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Functional Effects of Smoking, Alcohol Consumption, and Drug Abuse on Human Metabolism, Hormonal, and Reproductive Health

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ABSTRACT

The central aim of this study is to conduct a comprehensive analysis of the impact of smoking, alcohol intake, and drug abuse on human metabolic, endocrine, and reproductive functions. Hitherto, these factors have been detrimental to the multifaceted changes in systemic physiological functions, including, but not limited to, increased oxidative stress, organ dysfunction, and hormonal imbalance. The findings of the current study highlighted reduced hemoglobin concentration and elevated WBC count among participants in the exposed group, suggesting that the exposure is associated with chronic inflammatory responses and hematopoietic dysfunction. Furthermore, signs of liver dysfunction (ALT, AST) and elevated creatinine levels, suggesting strain on liver and kidney function, were observed during this study. Subsequently, significant decreases in LH and FSH were observed in the endocrine system, suggesting dysfunction of the hypothalamic-pituitary-gonadal axis. Concurrently, a marked decrease in sperm count was confirmed, clearly indicating a decline in reproductive capacity. These changes were most pronounced, particularly in the methamphetamine exposure group. Overall, this study reveals that lifestyle-related harmful exposures cause complex and significant impairments in metabolic, endocrine, and reproductive functions, and underscores the established scientific fact that LH and FSH are important biomarkers for assessing these impairments.

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1. Introduction

Human metabolic, endocrine, and reproductive functions are vital physiological indicators of overall health, and the interaction among multiple organ systems helps maintain their balance [1]. Albeit, in recent years, there has been a growing interest in the effects of lifestyle-related factors such as smoking, alcohol consumption, and drug abuse on these physiological functions, and their association with an increase in chronic diseases and male infertility has been alluded to as pernicious factors [2]. These deleterious factors are reported to act on the hypothalamic-pituitary-gonadal (HPG) axis, thereby impairing Luteinizing hormone (LH) and Follicle-Stimulating Hormone (FSH) secretion and decreasing testosterone production and spermatogenesis [3]. Furthermore, psychoactive substances, including nicotine, alcohol, and methamphetamine, have been shown to increase oxidative stress, induce cellular damage and metabolic dysfunction in testicular tissue, and even cause liver and kidney dysfunction [4].

Additionally, prevalent studies indicate that methamphetamine users suffer from a significant reduction in LH and FSH, and a decline in semen parameters, which clearly shows that both drugs have a strong suppressive effect on the reproductive endocrine system [5]. Conversely, epidemiological research has demonstrated that smoking and drinking alcohol are linked to low levels of male hormones and decreased [6].

Hitherto, prevailing research in this field has focused on the impact of each factor in isolation. In contrast, few studies have examined the cumulative effects of multiple adverse factors on metabolic, endocrine, and reproductive functions [7].

2. Background

This medical study was conducted at the O'Bryan Lab - Male Infertility and Germ Cell Biology of the University of Melbourne, Victoria 3010, Australia, where 210 participants were tested. These participants were adult men aged between 20 and 45 years who were enrolled in the study and were equally divided into five groups (42 men each): healthy, drug users, methamphetamine users, smokers, and alcohol consumers. Infertility, defined as the inability to achieve pregnancy after one year of unprotected, frequent sexual intercourse, is a global burden that affects approximately 15% of couples, or 190–230 million people worldwide, who are trying to start a family. The male contributes significantly, directly accounting for 30–35% and up to 52% of

total couple infertility, affecting approximately 7–8% of all men [8]. The study was highly valuable due to the wealth of information it provided, ranging from potential diagnoses to pregnancy prognoses. Hitherto, comprehensive, quality-controlled semen analysis has provided reliable baseline information for assessing reproductive tract patency, basic sperm parameters, and fertility potential. However, it is not a determinant of fertility. It should be complemented with sperm functional tests, including but not limited to biomarkers of oxidative stress, sperm immaturity, and DNA fragmentation, as the primary goal was to evaluate repercussions on male fertility due to drug overdose. Many cases of infertility require evaluation by a specialist in andrology; nonetheless, the understanding and rationale of the initial assessment of the infertile male can be undertaken by non-specialists, thus improving the care and counseling of couples facing this troubling issue and avoiding unnecessary use of assisted reproductive technologies (ART) [9], Since significant cases of male infertility can be treated and reversed by medical or surgical interventions, and the fertility status can be restored, to achieve a natural pregnancy, the use of ART should not be the initial offered resource, and was not taken as the primary consideration[10].

3. Research Objectives

The following research objectives are proposed for this study:

RO1- The current study evaluates reduced hemoglobin concentration and elevated WBC count among participants

RO2- signs of liver dysfunction (ALT, AST) and elevated creatinine levels, suggesting strain on liver and kidney function, were to be determined.

RO3- Testing to check LH and FSH in the endocrine system, evaluating dysfunction of the hypothalamic-pituitary-gonadal axis.

1.2: Significance of this Study

The significance of this study lies in its evaluation of the multifaceted, simultaneous effects of smoking, alcohol consumption, and drug abuse on subsequent vital homosapien metabolic function *(hematological and biochemical indicators)*, endocrine function *(LH, FSH)*, and reproductive function *(sperm count)*. Moreover, this research underscores the significant academic interest in analyzing these physiological modifications, not limited to individuals, but rather collective issues, through multi-tasking of the mechanisms

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underlying systemic functional impairment resulting from lifestyle-related toxic exposure [11].

2. Materials and Methods

2.1: Study Design and Participants

A cross-sectional comparative study was carried out to find out the effect of alcohol, cigarette, and methamphetamine consumption on the hematological, biochemical, and reproductive parameters of adult males. A total of 210 adult men aged between 20 and 45 years were enrolled in the study and equally divided into five groups (42 men each): healthy, drug users, methamphetamine users, smokers, and alcohol consumers. Since our testing ground, Australia, is home to diverse ethnic groups, we chose participants from Aboriginal, Middle Eastern, Caucasian, South Asian, and African backgrounds. Individuals in the control group had no history of cigarette, alcohol, or drug use. The smoker group included individuals who had been smoking regularly for at least one year. The alcohol consumer group had a history of regular alcohol consumption, and the methamphetamine and drug user groups were selected based on a confirmed history of substance abuse. This information is presented in a flowchart for the audience's convenience, as shown in Fig 1.

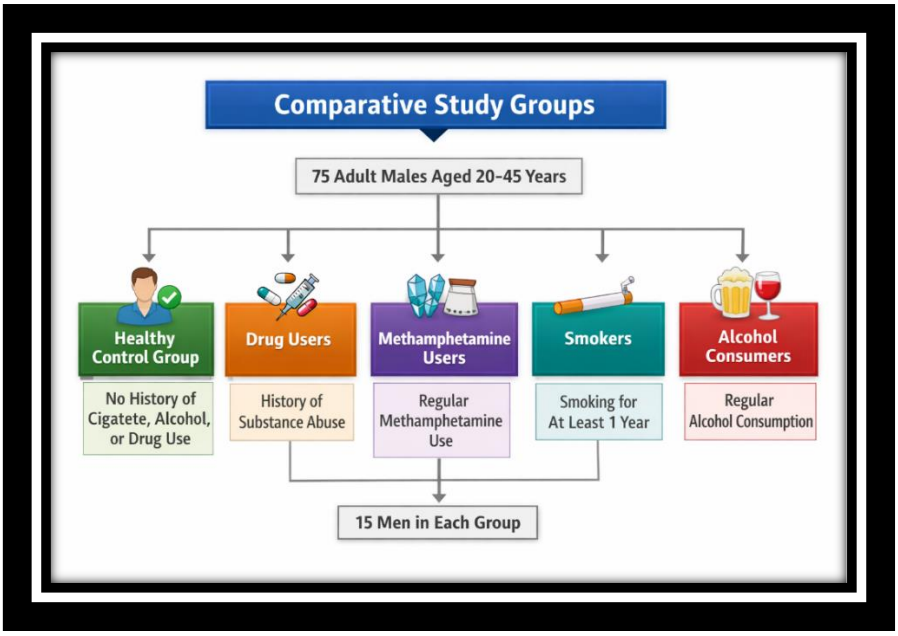

Figure 1: Comparative study groups of all 210 participants

2.2: Inclusion and Exclusion Criteria

Inclusion criteria for participants were adult men who voluntarily participated in the study and signed an informed consent form. Individuals with chronic diseases such as diabetes, cardiovascular diseases, kidney failure, liver dysfunction, endocrine disorders, infertility unrelated to substance use, or users of hormonal medications were excluded from the study. Additionally, individuals with acute infection or inflammation at the time of sampling were excluded to reduce confounding.

Figure 2-Explains clearly the inclusion or the exclusion criteria

2.3: Sample Collection

Venous blood samples were collected from all participants after 8 to 12 hours of fasting and under sterile conditions, as in the study by La Vignera, Sandro, and Rosita A. Condorelli [12]. Approximately 5 mL of blood was collected in tubes containing EDTA for hematology tests and tubes without anticoagulant for biochemical tests, as explained by Nikler in their article [13]. The samples were then centrifuged at 3000 rpm for 10 minutes, and the resulting serum was stored at -20°C until analysis, as explained by Ebisintei, Precious, in their article [14].

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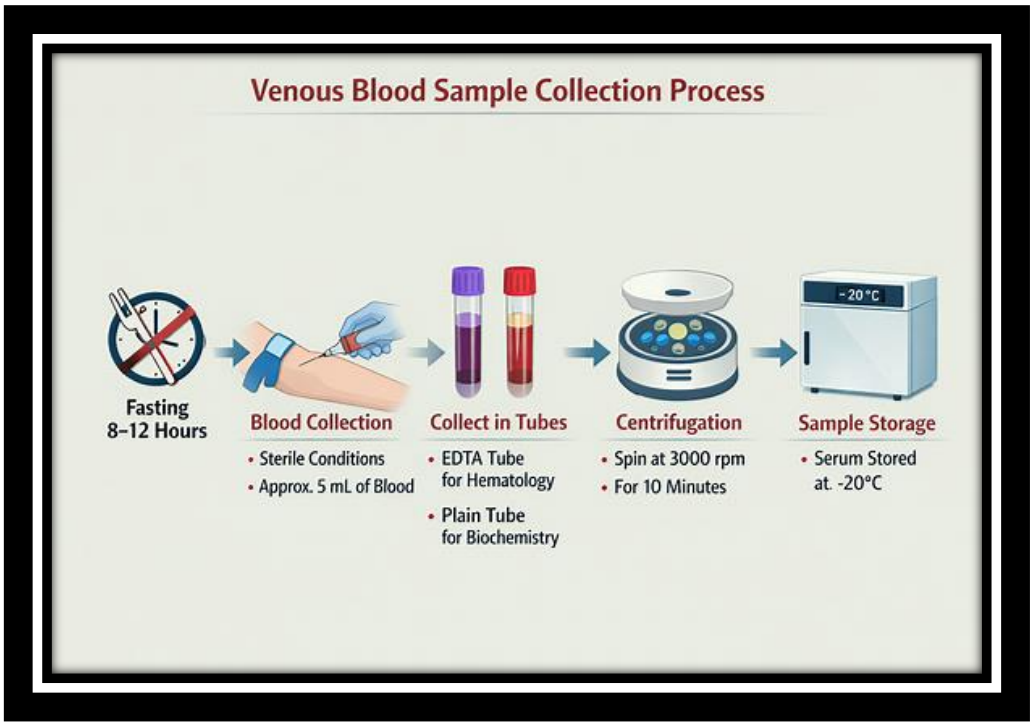

Figure 3- It shows the venous blood sample collection process.

2.4: Hematological and Biochemical Analyses

Hemoglobin concentration and white blood cell (WBC) count were measured using an automated hematology analyzer. Liver function was evaluated by determining the levels of the enzymes ALT and AST using enzymatic colorimetric methods. Serum creatinine was also used as a measure of kidney function, guided by the due diligence of the authors, Ndaba and Londeka Nontobeko, who prompted the researcher to develop this framework for biochemical analyses [15].

2.5: Hormonal Evaluation

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were quantified in serum [16], using an ELISA kit according to the manufacturer's instructions [17]. All tests were carried out twice to improve the accuracy and reliability of the results.

2.6: Semen Analysis

Semen samples were obtained after 3-5 days of sexual abstinence and analyzed as per the World Health Organization guidelines [18]. Sperm count was done by the microscopic method and expressed as millions/ml. All samples were tested within 1 hour of collection.

2.7: Statistical Analysis

These data were presented as mean ± standard deviation (Mean ± SD). Data analysis was carried out using IBM SPSS Statistics software. One-way ANOVA and Tukey's post hoc test were used to compare group means. Statistically significant results were defined as p-values < 0.05.

2.8: Ethical Considerations

The institutional ethics committee approved the study protocol. The institutional ethics committee approved the study protocol, and research procedures were performed in accordance with it. All research procedures were performed in accordance with the ethical principles of the Declaration of Helsinki [19]. All participants provided written informed consent before entering into the study.

3. Results

Results of the study indicated that there were significant differences between the control group and the smoking, alcohol use, and drug use groups. Hemoglobin concentration was significantly reduced in all exposed groups compared with the control group, as evidenced by the data. The greatest reduction was in the methamphetamine users (11.96 ± 0.30 g/dL) compared with the controls (15.08 ± 0.33 g/dL). In addition, the number of white blood cells was also found to be increased in the exposed groups, particularly the methamphetamine users who had the highest value of (12.21 ± 1.44 $\times 10^3/\mu L$), which may indicate an inflammatory response or physiological changes due to chronic exposure to toxic substances, as presented in Table 1 and Figure 1.

Table (1): The effect of smoking, alcohol, and drugs on blood, biochemical, and reproductive indicators in males (Mean ± SD)

Variable	Control (n=15)	Drug users (n=15)	Methamphetamine	Smokers (n=15)	Alcohol consumers

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			users (n=15)		(n=15)	
Hemoglobin (g/dL)	15.08 ± 0.33	13.42 ± 0.54	11.96 ± 0.30	12.84 ± 0.41	13.17 ± 0.48	
WBC (×10³/µL)	7.12 ± 0.88	10.14 ± 1.11	12.21 ± 1.44	11.25 ± 1.30	10.82 ± 1.05	
ALT (U/L)	24.40 ± 4.32	61.47 ± 9.18	68.60 ± 10.24	45.20 ± 7.84	52.87 ± 8.66	
AST (U/L)	27.73 ± 4.81	66.27 ± 8.74	73.40 ± 9.35	49.13 ± 7.62	58.20 ± 8.11	
Creatinine (mg/dL)	0.91 ± 0.13	1.36 ± 0.12	1.42 ± 0.15	1.18 ± 0.11	1.27 ± 0.14	
LH (mIU/mL)	5.14 ± 1.25	4.30 ± 1.43	2.69 ± 0.78	5.07 ± 1.00	3.54 ± 0.90	
FSH (mIU/mL)	5.37 ± 1.88	4.08 ± 1.26	3.28 ± 1.26	5.24 ± 1.38	4.26 ± 1.07	
Sperm Count (million/mL)	57.93 ± 4.08	29.47 ± 4.90	14.87 ± 2.97	26.20 ± 2.27	28.27 ± 3.95	

Table 1 shows the different effects of smoking, alcohol, and drug abuse on blood indicators, biochemicals, reproductive hormones, and sperm count in males compared to the control group, where the methamphetamine-abusing group showed the most obvious negative effects in most studied variables.

Liver function results also showed a significant increase in ALT and AST enzyme levels in all groups compared to the control group, with methamphetamine users recording the highest values for both enzymes at (68.60 ± 10.24 U/L) and (73.40 ± 9.35 U/L), respectively. In contrast, the control group recorded the lowest values.

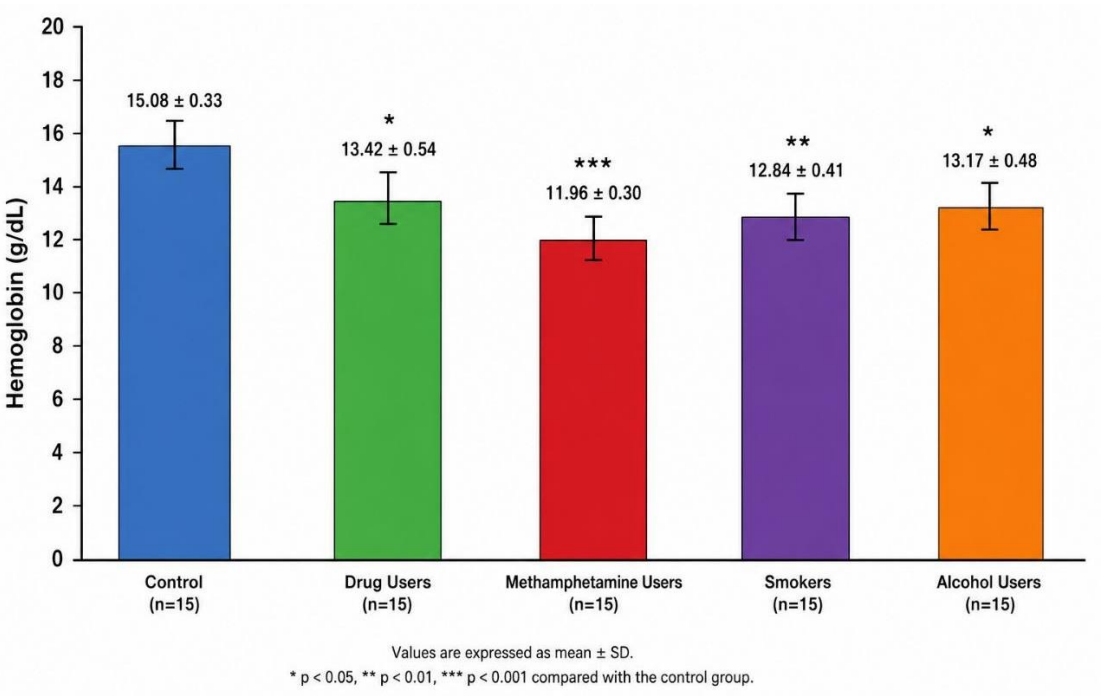

Figure (4): Hemoglobin Levels Among the Studied Groups

This shows stress or damage to the liver due to the use of different substances, as shown in Table 1 and Figure 5. Concerning kidney function, the results revealed that the levels of creatinine were increased in all exposed groups when compared with the control group, with the highest level of creatinine in the methamphetamine group being (1.42 ± 0.15 mg/dL), which indicated that chronic exposure to toxic chemicals might affect kidney function. The results revealed a significant reduction in LH and FSH levels among the drug users and methamphetamine users compared to the control group.

The most significant reduction was seen in methamphetamine users, LH (2.69 ± 0.78 mIU/mL) and FSH (3.28 ± 1.26 mIU/mL). This indicates that there has been a disruption in the reproductive hormonal axis as described in Table 1 and Figure 3 from the psychoactive substances. In addition, semen analysis revealed a significant reduction in sperm count in all the exposed groups as compared to the control group. The highest sperm count was found in the control group (57.93 ± 4.08 million/mL), followed by the smoking group (26.20 ± 2.27 million/mL), and the lowest in methamphetamine users (14.87 ± 2.97 million/mL).

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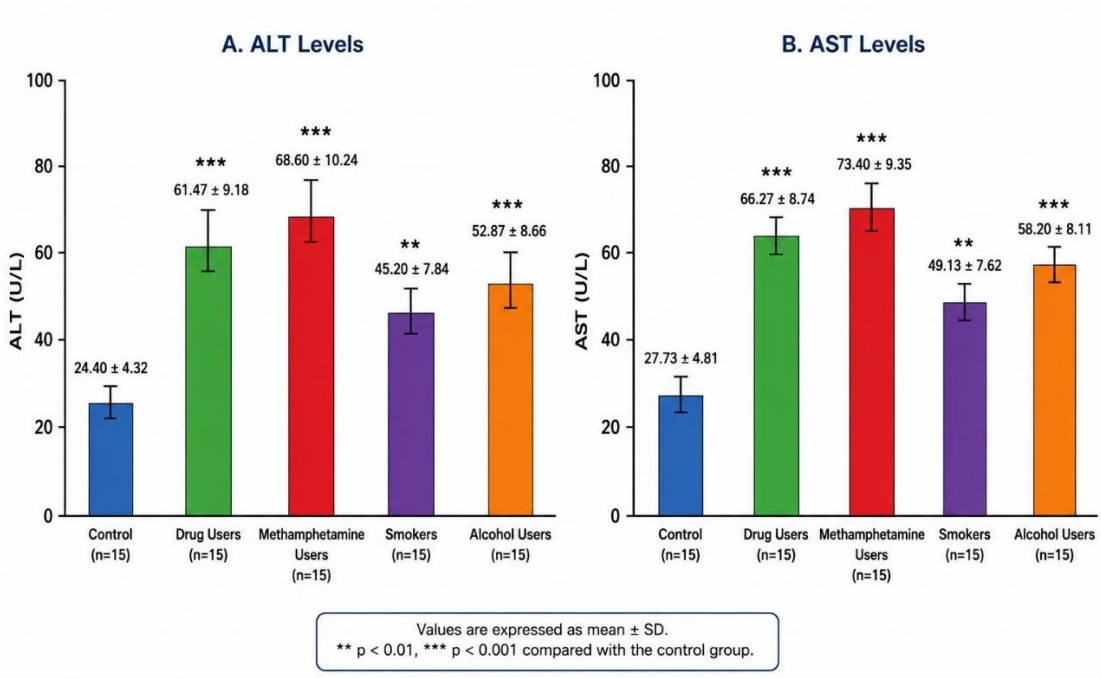
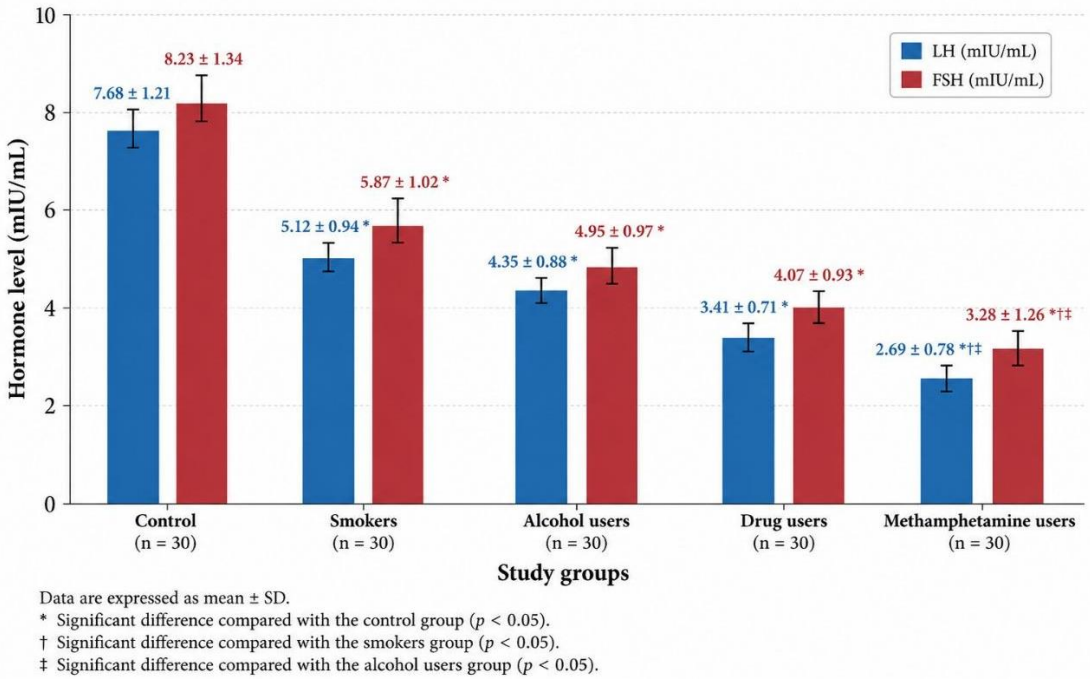


Figure 5: Serum ALT and AST levels among control and exposed groups (smoking, alcohol consumption, and drug abuse).



Data are expressed as mean ± SD.
* Significant difference compared with the control group ($p < 0.05$).
† Significant difference compared with the smokers group ($p < 0.05$).
‡ Significant difference compared with the alcohol users group ($p < 0.05$).

Figure (6): Serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels among control and exposed groups (smoking, alcohol consumption, and drug abuse)

This reflects the direct negative impact of toxic substances on male fertility, as shown in Table 1 and Figure 7.

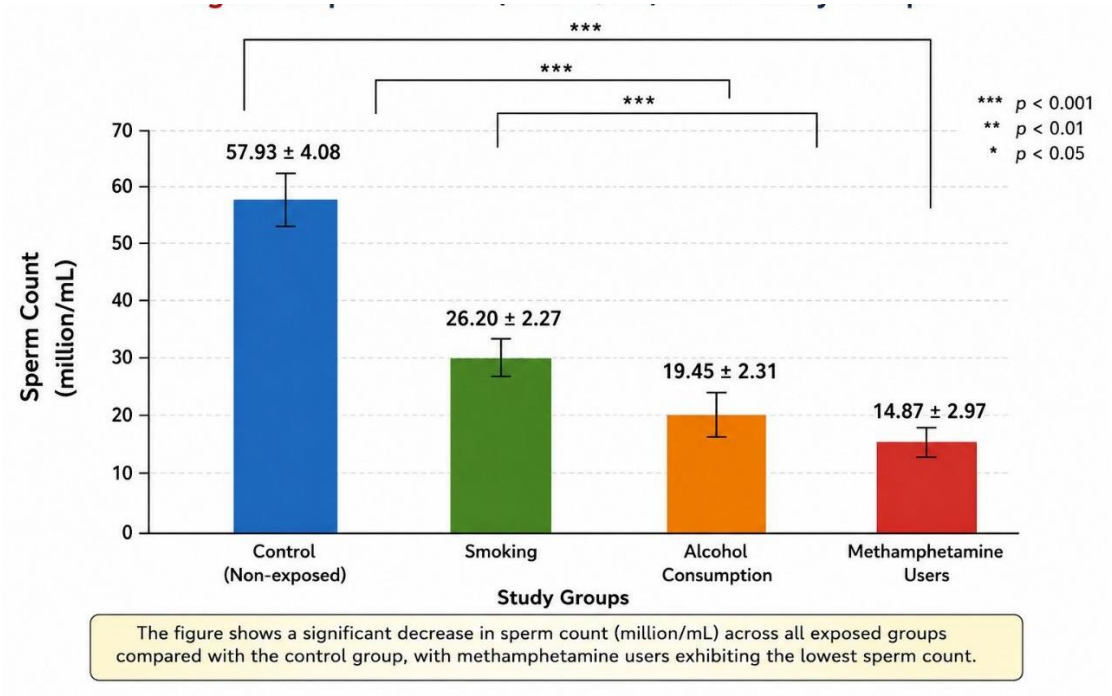


Figure 7. Sperm Count (million/mL) in the Study Groups

Furthermore, the results of the effect of age on reproductive indicators revealed that LH, FSH, and sperm count decreased with age. Sperm count was lowest in the age group >35 years (24.60 million/mL) as compared to the age group <25 years (42.80 million/mL). The levels of LH and FSH also decreased gradually, indicating an inverse relationship between advancing age and reproductive efficiency in males, as shown in Table 2 and Figure 8.

Table 2. Age-Related Variations in Reproductive Hormones and Sperm Count

Age Group (Years)	LH (mIU/mL) Mean ± SD	FSH (mIU/mL) Mean ± SD	Sperm Count (million/mL) Mean ± SD	-value

<25	5.82 ± 0.94	6.31 ± 1.08	42.80 ± 3.65	0.05
25–35	4.17 ± 0.83	4.92 ± 1.14	33.40 ± 3.12	0.05
>35	2.95 ± 0.71	3.54 ± 0.96	24.60 ± 2.88	0.05

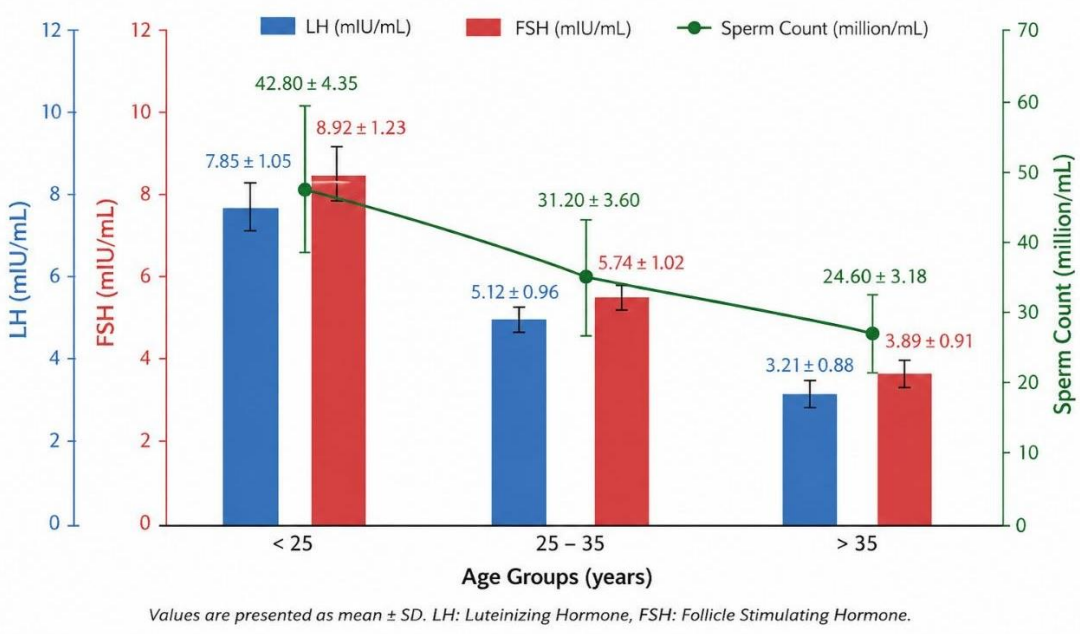


Figure 8: Effect of Age on Reproductive Hormonal and Semen Parameters in Male Participants

4. Discussion

The findings of the present study are in line with earlier published scientific findings that have demonstrated a significant decrease in the male reproductive hormones, particularly LH and FSH, due to an altered hypothalamic-pituitary-gonadal axis following chronic use of tobacco, alcohol, and drugs. Several clinical investigations have shown that the use of drugs with psychoactive properties, including methamphetamine, can suppress the secretion of GnRH at the hypothalamic level [20], which in turn decreases the amount of

LH and FSH secreted by the pituitary and results in reduced production of testosterone and impaired male reproductive function [21]. Similarly, systematic reviews have shown that smoking and alcohol use are correlated with substantial hormonal changes, such as decreased levels of LH, FSH, and testosterone, with a greater effect of chronic use or simultaneous use of toxic agents [22].

Similarly, previous studies in infertile male populations have shown significantly reduced levels of LH and FSH compared to healthy individuals, reinforcing the role of these hormones as sensitive biomarkers of testicular function [23]. Furthermore, the decrease in LH and FSH has been directly related to the dysfunction of Sertoli and Leydig cells, resulting in altered spermatogenesis and reduced male fertility [24]. These findings support the results obtained in the present study, where a marked decrease in LH and FSH was observed in the exposed groups, especially in methamphetamine users, along with a significant reduction in sperm count.

Taken together, these results confirm that the disruption of the hypothalamic–pituitary–gonadal axis induced by toxic substances represents a key mechanism in the deterioration of male reproductive function, in accordance with the existing scientific literature [25].

5. Conclusion

The results of this study revealed that chronic exposure to smoking, alcohol consumption, and drug use has significant adverse effects on hematological, liver function, kidney function, reproductive hormones, and semen parameters in men. Particularly in methamphetamine users, a remarkable decrease in hemoglobin levels, an increase in white blood cell count, elevated ALT and AST, and an increase in creatinine levels were prominent, suggesting systemic toxic stress and organ dysfunction.

Regarding the reproductive endocrine system, a significant decrease in LH and FSH levels was observed, strongly indicating dysfunction of the hypothalamus-pituitary-gonadal axis. Concomitantly, sperm count was also markedly reduced, showing the lowest values, particularly in methamphetamine users. Furthermore, a gradual decrease in LH, FSH, and sperm count was confirmed with increasing age, suggesting that both aging and exposure to harmful substances contribute to the decline in male reproductive function.

Conclusively, this study clearly demonstrates that exposure to harmful substances has multifaceted adverse effects on men's overall health and that LH and FSH are important biomarkers for assessing these effects.

6. Recommendations

Based on the results of this study, the following recommendations are presented.

1. It is necessary to strengthen public health education programs aimed at the prevention and reduction of smoking, alcohol, and drug use, as these substances have a significant adverse effect on men's health, particularly reproductive function.

2. For the early diagnosis of male infertility, it is recommended to conduct hormonal tests, including LH and FSH, regularly, and to introduce the evaluation of endocrine function as a standard examination.

3. For drug abusers, regular clinical monitoring should be performed to detect hormonal abnormalities and changes in semen parameters early on.

4. It is necessary to conduct molecular-level and long-term follow-up studies to clarify the effects of psychoactive substance use, including methamphetamine, on the hypothalamic-pituitary-gonadal axis.

5. To maintain male reproductive health, the promotion of healthy lifestyle habits (nutritional management, exercise, stress management) is important, and enhanced preventive education, especially for young people, is desired.

Ethical Considerations

Ethical approval for this study was obtained from the Human Research Ethics Committee (HREC) of the University of Melbourne, Victoria, Australia, prior to the commencement of the research. The study was conducted in accordance with the principles of the Declaration of Helsinki and the Australian National Statement on Ethical Conduct in Human Research (referenceH62148)

Written informed consent was obtained from all participants after they had received a comprehensive explanation of the study objectives, procedures, potential risks, and expected benefits. Participation was entirely voluntary, and participants were informed of their right to withdraw from the study at any stage without consequence. All personal

information and research data were treated with strict confidentiality, anonymized before analysis, and used solely for scientific and academic purposes.
The study was conducted within an academic research framework in Montréal, Quebec, Canada, involving students from CHU Sainte-Justine and Université de Montréal, which provided the institutional setting for recruitment, coordination, and full compliance with Canadian ethical research standards.

List of Abbrevations: (HPG): hypothalamic-pituitary-gonadal; (LH)Luteinizing Hormone; (FSH); Follicle-Stimulating Hormone; (ART): assisted reproductive technologies; (WBC): white blood cell

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Declaration of generative AI and AI-assisted technologies in the writing process
The authors hereby declare that no generative artificial intelligence or AI-assisted technologies were used at any stage during the preparation of this manuscript, including language editing, proofreading, or content development. The authors take full responsibility for the originality and integrity of the work presented in this publication.

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