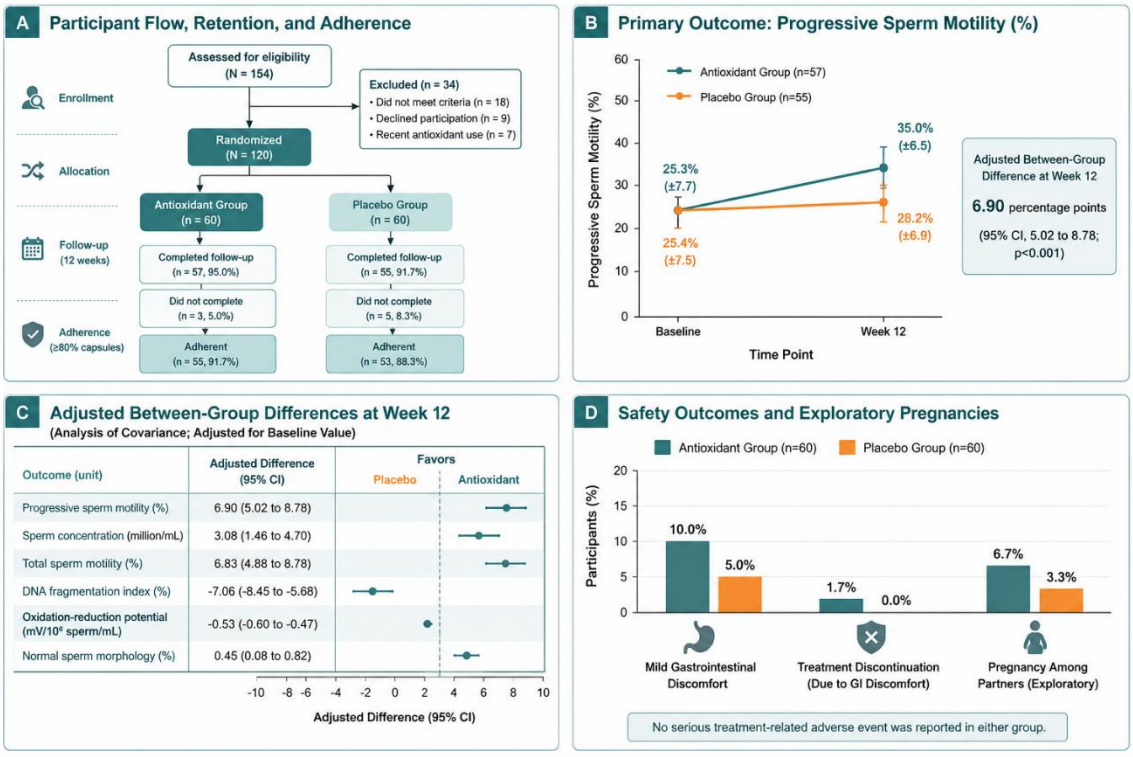

Figure 1: Participant flow, primary outcome trajectory, adjusted treatment effects, and safety outcomes following 12 weeks of antioxidant supplementation. Panel A presents eligibility assessment, randomization, retention, and adherence. Panel B shows progressive sperm motility at baseline and week 12, with error bars representing reported standard deviations. Panel C presents adjusted between-group effects with 95% confidence intervals in their native measurement units. Panel D compares gastrointestinal discomfort, treatment discontinuation, and exploratory pregnancy events. Progressive sperm motility increased from 25.3% to 35.0% in the antioxidant group compared with 25.4% to 28.2% in the placebo group, producing an adjusted difference of 6.90 percentage points (95% CI, 5.02–8.78; p<0.001). Significant treatment effects also favoured antioxidant supplementation for sperm concentration, total motility, DNA fragmentation, morphology, and oxidation-reduction potential. Mild gastrointestinal discomfort occurred in 10.0% versus 5.0%, while pregnancy events occurred in 6.7% versus 3.3%; the latter remained exploratory because of the small number of events.

DISCUSSION

The present randomized, double-blind, placebo-controlled trial found that 12 weeks of combined vitamin C, vitamin E, and coenzyme Q10 supplementation produced a greater improvement in progressive sperm motility than placebo among men with abnormal semen findings and laboratory evidence of seminal oxidative stress. The antioxidant group also demonstrated higher sperm concentration and total motility and lower sperm DNA fragmentation and oxidation-reduction potential at week 12. Normal sperm morphology showed a smaller between-group difference. The intervention was generally well tolerated, with no serious treatment-related adverse events reported. These findings indicate that the studied antioxidant combination affected several laboratory measures of sperm function and seminal redox status, although the trial did not establish an improvement in clinical pregnancy or live birth.

The primary finding was the adjusted between-group difference of 6.90 percentage points in progressive sperm motility. This result was supported by an observed increase from 25.3% to 35.0% in the antioxidant group, compared with an increase from 25.4% to 28.2% in the placebo group. Progressive motility is an important functional semen characteristic because forward sperm movement contributes to transport through the female reproductive tract and interaction with the oocyte. Nevertheless, semen parameters are surrogate laboratory outcomes and should not be interpreted as direct evidence of improved natural conception, clinical pregnancy, or live birth.

The improvement in progressive motility was consistent with previous randomized trials and evidence syntheses reporting beneficial effects of coenzyme Q10 and selected antioxidant preparations on sperm motility. Balercia et al. found improved motility after coenzyme Q10 treatment among men with idiopathic asthenozoospermia, while Alahmar reported improvements in motility and antioxidant status among men with idiopathic oligoasthenospermia (19,20). Systematic reviews have similarly identified coenzyme Q10 as one of the more consistently promising antioxidant interventions for sperm concentration and motility, although substantial heterogeneity has remained across trials (16,17).

A biologically plausible explanation for the motility findings is the combined action of the three antioxidant components. Coenzyme Q10 participates in mitochondrial electron transport and may support adenosine triphosphate production required for sperm movement. Vitamin E may reduce lipid peroxidation within the polyunsaturated fatty acid-rich sperm membrane, while vitamin C may contribute to antioxidant protection within seminal plasma. The observed improvement in motility was therefore consistent with, but did not directly prove, an effect on mitochondrial function, membrane integrity, or intracellular energy metabolism because these mechanisms were not independently measured in the trial (12,13,16).

Sperm concentration also increased more in the antioxidant group than in the placebo group. The adjusted difference of 3.08 million/mL was smaller in relative magnitude than the effect observed for progressive and total motility. Oxidative stress may impair developing germ cells through membrane, protein, mitochondrial, and DNA damage, and reducing this burden could improve sperm survival or preservation during spermatogenesis and epididymal maturation (1–8). However, the 12-week intervention covered only a limited observation period, and the trial did not evaluate testicular histology, endocrine function, germ-cell apoptosis, or spermatogenic kinetics. The concentration result should therefore be interpreted as a change in the measured semen parameter rather than evidence of a specific regenerative mechanism.

Total sperm motility improved by an observed 7.2 percentage points in the antioxidant group but changed minimally in the placebo group. This pattern was aligned with the primary progressive-motility result and suggested that the intervention predominantly affected functional sperm movement. Previous trials of coenzyme Q10 and multimicronutrient formulations have also reported improvements in motility-related outcomes, although differences in intervention composition, dose, baseline nutritional status, and participant selection limit direct comparisons (19–22).

A clinically relevant biological finding was the reduction in sperm DNA fragmentation. The antioxidant group showed an observed decline of 9.4 percentage points, compared with a 2.1-point decline in the placebo group, with an adjusted between-group difference of −7.06 percentage points. Excessive reactive oxygen species may induce oxidative base modification, strand breaks, mitochondrial dysfunction, and membrane injury in spermatozoa, which have limited DNA-repair capacity (3–8). The present result was consistent with the meta-analysis by Noegroho et al., which found that antioxidant supplementation may reduce sperm DNA fragmentation while improving selected semen parameters (18).

The DNA-fragmentation finding was not fully consistent with all previous trials. Stenqvist et al. did not identify a significant improvement in DNA fragmentation after combined antioxidant treatment (24). Differences in eligibility criteria may have contributed to the contrasting findings. The present trial selected participants with laboratory evidence of oxidative stress, whereas broader infertility trials may have included men with normal redox balance who had less potential to respond to antioxidant therapy. This explanation remains a hypothesis because the study did not include a prespecified interaction analysis comparing participants across different baseline oxidative-stress levels.

The reduction in seminal oxidation-reduction potential provided evidence that the intervention affected the biological pathway it was intended to target. Oxidation-reduction potential decreased from 1.75 to 1.11 mV/10^6 sperm/mL in the antioxidant group and from 1.88 to 1.73 mV/10^6 sperm/mL in the placebo group. The adjusted difference of −0.53 mV/10^6 sperm/mL was statistically precise. The concurrent changes in oxidation-reduction potential, progressive motility, total motility, and DNA fragmentation were consistent with a relationship between improved seminal redox balance and sperm function. However, mediation could not be established because the trial did not report a formal analysis examining whether the change in oxidative status explained the treatment effects on semen outcomes.

The findings should also be considered in relation to the Males, Antioxidants, and Infertility trial, which did not demonstrate clear benefits of a combined antioxidant formulation for semen parameters, sperm DNA fragmentation, pregnancy, or live birth (23). The discrepancy may reflect differences in supplement composition, dosage, treatment duration, baseline infertility characteristics, laboratory methods, adherence, and participant selection. In particular, enrolment based on evidence of seminal oxidative stress may have increased the likelihood of observing a laboratory response in the present study. Nevertheless, the present results should not be interpreted as disproving the MOXI findings or establishing that all men with infertility and oxidative stress will benefit from supplementation.

Normal sperm morphology showed an adjusted difference of only 0.45 percentage points. Although the confidence interval excluded zero, the magnitude was modest and its clinical importance is uncertain. Morphology may be influenced by testicular development, genetic factors, environmental exposures, laboratory staining and classification procedures, and observer variability. It may also respond less rapidly than motility or redox-related outcomes. Previous evidence has similarly shown less consistent effects of antioxidant supplementation on morphology than on motility and concentration (16,17,19).

Both groups showed some improvement in selected semen outcomes, including progressive motility and DNA fragmentation. Several factors may account for this pattern. Semen parameters demonstrate natural intra-individual variability, and enrolment based on abnormal baseline results may introduce regression toward the mean during repeated testing. Both groups also received advice concerning diet, physical activity, sleep, smoking cessation, and avoidance of prolonged heat exposure. Behavioural changes associated with this advice could have contributed to improvements independent of the allocated capsules. Repeated contact with study personnel, adherence monitoring, and avoidance of other supplements or fertility medicines may also have influenced participant behaviour.

No serious treatment-related adverse events were reported. Mild gastrointestinal discomfort occurred in 10.0% of participants assigned to antioxidants and 5.0% assigned to placebo, and one participant discontinued antioxidant treatment because of persistent discomfort. This safety pattern was broadly

consistent with previous reviews in which major harms were uncommon but mild gastrointestinal symptoms occurred in some participants (14). The relatively short intervention and modest sample size, however, limited the ability to detect uncommon, delayed, or dose-related adverse effects.

Four pregnancies occurred among partners of men in the antioxidant group and two among partners of men in the placebo group. These event numbers were too small to support a reliable comparison, and pregnancy was not the outcome on which the sample size was based. Conception is influenced by numerous factors not captured by semen analysis alone, including female-partner age and reproductive health, intercourse timing, duration of infertility, use of assisted reproductive procedures, and embryo-related factors. The numerical difference in pregnancy events should therefore be treated as exploratory and should not be used to claim improved fertility or reproductive success.

The study had several strengths. Random allocation, use of a matching placebo, masking of participants and outcome assessors, repeated follow-up, and assessment of both conventional semen parameters and biologically relevant measures strengthened the trial design. The evaluation of sperm DNA fragmentation and seminal oxidation-reduction potential provided information beyond routine semen analysis. Selecting men with evidence of oxidative stress also addressed a clinically relevant limitation of previous trials that evaluated heterogeneous infertility populations without biomarker-based selection.

Several limitations should be acknowledged. The trial was conducted at a single centre and included a relatively modest sample, which restricted generalizability and the precision of uncommon safety and pregnancy outcomes. The intervention lasted 12 weeks, and longer-term persistence of the observed laboratory changes was not assessed. Clinical pregnancy and live birth were not adequately powered outcomes. Female-partner characteristics, fertility treatment during follow-up, dietary antioxidant intake, environmental exposures, and objective behavioural changes were not comprehensively reported and may have influenced reproductive outcomes.

Eight randomized participants did not complete follow-up, and the available manuscript information did not establish a specific imputation or model-based procedure for missing outcome data. The revised analysis therefore requires clear reporting of outcome-specific denominators and the actual missing-data approach. In addition, multiple secondary outcomes were tested without a reported multiplicity adjustment, and these findings should be interpreted as supportive rather than independently confirmatory. The exact assay specifications and positivity threshold used to define seminal oxidative stress also require complete reporting to permit replication. Trial-registration information, full ethics-approval details, supplement and placebo manufacturing information, and the complete allocation and masking procedures must be documented in the final manuscript from authentic study records.

The findings support further evaluation of a targeted rather than indiscriminate approach to antioxidant use in male infertility. Future multicentre trials should prospectively register a detailed protocol, use standardized oxidative-stress definitions and assay procedures, prespecify clinically meaningful treatment effects, and apply robust methods for handling missing data and multiple outcomes. Follow-up should extend beyond semen analysis to clinical pregnancy, pregnancy loss, and live birth, with appropriate evaluation of both partners. Comparative trials could also determine whether baseline oxidation-reduction potential identifies men most likely to respond and whether individual antioxidants, combined regimens, or different treatment durations provide the most favourable balance of efficacy and safety.

CONCLUSION

A 12-week daily combination of vitamin C 500 mg, vitamin E 400 IU, and coenzyme Q10 200 mg produced greater improvements than placebo in progressive sperm motility, sperm concentration, total motility, sperm DNA fragmentation, and seminal oxidation-reduction potential among men with

abnormal semen findings and laboratory evidence of oxidative stress. The difference in normal morphology was comparatively small, and the limited pregnancy events did not establish an effect on conception or live birth. The regimen was generally well tolerated, although mild gastrointestinal discomfort occurred more frequently in the antioxidant group. These results support further investigation of biomarker-targeted antioxidant therapy, but larger prospectively registered multicentre trials with standardized laboratory methods and clinically relevant reproductive outcomes are required before routine treatment recommendations can be made.

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