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Exploring Risk Factors and Functional Aspects of Semen Quality in Male Infertility: The Intersection of Reproductive Health and Lifestyle

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Abstract:
Infertility is a prevalent health issue that affects millions of couples worldwide, with male infertility rates steadily increasing. Abnormal spermatogenesis and spermiogenesis are major contributors to male infertility. Various risk factors, including socio-demographic, environmental, behavioral/lifestyle, genetic factors, etc., play an intertwined role in the onset of male infertility. Although assisted reproductive technologies (ART) offer hope, their limited accessibility and affordability discourage couples from seeking infertility treatment. Semen analysis is a vital laboratory test that measures various physical and microscopic parameters to assess semen quality. This study aimed to evaluate the impact of multiple factors, including age, BMI (Body Mass Index), and lifestyle, on semen quality associated with male infertility. The findings of this study highlight the importance of a comprehensive approach to diagnosing male infertility. Furthermore, this approach advances our understanding of the association between the aetiology and pathophysiology of male infertility, offering insights for developing prevention and treatment strategies.

Keywords: Male infertility, risk factors, lifestyle, semen analysis, sperm quality

1. Introduction

Since infertility is a prevalent concern affecting millions of couples worldwide, it is gaining high importance in research trends. Though diagnosing and addressing infertility can be challenging, it's a condition that can impact couples rather than individuals. There are various factors contributing to infertility, and male infertility rates are on the rise globally, often stemming from issues like abnormal spermatogenesis or spermiogenesis. Lifestyle factors in addition to stress, sleep quality, physical activity, and diet can significantly affect semen quality.

Several studies indicate that infertility affects an estimated 60-80 million couples globally [1].

Diagnostic efforts are primarily aimed at uncovering the root causes of infertility as it pertains to couples rather than isolated individuals. Male infertility, often related to problems in spermatogenesis or spermiogenesis, as well as mechanical obstacles, can impede the healthy merging of sperm and egg [2]. Sperm parameter assessment, including count, motility, morphology, and progressive motile sperm count, is typically conducted by specialized diagnosticians or through precise computer methods like CASA (Computer Assisted Sperm Analysis). According to WHO (World Health Organization) guidelines, this assessment encompasses sperm count, motility, morphology, pH, semen volume, and more [3]. Sperm quality is influenced by numerous factors, spanning genetics, diseases, and lifestyle elements such as diet, physical activity, and sleep quality, among others [4]. The figure shows different risk factors included in several studies based on male infertility.

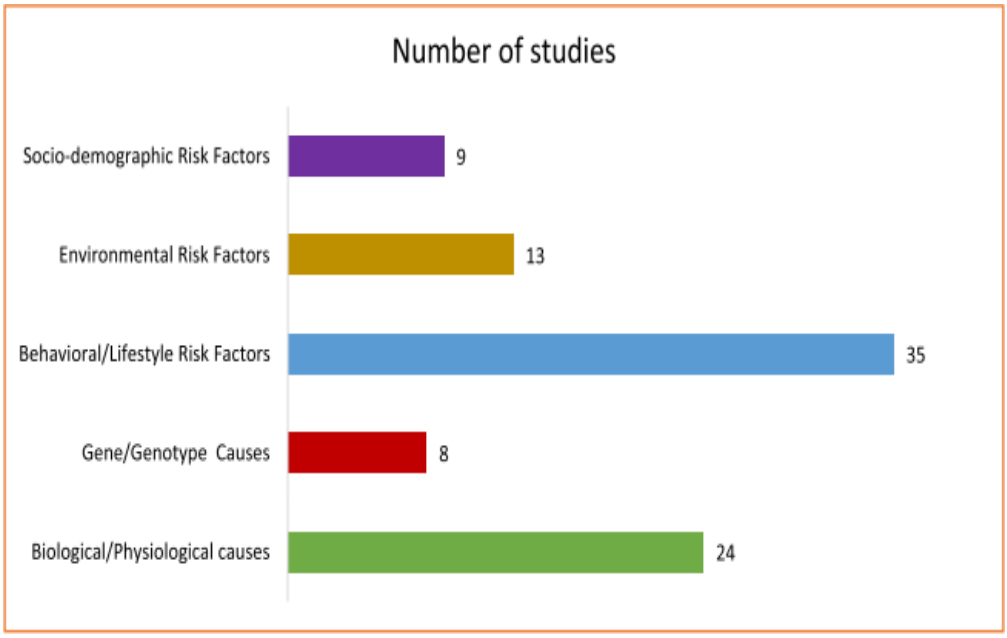

Figure 1: Major causes of male infertility [5]

Male infertility results from various risk factors [5] encompassing socio-demographic factors while including environmental factors as well as genetic and behavioral/lifestyle factors. Lifestyle choices are notably influential in male infertility, with biological factors like azoospermia also playing a significant role. Genetic and socio-demographic risk factors including chromosomal abnormalities, abnormal BMI and age can cause an increase in infertility [6]. Research has explored individual risk factors affecting semen quality associated with male infertility through various studies.

Environmental factors, including exposure to toxins and pollution, can substantially influence sperm quality [7]. It is observed that toxins like heavy metals, pollutants, pesticides, or industrial chemicals are connected to reduced sperm quality as well as male infertility [8]. They can induce oxidative stress, DNA damage, and apoptosis in spermatozoa, impairing fertilization and reducing pregnancy rates. Moreover, the effect of Diet, physical activity, and smoking habits is observed by several studies influencing sperm quality. These studies have shown an association of smoking, and inadequate dietary habits, as well as sedentary lifestyles with poor sperm quality [9]. Environmental factors lead to reduced fertility rates and harm to spermatozoa due to oxidative stress, DNA damage, and apoptosis.

Evaluating male infertility involves assessing reproductive history and conducting semen quality analyses. Semen analysis, a vital laboratory test, gauges semen quality and quantity by examining

various Macroscopic and microscopic parameters. Physical parameters, including volume, viscosity, color (whitish-grey), and pH (slightly alkaline), are assessed to investigate sperm quality. However, microscopic parameters encompass sperm count, motility, morphology, and viability [10]. Additionally, tests are conducted to detect substances like antibodies and infections that can affect fertility. These parameters provide crucial insights into the fertility potential of men.

Semen analysis involves assessing several critical parameters to understand male infertility. Sperm count signifies the quantity of sperm in the semen, while sperm movement is categorized as immotile, progressively motile, or non-progressively motile. Morphology examines sperm shape and size, and viability measures the percentage of live sperm. These parameters aid in pinpointing the cause of male infertility, guiding treatment decisions, and predicting the success of assisted reproductive techniques. Conditions such as a low sperm count, poor sperm motility, or abnormal sperm morphology can hinder the fertilization of an egg, ultimately leading to infertility. Additionally, the Fructose Test is vital as it provides insights beyond standard semen parameters. This test determines fructose levels in sperm, a substance produced by seminal vesicles and used as an energy source for sperm. Low fructose levels may indicate issues with seminal vesicle function or ejaculatory duct occlusion. Thus, the research aim was to evaluate the impact of various risk factors, including age, BMI, and lifestyle, on the functional aspects of semen quality associated with male infertility.

2. Methods

2.1 Design of Study

A cross-sectional approach was employed in this study. The study design is shown in Figure 2, which highlights the essential steps and parameters for the evaluation of semen quality and functional aspects such as semen volume, sperm count, sperm motility, and morphology. Written consent, including the creation of a questionnaire for data collection from the participants, was obtained before semen samples were collected.

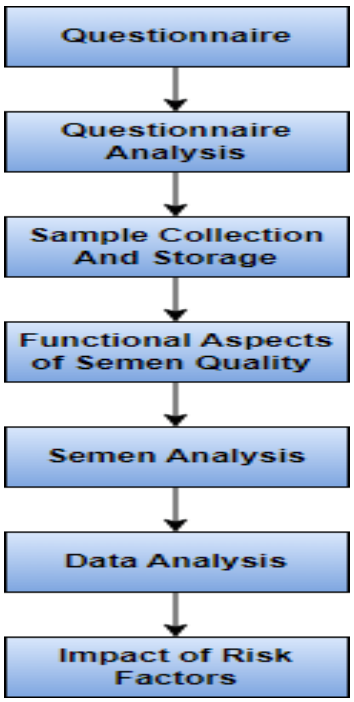

Figure 2: Design of study

2.2 Data Collection

This study was conducted at an *in vitro* fertilization center providing services for infertility issues. As previously mentioned, the study sourced data from the well set-up Test Tube Baby Center in Pune, Maharashtra, with prior permission and written consents both from the center and the participants. A comprehensive questionnaire in this study, which included all relevant information about demographic features and lifestyle habits, was administered to the participants prior to semen collection.

Semen samples were collected, stored, and maintained strictly adhering to the guidelines defined by the WHO. The procedures utilized in the study are meticulously conducted in the Andrology laboratory to ensure the preservation of sample quality and integrity. The study encompassed men aged 18 to 45 who willingly provided semen samples for analysis. During February 2020 – December 2023, a total of 1,006 men facing fertility challenges were recruited for this research. Participants received comprehensive information about the study and provided written consent. They were asked to provide information about demographic features, including age, occupation, education, and lifestyle habits like smoking, consumption of alcohol, or tobacco, etc. These contributors were carefully selected based on inclusion criteria, which include men aged 18 to 50 who have been trying to conceive for over a year without success. Exclusion criteria were applied to men with a history of genital tract infections, trauma or surgery, as well as those with long-term chronic illnesses, thyroid-associated syndromes, trauma and surgery associated with the reproductive system, diseases associated with the sexually diffused or genitourinary system, in addition to jobs with probable contact hazards or toxic exposure with high reproductive system risk. Additionally, participants underwent assessments for infertility types and prior surgeries, and received semen analysis reports.

2.3 Physical Inspection

An certified physician conducted a comprehensive assessment, physical inspection and interviewed all participants. The examination involved measuring height and weight, calculating BMI, conducting palpation, and performing a urogenital visual check. The interview covered various behavioural factors, including drinking habits, duration of abstinence, place of residence, frequency of intercourse, educational background, self-assessment of life, personal information, and current medication history.

2.4 Semen Collection and Semen analysis

The collection of semen samples and their analysis were done following the standard procedure and guidelines as recommended by the WHO [10]. Each male participant was pre-instructed about sample collection. The sample was carefully collected in a sterile plastic container and promptly transported to the testing facility for analysis. A qualified embryologist, after complete liquefaction of the specimens, performed standard semen analysis that included macro- and microscopic parameters.

The samples were obtained via masturbation after a period of abstinence lasting 2–7 days and were collected in sterile collection flasks made of non-contaminated, non-spermicidal, and non-pyrogenic materials at Test-Tube Baby Center Pune. To minimize the time between collection and analysis, it is crucial to collect the samples in close proximity to the laboratory. Subsequently, these samples were transferred to the andrology lab at the Test Tube Baby Center for advanced examination. The samples were allowed to liquefy at 37°C for 30 minutes, and analysis began within an hour of collection. Post-liquefaction, a small quantity of semen (approximately 6–10 µL) was placed in a Makler's counting chamber, where sperm count and motility were assessed under a bright field microscope at ×400 magnification. An additional drop of 10 µL was also used for the diff-

quick staining method for the assessment of sperm morphology. A minimum of 200 sperm were counted, and the analysis was based on the average of duplicate measurements for both assessments.

3. Materials

The human semen samples were sourced from a study population comprising a total of 1,006 participants. A well-equipped and meticulously maintained and ART lab was used for the collection, storage, and analysis of semen samples. The lab contained all the essential equipment's and instruments necessary for semen analysis, including a microscope, laminar airflow, centrifuge, cryo-tank, micropipettes and refrigerator etc. as well as disposables like sterile semen collection containers, glass slide and microslide etc. Every material utilized in the research was cautiously selected and designed to ensure the utmost accuracy and reliability of the findings. The integration of a well-equipped ART lab, specialized analysis tools, and IBM SPSS Statistics software enabled a comprehensive analysis of the collected semen samples, and the assessment of diverse risk factors impacting semen quality was done.

3.1 Statistical analysis

For the purpose of data analysis and report generation, SPSS Statistics Software, Version 20.0 (IBM Corp., Armonk, NY, USA) was utilized. The statistical analysis included vivid statistics of semen parameters, correlation analysis and factor analysis with semen volume, progressive motility, motility rate, and total sperm count, which describe the relationship between semen parameters, and risk factors. The parameters were then compared with demographic and medical attributes, such as age, smoking, tobacco use, alcohol consumption, and infertility status. The statistical inference employed two-sided tests with a significance level of 0.05. Quantitative variables of semen quality were presented as mean values with standard deviations, indicating the significance level of the analysis.

3.2 Ethical Considerations

Before sample collection, explicit informed consent was diligently obtained from all participants, ensuring their comprehensive understanding of the study objectives. The utmost care was taken to safeguard the confidentiality and privacy of all individuals involved throughout the study. All the investigations were conducted at the approved ART Centre after obtaining ethical approval from the Institutional Ethics Committee (ECR/440/INST/MH/2013/RR-2016) as well as with unwavering adherence to the ethical guidelines and regulations as set by the WHO.

3.3 Risk Factors:

The analysis was focused on specific risk factors to assess their impact on semen parameters. These risk factors were categorized into health factors, including age and BMI, and lifestyle factors, which encompass various addictions such as cigarette smoking, tobacco consumption, and alcohol use, to investigate their effects on men's reproductive health.

4. Results

In this study, a total of 1006 semen samples were collected and analyzed to investigate the functional aspects and their impact on semen quality. Various parameters were assessed, such as semen quality, macroscopic parameters such as semen volume, and microscopic parameters including sperm count, motility (total motility and progressive motility), and morphology. Additionally, we conducted a questionnaire-based analysis to gather information on factors like age, BMI, and

lifestyle choices. These factors were assessed for their influence on sperm quality.

4.1 Impact of Health Factors – Age and BMI

Semen samples analyzed for the impact of health factors such as age and BMI lead to the categorization of participants into different age and BMI groups. Semen samples were distributed across six age groups: <25 years, 26–30 years, 31–35 years, 36–40 years, 41–45 years, and >45 years, facilitating parameter evaluation. Additionally, BMI groups were established as underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥30 kg/m^2), enabling the observation of obesity's impact on semen quality.

Impact of Age on semen parameters: The data presented in Figure 3 suggests that sperm count increased with age, highest sperm count was observed in the age group above 40 yrs ($p<0.01$). Figure 4 shows that semen volume decreased with age. Whereas Figure 5 and Figure 6 results suggest a variation in sperm motility in different age groups. Highest total motility and progressive motility was observed to be in the lower age group than 25 yrs.

Impact of BMI on semen parameters: Figures 7,9 and 10 reveal that the normal weight group showed the highest values (sperm count, TM, PR motility) for these parameters. Underweight and obese BMI groups exhibited decreased sperm count and motility. Figure 8 shows that semen volume decreased as BMI increased ($p<0.05$).

4.2 Impact of Lifestyle Factors

Semen parameters were analyzed to investigate the impact of lifestyle factors including consumption of cigarette smoking, tobacco and alcohol. The participants were categorized by level of consumption.

Impact of Smoking on semen parameters: Figure 11 to 14 show the impact of cigarette smoking on semen parameters, where the impact of smoking was evaluated for 0, 1–2, 3–4, and >5 cigarettes per day consumption. Figure 11 depicts the sperm count, which was observed to be highest in the chain smoker group. Although Figures 12,13 and 14 don't show any significant impact of cigarette smoking on semen volume, total motility, and progressive motility, respectively ($p<0.05$).

Impact of Tobacco Chewing on semen parameter: Figures 15, 17 and 18 show that a daily but very low amount of tobacco (1–2 times/day) consumption had a significantly positive impact on the semen parameters. The values for sperm count, progressive motility, and total motility were observed to be highest in these group. Whereas Figure 16 shows that semen volume was increased in the highly addicted to tobacco consumption (>10 times per day) group ($p<0.05$).

Influence of Alcohol Consumption on semen parameters: As depicted in Figures 19, 20, 21 and 22, we did not find any significant relationship between the alcohol consumer and alcohol non-consumer groups. Further, we did not observe any significant correlation between alcohol consumption and semen parameters.

1. Discussion

1.1 Health factors

Male infertility rates are notably higher among men who have not fathered a child, indicating the role of age as a significant contributing factor in male infertility [13], [14]. A study [15] analyzing sperm concentration changes in African populations between 1965 and 2015 consistently identified

age as a risk factor, showing a noteworthy decline in sperm concentration with increasing age. In several studies, semen abnormalities are more prevalent in men aged 31–40 [16] and those over 40. Ugwuja et al. [16] showed that men aged 31–40 carry infections acquired before marriage, that influence their reproductive health. Additionally, a higher occurrence of *C. trachomatis* antibodies was found in men aged 20–29 as well as 30–39 [17]. Furthermore, Abayomi et al. [18] explored age and BMI for their impact on sperm parameters, observing that men under 45 years of age had significantly higher semen volume compared to those aged 45 and above, indicating an increased risk of infertility with high age and abnormal BMI. Notably, the 30–39 age group with the highest mean BMI exhibited the poorest sperm quality in terms of spermogram results [19]. Men who are both obese and above 45 years old [18] are nearly two and a half times more likely to produce less semen volume. From existing research, it is evident that age and BMI play a significant role in male infertility, with age being a consistent risk factor associated with declining sperm quality.

Further, studies show the significance of abnormal body mass index (BMI) as a notable threat to male infertility [20] [21]. In a study by Oghagbon et al., both low and elevated BMI were found to be linked to lower sperm count and motility [22]. While Wang et al. [23] described that obese men had notably lower volume, count, and motility compared to normal-weighted men. Maghsoumi-Norouzabad et al. showed that BMI and male infertility are positively correlated with decreased sperm count with increased BMI [24], while oestradiol and progesterone (ng/mL) are positively associated with BMI. In a prospective study involving infertile men, a BMI exceeding 25 kg/m^2 showed lower sperm counts per ejaculate with significantly lower sperm morphology and motility than fertile individuals [25]. Examining seminal fluid and BMI in infertile men established a significant association between BMI and infertility, linking low as well as high BMI, to unusual motility and sperm count. Men with a normal BMI are compared with those with a high or low BMI demonstrating the maximum semen parameters like sperm count and motility [22]. A Norwegian study [26] has found that obese and overweight men frequently experience infertility, even after accounting for the effects of sexual dysfunction. Similarly, an Iranian study [27] has reported that oligospermia in obese men is found 3.5 times compared to those with a normal BMI. Still, BMI is not identified as a noteworthy risk factor in some studies [28], including more cases of abnormal semen among men with a normal BMI than among those with normal semen. According to [29], sperm concentration is significantly lower in men with a high BMI compared to those with a normal BMI. Thus, several studies have linked abnormal BMI to male infertility, with findings indicating associations with sperm count, motility, and other sperm parameters. Hypotestosteronaemia, a hormonal issue in obese men [30], is also identified as a primary mechanism affecting fertility, but the causes of infertility in overweight and obese men are considered potentially reversible. As compared to these studies, our investigation found that health factors such as age and BMI show a moderate negative impact on semen quality. However, further research is needed for a comprehensive understanding of their relationship with semen quality. Conducting more extensive studies with adequate sample sizes will offer deeper insights into these impacts.

1.2 Lifestyle factors

Lifestyle factors, like cigarette smoking, demonstrate a consistent negative effect on semen parameters as smoking frequency increases. Smoking has been identified as a detrimental factor for sperm quality in a study [31], showing male infertility linked to longer durations of smoking. Specifically, moderate to heavy alcohol consumption (daily 1–2 glasses) is positively correlated with male infertility when related to an intermittent intake of alcohol [32]. Concerning health performance, a report on seminal fluid analysis [33] revealed a key impact of smoking on semen

motility. Heavy smokers (20 or more cigarettes per day) exhibited lower sperm concentration with a higher abnormal sperm, and increased leukocyte infiltration in semen compared to non-smokers. An organized literature review relates smoking to male infertility, indicating that the majority of research found a significant decrease in sperm creation, motility, normal sperm forms, and fertilizing capacity among smokers. This is attributed to an enlarged OS of the semen seminal with DNA damage. In previous studies, civil servants found a higher prevalence of semen abnormalities compared to other professionals. This discrepancy was attributed to social activities, including excessive smoking and alcohol intake [16], which may adversely affect semen quality.

Garba-Alkali et al. [34] investigated the connection between semen analysis and numerous carefully chosen variables related to male infertility. They found that semen abnormalities were statistically associated with several risk factors, including a history of past sexually transmitted disease (STD) treatment, smoking, and alcohol consumption. Notably, a higher abnormal semen proportion is observed across all groups compared to normal semen, with a statistically significant association between semen quality and these risk factors. In another study [35], infertile men were analysed using their seminal information, revealing behavioral risk factors for male infertility like regular alcohol consumption, and a history of smoking. Only a few studies reported the relationship between them as irrelevant [21].

In our study, cigarette smoking has been found to significantly affect semen quality, which is crucial for men's reproductive health. Conversely, tobacco consumption primarily affects sperm count, but no statistically significant difference was observed at high levels of tobacco consumption. Overall, it seems to have a positive impact on semen quality. However, the small sample size in some groups underscores the need for larger studies to better grasp the effects of tobacco consumption on semen quality. Additionally, while higher semen parameter values in the alcohol-consuming group suggest no significant differences compared to non-consuming groups, the overall impact of alcohol consumption on semen quality appears negative. Nevertheless, alcohol frequency appears to positively influence semen quality. However, the small sample size can affect a comprehensive understanding of the impact of alcohol consumption on semen quality. Furthermore, the combined impact of tobacco, cigarette smoking, and alcohol shows minimal differences in semen parameters, suggesting that the overall effect of these addictions may not substantially impact semen quality. However, these effects may have implications for male fertility and reproductive health.

2. Conclusion

This study assessed the impact of factors like age, BMI and lifestyle on sperm quality on various parameters such as semen volume, sperm count, motility, and morphology. The findings revealed that tobacco, cigarette smoking, and alcohol use have adverse effects on sperm quality, while age and BMI moderately affect it. Healthcare providers can design tailored interventions to address risk factors like age, BMI, and lifestyle, enhancing sperm quality and increasing conception chances.

3. Clinical significance

This investigation sheds light on the complex relationship between risk factors and sperm quality in male infertility. It underscores the importance of considering various criteria in assessing and treating male infertility. Further research is necessary to enhance effectiveness, optimize interventions, and develop focused techniques to improve sperm quality and address the challenges faced by infertile couples.

4. Limitations

Despite the study revealing significant impacts of various risk factors on sperm quality, it has several

limitations. The limited sample size in the study may have hindered its ability to establish strong associations between risk factors and sperm quality. This emphasizes the importance of inclusion of larger sample sizes for more generalizable findings. Additionally, the retrospective methodology employed in the study, relying on historical data, introduces the potential for recall bias and incomplete data. A prospective study design would enhance the reliability and accuracy of results. Furthermore, the study may not have considered all potential confounding factors affecting sperm quality, potentially influencing the observed associations. Some risk factors, such as lifestyle and sexual function, rely on self-reported data, which can introduce errors and biases. The focus of the study on specific risk factors might have limited a comprehensive understanding of their implications on sperm quality. Moreover, due to cultural, genetic, and environmental variations, the study's conclusions may not be generalizable to other populations or regions.

5. Future Scope

In this study, risk factors like age, BMI, and lifestyle are explored, examining their effects on sperm quality and the associated male infertility. Increasing the sample size and diversity of participants from various backgrounds can enhance the research by reinforcing statistical power and generalizability. Furthermore, a prospective study design with real-time data collection can reduce recall bias. Evaluation of genetic factors and specific medical conditions can further enhance understanding of the complex relationships between risk factors and sperm quality. The study also needs standardized and reliable measurement techniques to improve data accuracy and consistency across diverse settings. Comparing the impact of risk factors across demographics and cultures can illuminate contextual influences. By addressing these research areas, the influence of risk factors on sperm quality can be comprehensively studied to develop targeted interventions to alleviate the burden of male infertility.

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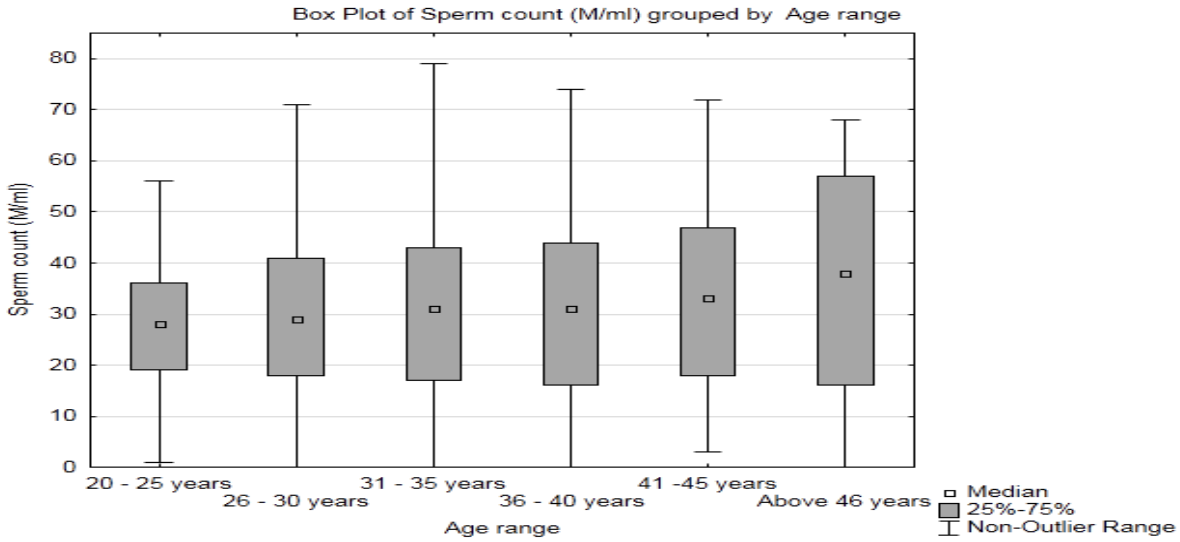

Figure 3 Impact of Age on sperm count

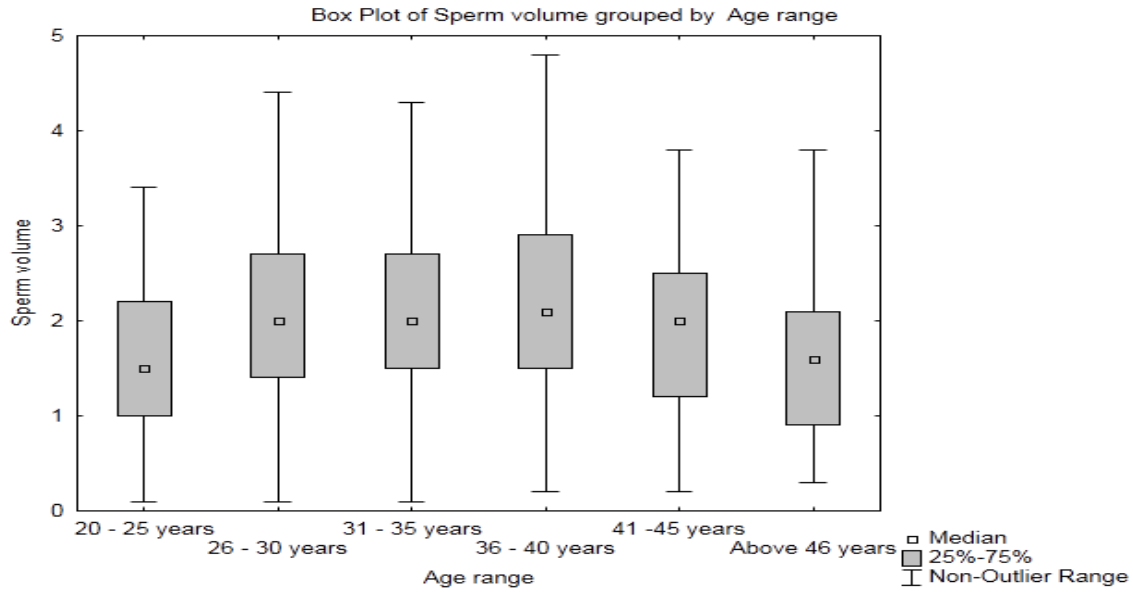

Figure 4 Impact of Age on semen volume

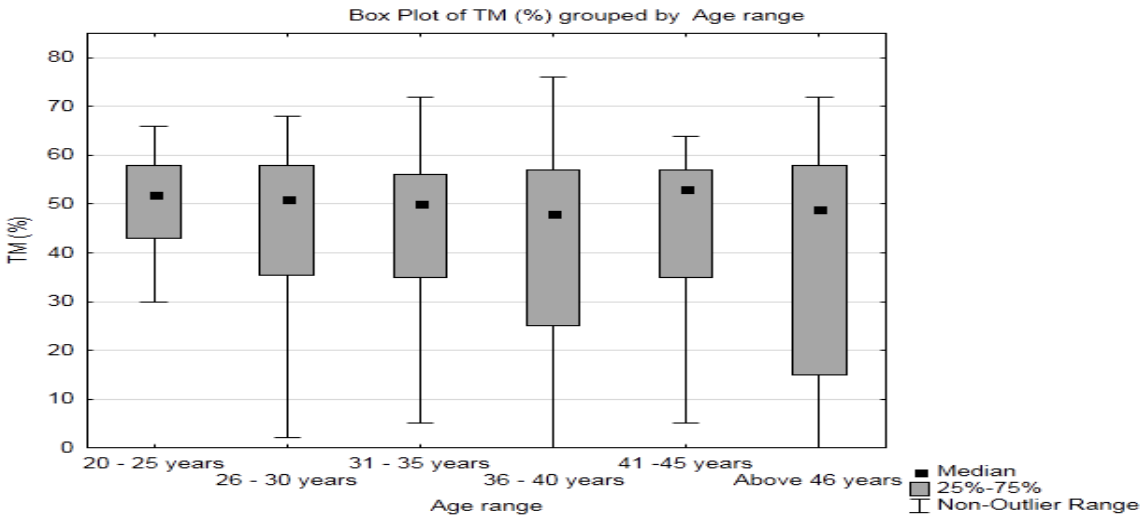

Figure 5 Impact of Age on Total motility

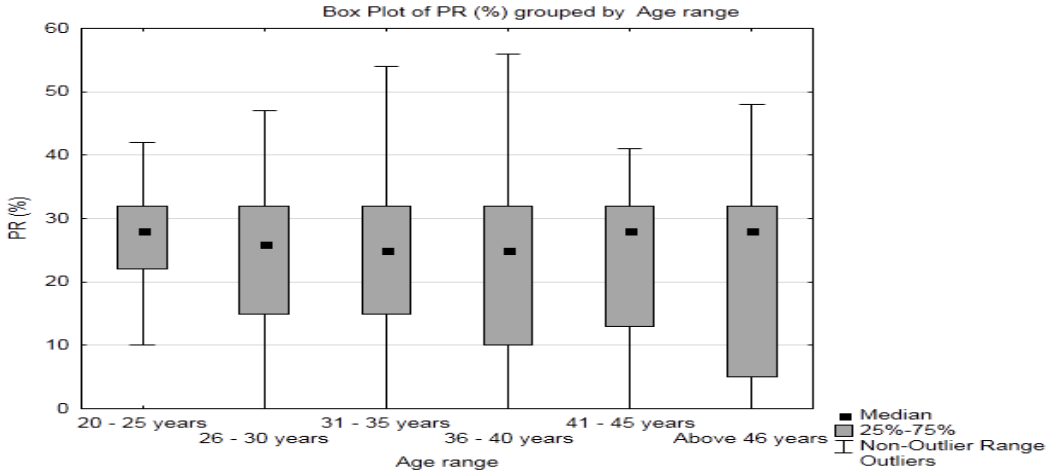

Figure 6 Impact of Age on Progressive Motility

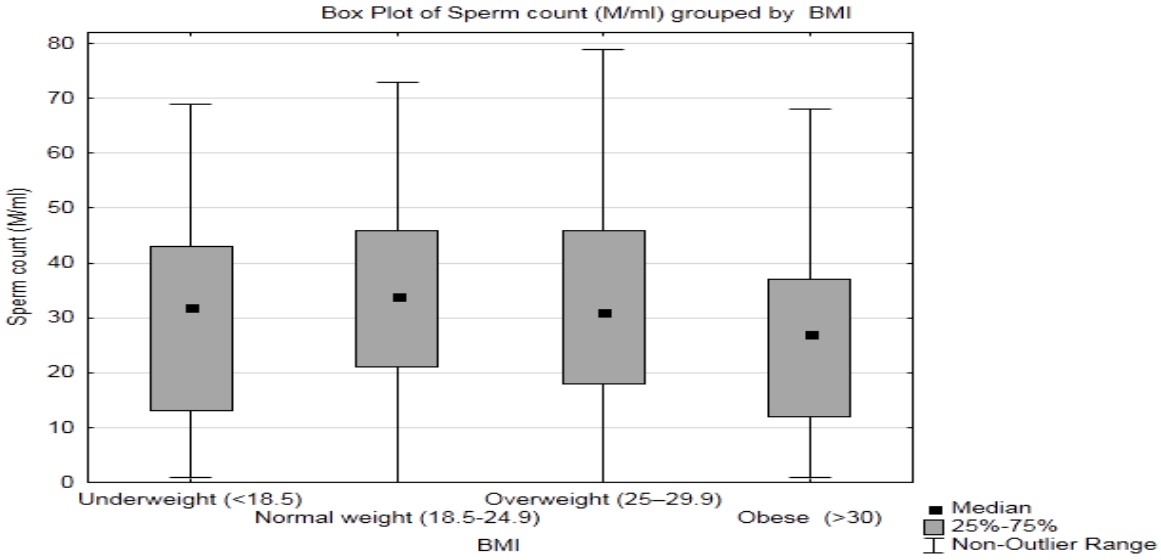

Figure 7 Impact of BMI on Sperm count

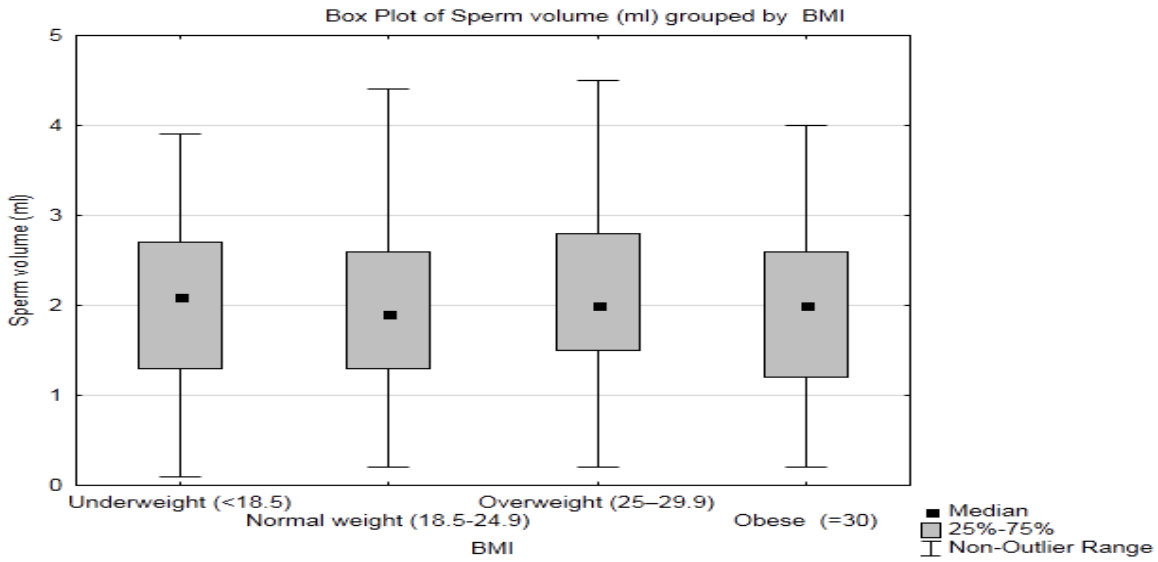

Figure 8 Impact of BMI on semen Volume

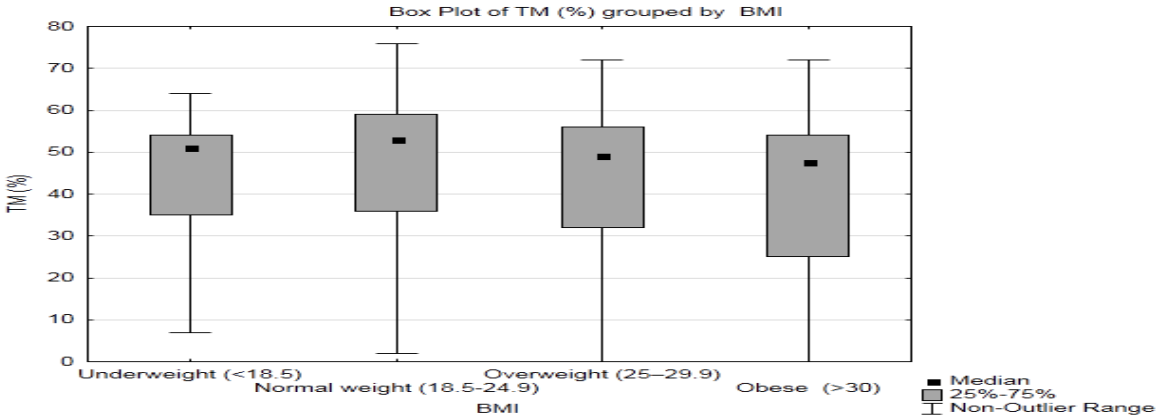

Figure 9 Impact of BMI (body mass index on Total Motility

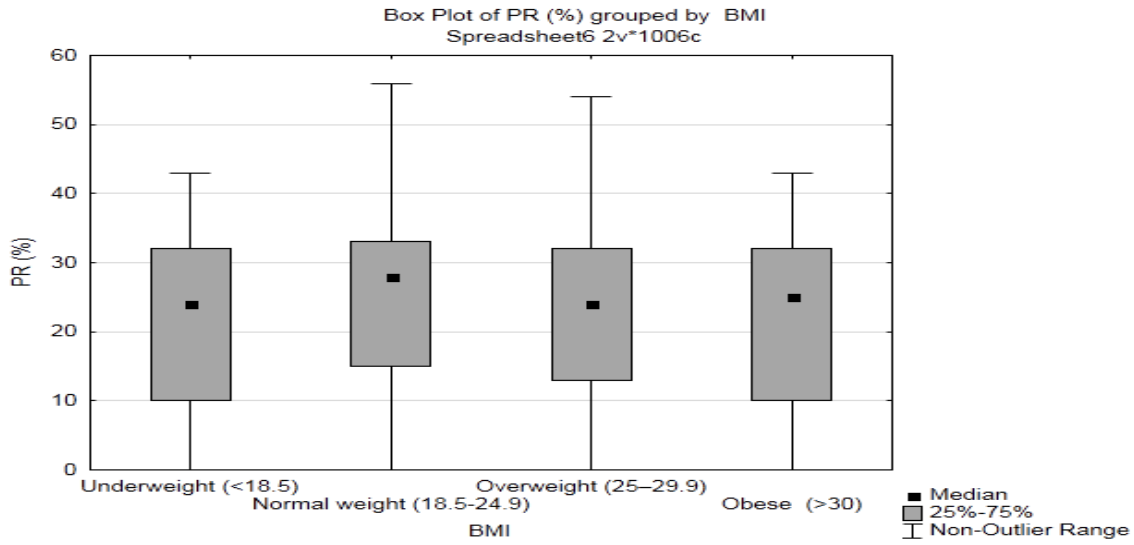

Figure 10 Impact of BMI on Progressive Motility

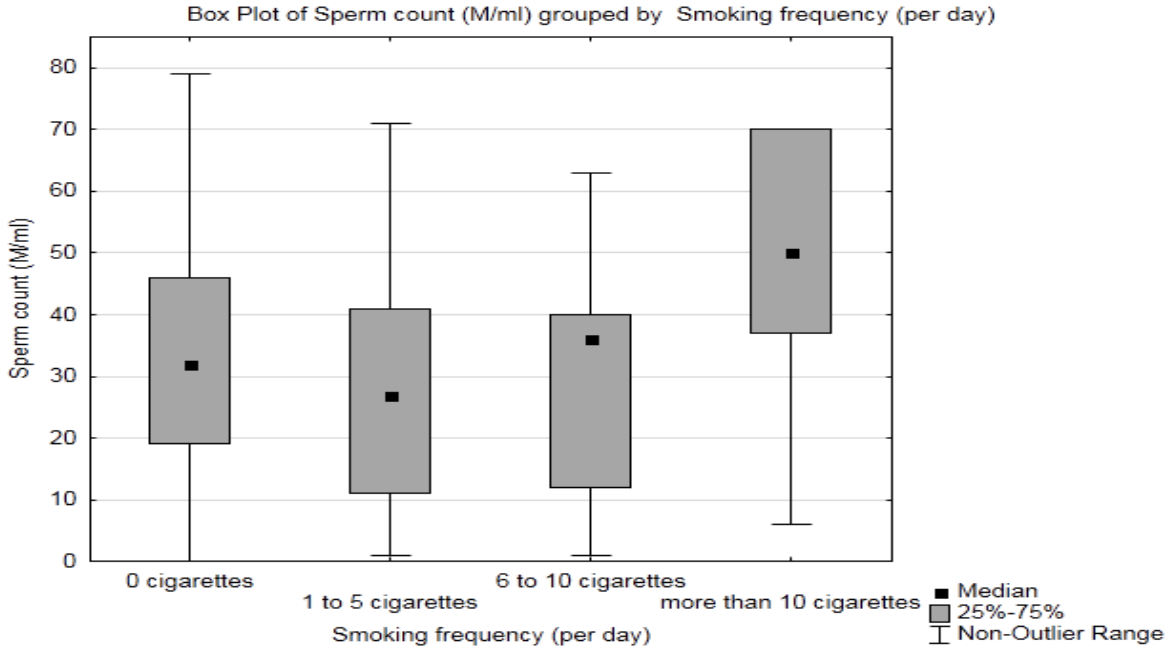

Figure 11 Impact of Cigarette smoking on sperm count

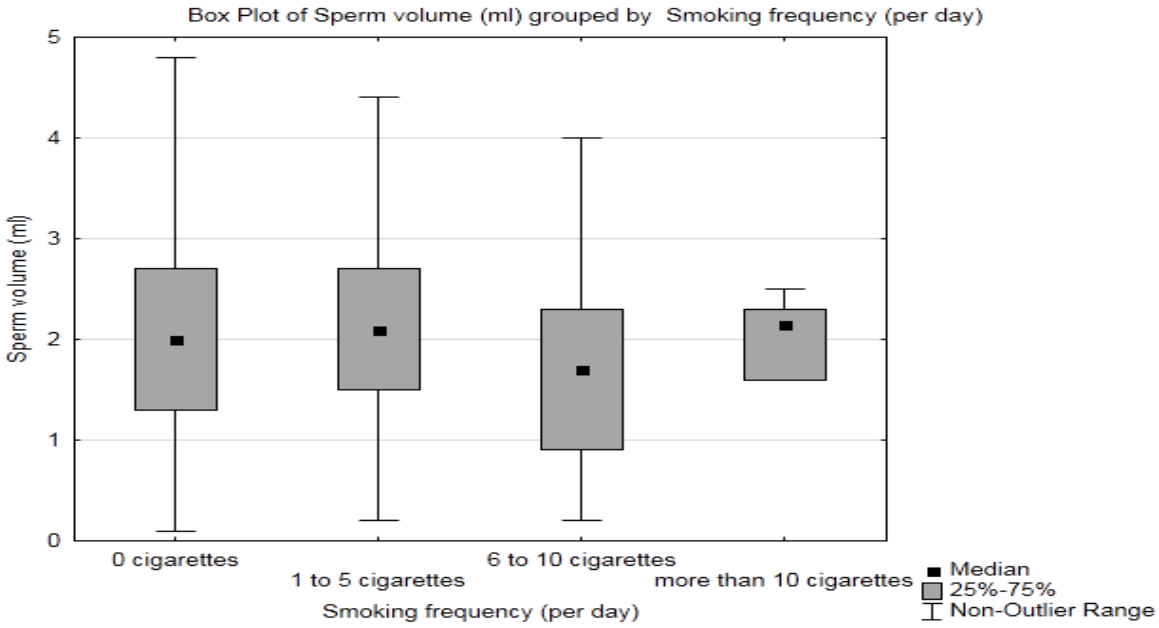

Figure 12 Impact of Smoking on Semen Volume

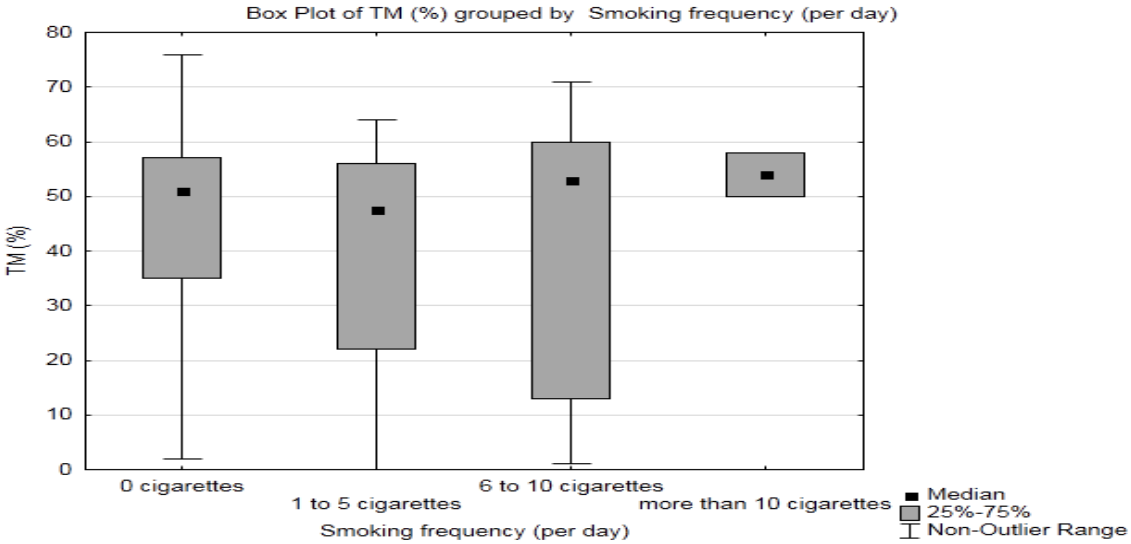

Figure 13 Impact of Smoking on Total Motility

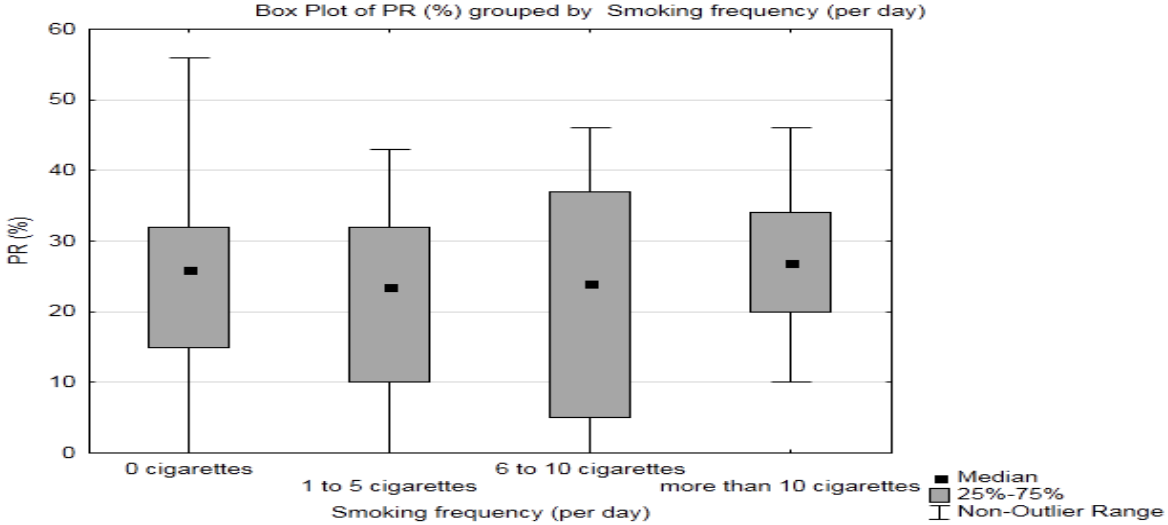

Figure 14 Impact of Smoking on Progressive Motility

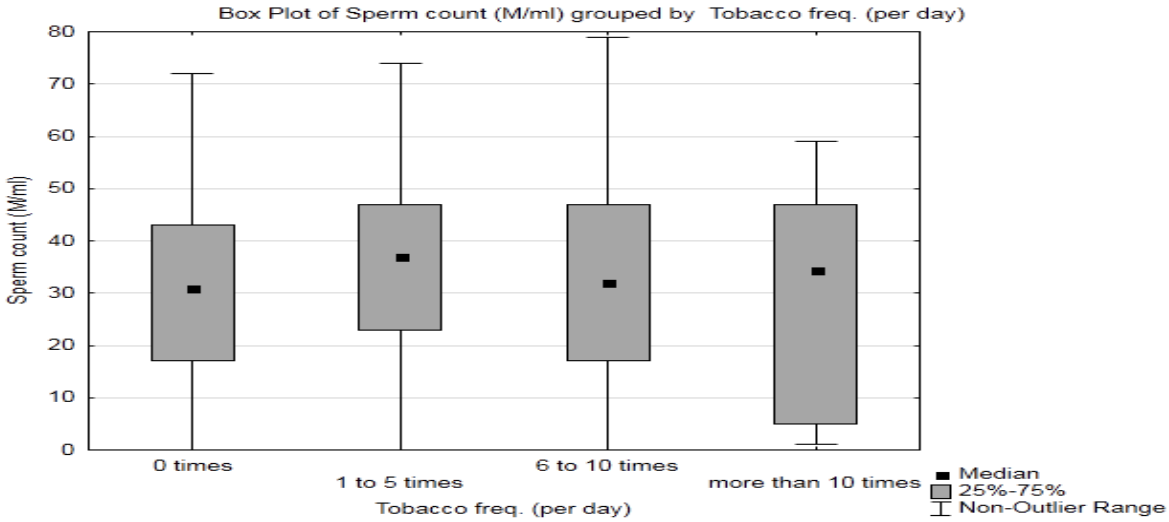

Figure 15 Impact of Tobacco chewing on Sperm Count

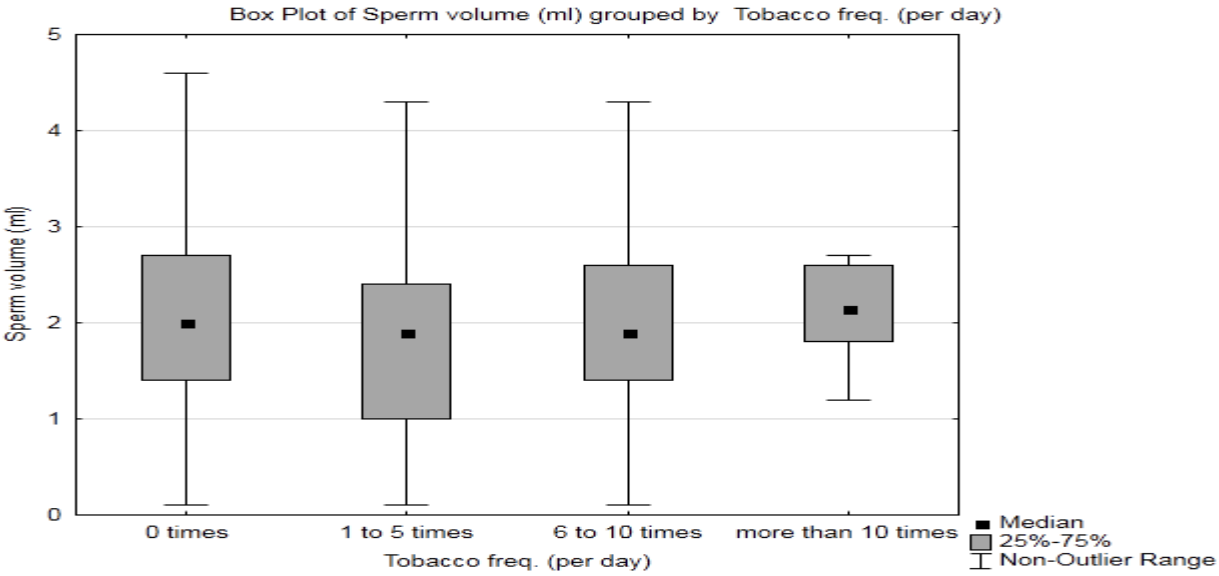

Figure 16 Impact of Tobacco chewing on Semen volume

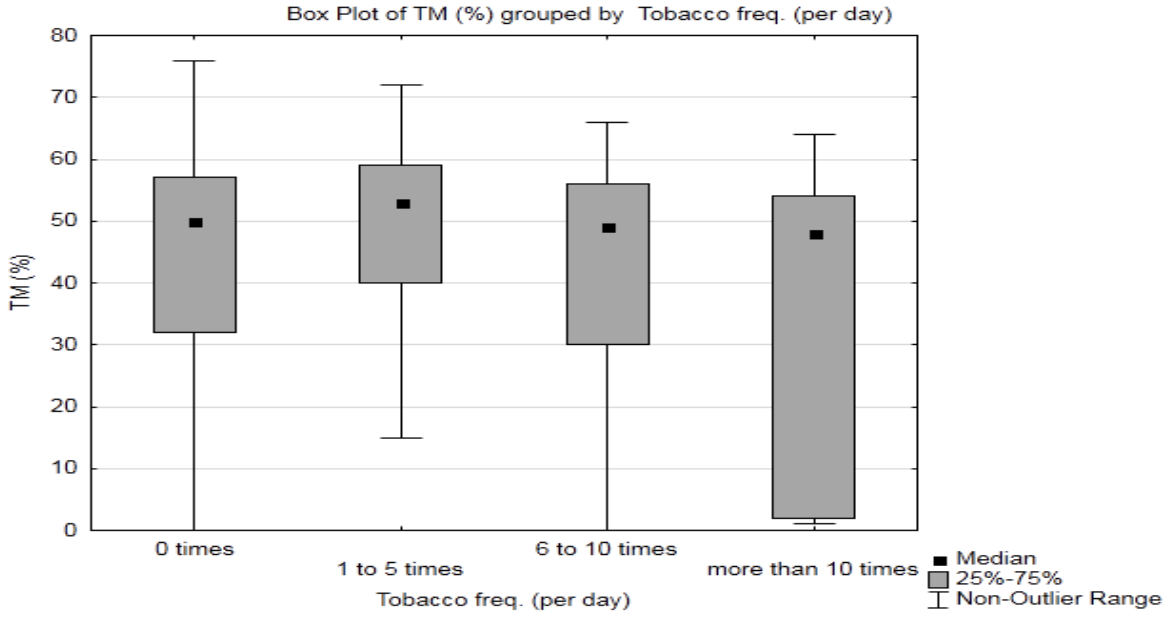

Figure 17 Impact of Tobacco chewing on Total Motility

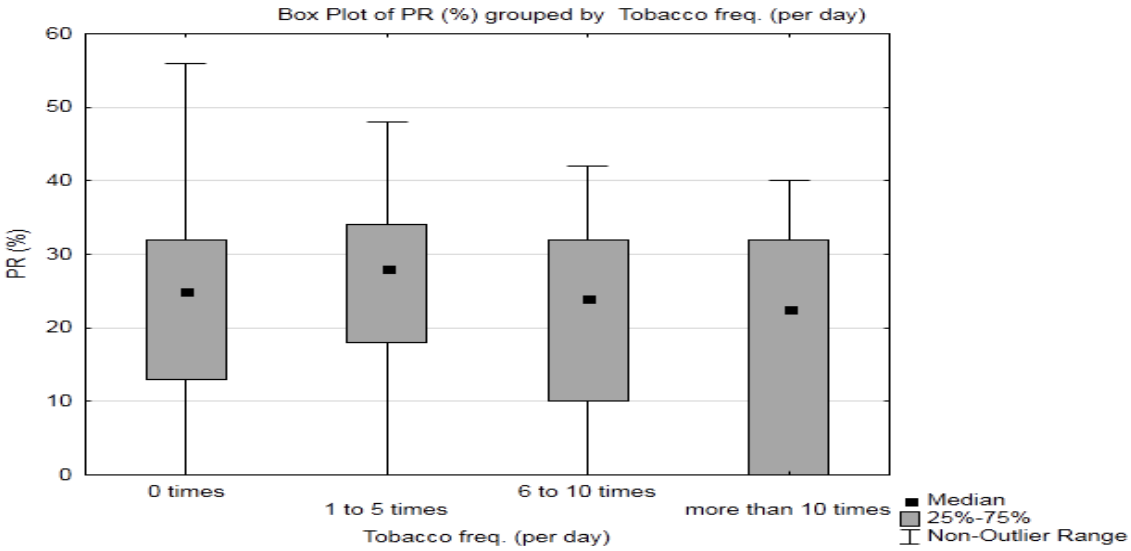

Figure 18 Impact of Tobacco chewing on Progressive Motility

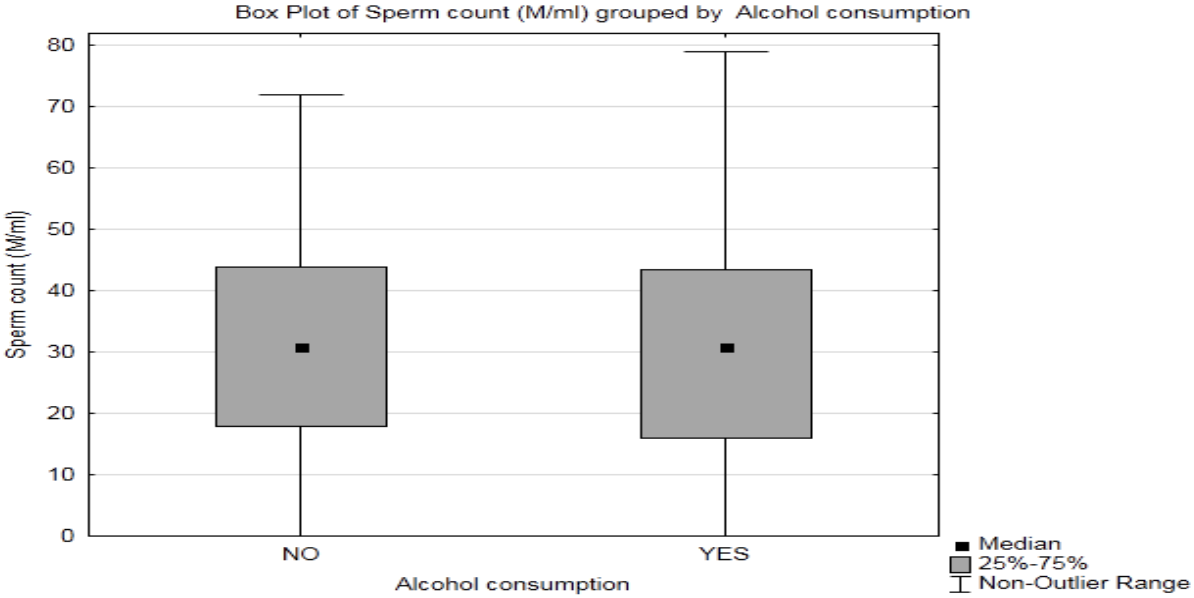

Figure 19 Impact of Alcohol consumption on sperm count

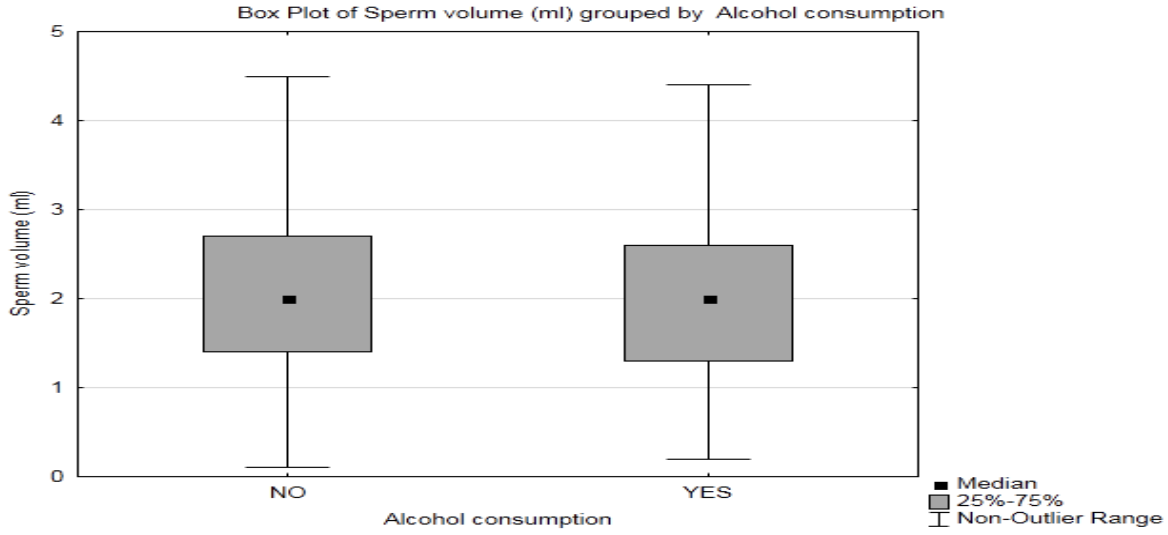

Figure 20 Impact of Alcohol consumption on semen volume

Figure 21 Impact of Alcohol consumption on Total Motility

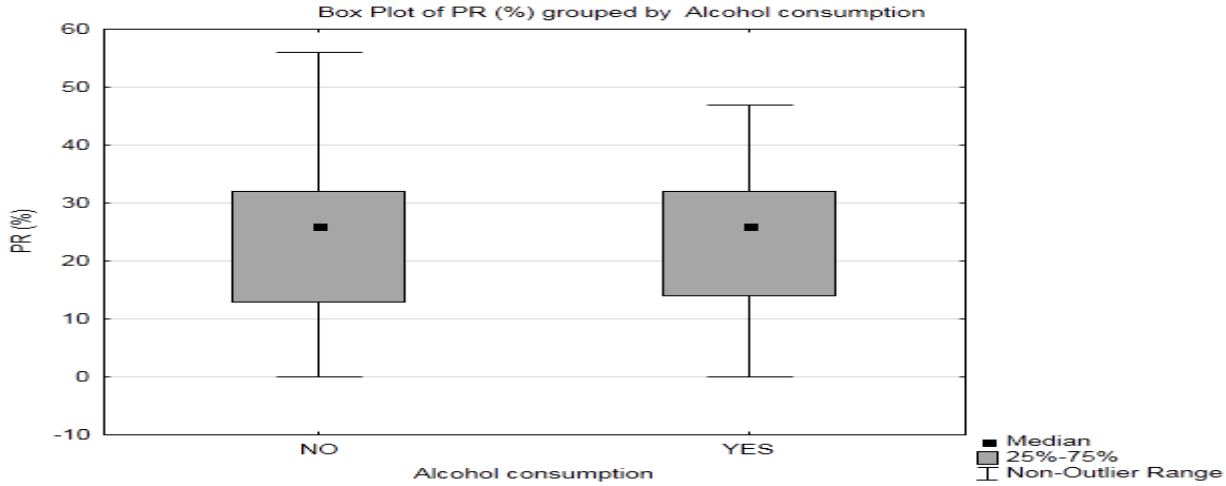

Figure 22 Impact of Alcohol consumption on Progressive Motility