CLINICAL STUDY

Effect of Alcohol on Clinical Outcomes and Its Relationship with Semen Parameters

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ABSTRACT

Background: The incidence of infertility is 10%-15% globally and this has risen in recent years. Alcohol has been consumed in India for centuries, both in rural and urban areas, with prevalence rates ranging from 20% to 38% in males, according to various reports. Studies in northern India found the 1 year prevalence of alcohol use to be between 25% and 40%. In southern India, the prevalence of current alcohol use varies between 33% and 50%, with a higher prevalence among the lesser educated and the poor. **Aim:** To determine the effect of alcohol on seminal parameters. **Design:** Retrospective study. **Setting:** Morpheus Lucknow Fertility Center, Lucknow, Uttar Pradesh. **Time duration:** From January 2017 to December 2020. **Sample size:** Total 130 patients consisting of 57 patients as nonalcoholic control and 73 patients as alcoholic. **Main outcome measure(s):** The outcome of interest was seminal parameters, including count, motility, volume and morphology. **Method:** The study included two subject groups, controls and alcoholics. Subjects in the control group were volunteers who were free from any disease and who had never consumed alcoholic drinks and who had never smoked. Subjects in the alcoholic group were nonsmokers who had consumed a minimum of 180 mL of alcohol (brandy and whisky, both 40%-50% alcohol content) per day for a minimum of 5 days per week in the past year. Semen samples were collected after at least 48 hours but no more than 7 days of sexual abstinence. Semen parameters - volume, count, motility and morphology - were analyzed. **Results:** In the alcoholic group, volume ($p < 0.005$), count ($p < 0.005$), percentage of rapid progressively motile sperm ($p < 0.005$), were statistically significantly decreased, while percentage of nonprogressive sperm and percentage of immotile sperm ($p < 0.005$) were statistically significantly increased, compared with the control group. The percentages of slow progressively motile sperm and morphology were not statistically significant. **Conclusions:** The present study found statistically significant results that chronic alcoholism suppresses semen quality, at the seminiferous tubular level. Alcohol decreases semen volume, total sperm concentration, motility of sperm and viability of sperm. This study has proved beyond doubt that chronic alcohol consumption has a detrimental effect on the quality of semen, which in turn, may have effect on their reproductive outcomes.

Keywords: Alcohol, semen, sperm, semen quality, volume, count, motility

Infertility affects about 15% of the general population, where male infertility appears to play a role in up to 30% of cases[1]. Men's reproductive health has been known to be influenced by lifestyle and environmental factors, such as eating patterns, obesity, cigarette smoking, alcohol intake, substance abuse and exposure to environmental toxins[2]. Although the evidence for a causal correlation between environmental factors and male infertility is still inconclusive.

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Alcohol has been consumed in India for centuries. A number of mythological and religious books have highlighted the role it played in society. The pattern of drinking in India has undergone a change from occasional and ritualistic use to being a social event. Alcohol consumption is widespread in India, both in rural and urban areas, with prevalence rates ranging from 20% to 38% in males, according to various reports. Studies conducted in northern India reported the 1 year prevalence of alcohol use to be 25%-40%, while in southern India, the prevalence of current alcohol use has been reported to range from 33% to 50%. The prevalence has been reported to be higher among the lesser educated and the poor[3].

Excessive alcohol consumption (more than 3 days a week for more than a year) has been shown to have a negative effect on health. Alcohol reduces the amount of spermatozoa with regular morphology and increases the number of permanent tail defects[4]. Evidence suggests

that ethanol is a Leydig cell toxin[5], although dose-dependent effects of alcohol on human spermatogenesis are not well-known. Seminiferous tubules in alcohol users mostly contain degenerated spermatids with a consequent azoospermia[6].

Table 1 outlines the mechanisms underlying the connection between alcohol intake and reduced sperm content, which have been linked to a direct negative impact on testosterone metabolism and spermatogenesis. Alcohol consumption alters the ratio of free estradiol to free testosterone, and spermatogenetic arrest and Sertoli-cell-only syndrome are more commonly associated with heavy drinking.

Alcohol appears to have a dual impact on the hypothalamic-pituitary-gonadal axis, preventing the release of luteinizing hormone (LH)-releasing hormone/LH from the hypothalamic-pituitary axis and inhibiting testicular steroidogenesis. Moderate alcohol intake has been linked to a lower risk of mortality and morbidity, but not always. Excessive alcohol consumption, on the other hand, is harmful to one's health (e.g., coronary heart disease, stroke and liver disease). Some studies have also indicated a connection between alcohol consumption and sperm quality, but others have not confirmed these findings.

The areas of interest regarding the use of alcohol and its effects on fertility are described in Figure 1[7]. Men who drink too much alcohol can have problems conceiving. Reduced gonadotropin release, testicular atrophy, and decreased testosterone and sperm output have all been identified in studies of long-term, heavy alcohol use. Other studies of men who drink excessively have found increased gonadotropins and estradiol levels in the absence of liver disease, as well as reduced testosterone.

Table 1. Alcohol Intake and Male Reproductive Function

Level of alcohol consumption	Effect on male reproduction
Moderate alcohol consumption	No effect on fecundability
	No increased subfecundity
	No effect on any semen parameters or pregnancy rate
	No difference in any semen parameters
Excessive alcohol intake	Increased serum free testosterone (19.7-24.6 pmol/L higher) and total testosterone (0.9-1.0 nmol/L higher)

Although most studies found that the semen characteristics were lower at higher levels of recent alcohol intake; however, there was no statistically significant dose-response association. The hormonal changes observed in men with a high alcohol intake may, overtime, lead to adverse effects on semen quality. More longitudinal studies are needed to verify these results. Hence, the aim of this study is to find the relationship between alcohol intake and the semen characteristics.

MATERIAL AND METHODS

Subjects

This study was conducted at the Morpheus Lucknow Fertility Center, Lucknow, Uttar Pradesh, India. We screened a total of 73 alcoholics who had reported to the Morpheus Fertility Center and 57 nonalcoholic nonsmoking volunteers (as controls) from Lucknow city. The study population consisted of 66 nonsmoking alcoholics, aged 36.6 ± 5.7 years (mean ± SD). Alcoholics consuming drugs like diazepam, pethidine, cannabis and marijuana along with alcohol were excluded from the study. The control population consisted of 30 normal healthy persons aged 35.0 ± 6.1 years.

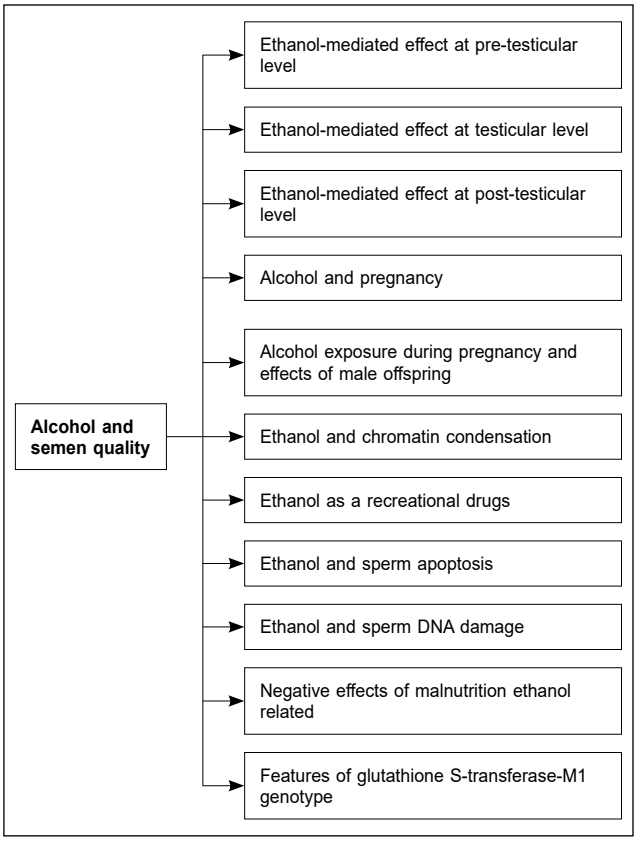

Figure 1. Main areas of interest regarding the use of alcohol and its effects on fertility (adapted from Condorelli et al, 2015).

The subjects were examined by a physician before inclusion in the study. Personal interviews were conducted with all alcoholic and control subjects to obtain relevant clinical data: age, sex, domicile (urban vs. rural dwelling), marital status, diet, history of alcohol consumption, infertility status, past medical illness and treatment, history of smoking, sexual urgency and frequency and premarital and extramarital sexual history. Sexual function (e.g., erectile function, libido potency, frequency of ejaculation) was also noted in the questionnaire.

Experimental Design

The study included two subject groups - controls and alcoholics. Subjects in the control group were volunteers who were free from any disease and who had never consumed alcoholic drinks and who had never smoked. Subjects in the alcoholic group were nonsmokers who had consumed a minimum of 180 mL of alcohol (brandy and whisky, both 40%-50% alcohol content) per day for a minimum of 5 days per week in the past year.

Semen Collection

The participant was asked to collect semen in the collection room near to the laboratory in order to limit the exposure of the semen to fluctuations in temperature and the time between the collection and analysis was maintained. The sample was collected with minimum 2 days and maximum 7 days of sexual abstinence.

Before collection, partner was given clear instruction concerning the collection of semen sample as the semen sample should be complete and there should be no loss of any fraction of the sample. The sample was obtained by masturbation and was ejaculated into a clean wide-mouthed plastic container. Container should not be touched on the inner surface with wet hands was instructed to the participant. After collection, sample was stored at 37°C. It was left for liquefaction for 30 minutes at 37°C in incubator. If it was not liquefied, then needling was done with (18G) needle attached to 2 cc syringe.

Semen Analysis

Semen analysis was performed prior to semen processing. Semen analysis mainly accounted for sperm count and sperm motility and values were evaluated in reference of World Health Organization (WHO) manual 2010.

Sperm Count

Sperm count was performed using a hemocytometer having two chambers, and each chamber has a microscopic grid attached to the glass surface. The chambers are overlaid with a special heavy glass cover slip that stays on pillars exactly 0.1 mm above the chamber floor. The main divisions separate the grid into 9 squares. Each square has a surface area of 1 mm^2, a depth of 0.1 mm and a total volume of 0.1 mm^3 or 10^{-4} cm^3. The central square consists of 25 large squares, and each of these contains 16 smallest squares. Each horizontal and vertical count was taken for 10 consecutive boxes and average was taken in count.

Sperm Motility

The collected sample was allowed to liquefy and a wet preparation was made using counting chamber. The chambers were overlaid with a special heavy glass cover slip that rests on pillars exactly 0.1 mm above the chamber floor. The slide was examined with phase-contrast optics at x200 or x400 magnification. At least 100 sperms for different categories of motility were counted.

Sperm Morphology

Diff-Quik staining was performed according to strict criteria; the length of the head should be 4.0-5.0 μm and the width should be 2.5-3.5 μm with a length/width ratio of 1.50 to 1.75. There should be a well dense acrosomal region which comprises of 40-70% of the head area. The mid-piece should be slender, <1 μm wide, about 1.5 times the length of the head and attached axially. Cytoplasmic droplets should be less than half the size of a normal head. The tail should be straight (uncoiled), thinner than the mid-piece and approximately 45 μm long. For a spermatozoon to be considered normal, the head, neck, mid-piece and tail should all be normal. At least 100 sperms were counted.

Seminal Parameters

Semen samples were collected after at least 48 hours but no more than 7 days of sexual abstinence. The semen sample was collected by masturbation and delivered to the laboratory within ½ hour from the time of collection. After liquefaction, semen appearance, volume, consistency, pH, fructose and sperm motility, concentration, viability and morphology were analyzed as per the criteria of the WHO manual 2010. Motility was expressed as percentages of rapid progressively motile, slow or sluggishly motile, nonprogressive motile and immotile sperm. Sperm viability was expressed as percentages of live and dead sperm, and sperm morphology.

STATISTICAL ANALYSIS

The patients were recruited into two groups namely, Group 1 Nonalcoholics (n = 57) and Group 2 Alcoholics (n = 73). Descriptive statistics was done using tables, columns, charts and measure of central tendency and dispersion was also calculated. The results for both groups are expressed as mean ± SD. The results were analyzed statistically with commercial software (SPSS for Windows 7.5.1; SPSS, Chicago, IL). Student's-test was used to determine the degree of significance for the various mean variables obtained. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 130 patients was recruited in the study, containing 57 nonalcoholics and 73 alcoholics. Table 2

Table 2. The Descriptive Statistics of All Seminal Parameters in Alcoholics and Control Group

Group Statistics					
	Group	**N**	**Mean**	**SD**	**SE Mean**
Volume	Nonalcoholics	57	2.7895	0.99187	0.13138
	Alcoholics	73	1.5767	0.56900	0.06660
Count	Nonalcoholics	57	117.5789	48.23638	6.38906
	Alcoholics	73	48.7534	18.48857	2.16392
Rapid progressive motility	Nonalcoholics	57	56.1579	6.25582	0.82860
	Alcoholics	73	14.9041	7.54462	0.88303
Slow progressive motility	Nonalcoholics	57	21.4912	2.67343	0.35410
	Alcoholics	73	23.9863	6.41286	0.75057
Nonprogressive motility	Nonalcoholics	57	2.9474	1.04234	0.13806
	Alcoholics	73	27.7123	7.66391	0.89699
Immotile	Nonalcoholics	57	20.2807	4.00337	0.53026
	Alcoholics	73	33.3973	13.26518	1.55257
Morphology	Nonalcoholics	57	5.9649	1.68994	0.22384
	Alcoholics	73	5.1096	2.21461	0.25920

Table 3. The Seminal Parameter Value in Nonalcoholics and Alcoholics

Seminal parameter	Nonalcoholics (57)	Alcoholics (73)	't' value
Semen volume (mL)	2.789 ± 0.991	1.576 ± 0.569	8.234[a]
Sperm count (10^6/mL)	117.578 ± 48.236	48.753 ± 18.488	10.203[a]
Rapid progressively motile sperm (%)	56.157 ± 6.255	14.904 ± 7.544	34.068[a]
Slow progressively motile sperm (%)	21.491 ± 2.673	23.986 ± 6.412	-2.754649[NS]
Nonprogressively motile sperm (%)	2.947 ± 1.042	27.7123 + 7.663	-24.202[a]
Immotile sperm (%)	20.281 ± 4.003	33.397 ± 13.265	-7.994850[a]
Morphologically normal sperm (%)	5.9649 ± 1.689	5.109 ± 2.214	2.417026[NS]

Note: Values are expressed as mean ± SD. NS = Nonsignificant.

[a]$P < 0.05$

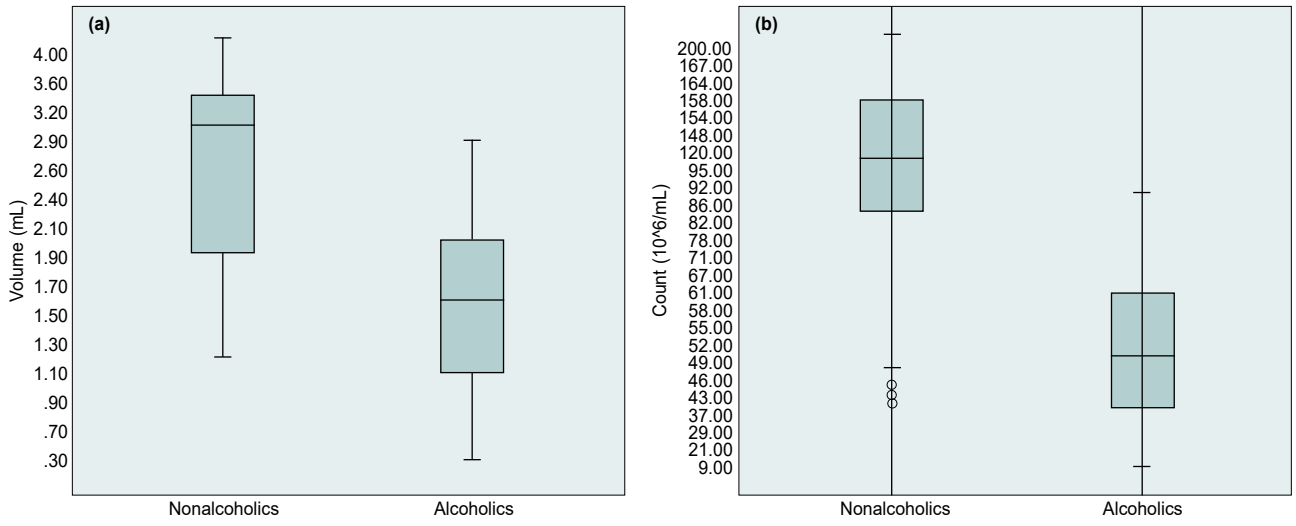

Figure 2 a) Box chart of volume in alcoholics and nonalcoholics, **(b)** Box chart of count in alcoholics and nonalcoholics.

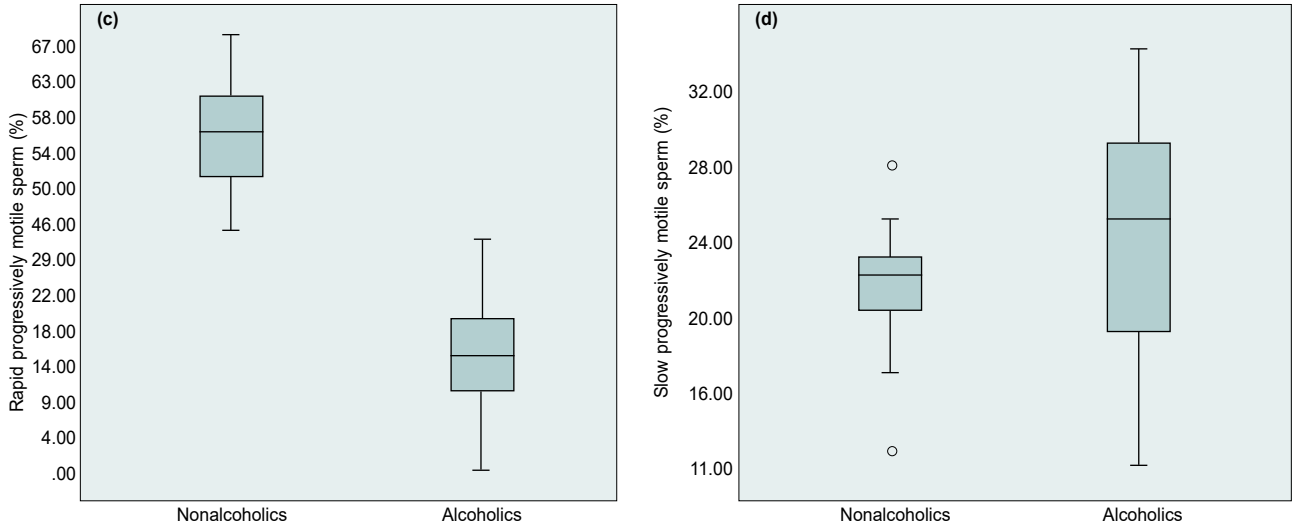

Figure 2 c) Box chart of rapid progressive motility in alcoholics and nonalcoholics, **(d)** Box chart of slow progressive motility in alcoholics and nonalcoholics.

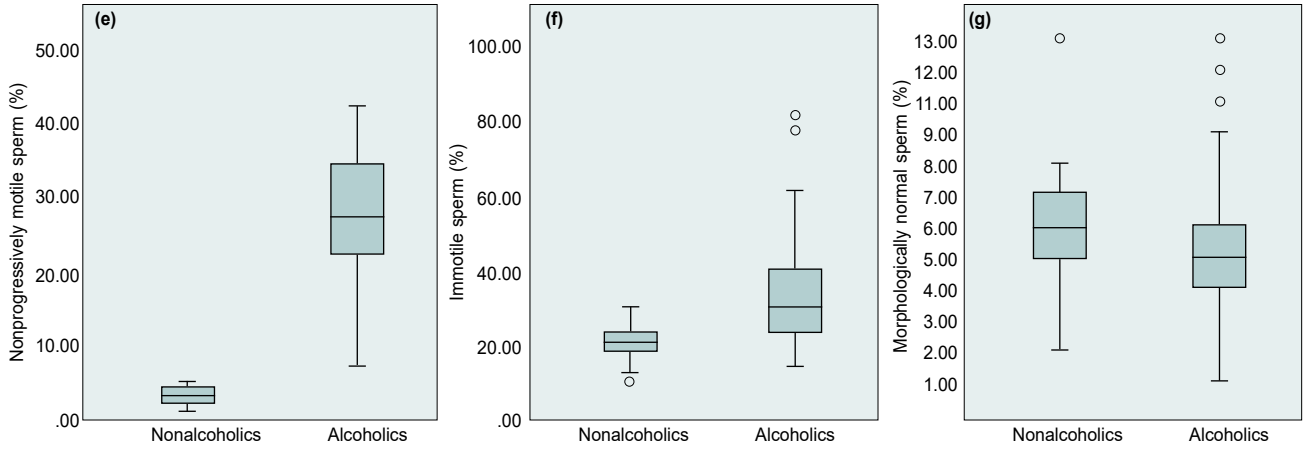

Figure 2 e) Box chart of nonprogressive motility in alcoholics and nonalcoholics, **(f)** Box chart of immotile sperms in alcoholics and nonalcoholics, **(g)** Box chart of morphology in alcoholics and nonalcoholics.

shows the descriptive statistics of seminal parameters in controls and alcoholics. Total average volume in alcoholics and nonalcoholics was 1.576 ± 0.569 and 2.789 ± 0.991, respectively; average count in alcoholics and nonalcoholics was 48.753 ± 18.488 and 117.578 ± 48.236, respectively. Average rapid progressive motility, average slow progressive motility, average nonprogressive motility, immotile sperm and average morphology are also presented in Table 2.

In the alcoholic group, volume ($p < 0.005$), count ($p < 0.005$), percentage of rapid progressively motile sperm ($p < 0.005$), were statistically significantly decreased, while percentage of nonprogressive sperm and percentage of immotile sperm ($p < 0.005$) were statistically significantly increased, compared with the control group (Table 3). The percentages of slow progressively motile sperm and morphology were not statistically significant. Figure 2 a-g depict the seminal parameters as box charts.

DISCUSSION

In this study, where 130 patients were recruited, including 57 nonalcoholics and 73 alcoholics, there was a statistically significant association in the semen parameters where the alcoholics (>180 mL of alcohol 5 times a week) had a reduced semen volume, count, rapid motile sperms and increased nonprogressive motile sperms and immobility. However, in terms of morphology and slow progressive motility, the results were not statistically significant.

Previous studies on alcohol intake and semen quality have shown inconsistent results[8-19], but most have been conducted among patients attending andrology or infertility clinics. Infertile men may have changed their drinking habits as a consequence of the infertility. Only four studies were conducted among unselected men, similar to our study, and they also found no association between semen quality and moderate or high alcohol intake or any statistically significant dose-response association[11,15,17,19]. We found no association between beer, wine or liquor consumption and semen quality.

The duration of human spermatogenesis is approximately 72 days[20], and the time window of alcohol exposure in this study was the last 5 days prior to semen sampling. Since, alcohol habits often follow long time trends, the recorded exposure is expected to correlate with exposure during spermatogenesis. Alcohol exposure during the late stages of spermatogenesis may disturb maturation of spermatozoa during epididymal transfer, which in particular can affect sperm motility and morphology. Continued alcohol exposure throughout spermatogenesis could affect the other semen characteristics as well. However, we found no tendency towards sperm morphology and slow progressive motility.

Sex hormone-binding globulin (SHBG) is the key carrier protein of testosterone and estradiol. It is produced in the liver, and the levels and regulation depend on diet, age and body mass index (BMI)[21]. The association between alcohol intake and SHBG is not clear. Considering the fact that SHBG affects free nonbound testosterone and estradiol, the observed rise in free testosterone and estradiol in the study by Hansen et al[17] appears to be likely guided by changes in SHBG. The study revealed that increasing recent alcohol exposure was associated with lower SHBG levels and higher testosterone levels. Similar findings were reported from the cross-sectional Third National Health and Nutrition Examination Survey (NHANES III) study conducted on healthy nonalcoholic men[22]. Studies conducted among men with chronic alcoholism and fatty liver point to a significant rise in SHBG levels with increasing alcohol exposure[23]. A detoxification study on alcoholics revealed a positive link between testosterone and SHBG, thus indicating SHBG regulation may be different in men with a high alcohol intake[24].

The present study affirmed that there is decline in seminal parameters in alcohol-dependent patients, who consumed minimum of 180 mL of alcohol (5 times/week). There was a decline in count, volume, and motility. This finding has implications for clinical practice. There were certain limitations of this study. The study was carried out in a small sample of clinic-based population, and hence the findings could not be generalized to other population groups.

Future studies should try to overcome these limitations. In addition, future research should focus on alcohol consumption in a dose-dependent manner and its effects on the seminal parameters, on structured assessment of sexual dysfunction in partners of alcohol-dependent men. If the patient has a history of alcohol and drug use/abuse/dependence, efforts must be made to delineate the relationship of sexual dysfunction with the alcohol use and efforts must be made to achieve abstinence.

CONCLUSION

In conclusion, the present study found statistically significant results that chronic alcoholism suppresses semen quality, at the seminiferous tubular level. Alcohol

decreases semen volume, total sperm concentration, motility of sperm and viability of sperm. This study has proved beyond doubt that chronic alcohol consumption has a detrimental effect on the quality of semen, which in turn, may have effect on their reproductive outcomes.

Hence, men are advised to refrain from chronic alcohol consumption if they want to procreate and lead a normal sexual life.

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