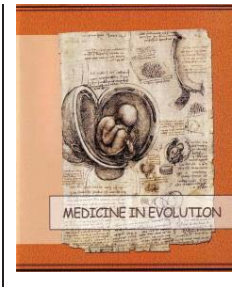


The impact of lifestyle and demographic factors on semen parameters



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Abstract

Aims and objectives: To identify the possible associations between semen parameters and different demographic or lifestyle factors with known roles in fertility.

Material and methods: The present retrospective study has taken place over a period of 12 months and has included 876 male patients who have presented themselves for fertility medical testing in a Fertility Center. They provided semen samples which were analysed through the use of semen analysis, according to the World Health Organisation (WHO) standards, providing basic information about spermatogenesis.

Results: Some significant statistical correlations were observed between different sperm parameters and demographic and lifestyle factors.

Conclusions: The present study shows that age, the number of abstinence days, obesity, smoking, some medical condition like varicocele or genetic factors,, as well as correct patient sample collection and analysing methods can greatly influence the different diagnostics decisions, on the basis of the sperm analysis, with different significations regarding the masculine fertility prognostic.

Keywords: Semen analysis/lifestyle/male factor/smoking/fertility

INTRODUCTION

Fertility represents the capacity of a healthy couple to reproduce through normal sexual activity (1). Today, on a world scale, infertility affects approximately 15% of couples that are of reproductive age (2) and in approximately 20-50% of cases, the medical reasons are of a masculine nature (3). There are a number of tests that try to establish the reference values for semen function evaluation. The World Health Organisation (WHO) has elaborated many editions of the manuals that define the optimal parameters of spermatogenesis, as dysregulations of the semen functions represent a major factor of masculine infertility (4).

The semen analysis is a laboratory standard test which offers basic information about spermatogenesis, sperm production and sperm quality, and some information about the secretory activity of the anexe glands and the potency of the masculine genital tract, it being the simplest masculine fertility test (5).

Aim and objectives

The objective of this study has been to identify the possible associations between some semen parameters and demographic or lifestyle factors, with a known role in fertility.

MATERIAL AND METHODS

Study Population: The present retrospective study has taken place over a period of 12 months and has included 876 male patients who have presented themselves for fertility medical testing (semen analysis) in a Fertility Center.

Semen parameters evaluated: semen volume, sperm cell concentration/ml, sperm cell concentration/ejaculate and the progressive motility.

The variables used in testing correlations were: the months of the year, the season, the number of abstinence days, age, some associated risk factors, the presence of varicocele, smoking, genetic factors and some associated infections.

The concentration and motility of sperm cells has been evaluated using the Makler counting chamber (Sefi Medical Instruments Ltd., Israel), especially conceived for evaluating the concentration and motility of sperm cells.

Determining the morphology of sperm cells has been done with the help of the May-Grünwald and Giemsa staining methods which have an affinity for the cellular components.

Normal and abnormal semen parameters

The semen parameter values have been fitted according to WHO²⁰¹⁰ (4), and have been taken into account for a correct evaluation of the sperm (6):

- *semen concentration* represents the number of sperm cells present in a volume of semen (per millilitre). The total number of sperm cells is referring to the number of sperm cells present in the entirety of the ejaculated material and is obtained by multiplying the concentration of sperm cells with the total volume of semen (7).
- *sperm cell motility* represents the speed with which the sperm cells are travelling; the speed with which they progress is directly linked with their chance of generating a pregnancy; *progressive motility*: represents the actively moving sperm cells, linearly or in a circle, no matter their speed.
- *sperm morphology (the shape of the sperm cells)*: sperm can be considered normal if they present an oval shaped head and a long, slim and straight tail. Any other potential shapes are considered abnormal (4).

Statistical data analysis

In this study, statistical data analysis and graphical representations have been accomplished with the help of the SPSS 20 program (Statistical Package for the Social Sciences, IBM Corp.). A $p < 0.05$ was considered to indicate a statistically significant

difference. During the study, apart from descriptive variable analysis (average, median, modal value, standard deviation, minimum and maximum), taking into account the type of data obtained and the end goals of the study, the Kruskal-Wallis H, Mann-Whitney U Tests and the Spearman Correlation Coefficient have also been used.

RESULTS

The average age of the participants has been 33.66 years, with a minimum of 17 years and a maximum of 69 years. The most frequently met age was 34 years, and the predominant group was the 31-35 years of age (32.42%) followed by the 36-40 years of age (31.85%). The samples have been collected in all seasons, in approximately equal percentages: 23.5% in winter, 26.9% in spring, 24.4% in summer and 25.1% in autumn.

Following this study, it has been noticed that 80.4% of the patients have presented a normal semen volume according to WHO.

Sample collection was made taking into account the average number of abstinence days (4.23 days), therefore keeping in line with the international recommendations for testing (the required 2-7 days of abstinence between intercourse)(4).

Over 79% of patients have presented a normal semen concentration, while from the rest of 21%, 14.5% have been diagnosed with oligozoospermia (low sperm concentration) and 6.1% with azoospermia (the absence of sperm cells in the semen sample). Approximately half of the patients have presented sperm progressive motility dysfunctions, therefore 51.4% had the diagnosis of astenozoospermia (low progressive motility). According to sperm morphology, for 17.9% of the subjects, the diagnosis of teratozoospermia (abnormal sperm shape morphology) has been chosen.

From the subjects of this study, 10.2% have presented associated risk factors. The presence of the varicocele has been noticed in a percentage of 3.4% of the subjects and in an extremely small number of patients, the presence of associated genetics factors has been observed.

For the analysed patient samples, the identification of correlations between different variables and studied semen parameters has been attempted.

The season in which semen sample collection has taken place

The Kruskal-Wallis H Test has been applied due to the abnormal distribution of the variables that express the semen volume, semen concentration, total semen concentration/ejaculate and progressive motility. No significant statistical relationship between the season when the samples were collected and any of the parameters has been observed ($p > 0.05$).

Age of the patients

A significant statistical correlation, negative, but of a very low intensity, has been observed between age and semen volume ($\rho = -0.095$; $p = 0.005$).

Apart from this, age does not seem to significantly influence any other studied parameter; no significant statistical correlations have been identified. It can be affirmed that as one ages, a drop in semen volume can be observed (**Fig.1**).

The number of abstinence days

In order to determine the relationship between the number of abstinence days and different semen parameters, the Spearman Correlation Coefficient has been employed (**Fig.2**).

The presence of significant statistical correlations has been observed between the number of abstinence days, on one side and the semen volume ($\rho = 0.163$; $p < 0.001$), semen concentration ($\rho = 0.148$; $p < 0.001$), total semen concentration/ejaculate ($\rho = 0.204$; $p < 0.001$) and sperm cell morphology ($\rho = 0.102$; $p = 0.003$), on the other side. Alternatively, no significant statistical correlations have been observed between the number of abstinence days and progressive motility ($\rho = 0.019$; $p = 0.591$).

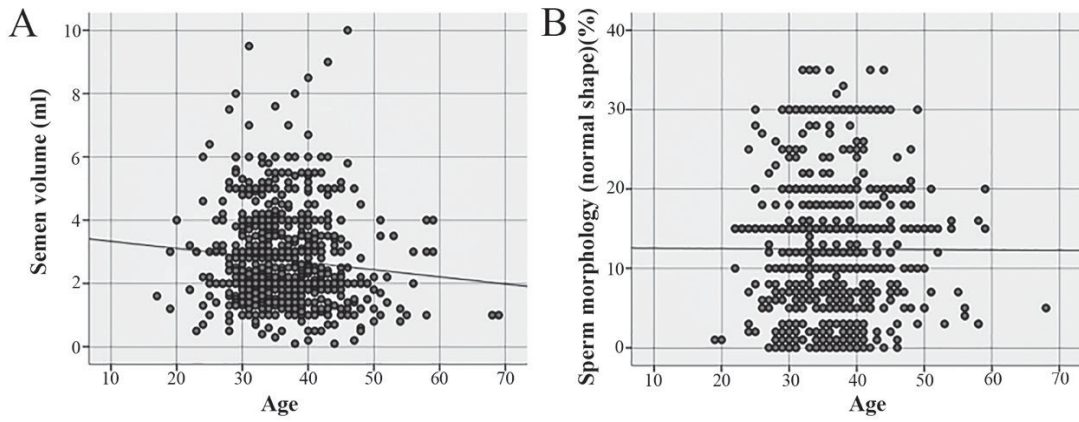


Figure 1. The relationship between age and different semen parameters. A) Semen volume (ml); B) Sperm morphology (normal shape)(%)

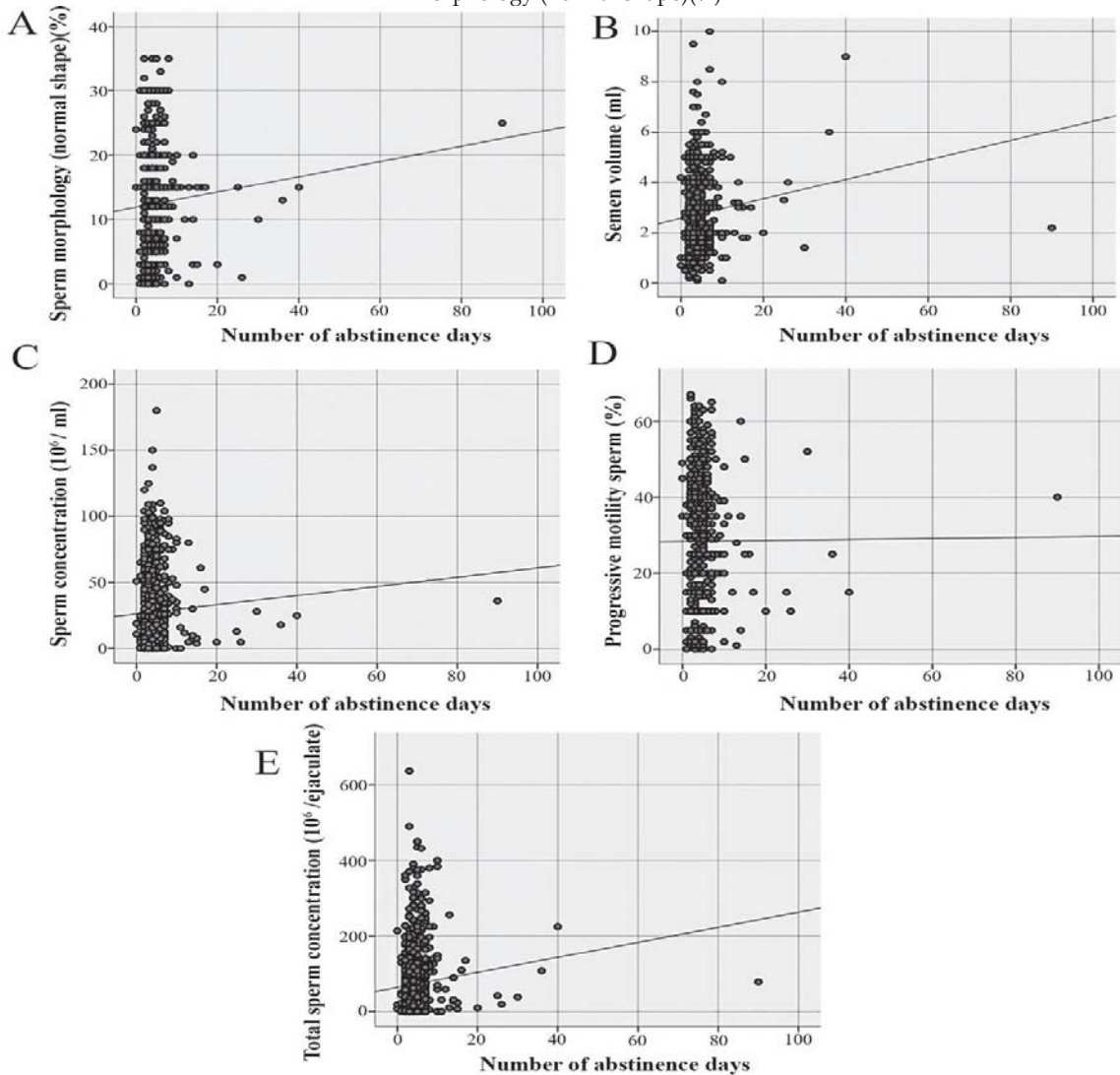


Figure 2. Relationship between the number of abstinence days and different semen parameters. A) Sperm morphology (normal shape)(%); B) Semen volume (ml); C) Sperm concentration (10^6 / ml); D) Progressive motility sperm(%); E) Total sperm concentration (10^6 / ejaculate)

Lifestyle and the presence of risk factors

Only 89 patients have presented risk factors (10.2% from the studied total); the majority (80.9%) presented obesity, 9% had diabetes, 6.7% had testicular afflictions and 3.4% had consumed recreational drugs.

Between risk factors and the studied semen parameters, no statistically significant relationships have been noticed. A very small effect of the risk factors on semen volume has been observed ($U = 30462$; $p = 0.043$; $r = 0.06$), as well as on semen concentration ($U = 29697$; $p = 0.019$; $r = 0.08$) and total semen concentration/ejaculate ($U = 27881.5$; $p = 0.002$; $r = 0.07$). In all cases, the presence of risk factors has led to decreases in semen characteristics.

Varicocele

Semen concentration and total semen concentration/ejaculate is significantly lower in the case of patients that present a varicocele. The measure in which the varicocele affects the semen concentration ($r = 0.11$) and the total semen concentration ($r = 0.09$) is very reduced. The presence of normal sperm cells is significantly lower in patients with this affliction, while the measure in which it affects their morphology is still very reduced ($r = 0.09$).

Smoking

According to the results of the statistical analysis, smoking does not have a significant effect over the morphology of sperm cells ($U = 1240.5$; $p = 0.054$; $r = 0.17$). However, smoking does have a statistically significant effect over semen concentration ($U = 1408$; $p = 0.014$; $r = 0.21$), total semen concentration/ejaculate ($U = 1331$; $p = 0.005$; $r = 0.25$) and progressive motility ($U = 1162$; $p = 0.018$; $r = 0.22$), through increasing these parameters.

DISCUSSIONS

Keeping in line with other published works, the differences in parameters and diagnostics on the basis of the semen analysis can be due to the differences in geographical zones, lifestyles, workplaces and environmental factors (8).

In our study, a decrease in sperm cell motility has been noticed, in 46.81% of the smoking patients. These results are backed by other examples from literature which have identified a decrease in sperm cell motility and concentration (9).

Cigarette smoke contains a high number of compounds recognised as carcinogenic and mutagenic factors. In spite of this, the toxicity of the many constituents of cigarette smoke has not been properly evaluated for its effect over sperm cells. Even though the effect of smoking over sperm cell dysfunctions has been observed a long time ago, the mechanism through which tobacco smoke affects sperm cells still remains misunderstood (10). On the other hand, some studies do show that the effect of nicotine can lead to a decrease in sex hormones which in turn influences the seminal parameters, but this hypothesis is still being investigated (11).

Testing statistical correlations between different parameters and variables has shown that no significant differences exist, depending on the month of semen collection. According to another study (12), an increased concentration of sperm cells, a better motility and morphology have been noticed in patients that have undertaken a semen analysis in spring, compared to the other seasons. This discrepancy could be explained by the different geographical zones, where changes in temperature could lead to seasonal variations in semen analysis results.

The presence of significant statistical correlations between the number of abstinence days and semen volume, semen concentration, total semen concentration/ejaculate have been observed. It could be inferred that as the number of abstinence days grows, the values of the previously mentioned parameters also grow, as well as the number of morphologically normal sperm cells. These data are in accordance with other available studies, which have also registered an increase in seminal parameters values as the number of abstinence days

grows (13, 14). Contrary, an increase in the percentage of sperm DNA (deoxyribonucleic acid) fragmentation has also been observed in longer periods of abstinence, a fact that is associated with reactive oxygen species (ROS) and a reduced fertility capacity (15).

Speaking about age, it can be affirmed that as men grow older, a decrease in semen volume takes place. Between age and all the other parameters, no statistically significant correlation has been found. The results of this study are in accordance with previously published works which have also proved that age does not exert an influence over the majority of the seminal parameters, with the exception of the semen volume in older individuals (16). Opposed to our data, according to another published study, a decrease in all seminal parameters values has been found in all patients over 45 years of age (17).

Regarding semen volume, semen concentration, total semen concentration/ejaculate and progressive motility, their values do not significantly differ according to certain risk factors. There is, however, a very small effect of the presence of these factors (no matter their type) over the mentioned parameters. In our study, the presence of obesity and varicocele leads to a decrease in the characteristics regarding semen quality and the total/ejaculate semen concentration, leading to a cause of potential masculine infertility.

Our results are backed-up by other available studies that have analysed the correlation with the masculine body mass index (BMI) and have found that there is a decrease in seminal parameters with gaining weight. This because a high masculine BMI is associated with reduced plasmatic concentrations of globulin which binds the sex hormone (SHBG) testosterone and with a concomitant rise of the plasmatic concentrations of follicular hormone (FSH). Low levels of testosterone and high levels of FSH have been associated for a long time with subfertility (18) and a reduction in the number of sperm cells through the interruption of the negative feedback loop of the hypothalamic pituitary gonadal axis (19). In addition, the damaging effect of heat which results from the increase in scrotum adiposity has been associated with a reduced motility of sperm cells and an increased fragmentation of sperm DNA (20), and also an increase in the oxidising stress of semen (21).

Other authors have observed a lower concentration of sperm cells, a lower rate of progressive motility, but also of abnormal morphology in patients and compare the semen analysis with before and after the surgical treatment of the varicocele, noting a significant improvement of some parameters, posttreatment (22). The varicocele represents an abnormal dilation of the testicular veins (the pampiniform plexus) at scrotum level and can be a cause of infertility (23). The scrotum is a temperature regulator for the testicles and the varicocele can determine an increase in temperature at this level and can affect spermatogenesis (24, 25). The varicocele is also associated with the deterioration of semen DNA and can affect the patency of the efferent ducts or the epididymis channel, which can affect the maturing of the sperm cells in the epididymis and can lead to motility disorders (26).

In our study, we have identified that the presence of genetic factors has a statistically significant effect on semen concentration, total semen concentration/ejaculate and progressive motility, but the size of the effect is extremely reduced. These parameters are reduced in patients that present certain genetic factors. Azoospermia has been identified in 6% of patients and this can be due to genetic anomalies (8), certain hormonal dysregulations, varicocele or testicular torsion (27). In addition, the percentage of normal shaped sperm cells is reduced in patients which present these factors, coming also in correlation with other studied works (8).

CONCLUSIONS

There are a series of factors that can influence significantly semen parameters along with deciding different diagnostics on the basis of the semen analysis, with implications in the evaluation of the masculine fertility prognostic. Morphological sperm cell defects can be influenced by diverse variables and are in most cases irreversible, being the result of the

effects of environmental factors or pathologies of the masculine genital tract. These can induce epigenetic modifications which can partially explain the variations in sperm cell parameters, especially regarding volume, concentration, motility and morphology.

The results of the present study can be affected by the following limitations that need to be mentioned: Firstly, limitations regarding population selection: the samples came from patients that have contacted a Fertility Centre and therefore, any attempt to extrapolate the results to the general population can be invalidated. On the other hand, the retrospective examination of data can include possible methodological variations between different operators. Therefore, future prospective analysis and the use of standardised evaluation equipment that can automatically analyse semen samples will be able to provide much more robust evaluations in this domain.

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REFERENCES

1. Optimizing natural fertility: a committee opinion. *Fertil Steril.* 2017;107(1):52-8.
2. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. *Reprod Biol Endocrinol.* 2015;13:37.
3. Kumar N, Singh AK. Trends of male factor infertility, an important cause of infertility: A review of literature. *J Hum Reprod Sci.* 2015;8(4):191-6.
4. DoRHaR WHO. WHO laboratory manual for the examination and processing of human semen. 2010;Fifth edition:1 - 287.
5. Bunting L, Tsibulsky I, Boivin J. Fertility knowledge and beliefs about fertility treatment: findings from the International Fertility Decision-making Study. *Hum Reprod.* 2013;28(2):385-97.
6. Gottardo F, Kliesch S. [Semen analysis: spermogram according to WHO 2010 criteria]. *Urologe A.* 2011;50(1):101-8.
7. Li W, Jia M, Peng Y, Ding R, Fan L, Liu G. Semen quality pattern and age threshold: a retrospective cross-sectional study of 71,623 infertile men in China, between 2011 and 2017. *Reproductive Biology and Endocrinology.* 2019;17.
8. Karabulut S, Keskin I, Kutlu P, Delikara N, Atvar O, Ozturk M. Male infertility, azoospermia and cryptozoospermia incidence among three infertility clinics in Turkey. *Türk Üroloji Dergisi/Turkish Journal of Urology.* 2018;44:109-13.
9. Parmar N, Gohel V, Sarvaiya J, Patel N, N V. Effect of tobacco chewing on semen parameters. *Int J Med Sci Public Health.* 2016;5(6):1139-42.
10. Meri Z, Irshid I, Migdadi M, Irshid A, Mhanna S. Does Cigarette Smoking Affect Seminal Fluid Parameters? A Comparative Study. *Oman medical journal.* 2013;28:12-5.
11. Al-Turki HA. Effect of smoking on reproductive hormones and semen parameters of infertile Saudi Arabians. *Urol Ann.* 2015;7(1):63-6.
12. Chen Z, Godfrey-Bailey L, Schiff I, Hauser R. Impact of seasonal variation, age and smoking status on human semen parameters: The Massachusetts General Hospital experience. *Journal of experimental & clinical assisted reproduction.* 2004;1:2.
13. De Jonge C, LaFromboise M, Bosmans E, Ombelet W, Cox A, Nijs M. Influence of the abstinence period on human sperm quality. *Fertil Steril.* 2004;82(1):57-65.
14. Demick J, Blanchard A, Centola G. Increased abstinence period results in improved semen volume, sperm concentration and total motile concentration in sperm banking patients. *Reproductive BioMedicine Online.* 2016;33:e7-e8.
15. Comar VA, Petersen CG, Mauri AL, Mattila M, Vagnini LD, Renzi A, et al. Influence of the abstinence period on human sperm quality: analysis of 2,458 semen samples. *JBRA Assist Reprod.* 2017;21(4):306-12.
16. Ng KK, Donat R, Chan L, Lalak A, Di Pierro I, Handelsman DJ. Sperm output of older men. *Human Reproduction.* 2004;19(8):1811-5.

17. Hellstrom WJ, Overstreet JW, Sikka SC, Denne J, Ahuja S, Hoover AM, et al. Semen and sperm reference ranges for men 45 years of age and older. *J Androl*. 2006;27(3):421-8.
18. Dutta S, Biswas A, Sengupta P. Obesity, endocrine disruption and male infertility. *Asian Pacific Journal of Reproduction*. 2019;8(5):195-202.
19. Du Plessis S, Cabler S, McAlister D, Sabanegh E, Agarwal A. The effect of obesity on sperm disorders and male infertility. *Nature reviews Urology*. 2010;7:153-61.
20. Katib A. Mechanisms linking obesity to male infertility. *Cent European J Urol*. 2015;68(1):79-85.
21. Leisegang K, Sengupta P, Agarwal A, Henkel R. Obesity and male infertility: Mechanisms and management. *Andrologia*. 2020.
22. Taha E, Kamal E, Abdulwahed S, Elktatny H. Impact of varicocele recurrence on semen parameters and pregnancy outcome. *Human Andrology*. 2012;2:65-9.
23. Miyaoka R, Esteves SC. A Critical Appraisal on the Role of Varicocele in Male Infertility. *Advances in Urology*. 2012;2012:1-9.
24. Kantartzi PD, Goulis Ch D, Goulis GD, Papadimas I. Male infertility and varicocele: myths and reality. *Hippokratia*. 2007;11(3):99-104.
25. Mohammed A, Chinegwundoh F. Testicular varicocele: an overview. *Urol Int*. 2009;82(4):373-9.
26. Zini A, Agarwal A. *A Clinician's Guide to Sperm DNA and Chromatin Damage*: Springer International Publishing; 2018.
27. Patel AS, Leong JY, Ramasamy R. Prediction of male infertility by the World Health Organization laboratory manual for assessment of semen analysis: A systematic review. *Arab J Urol*. 2018;16(1):96-102.