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## **Sexual Functions, Sexual Organs and Sex Hormone Level in Chronic Alcohol Intake**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author AEO initiated the topic and wrote the first draft of the manuscript. Author OTH compiled the literature papers. Author ADA edited the manuscript and author NVU managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

A general knowledge among youths is that alcohol enhances sexual desire and sexual performance. In contrast to this, studies have reported various adverse effects of alcohol on reproductive and sexual functions in both male and female. Male alcoholics frequently suffer from erectile dysfunction, intermittent delay in or absence of orgasm, and premature or delayed ejaculation. Alcohol is a toxin that can damage sperm-producing cells in the testicles, decrease testicular size, increase number of abnormally-shaped sperm and lower sperm count. Studies found that heavy alcohol consumption results in reduced testosterone and elevated estrogen levels in the blood and it can decrease the production, release and/or activity of luteinizing hormone and follicle-stimulating hormone. Female alcoholics have problems in producing enough natural lubrication for pain-free sex. Alcohol has a disruptive effect on menstrual cycle which can result in amenorrhea and anovulation. It affects estrogen and progesterone levels and also leads to hyperprolactinemia. It has been observed that when a man stops drinking alcohol, the

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negative effects on fertility and sexual abilities reverse quickly. Long term excessive intake of alcohol can lead to damage to the central nervous system and the peripheral nervous system resulting in loss of sexual desire and infertility in men and women.

*Keywords: Alcohol; sexual function; primary sexual organs; accessory sexual organs; sex hormone; male; female.*

## 1. INTRODUCTION

Procreation in human beings is achieved by different processes, which work in synergy to bring about a new life. These processes are gametogenesis, female monthly cycle, sexual functions, fertilization and implantation [1] impairment of any of this result in infertility. Fertility in both male and female has been reported to be impeded by many factors: nutrition [2], emotional and physical stress [3,4], environmental chemicals and pollutants [5,6], life style factors such as cigarette smoking [7], illicit drug use [8] and alcoholism [9,10,11].

Ethanol is the type of alcohol found in alcoholic beverages [12]. It is oxidized by alcohol dehydrogenase in the liver to aldehydes (e.g. acetaldehyde) or carboxylic acids. Its toxicity is largely caused by its primary metabolite- acetaldehyde and secondary metabolite- acetic acid [13]. The metabolite toxicity of alcohol is reduced in rats fed with N-acetylcysteine [14]. Alcohol is the most abused drug that young adults indulge in to reduce their anxiety and fear, improve their confidence and they believe it increase their sexual desire and performance. The present review will discuss the effects of alcohol on sexual function, sex organs and sex hormones in male and female. Examining this information is essential in planning, designing, and elucidating researches to evaluate the mechanism of alcohol's effects on reproduction which will facilitate therapeutic interventions.

## 2. EFFECT OF ALCOHOL ON SEXUAL FUNCTION

Alcohol may help to alleviate some of the symptoms of anxiety and relaxes the individual about sexual performance and sexuality but chronic alcohol consumptions can have negative impact on sexual function. Alcohol abuse is the leading cause of impotence and other disturbances in sexual dysfunction and most commonly reported is erectile dysfunction in male alcoholics [15]. Miller and Gold 1988 [16] reported that acute and chronic alcohol intake affects virtually all aspect of male sexual functions especially sexual desire and erection. Vijayasenan 1981 [17] in his report stated that out of 97 male in-patients admitted for the treatment of alcoholism, 71% suffered from sexual dysfunction and the disturbances noted were diminished sexual desire (58%), ejaculatory incompetence (22%), erectile impotence (16%) and premature ejaculation (4%). More recent studies have also demonstrated the harmful effect of alcohol on sexual functions. Okulate etal 2003 [18] screened 829 men for erectile dysfunction (ED) using the Patient Health Questionnaire (PHQ) and the International Index of Erectile Function (IIEF), they observed that among the men identified as having ED 10.3% are involved in alcohol abuse, Bijil and Vivek 2007 [19] assessed one hundred male subjects admitted to a deaddiction centre for sexual dysfunction, using a sexual dysfunction checklist containing items corresponding to 12 areas of sexual dysfunction described in the Diagnostic Criteria for Research, ICD-10 Classification of Mental and Behavioural Disorder reported that seventy-two per cent had one or more sexual dysfunction, the most common being premature ejaculation, low sexual desire and erectile dysfunction and they also stated that the amount of alcohol consumed appeared to

be significant predictor of developing sexual dysfunction. In contrast, a study interviewed forty-five chronically alcoholic men and a control group of thirty healthy non-alcoholic volunteers using a sexual dysfunction questionnaire reported that the sexual desire and erection scores of alcoholic men were not statistically different from those of the control group, but they stated that fourteen out of the 45 alcoholic men complained of loss of erection during sexual activity [20]. The limitation in the reports of the above studies is that they are gotten from individual self-assessment and not from objective assessment of sexual dysfunction. However a study assessed nocturnal penile tumescence (NPT) responses in twenty-six chronic male alcoholics in the process of detoxification. They observed in the alcoholic subjects significant reduction in latency to tumescence (slower erection), decreased number and rigidity of erection, and more semi-erection when compared to an age-matched non-alcoholic control group [21]. Alcohol-induced sexual dysfunction can be reversible with abstinence as postulated by Schiavi et al. 1995 [22]; they did a comparison study on sexual dysfunction in alcoholics abstinent for 2-3 months with a nonalcoholic control group and they observed no difference between the two groups. Basic researches describing effects of chronic alcohol intake on women's sexual physiology are very limited and also the report of these studies has limitation in that it gotten from individual self assessment. Covington and Kohen (1984) [23] stated that of the female alcoholics they interviewed 64% experience lack of orgasm, 64% lack of sexual interest, 61% lack of sexual arousal or pleasure, 46% lack of lubrication, 24% experience painful intercourse and 6% suffered muscular spasms (Vaginismus) (Table 1.). Recent studies have demonstrated alcohol's effect on physiological genital arousal in women using a vaginal photoplethysmography, but the studies focused mainly on the acute effect and reported that alcohol reduces Vaginal Pulse Amplitude (VPA) in women exposed to erotic film [24,25,26,27]. In contrast, a study reported that alcohol increases sexual desire in female, ascribing this to increased testosterone level in alcoholic female, testosterone is known to control the strength of libido in women [28]. In line with this report studies have associated alcohol intake with elevated plasma testosterone levels in female [29].

The underlying mechanisms of alcohol's effect on sexual function are not well understood. The brain cells are particularly sensitive to alcohol, which acts as a depressant and sedates all the nerve cells of the brain [30], it has also been reported that alcohol abuse may result to vagal neuropathy [31]. Sexual activity or function is initiated by the autonomic nervous system damage or depression of this centre consequently will inhibit every aspect of sexual function or act. Chronic intake of alcohol is also known to significantly decrease testosterone level in male [11], thus the decreased level of testosterone might be responsible for various sexual dysfunctions experience by male alcoholics. Some studies have suggested that hormonal response to alcohol may constitute important mechanisms in attenuation of genital arousal in alcoholic women [32]. Alcohol has been reported to retard blood congestion and swelling in the genitals [33], similarly Malatesta et al. [34] reported that alcohol decreases vaginal blood volume, thus the erectile dysfunction might be due to altered blood flow to genitalia and/or inability of arterioles of genitalia to dilate properly as well as venous leakage resulting from contraction of the cavernous smooth muscle.

**Table 1. Effects chronic alcoholism on sexual function**

Author/ Date	Subjects	Sexual function assessment	Major findings
Vijayasenan [11]	97 alcoholism inpatients in porirua hospital, porirua.	Interview.	71% suffered from sexual dysfunction; 58% diminished sexual desire, 16% erectile impotence, 4% premature ejaculation, 22% ejaculatory in competence
Okulate et al. [13]	862 military personnel of the Nigerian army based within the Lagos area	the Patient Health Questionnaire (PHQ) and The International Index Of Erectile Function (IIEF)	39.6% had erectile dysfunction and of these 10.3% are chronic alcoholics
Bijil and Vivek [14]	100 admitted to the deaddiction centre of the national institute of mental health and neurosciences, bangalore, india	sexual dysfunction checklist constructed using items from the diagnostic criteria for research [ICD-10] for sexual dysfunction	71% had sexual dysfunction: 37.5% complaints of ejaculating within the first to three minutes of intromission, 33.3% had erectile dysfunction; difficulty in achieving erection and difficulty in maintaining erection. 14.58% had anorgasmia and 10.41% had inhibited or delayed ejaculation.
Gumuş et al. [15]	45 chronically alcoholic men + 30 healthy non-alcoholic volunteers	sexual dysfunction questionnaire constructed by an urologist and comparison with non-alcoholic controls	The sexual desire and erection of alcoholic men and those of the control group were not statistically different.
Snyder and Karacan, [17]	26 detoxified, chronic male alcoholics + 26 non-alcoholic control group	Nocturnal Penile Tumescence (NPT) assessment	Significant reduction in latency to tumescence, decreased number and rigidity of erection, and more semi –erection compared to non-alcoholic group
Covington and Kohen [19]	35 alcoholic women + 35 nonalcoholic women	interview and comparison with non-alcoholic controls	Lack of orgasm was reported by 64% of alcoholic women and 27% of nonalcoholic women, lack of sexual arousal or pleasure by 61% of alcoholic women and 30% of nonalcoholic women, lack of lubrication by 46% of alcoholic women and 24% of nonalcoholic.

The relaxation of cavernous smooth muscle is essential for inducing and maintaining a penile erection [35]. Yang et al. [36] in their study on the isolated rabbit corpus cavernosum reported that ethanol significantly augmented the corporal relaxation induced by isoprenaline and the ethanol-induced relaxation was inhibited by an adenylate cyclase inhibitor, from their study they concluded that ethanol has a relaxant effect, which may be associated with the cAMP signaling pathway. Differing, Aydinoglu et al. [35] demonstrated in their study in mouse that ethanol treatment was able to stop the endothelium-dependent relaxations induced by acetylcholine but failed to alter the relaxation initiated by exogenous nitric oxide and therefore concluded that ethanol impaired the endothelial function of corpus cavernosum and that this may lead to erectile dysfunction through a reduced nitric oxide release as result of the endothelial impairment. Chronic alcohol intake has been associated with hyperestrogenemia [11], high estrogen level has been reported to attenuate the relaxation of rabbit penile corpus cavernosum induced by acetylcholine, nitroglycerin, and nitrenergic transmission and potentates norepinephrine-induced antierectile contraction of corpus cavernosum [37].

### **3. EFFECT OF ALCOHOL ON SEXUAL ORGANS**

The consumption of alcohol can cause damage to cells of the reproductive organs. There is paucity of reports on effect of alcohol on accessory reproductive organs, researches concentrated mostly on the testes, while very limited reports are on the ovaries. Research should also be conducted to examine the effect of alcohol on accessory organ, they are also essential for human fertility; however a study observed that retro-injection of 30% ethanol into the vas deferens of rats increases sperm deformity rate in the treated animals compared to the control but the apoptosis index of spermatogenic cells was not affected by alcohol [38]. Emanuele and Emanuele, 1998 [39] explained in their review that testicular atrophy mainly results from the loss of sperm cells and decrease in the diameter of seminiferous tubules, they suggested that the atrophy caused by chronic alcohol intake might be caused by its damaging effects on the testicular cells as well as its effects on LH and FSH production which are essential stimulants for testicular growth. Study has shown that Male alcoholic have a decrease sperm count, percentage of rapid progressively motile sperm, percentage of live sperm, and percentage of morphologically normal sperm and an increase in the percentages of slow progressively motile sperm, nonprogressively motile sperm, immotile sperm, dead sperm, head-defective sperm, neck-defective sperm, and tail defective sperm when compared non alcoholic male [11]. Teratozoospermia and oligozoospermia have been observed in alcoholics engaged in heavy drinking [40]. Alcohol has also being reported to decrease LH and FSH level in the blood [41]. Ovarian atrophy has been observed in animal study; a study by Van Thiel et al. [42] on rats fed alcohol as 36% of their calories for 7 weeks showed noticeable structural and functional ovarian failure compared with animals that did not receive alcohol but were fed the same number of total calories. Alcoholic women have been reported to have pelvic inflammatory disease and endometriosis [43] and array of menstrual and reproductive disorders, which include irregular menstrual cycles, complete cessation of menses and absence of ovulation [9]. Alcohol abuse has also been associated with early menopause [9].

Alcohol is a small molecule soluble in both water and lipid; therefore it easily permeates all tissues of the body, causing damage to the tissue and affects most vital functions [44]. Alcohol is oxidized by alcohol dehydrogenase in the liver to acetaldehyde, which is responsible for alcohol toxicity, acetaldehyde is rapidly metabolised to acetate mainly by mitochondrial aldehyde dehydrogenase [45]. The activity of mitochondrial aldehyde dehydrogenase has been reported to be significantly reduced by chronic alcohol

consumption [46]. High level of acetaldehyde is highly toxic, its toxicity is partly due to its capacity to form protein adducts, which result to antibody production, enzyme inactivation and decreases DNA repair [47], furthermore acetaldehyde promotes glutathione depletion, free radical mediated toxicity and lipid peroxidation which are responsible for tissue damage [45]. In line with this a study reported that the plasma concentrations of antioxidant vitamins (alpha-tocopherol and ascorbic acid) were lower and malondialdehyde (MDA) and autoantibodies directed to MDA adducts to proteins (Ig-NH<sub>2</sub>-MDA) were higher in alcoholics than in men who drank low amounts of alcohol [48], another study reported a decrease in the activities of Glutathione S-Transferase (GST) and total antioxidant capacity (TAC) in alcohol-dependent males compared to non-alcoholics males [49] and also an animal study showed that antioxidant activity was decreased both in the serum and brain of rats treated with alcohol [50].

### **3.1 Effect of alcohol on sex hormones**

Chronic alcohol abuse has been linked with irregularity in synthesis and secretion of hormones; several studies have reported changes in sex hormones concentration in the blood of both male and female alcoholics. Acute effect of alcohol on sex steroids has been ascribed to its effect on the hypothalamic-pituitary-gonadal and-adrenal axes, but the exact mechanisms are not cleared [51]. There are conflicting reports on the alcohol's effect on GnRH secretion; for instance, a study by Ching et al. [52] in male rats established that alcohol administration significantly lowered GnRH levels in the blood vessels connecting the hypothalamus to the pituitary gland, but some researches isolated hypothalami from male rats or GnRH producing cells obtained from genetically engineered mice, failed to demonstrate any reduction in GnRH secretion in response to alcohol treatment [53,54]. Also, no alcohol-induced reduction in the expression of the gene that is responsible for generating GnRH was detected from the study, thereby suggesting that alcohol probably does not affect GnRH production [54]. However, they reported that the process involving the conversion of inactive precursor GnRH to its active molecule diminished after alcohol exposure [54]. Emanuele and Emanuele [39] in their review suggested that alcohol decreases GnRH secretion by acting at a site outside the hypothalamus and that alcohol's breakdown products (e.g., acetaldehyde) rather than alcohol itself reduces GnRH secretion. Rettori and McCann [55] explained that the release of LHRH is controlled by nitric oxide (NO) and the pathway via the norepinephrine-induced release of nitric oxide from NOergic neurons, which activates LHRH release. From their findings they reported that the suppressive effect of alcohol on LHRH release was due to stimulation of beta-endorphinergic neurons that inhibit the release of norepinephrine, which drives the NOergic release of LHRH. Another study showed that Norepinephrine increased the release of NO by increasing the conversion of [14C] arginine to [14C] citrulline. NO stimulate LHRH release via activating guanylate cyclase, which leads to an increase in cGMP and at the same time activates cyclooxygenase. The increase in cGMP increases intracellular free calcium, which activates phospholipase A2 and cyclooxygenase. Phospholipase A2 produces arachidonic acid, which is converted to prostaglandin E2 under the influence of cyclooxygenase, prostaglandin E2 then stimulates the release of LHRH. From their findings they observed that alcohol has no effect on the production of NO by medial basal hypothalamic neurons nor does it have effect on the increased release of NO induced by norepinephrine but alcohol was able to inhibit the conversion of labeled arachidonic acid to prostaglandin E2, concluding that alcohol acts either by directly inhibiting cyclooxygenase or by blocking the increase in intracellular free calcium induced by cGMP, which is necessary for activation of both phospholipase A2 and cyclooxygenase [56].

Researchers have reported decrease in LH level in response to alcohol intake [41], similarly a study by Sarkola et al. [57] reported decrease in LH level in women using oral contraceptives but no effect of alcohol on luteinizing hormone levels was observed among women not using oral contraceptives. In contrast studies have observed no effects of alcohol on LH level in women or men [58]. Emanuele et al. [59] concluded that the decrease in LH blood levels resulted from impairments in both LH production and LH secretion, supporting this claim some studies removed anterior pituitary glands from animals and grew them in vitro in the presence or absence of alcohol, the results suggested that alcohol can decrease LH secretion even from isolated pituitary glands inferring that alcohol lowers LH levels at least in part by acting directly on the pituitary [60]. Few information is available on alcohol's effect on FSH, researches have pointed out that alcohol reduces FSH levels in the blood, although this effect is not as consistent as its effect on LH levels [61,62]. In contrast, a study compared FSH and LH levels in alcoholics and nonalcoholic male, observed an increase in levels of these hormones in alcoholics [11]. There are no available data on alcohol's effect on inhibin and activin secretion these two hormones regulate FSH secretion in both male and female. Alcohol's effect on FSH secretion might be via these hormones, therefore its effect on their secretion and release is suggested for future research.

Chronic alcohol intake has been associated with an elevation in plasma estradiol levels in male alcoholic [11]. Studies have shown that acute alcohol consumption cause increased levels of estradiol levels in premenopausal women [63] as well as in postmenopausal women on estrogen replacement therapy [64], accordingly a study reported that alcohol intake causes elevation in estradiol level among premenopausal women using oral contraceptives but observed no effect among premenopausal women not using oral contraceptives [57]. Results of same study indicated that alcohol intake causes a decline in progesterone levels among women using oral contraceptives as well as among non-user, similarly Teoh et al. [63] demonstrated similar progesterone effects among premenopausal women not using oral contraceptives. Increased estrogen level might be as a result of alcohol-induced aromatization, alcohol has been reported to increase the conversion of testosterone into estradiol [65]. A study by Gavaler 1998 [66] reported that alcoholic beverages contain estrogen like substance called phytoestrogens, which has been observed to exert estrogenlike effects.

Muthusami and Chinnaswamy, [11] assessed 1300 alcoholics who had 180 ml of alcohol per day for a minimum of 5 days per week in the past year and 300 non alcoholic volunteers, they observed a decreased testosterone level in the alcoholic group compared to the nonalcoholic group. However, studies have shown that alcohol intake elevates plasma testosterone levels both in premenopausal women using oral contraceptives as well as among non-users [67], elevated testosterone levels have also been reported among drunken female adolescents [29]. A study by Sarkola et al. [68] reported an elevation in plasma testosterone after intake of alcohol in both premenopausal women using oral contraceptives as well as non-users, the study observed that the increase in the testosterone level was accompanied by a decrease in the androstenedione level in plasma as well as a decrease in the urine etiocholanolone and androsterone levels, which are principal catabolic products of androgens suggesting that the testosterone elevation was as a result of an inhibition of testosterone catabolism in the liver, which is mediated by alcohol-induced elevation in the ratio of reduced nicotinamide adenine dinucleotide (NADH) to oxidized nicotinamide adenine dinucleotide (NAD<sup>+</sup>), NAD<sup>+</sup> is essential for catabolism of testosterone in liver. The increased testosterone in female alcoholics might be due to the stimulatory effect of alcohol on adrenal cortex. It has been demonstrated that alcohol activate the hypothalamic-pituitary-adrenal (HPA) axis [69] and the hypothalamic-pituitary-adrenal axis of female rats is more

responsive to alcohol than that of males [70]. The ethanol-induced steroidogenesis in the adrenal cortex is dependent on the pituitary release of ACTH [71]. Rivier and Lee [72] reported that acute alcohol administration stimulates the activity of hypothalamic neurons that express corticotrophin-releasing hormone (CRH), findings from another study showed that ethanol upregulates the expression of CRH gene through cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA)-dependent signal transduction pathway [73]. Acute intragastric administration of alcohol to adult male rats elevated plasma adrenocorticotrophic hormone (ACTH) levels and activated hypothalamic corticotrophin-releasing factor neurones. Findings from this study showed that alcohol up-regulated factor c-fos (Foc) signals in the locus coeruleus, the main noradrenergic brain cell group and activated (nor) adrenergic medullary cells (A1-A2/C1-C3). They demonstrated that blockade of  $\alpha(1)$ -but not  $\beta$ -, adrenergic receptors interfered with alcohol-induced ACTH secretion, the depletion of catecholaminergic input to the paraventricular nucleus (PVN) by toxin 6-hydroxydopamine decrease the ACTH response to alcohol and the destruction of the A1-A2/C1-C3 region with the immunotoxin anti-dopamine-B-hydroxylase-saporin interfered with the catecholaminergic input to the PVN. From their findings they concluded that alcohol up-regulate catecholamine circuitry in the rat brain and medullary catecholamine innervation of the hypothalamus plays an important role in modulating the stimulatory effect of alcohol on the HPA axis and that this effect of alcohol is via activation of  $\alpha(1)$ -adrenergic receptors [74]. In consistent, a study observed that alcohol increased the number adrenocorticotropin cells in Wistar rats given 15% ethanol compared to the control group and via the influence ACTH there was a significant increase of the synthetic active elements in the zona fasciculata and zona reticularis of adrenal cortex in the treated rats, concluding that alcohol primarily acts at the level of hypothalamus and hypophysis and the adrenal cortex react to hypersecretion of ACTH cells [75]. However, most of these studies focus mainly on alcohol's effect on adrenal cortisol secretion, research on alcohol's effect on adrenal androgen secretion especially in female is necessary.

Several mechanisms have been recommended via which alcohol induced the decreased testosterone level in male alcoholics. For instance, researchers have demonstrated that the metabolism of alcohol reduces the NAD<sup>+</sup>/NADH ratio both in the liver and the testes, NAD<sup>+</sup> is necessary for the synthesis of testosterone in testes, thereby reducing testosterone production [76]. Another study has pointed out an increase in  $\beta$ -endorphin levels in the testicular fluid after acute alcohol exposure [41], testicular  $\beta$ -endorphin inhibits testosterone production and/or release. This was confirmed through a study in which rats were treated with naltrexone; a substance that inhibits  $\beta$ -endorphin activity [77]. They observed that naltrexone prevented the decrease in testosterone level after both acute and chronic alcohol ingestion. Nitric oxide (NO), a ubiquitous gas that results in the dilation of blood vessels has also been suggested to contribute to alcohol's toxic effects [39], NO has been shown to decrease testosterone secretion in the testes as well as in many other tissues [78]. NO is synthesized in the testes by an enzyme called NO synthase (NOS), and inhibition of this enzyme by a variety of NOS inhibitors successfully avert the decrease in testosterone associated with alcohol consumption [79]. Elevated estrogen level in male alcoholics might also be responsible for the decrease testosterone level; chronic treatment with estradiol has been reported to reduce testosterone levels in the blood of New Zealand white male rabbits [37]. Studies have demonstrated that estrogen decreases testicular androgen secretion by inhibiting gonadotropin-stimulated androgen production, and this inhibitory effect is via altering the activity of steroidogenic enzymes which include 17 $\alpha$ -hydroxylase, C17, 20-lyase (desmolase), and 17 $\beta$ -dehydrogenase [80]. In consistent, Anna and peter [81] reported that estrogen decreases gonadotropin-stimulated 11-ketotestosterone (11-KT) production in Atlantic croaker, suggesting that it act along the pathway for 11-KT synthesis after

production of androstenedione and in addition they reported that this action of estrogen is not mediated through the classical nuclear estrogen receptor to influence androgen production, but instead it is act at the cell surface via a membrane estrogen receptor.

Alcohol has been reported to elevate prolactin level in the blood in both male and female alcoholics [82], in another study a transient acute elevation in plasma prolactin was observed among premenopausal women using oral contraceptives as well as among non-users after intake of alcohol [52]. Deferring, a study observed no change in prolactin level male alcoholic when compared to nonalcoholic male [11]. Although it is known that alcoholism can cause hyperprolactinemia the mechanism by which this occurs is not very clear [83]. Tuomisto and Männistö [84] in their review suggested that the elevated prolactin level might involve the opioid peptides and dopamine; these participate in the hypothalamic regulation of pituitary prolactin secretion. Acute alcohol intake has been described to release  $\beta$ -endorphin peptides in the rat hypothalamus [85] and elevate plasma  $\beta$ -endorphin in man [86].

An animal study examined whether alcohol-induced hyperprolactinemia is the result of increased pituitary production of prolactin as consequent of increased cell number and/or increased cell production of prolactin in the pituitary and also whether its action directly on the pituitary lactotropes or it is dependent on the presence of estradiol. it was demonstrated that the pituitary of ethanol fed rats revealed an increased number of proliferating lactotrophic cells when compared to those rats fed diets without ethanol after fifteen days, it was observed that the administration of ethanol potentate the effects of estradiol in the rats. Same study also observed that ethanol increased prolactin production in vitro enriched lactotropes thus they established that ethanol acts directly on lactotropes cells of the pituitary gland. However the exact mechanism in which ethanol affects lactotropes was not determined, they suggested that it may involve cytokines, or intercellular mediators produced locally in the pituitary [87]. One cytokine, Transforming Growth Factor (TGF- $\beta$ -I), has been demonstrated to inhibit prolactin production and cell proliferation. The production of this cytokine is inhibited by estradiol administration and further reduced by ethanol administration [83]. Prolactin secretion is known to be stimulated by estrogen [88], therefore it can be suggested that the elevated prolactin might be due to high estrogen level in alcoholics.

#### **4. CONCLUSION**

The findings in this review exposed the various harmful effect of alcohol on reproductive functions of male and female. Alcohol abuse is associated with hormonal changes in men and women, negatively affect sexual desire as well as performance and has a destructive effect on sex organs, these harmful effects of alcohol can also occur even at moderate drinking levels. The oxidized product of alcohol which is acetaldehyde has been suggested to be responsible for its toxicity. Acetaldehyde has been demonstrated to act via promoting depletion of antioxidants, mediating free radical production and lipid peroxidation, suggesting that alcohol's effect on reproductive system might be alleviated by antioxidants. It is therefore proposed that future research should investigate the consequences of antioxidants usage on alcohol's effects on reproductive functions and also if antioxidants administration can reverse the tissue damage induced by chronic alcohol intake. Furthermore, alcoholic beverages have been demonstrated to contain phytoestrogens which exerted estrogenic effects, further study is needed to investigate the cellular mechanisms underlying its effects in order to develop effective approaches to reverse or prevent its effects.

## CONSENT

Not applicable.

## ETHICAL APPROVAL

Not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- 1 Zinaman MJ, Clegg ED, Brown CC, O'Connor J, Selevan SG. Estimates of human fertility and pregnancy loss. *Fertil and Steril*. 1996;65:503-509.
- 2 Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Protein intake and ovulatory infertility. *Am J Obstet Gynecol*. 2008;198:210.
- 3 Barnea ER, Tai J. stress –related reproductive failure J. invitro fertile. *Embryo Transfers*. 1991;8:15-23.
- 4 Pook M, Krause W, Röhrle BA. Validation study on the negative association between an active coping style and sperm concentration. *J Reprod Infant Psychol*. 2000;18:249–252.
- 5 Gerhard I, Runnebaum B. The limits of hormone substitution in pollutant exposure and fertility disorders. *Zentralbl Gynakol*. 1992;114:593-602.
- 6 Chalupka S, Chalupka AN. The impact of environmental and occupational exposures on reproductive health. *JOGNN*. 2010;39:84–102.
- 7 Kapawa A, Giannakis D, Tsoukanelis K, Sofikitrs N. Effect of paternal cigarette smoking on testicular function, sperm fertility capacity, embryonic development and blastocyst capacity for implantation in rats. *Andrologin*. 2004;36:57-68.
- 8 Park B, McPartland JM, Glass M. Cannabis, cannabinoids and reproduction. *Prostaglandins Leukot Essent Fatty Acids*. 2004;70:189–197.
- 9 Mello M, Mendelson J, Teol S. An overview of effect of alcohol on neuroendocrine function in women: Zatkhari, S. ed. *Alcohol and Endocrine system*. National institute on alcohol abuse and alcoholism research monograph. Bethesda, MD: the institute. 1993;23:139-169.
- 10 Eggert J, Theobald H, Engfeldt P. Effects of alcohol consumption on female fertility during an 18-year period. *Fer til Steril*. 2004;81:379–383.
- 11 Muthusami KR, Chinnaswamy P. Effect of chronic alcoholism on male fertility hormones and semen quality. *Fer til Steril*. 2005;84:919–924.
- 12 Maxwell CR, Spangenberg RJ, Hoek JB, Silberstein SD, Oshinsky, ML. Acetate Causes Alcohol Hangover Headache in Rats. In Skoulakis, Efthimios M. C. *PLoS ONE*. 2010;5:12.
- 13 Cassarett L, Doull J. *Toxicology: The Basic Science of Poisons*. ed 3. 1986;48-653.
- 14 Ozaras R, Tahan V, Aydin S, Uzun H, Kaya S, Senturk H. N-acetylcysteine attenuates alcohol-induced oxidative stress in the rat. *World J of Gastroenterol*. 2003;9:125–128.
- 15 Mendelson JH, Mello NK. Medical progress, Biologic concomitants of Alcoholism. *N Engl J Med*. 1979;301:912–921.
- 16 Miller NS, Gold MS. The human sexual response and alcohol and drugs. *J Subst Abuse Treat*. 1988;5:171–177.

- 17 Vijayasenana ME. Alcohol and sex. *N Z Med J.* 1981;93:18–20.
- 18 Okulate G, Olayinka O, Dogunro AS. Erectile dysfunction: prevalence and relationship to depression, alcohol abuse and panic disorder. *Gen Hosp Psychiatry.* 2003;25:209–13.
- 19 Bijil SA, Vivek B. Prevalence of sexual dysfunction in male subjects with alcohol dependence. *Ind J Psych.* 2007;49:109–112.
- 20 Gumus B, Yigitoglu MR, Lekili M, Vyanik BS, Muezzinoglu T, Buyuksu C. Effect of long term alcohol abuse on male sexual function and serum gonadal hormone levels. *Int Urol Nephrol.* 1998;30:755–759.
- 21 Snyder S, Karacan I. Effect of chronic alcoholism on nocturnal penile tumescence. *Psycho Med.* 1981;43:423-429.
- 22 Schiavi RC, Stimmel BB, Mandelli J, White D. Chronic alcoholism and male sexual function. *Am J Psychiatry.* 1995;152:1045–1051.
- 23 Covington SS, Kohen J. Women, alcohol, and sexuality. *Advances in Alcohol and Substance Abuse.* 1984;4:41-56.
- 24 George WH, Davis KC, Norris J, Heiman JR, Stoner SA, Schacht RL, Hendershot CS, Kajumulo KF. Indirect effects of acute alcohol intoxication on sexual risk-taking: The roles of subjective and physiological sexual arousal. *Arch of Sex Behav.* 2009;38:498–513.
- 25 George WH, Davis KC, Heiman JR, Norris J, Stoner SA, Kajumulo KF. Sexual abuse history, alcohol intoxication, and women's sexual risk behavior. *Arch of Sex Behav.* 2010;39:898–906.
- 26 Schacht RL, George WH, Otto JM, Davis KC, Heiman JR, Norris J, Kajumulo KF. Assessing women's sexual arousal in the context of sexual assault history and acute alcohol intoxication. *J of Sex Med.* 2010;7:2112–2119.
- 27 George WH, Davis KC, Heiman JR, Norris J, Stoner SA, Kajumulo KF. Sexual abuse history, alcohol intoxication, and women's sexual risk behavior. *Arch of Sex Behav.* 2010;39:898–906.
- 28 Beckman LJ, Ackerman KT. "Women, alcohol, and sexuality". *Recent Developments in Alcoholism.* 1995;12:267–285.
- 29 Frias J, Rodrigues R, Torres JM, Ruiz E, Ortega E. Effects of acute alcohol intoxication on pituitary-gonadal axis hormones, pituitary-adrenal axis hormones, endorphin and prolactin in human adolescents of both sexes. *Life Sci.* 2000;67:1081-1086.
- 30 Murty BR. The Biochemistry of Alcohol Toxicity. *Resonance.* 2004;41-47.
- 31 Villalta J, Estruch R, Antunez E, Valls J, Urbano-Marquez A. Vagal neuropathy in chronic alcoholics: Relation to ethanol consumption. *Alcohol Alcohol.* 1989;24:421–428.
- 32 Pfaus JG, Wilkins MF, Dipietro N, Benibgui M, Toledano R, Rowe A, Couch MC. Inhibitory and disinhibitory effects of psychomotor stimulants and depressants on the sexual behaviour of male and female rats. *Hormones and Behaviour.* 2010;58:163–176.
- 33 Stephanie SC. Women, Addiction, and Sexuality. *Gender Issues in Addiction: Men and Women in Treatment.* eds L. Straussner and E. Zelvin, Jason Aronson. 1997.
- 34 Malatesta VJ, Pollack RH, Crotty TD, Peacock LJ. Acute alcohol-intoxication and female orgasmic response. *Journal of Sex Research.* 1982;18:1–17.
- 35 Aydinoglu F, Yilmaz SN, Coskun B, Daglioglu N, Ogulener N. Effects of ethanol treatment on the neurogenic and endothelium-dependent relaxation of corpus cavernosum smooth muscle in the mouse. 2008;60:725-734.
- 36 Yang L, Tang Q, Hu BR, Xiang JZ. Relaxant effect of ethanol on isolated rabbit corpus cavernosum and its mechanism. *Zhonghua Nan Ke Xue.* 2007;13:910-914.

- 37 Srilatha B, Adaikan PG. Estrogen and phytoestrogen predispose to erectile dysfunction: do ER-alpha and ER-beta in the cavernosum play a role? *Urol.* 2004;63:382-386.
- 38 Zhou ZY, Hu LQ, Wang HP, Li SW, Ma SL, Tang Q. Antifertility effect of 30% ethanol retro-injection into rat vas deferens. *Zhonghua Nan Ke Xue.* 2006;12:602-4.
- 39 Emanuele MA, Emanuele NV. Alcohol's Effects on Male Reproduction. *Alcohol Health & Research World.* 1998;22:195-201.
- 40 Gaur DS, Talekar MS, Pathak VP. Alcohol intake and cigarette smoking: Impact of two major lifestyle factors on male fertility. *Indian J Pathol Microbiol.* 2010;53:35-40.
- 41 Adams ML, Cicero TJ. Effects of alcohol on  $\beta$ -endorphin and reproductive hormones in the male rat. *Alcohol Clin Exp Res.* 1991;15:685-692.
- 42 Van TDH, Gavaler JS, Lester R, Shreins RJ. Alcohol-induced ovarian failure in the rat. *Journal of Clinical Investigation.* 1978;61:624-632.
- 43 Eggert J, Theobald H, Engfeldt P. Effects of alcohol consumption on female fertility during an 18-year period. *Fertil Steril.* 2004;81:379-383
- 44 Lieber CS. Medical and nutritional complications of alcoholism: mechanisms and management. New York. Plenum press. 1992;579.
- 45 Lieber CS. Ethanol metabolism, cirrhosis and alcoholism. *Clinica Chimica Acta.* 1997;257:59-84.
- 46 Hasumura Y, Teschke R, Lieber CS. Hepatic microsomal ethanol oxidizing system (MEOS): dissociation from reduced nicotinamide adenine dinucleotide phosphate-oxidase and possible role of form 1 of cytochrome P-450. *J pharmacol Exp Ther.* 1975;194:469-474.
- 47 Espina N, Lima V, Lieber CS, Garro AJ. In vitro and in vivo inhibitory effect of ethanol and acetaldehyde on o6-methylguanine transferase. *Carcinogenesis.* 1988;761-766.
- 48 Lecomte E, Herbeth B, Pirollet P, Chancerelle Y, Arnaud J, Musse N, Paille F, Siest G, Artur Y. Effect of alcohol consumption on blood antioxidant nutrients and oxidative stress indicators. *Am J Clin Nutr.* 1994;60:255-261.
- 49 Neethumol P, Kevin J, Chiramel AR, Shivashankara AR. Effect of Alcohol Withdrawal on Glutathione S-transferase, Total Antioxidant Capacity and Amylase in Blood and Saliva of Alcohol-Dependent Males. *J Clin Diagn Res.* 2013;7:797-800.
- 50 Kurban S, Mehmetolu I. The Effect of Alcohol on Total Antioxidant Activity and Nitric Oxide Levels in the Sera and Brains of Rats. *Turk J Med Sci.* 2008;38:199-204.
- 51 Veldman RG, Meinders AE. On the mechanism of alcohol-induced pseudo-Cushing's syndrome. *End Rev.* 1996;17:262-268.
- 52 Ching M, Valenca M, Negro-Vilar A. Acute ethanol treatment lowers hypophyseal portal plasma LHRH and systemic LH levels in rats. *Brain Research.* 1988;443:325-328.
- 53 Emanuele MA, Tentler JJ, Reda D, Kirsteins L, Emanuele NV, Lawrence AM. The effect of in vitro ethanol exposure on LHRH release from perfused rat hypothalamus. *Endocrine Research.* 1990;16:313-321.
- 54 Uddin S, Wilson J, Emanuele MA, Williams D, Kelley MR, Emanuele N. Ethanol-induced alterations in the posttranslational processing, but not secretion of luteinizing hormone-releasing hormone in vitro. *Alcohol Clin Exp Res.* 1996;20:556-560.
- 55 Rettori V, McCann SM. Role of nitric oxide and alcohol on gonadotropin release in vitro and in vivo. *Ann N Y Acad Sci.* 1998;840:185-93.
- 56 Canteros G, Rettori V, Franchi A, Genaro A, Cebral E, Faletti A, Gimeno M, McCann SM. Ethanol inhibits luteinizing hormone-releasing hormone (LHRH) secretion by blocking the response of LHRH neuronal terminals to nitric oxide. *Proc Natl Acad Sci U S A.* 1995;92:3416-20.

- 57 Sarkola T, Mäkisalo H, Fukunaga T, Eriksson CJP. Acute effect of alcohol on estradiol, estrone, progesterone, prolactin, cortisol, and luteinizing hormone in premenopausal women. *Alcohol Clin Exp Res.* 1999;23:976-982.
- 58 Välimäki, M., Tuominen, J.A., Huhtaniemi, I., and Ylikahri, R. The pulsatile secretion of gonadotropins and growth hormone, and the biological activity of luteinizing hormone in men acutely intoxicated with ethanol. *Alcohol Clin. Exp. Res.* 1990;14:928-931.
- 59 Emanuele MA, Tentler J, Emanuele NV, Kelley MR. In vivo effects of acute EtOH on rat and  $\beta$  luteinizing hormone gene expression. *Alcohol.* 1991;8:345-348.
- 60 Pohl CR, Guilinger RA, Van TDH. Inhibitory action of ethanol on luteinizing hormone secretion by rat anterior pituitary cells in culture. *Endocrinology.* 1987;120:849-852.
- 61 Salonen I, Huhtaniemi I. Effects of chronic ethanol diet on pituitary-testicular function of the rat. *Biology of Reproduction.* 1990;42:55-62.
- 62 Emanuele MA, Tentler J, Halloran MM, Emanuele NV, Wallock L, Kelley MR. The effect of acute in vivo ethanol exposure on follicle stimulating hormone transcription and translation. *Alcohol Clin Exp Res.* 1992;16:776-780.
- 63 Teoh SK, Mendelson JH, Mello NK, Skupny A, Ellingboe J. Alcohol effects on hCG-stimulated gonadal hormones in women. *J Pharmacol Exp Ther.* 1990;254:407-411.
- 64 Ginsburg ES, Mello NK, Mendelson JH, Barbieri RL, Teoh SK, Rothman M, Gao X, Sholar JW. Effects of alcohol ingestion on estrogens in postmenopausal women. *JAMA.* 1996;276:1747-1751.
- 65 Gordon GG, Southren AL, Vittek J, Lieber CS. Effect of alcohol ingestion on hepatic aromatase activity and plasma steroid hormones in the rat. *Metabolism.* 1979;28:20-24.
- 66 Gavaler JS. Alcoholic Beverages as a Source of Estrogens *Alcohol Health & Research World.* 1998;22:220-228.
- 67 Eriksson CJP, Fukunaga T, Lindman R. Sex hormone response to alcohol. *Nature.* 1994;369:711.
- 68 Sarkola T, Fukunaga T, Mäkisalo H, Eriksson CJP. Acute effect of alcohol on androgens in premenopausal women. *Alcohol.* 2000;35:84-90.
- 69 Milovanović T, Budeč M, Balint-Perić Lj. Effects of acute administration of ethanol on rat adrenal cortex. *J Stud Alcohol.* 2003;64:662-668.
- 70 Rivier C. Female rats release more corticosterone than males in response to alcohol: influence of circulating sex steroids and possible consequences for blood alcohol levels. *Alcohol Clin Exp Res.* 1993;17:854-859.
- 71 Boyd KN, Kumar S, O'Buckley TK. Ethanol induction of steroidogenesis in rat adrenal and brain is dependent upon pituitary ACTH release and de novo adrenal StAR synthesis. *J Neurochem.* 2010;112:784-796.
- 72 Rivier C, Lee S. Acute alcohol administration stimulates the activity of hypothalamic neurons that express corticotropin-releasing factor and vasopressin. *Brain Res.* 1996;726:1-10.
- 73 Li Z, Kang SS, Lee S. Effect of ethanol on the regulation of corticotropin-releasing factor (CRF) gene expression. *Mol Cell Neurosci.* 2005;29:345-354.
- 74 Lee S, Craddock Z, Rivier C. Brain stem catecholamines circuitry: activation by alcohol and role in the hypothalamic-pituitary-adrenal response to this drug. *J Neuroendocrinol.* 2011;23:531-541.
- 75 Somer L, Matavulj M, Hadzić B, Vucković N. The hypophyseal-adrenal axis in chronic alcoholism. *Med Pregl.* 1996;49:349-55.
- 76 Gordon GS, Vittek J, Southren AL, Munnangi P, Lieber CS. Effect of chronic ethanol ingestion on the biosynthesis of steroids in rat testicular homogenate in vitro. *Endocrinology.* 1980;106:1880-1885.

- 77 Emanuele MA, Lapaglia N, Steiner J, Jabamoni K, Hansen M, Kirsteins L, Emanuele N. Reversal of ethanol-induced testosterone suppression in peripubertal male rats by opiate blockade. *Alcohol Clin Exp Res*. 1998;22:1199–1204.
- 78 Mccann SM, Rettori V. The role of nitric oxide in reproduction. *Proceedings of the Society of Experimental Biology and Medicine*. 1996;211:7–15.
- 79 Adams ML, Forman JB, Kalicki JM, Meyer ER, Sewing B, Cicero TJ. Antagonism of alcohol-induced suppression of rat testosterone secretion by an inhibition of nitric oxide synthase. *Alcohol Clin Exp Res*. 1993;17:660–663.
- 80 Kalla NR, Nisula BC, Menard R, Loriaux DL. The effect of estradiol on testicular testosterone biosynthesis. *Endocrinology*. 1980;106:35–39.
- 81 Anna KL, Peter T. Effects of Estrogens and Xenoestrogens on Androgen Production by Atlantic Croaker Testes In Vitro: Evidence for a Nongenomic Action Mediated by an Estrogen Membrane Receptor. *Biology of Reproduction*. 2000;62:4995-5004.
- 82 Mendelson JH, Mello NK, Cristofaro P, Ellingboe J, Skupny A, Palmieri SL, Benedikt R, Schiff I. Alcohol effects on naloxone-stimulated luteinizing hormone, prolactin and estradiol in women. *J Stud Alcohol*. 1987;48:287-294.
- 83 Braund D, "Hyperprolactinemia" (2002). Honors Thesis. Paper 238.
- 84 Tuomisto J, Männistö P. Neurotransmitter regulation of anterior pituitary hormones. *Pharmacol Rev*. 1985;37:249-332.
- 85 Gianoulakis C. Characterization of the effect of acute ethanol administration on the release of endorphin peptides by the rat hypothalamus. *Eur J Pharm*. 1990;180:21-29.
- 86 Gianoulakis C, Béliveau D, Angelogianni P, Meaney M, Thavundail J, Tawar V, Dumas M. Different pituitary endorphin and adrenal cortisol response to ethanol in individuals with high and low risk for future development of alcoholism. *Life Sci*. 1989;45:1097-1109.
- 87 De Alok, Nadka B, Souichi O, Dipak KS. Ethanol Induces Hyperprolactinemia by Increasing Prolactin Release and Lactotrope Growth in Female Rats. *Alcohol Clin Exp Res*. 2002;26:1420-1429.
- 88 Donald LT, Sarah CC, Pamela BM, Lisa RE. Estradiol Effects on Secretagogue-Induced Prolactin Release: Disparity in Responses to Sulpiride, Exercise, Epinephrine, Prostaglandin-F<sub>2</sub>α, and Thyrotropin-Releasing Hormone. *Journal of Equine Veterinary Science*. 2013;33:607–614.

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