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Review Paper

Review Article on Impact of Alcohol Consumption on Male Fertility

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ABSTRACT

Alcohol consumption is an increasingly recognized modifiable risk factor in male infertility, contributing significantly to reproductive dysfunction through multiple interrelated mechanisms. This review highlights that ethanol metabolism generates reactive oxygen species, leading to oxidative stress, lipid peroxidation, and DNA damage in spermatozoa, while also disrupting the hypothalamic–pituitary–gonadal axis and altering key reproductive hormones such as GnRH, FSH, LH, and testosterone. These hormonal and oxidative changes impair the function of Leydig and Sertoli cells, ultimately compromising spermatogenesis and overall semen quality. Clinical and experimental evidence consistently shows that chronic and heavy alcohol consumption is associated with reduced semen volume, sperm count, motility, morphology, and increased DNA fragmentation. Although low-to-moderate alcohol intake may have minimal observable effects on conventional semen parameters in some individuals, underlying oxidative and endocrine disturbances remain a concern, and no clear safe threshold for reproductive health has been established. Additionally, emerging evidence suggests that alcohol-induced genotoxic and epigenetic alterations may adversely affect embryo development and offspring health. Importantly, these adverse effects are at least partially reversible, as alcohol cessation or significant reduction for a minimum of one spermatogenic cycle can lead to improvements in hormonal balance and semen parameters. Management strategies include lifestyle modification, antioxidant supplementation, hormonal therapy, and assisted reproductive techniques when necessary. However, limitations in existing studies, including variability in exposure assessment and reliance on cross-sectional data, highlight the need for further longitudinal and mechanistic research to better define dose–response relationships and individual susceptibility

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INTRODUCTION

The consumption of alcohol is one of the modifiable lifestyle factors that are increasingly linked with male infertility which accounts for approximately half of all cases of infertility globally (1,2). Thousands of millions of men who are of reproductive age suffer from drinking disorder which is on the rise in many areas. This creates a huge public health connection between andrology and addiction medicine. The effects of various alcohol use patterns occasional, moderate, heavy, and chronic on male reproductive potential have drawn increasing attention as a result of this (1,3). Alcohol (ethanol) is primarily metabolized in the liver, where it is converted into acetaldehyde and subsequently into acetate. This metabolic process leads to the generation of reactive oxygen species (ROS) and creates a reductive intracellular environment that can damage cellular components, including lipid membranes, proteins, and DNA (3,4). The male reproductive system, alcohol exerts its effects at several levels of the Hypothalamic Pituitary Gonadal (HPG) axis as well as directly within the testes. Alcohol consumption has been shown to alter the secretion of key reproductive hormones, including Gonadotropin Releasing Hormone (GnRH), Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Testosterone(1,5,67) . These hormonal disturbances may impair the normal functioning of Leydig and Sertoli cells, which play essential roles in spermatogenesis and testicular health(6,7). Both experimental animal studies and clinical investigations in humans have demonstrated that chronic or excessive alcohol exposure induces oxidative stress in testicular tissue and seminal fluid. This oxidative imbalance reduces antioxidant defense mechanisms, promotes lipid peroxidation, and contributes to DNA damage in spermatozoa, ultimately compromising male fertility potential(1,2,5,8). Clinically, alcohol use is linked to decreased semen volume, reduced normal morphology, and impairment of conventional semen indices, especially in heavy or chronic drinkers, according to a number of systematic reviews and meta-analyses(1,7,9,10). Alcohol consumption drastically decreased ejaculate volume, seminal antioxidant enzymes and circulating testosterone, FSH, and LH, with greater noticeable effects in heavy drinkers. According to a major meta-analysis involving over 23,000 males from five continents(5). Complementary data from addiction group and infertile populations reveals that chronic drinkers have typical hormonal alterations along with decreased sperm count, motility, and normal forms (7,10). However, although still altering sex hormone profiles low-to-moderate alcohol use may have little to no adverse effect on normal semen parameters, according to several meta-analyses and large cross-sectional studies of healthy men(9,11,12,13). The significance of dose, pattern (binge vs. habitual), duration of exposure, and co-factors like smoking, obesity, and other addictions are highlighted by these disparities. chronic alcohol usage has genotoxic and epigenetic effects that go beyond the immediate quality of semen. According to narrative reviews, exposure to acetaldehyde and ethanol-related oxidative stress can damage sperm DNA and change epigenetic markers, which may have an impact on the development of the embryo and the health of the progeny(1,3,14). Recent research suggests using OMICS-based methods to determine the molecular signs of male infertility linked to alcohol and to identify the most vulnerable men(1,3). However, a large portion of the available data is cross-sectional, unreliable in exposure assessment, and complicated by other lifestyle factors, leaving important questions unanswered, especially with regard to the point at which "moderate" chronic use starts to impair male reproductive potential (1,3,9,12).

Alcohol consumption is an important modifiable lifestyle factor increasingly associated with male infertility, which contributes to nearly half of all infertility cases worldwide. Rising alcohol use among men of reproductive age has strengthened the link between andrology and addiction medicine, prompting greater focus on how different drinking patterns from occasional to chronic affect reproductive health. Ethanol metabolism generates reactive oxygen species and oxidative stress, leading to cellular damage, while also disrupting the Hypothalamic Pituitary Gonadal axis and altering key reproductive hormones such as GnRH, FSH, LH, and testosterone. These changes impair leydig and sertoli cell function, compromise spermatogenesis, and negatively impact semen quality, particularly in heavy or chronic drinkers. Evidence from clinical and experimental studies shows associations with reduced sperm count, motility, morphology, semen volume, and increased DNA damage, although low-to-moderate consumption may have minimal effects in some cases. Variability in outcomes highlights the role of dose, duration, and co-existing lifestyle factors. Additionally, chronic alcohol exposure may induce genotoxic and epigenetic changes with potential effects on offspring health. Despite growing evidence, limitations in study design and exposure assessment leave uncertainties regarding safe consumption thresholds, emphasizing the need for advanced molecular approaches to better understand susceptibility and mechanisms.

PHYSIOLOGY OF MALE REPRODUCTIVE SYSTEM

The testis is a male reproductive gland, composed of seminiferous tubules (sperm production) and interstitial Leydig cells (testosterone production), responsible for spermatogenesis and androgen synthesis. Alcohol consumption, particularly heavy drinking, damages this structure by lowering testosterone, inhibiting Leydig cells, increasing Sertoli cell dysfunction, and reducing sperm count and quality, potentially causing testicular atrophy and infertility (3)

Structure and Function of the Testis

Seminiferous Tubules: The site of spermatogenesis, where sperm are produced. They contain Sertoli cells that support developing sperm cells(15,16)

Interstitial Cells (Leydig Cells): Located between the tubules, they produce testosterone, crucial for spermatogenesis and male secondary sex characteristics (15,16)

Function: The testis is responsible for producing testosterone and manufacturing sperm through a complex hormonal process mediated by the pituitary gland. (16,17)

Impact of Alcohol on Male Fertility

- **Testicular Damage and Atrophy:** Chronic alcohol abuse can cause testicular atrophy (shrinkage) and damage, with up to 75% of men with advanced cirrhosis showing signs of testicular injury (8)
- **Hormonal Imbalance:** Alcohol acts as a poison to the testes, causing lower serum testosterone levels. It often lowers testosterone and raises estrogen levels, reducing sperm quality (3)
- **Impaired Sperm Quality:** Alcohol is associated with reduced semen volume, reduced sperm count, decreased sperm motility, and increased morphological defects (e.g., tail curling, damaged sperm heads) (8)
- **Oxidative Stress and Cell Death:** Alcohol induced-oxidative stress triggers germ cell destruction (apoptosis), which impairs the

ability of cells to mature into healthy sperm (8)

- **Sertoli Cell Dysfunction:** Alcohol inhibits Sertoli cell function, affecting the nutrient support necessary for spermatogenesis, which can lead to infertility (3)

ALCOHOL METABOLISAM IN THE BODY

Absorption and distribution

- Ethanol is rapidly absorbed from stomach and small intestine, then distributed in total body water and reaches the liver, brain, and gonads.
- About 90–95% is metabolized; only a small fraction is excreted unchanged (18,19)

I.First oxidative step – ethanol → acetaldehyde

a. Alcohol dehydrogenase (ADH, mainly ADH1, cytosolic, hepatic)

Major pathway at low–moderate doses.

Reaction: ethanol + NAD^+ → acetaldehyde + NADH.

This causes a high NADH/NAD^+ ratio, altering redox state, lipid metabolism, and promoting steatosis and downstream injury (18,19)

b. Microsomal ethanol-oxidizing system (MEOS; CYP2E1)

- Located in endoplasmic reticulum; induction is prominent in chronic drinkers (18,19)
- Also converts ethanol to acetaldehyde but leaks electrons to O_2, generating superoxide and other ROS, driving lipid peroxidation and oxidative stress (18,20)
- CYP2E1-derived ROS are central in alcohol-induced liver injury and systemic oxidative stress (18,20)

c. Catalase/H_2O_2 system (peroxisomes)

- Catalase can oxidize ethanol using H_2O_2: ethanol + H_2O_2 → acetaldehyde + 2 H_2O.
- Long considered minor, but under conditions with high free fatty acids or lactate (which increase H_2O_2), catalase can contribute significantly to ethanol oxidation and ROS formation (18)

II.Second oxidative step – acetaldehyde → acetate

- Mainly via mitochondrial aldehyde dehydrogenase (ALDH2), producing acetate + NADH (19)
- Acetaldehyde forms protein and DNA adducts, disrupts cell function, and is a key mediator of toxicity (19)
- Genetic variants of ADH and ALDH alter acetaldehyde accumulation, influencing susceptibility to alcohol-associated tissue injury (19,20).

Acetate and downstream metabolism

Acetate enters the circulation, is taken up by peripheral tissues, and converted to acetyl-CoA.

In the brain, liver-derived acetate from alcohol can be used by ACSS2 to generate acetyl-CoA for histone acetylation, directly linking alcohol metabolism to epigenetic regulation and alcohol-related behaviors (21)

Non-oxidative metabolism (small fraction, high toxicity/biomarker value)

Formation of fatty acid ethyl esters, phosphatidylethanolamine, ethyl glucuronide, and ethyl sulfate; these are long-lived, membrane-associated metabolites often used as biomarkers and may contribute to cellular toxicity(21).

Oxidative stress as a unifying mechanism

- Ethanol metabolism via ADH, CYP2E1, and catalase increases ROS and disturbs antioxidant defenses, leading to oxidative stress (18,20)
- This oxidative stress contributes to inflammation, cell death, and organ damage in

alcohol use disorder and is a key mechanism relevant to germ-cell and testicular injury (20,22).

IMPACT OF ALCOHOL ON SPERM PARAMETERS

Alcohol consumption has been widely associated with deterioration of semen quality and male fertility potential. Both chronic heavy drinking and binge alcohol exposure can adversely affect several sperm parameters, including sperm count, motility, morphology, viability, and DNA integrity (6,23)

- **Sperm Count:** One of the most reported effects of alcohol is reduced sperm concentration.
- Chronic alcohol intake interferes with the hypothalamic–pituitary–gonadal (HPG) axis, leading to decreased testosterone production and impaired spermatogenesis (24)
- **Sperm Motility:** Alcohol significantly reduces progressive motility and total motility (3).

This happens mainly because alcohol induces:

- Oxidative stress
- Mitochondrial dysfunction
- ATP depletion
- Membrane damage

- **Sperm Morphology:** Alcohol has a negative impact on normal sperm morphology (6)

Abnormalities commonly seen include:

- Head defects
- Midpiece defects
- Tail abnormalities
- Double-headed sperm
- Coiled tail sperm

- **Sperm DNA Fragmentation**: Alcohol significantly increases DNA fragmentation index (DFI).

- Oxidative stress causes DNA strand breaks, chromatin damage, epigenetic alterations. This may lead to infertility, recurrent miscarriage, poor embryo quality, defective offspring development (3)

Alcohol-Induced Oxidative Stress And Male Fertility

Alcohol consumption is strongly associated with oxidative stress-mediated male reproductive dysfunction. Ethanol metabolism generates excessive reactive oxygen species (ROS) and weakens endogenous antioxidant defense systems, thereby impairing sperm function and fertility potential (24)

Oxidative stress occurs when there is an imbalance between ROS production and the antioxidant capacity of seminal plasma and testicular tissues. Spermatozoa are particularly vulnerable to oxidative injury because their plasma membrane is rich in polyunsaturated fatty acids (PUFAs) and they possess limited cytoplasmic antioxidant enzymes (25)

Mechanism of Alcohol-Induced Oxidative Stress

Ethanol is metabolized primarily into acetaldehyde by alcohol dehydrogenase and cytochrome P450 enzymes. During this process, excessive free radicals such as superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radicals (OH•) are generated (26)

These ROS exceed the neutralizing capacity of antioxidants such as superoxide dismutase (SOD),catalase, glutathione peroxidase ,vitamin c vitamin E leading to oxidative stress in the testes and semen (24)

Effect on Sperm Membrane (Lipid Peroxidation)

ROS attack the sperm membrane lipids, causing lipid peroxidation. This damages membrane fluidity and permeability, which are essential for sperm motility, capacitation, acrosome reaction, sperm oocyte fusion (27)

Mitochondrial Dysfunction

- Alcohol-induced ROS also damage sperm mitochondria
- Since ATP production occurs in mitochondria, this leads to
- low energy generation,
- poor sperm motility
- reduced viability (24).

Testicular Oxidative Damage

Chronic alcohol intake increases oxidative stress in Leydig cells, Sertoli cells and they disrupts spermatogenesis and testosterone synthesis, causing reduced sperm production (24)

How Alcohol Causes Testicular Damage and Reduces Male Fertility

Alcohol and aldehyde dehydrogenase primarily oxidize ethanol in the liver to acetaldehyde and acetate, producing excess NADH and a reduced cellular environment(28).

These mechanisms encourage lipid buildup, mitochondrial malfunction, and excessive ROS production, which paves the way for systemic oxidative stress and inflammation that have a secondary effect on the testis(28).

Oxidative Stress and Inflammation in the Testis

- Strong oxidative stress is indicated by prolonged alcohol exposure, which raises malondialdehyde (MDA) and lowers antioxidant enzymes (SOD, CAT, and GSH-Px) in testicular tissue
- Additionally, alcohol causes germ-cell death and decreased spermatogenesis in the testis by upregulating inducible nitric oxide synthase (iNOS), inflammatory cytokines (TNF-α, IL-1β, and IL-6), and apoptosis markers (caspase-3)
- One of the most critical factors contributing to male infertility is the complex interplay between oxidative stress and inflammation, which creates a self-perpetuating cycle of cellular damage affecting germ cells, Sertoli cells, and Leydig cells (28)

Disruption of the hypothalamic-pitutiary-gonadal axis and steroidogenesis

- Chronic alcohol consumption reduces testosterone, FSH, and LH while increasing estradiol, which is indicative of central (HPG) and testicular dysfunction, according to meta-analytic and experimental data.
- Ethanol directly impairs testosterone synthesis at the testicular level by suppressing important enzymes (3β-HSD, 17β-HSD), changing StAR and other steroidogenic proteins, and reducing the expression of the androgen receptor (AR).
- A two-way loop between ROS and endocrine imbalance is created when oxidative stress further interferes with hormonal signaling(2)

Direct testicular and spermatogenic damage

- Alcohol causes seminiferous tube atrophy, increased intercellular gaps, germinal epithelium sloughing, and decreased spermatocyte counts.
- Cell-cycle regulation is disrupted: long-term alcohol drinking raises p21 and lowers cyclin D1, which prevents germ-cell growth and lowers the quantity and quality of sperm.
- PI3K/mTOR pathways are also up-regulated in testis in both acute and chronic scenarios, which connects oxidative stress signaling to modified cell proliferation and survival (2)

Sperm quality, DNA integrity and epigenetic effects

- A human meta-analysis shows that heavy alcohol consumption reduces sex hormones, seminal antioxidants, and semen volume; at moderate amounts, fundamental semen parameters change more subtly.

- Increased aberrant sperm morphology, a compromised acrosome response, and DNA damage in germ cells and sperm following ethanol exposure are observed in experimental animals.
- Intergenerational epigenetic effects are supported by paternal alcohol consumption, which damages sperm DNA and modifies histones, resulting in aberrant embryo development and problems in male offspring's testicles and sperm(1).

Emerging systemic mechanisms: gut-testis axis and metabolism

- The long-term alcohol consumption results in intestinal dysbiosis, increased endotoxin and systemic cytokines, testicular inflammation, altered expression of genes related to cell division, meiosis, and mitochondrial function, and eventually poor sperm quality.
- Reproductive toxicity is integrated into a larger metabolic syndrome framework by alcohol-induced metabolic dysfunction (liver disease, dyslipidemia, insulin resistance), which further reduces testosterone and deteriorates testicular function (29)

Alcohol reduction

- Reduced semen volume, decreased antioxidant capacity in semen, and lowered levels of testosterone, FSH, and LH are all reliably associated with severe or chronic alcohol consumption, suggesting compromised spermatogenesis and hormonal regulation.
- When paired with smoking, heavy drinkers exhibit lower sperm motility and morphology as well as higher oxidative stress markers and DNA/chromatin damage.
- Semen indices and sex hormones are harmed by ≥7 units/week (or heavy patterns), according to meta-analysis; fundamental semen metrics did not clearly change with <7 units/week, but oxidative and hormonal impacts are still a concern.
- According to a number of reviews, the decline in sperm parameters can be partially reversed after quitting alcohol, which supports strong reduction or abstinence as a prophylactic measure(28)

Broader lifestyle modification package

Alcohol rarely acts alone combine risk factors worsen fertility review recommend bundled counselling on:

- **Stopping smoking**: Even with "normal" traditional semen characteristics, smoking plus alcohol significantly increases oxidative stress, antioxidant enzyme up-regulation, and sperm DNA fragmentation
- **Weight control and diet**: It is advised to lose weight and adopt a healthy diet because obesity, high-fat diets, and metabolic syndrome combine with alcohol to decrease testosterone, spermatogenesis, and metabolic health.
- **Physical activity**: Regular moderate exercise promotes reproductive and metabolic health; prolonged periods of inactivity (heat, scrotal temperature) are avoided.
- **Heat and radiation avoidance**: limiting device radiation near the testes and minimizing prolonged scrotal heat (tight underwear, hot baths, laptops on laps).
- **Stress and sleep**: Hormonal disruption and oxidative stress are caused by psychological stress and insufficient sleep(9)

Antioxidant and supportive measures

- A vital component mechanism is alcohol-related oxidative damage, which includes decreased seminal antioxidants, increased lipid peroxidation, and altered SOD, catalase, and glutathione reductase activities.

- Lifestyle modifications combined with dietary antioxidant supplements (vitamins C, E, carnitine, CoQ10, etc.) may help prevent oxidative damage, especially in men who experience high levels of oxidative stress, according to reviews on lifestyle and male fertility(30)

Public health and counselling approaches

- Men at fertility clinics are frequently unaware of how alcohol affects reproduction, but they are highly willing to change after being diagnosed with infertility, which supports focused education initiatives.
- Reviews contend that using ART alone is not as effective or economical as preventive (screening and changing alcohol and other lifestyle variables) (31)

Clinical Management and Treatment Approaches

I.Alcohol Cessation and Lifestyle Modification

➢ **First line management**

The most crucial intervention is to completely stop drinking alcohol or drastically cut back. Abstinence from alcohol aids in improving spermatogenesis and restoring hormonal equilibrium (7).

➢ **Duration of abstinence**

A minimum period of 3 months is generally recommended. This duration corresponds to one complete spermatogenic cycle (7).

➢ **Expected improvements**

- Increase in sperm concentration
- Improved sperm motility
- Better sperm morphology
- Reduction in sperm DNA fragmentation
- Improvement in semen volume

➢ **Additional lifestyle modifications**

- Smoking cessation
- Balanced diet
- Regular exercise
- Adequate sleep
- Stress management
- Avoidance of heat exposure and toxins (7)

2.Clinical Assessment and Diagnostic Evaluation

➢ **Detailed history taking**

- Duration and quantity of alcohol consumption
- Frequency of binge drinking
- History of infertility
- Sexual dysfunction
- Erectile difficulties
- Reduced libido
- Smoking and drug history
- Past medical and liver disease history (5)

➢ **Physical examination**

- Testicular size and consistency
- Presence of varicocele
- Signs of hypogonadism
- Gynecomastia
- Secondary sexual characteristics (5)

➢ **Laboratory investigations**

- Semen analysis
- Hormonal profile
- Liver function tests
- Oxidative stress markers (5)

Hormonal Evaluation and Therapeutic Option

Hormonal Evaluation

The hormonal profile should be assessed to identify endocrine disturbances associated with alcohol-induced male infertility.

- **Serum testosterone:** It evaluates androgen status, leydig cell function and help to detect hypogonadism.
- **Luteinizing Hormone (LH):** It assesses Pituitary Stimulation of testosterone production. Useful in differentiating primary and secondary hypogonadism.
- **Follicle-stimulating hormone (FSH):** Reflects Sertoli cell activity and spermatogenesis. Elevated levels may indicate impaired testicular function.
- **Prolactin:** Increased levels may contribute to reduced libido and infertility
- **Estradiol:** Assesses estrogen imbalance and elevated levels are commonly seen in chronic alcohol users (23)

Therapeutic Options

A. Clomiphene Citrate

- A selective estrogen receptor modulator (SERM)
- Stimulates endogenous testosterone production
- Enhances release of LH and FSH
- Preserves fertility potential
- Preferred over exogenous testosterone in infertile males (3)

B. Human Chorionic Gonadotropin (hCG)

- Mimics the action of LH
- Stimulates Leydig cells to produce testosterone
- Used in selected cases of hypogonadism
- Helpful in men with secondary hypogonadism who desire fertility (3)

C. Aromatase Inhibitors

- Reduce peripheral conversion of testosterone to estrogen
- Useful in cases of elevated estrogen levels
- Improve testosterone-to-estrogen ratio
- **Example:** Anastrozole (3)

➢ **Antioxidant Therapy**

Alcohol-induced infertility is strongly associated with oxidative stress and reactive oxygen species (ROS). (32)

Common antioxidants used : Vitamin C**,** Vitamin E, Zinc**,** Selenium, Coenzyme Q10**,** L-carnitine**,** N-acetylcysteine **(32)**

Clinical benefits

- Reduced oxidative damage
- Improved sperm motility
- Improved sperm viability
- Reduced DNA fragmentation
- Better fertilization potential (32)

➢ **Management of Sexual Dysfunction**

Chronic alcohol use may lead to erectile dysfunction, ejaculatory disorders, reduced libido (3)

Treatment options

- Sildenafil
- Tadalafil
- Psychological counseling
- Behavioral therapy (3)

Management of Alcohol Use Disorder

Pharmacological management: Naltrexone, Acamprosate, Disulfiram,

Non-pharmacological management:

- Cognitive behavioral therapy
- Motivational counseling
- Relapse prevention programs
- Psychiatric support (1)

➢ **Assisted Reproductive Techniques (ART)**

Considered when natural fertility does not improve despite treatment

Available options

- Intrauterine insemination (IUI)
- In vitro fertilization (IVF)
- Intracytoplasmic sperm injection (ICSI) (6)

Indications

- Severe oligospermia
- Poor sperm motility
- High DNA fragmentation
- Failed natural conception (6)

Future research directions

➢ **Dose–response and thresholds for harm in humans**

When meta-analyses indicate that moderate intake (<7 units/week) has little effect on conventional semen indices, but severe intake definitely degrades semen volume, hormones, and several morphological characteristics, it is important to clarify whether there is a true safe threshold for male fertility. It is necessary to conduct prospective cohort studies using standardized alcohol units, drinking habits (binge vs. routine), and repeated measurements of semen and hormones. (1,3,6)

➢ **From semen parameters to real fertility outcomes**

Many research focus only on hormones and semen quality; effects on live birth, miscarriage, and time to pregnancy are still unknown and occasionally inconsistent with semen results. Male alcohol consumption and clinical outcomes (such as IUI/IVF/ICSI success) must be concurrently measured by large longitudinal couple-based studies and ART cohorts. (33)

➢ **Mechanistic and OMICS-based pathways**

The hypothalamic-pituitary-gonadal axis is disrupted, oxidative stress is increased, and testicular steroidogenesis is altered by chronic alcohol consumption; however, the molecular fingerprints in human sperm are not well understood. urge the use of OMICS techniques (proteomics, metabolomics, and epigenomics) on semen in order to find biomarkers of alcohol-related infertility and its impacts across generations. (34)

➢ **Genetic, epigenetic, and intergenerational effects**

There is conflicting evidence about changes in DNA integrity; despite significant hormonal and antioxidant changes, some meta-analyses reveal no discernible impact on sperm DNA fragmentation. Sperm chromatin structure, short RNAs, DNA methylation, and connections to the metabolic and neurological consequences of offspring require further investigation. (35)

➢ **Interaction with other lifestyle and environmental exposures**

Alcohol is rarely found alone. Multi-exposure designs are necessary to account for the combined effects of smoking, obesity, poor food, heat, endocrine disrupting chemicals, and recreational substances on oxidative stress and male fertility. Exposome-oriented models should replace single-factor analyses in research. (36)

➢ **Reversibility and timing (preconception windows)**

Chronic alcohol exposure may result in long-term testicular damage, but some animal and human evidence indicate partial reversibility after quitting alcohol. There is a significant unmet need for controlled cessation trials with defined wash-out intervals and serial semen/epigenetic evaluations in men intending conception. (37)

➢ **Moderate vs binge patterns and type of beverage**

The majority of research categorize average weekly units; although clinically significant, binge

drinking patterns and beverage type (wine/beer vs. spirits) are not well differentiated. Pattern, frequency, and context (e.g., weekend binges vs. daily low doses) should be broken down in future observational and experimental research. (38)

➢ **Clinical guidelines and intervention trials**

Male preconception guidelines are either ambiguous or derived from general health data, despite proven links between chronic alcohol abuse and poor semen quality. The effects of systematic alcohol-reduction therapies (perhaps in conjunction with antioxidant or lifestyle programs) on semen quality and ART outcomes require randomized or pragmatic trials. (38)

CONCLUSION

Alcohol consumption is a significant and modifiable factor contributing to male infertility, exerting its effects through hormonal disruption, oxidative stress, and direct testicular damage that impair spermatogenesis and overall semen quality. Chronic and heavy alcohol use is consistently associated with reduced sperm count, motility, morphology, and DNA integrity, primarily due to alterations in the hypothalamic–pituitary–gonadal axis, increased reactive oxygen species, and impaired function of Leydig and Sertoli cells. Although low-to-moderate intake may show minimal impact on conventional semen parameters in some cases, underlying oxidative and hormonal changes suggest that no clearly safe threshold exists for reproductive health. Importantly, these adverse effects are at least partially reversible, as alcohol cessation or reduction over a complete spermatogenic cycle can significantly improve hormonal balance and semen parameters. Furthermore, emerging evidence of genotoxic and epigenetic effects highlights potential implications for offspring health, reinforcing the need for caution. Despite existing knowledge, uncertainties remain regarding dose–response relationships and individual susceptibility, underscoring the importance of further research. Overall, reducing or eliminating alcohol intake, alongside comprehensive lifestyle modification and appropriate clinical management, should be strongly emphasized in male infertility prevention and treatment strategies.

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