

A Prospective, Single Centre, Observational Study for the Impact of Lifestyle Modifications on Semen Parameters in Patients Diagnosed with Abnormal Semen Analysis

Prof. Rahul Jagadale, Amol Khairnar, Laxmi Pardeshi, Yash Dhikale

Matoshri Institute of Pharmacy, Yeola, Nashik, Maharashtra, India

ABSTRACT

The male factor is a major contributory factor in the development of infertility. Male fertility can arise for a variety of reasons, including both reversible and irreversible diseases. Numerous studies conducted around the world have revealed that these modifiable lifestyle factors negatively impact not only sperm count, but also morphology, vitality, and motility. Semen analysis, when performed along with a detailed medical and sexual history, can help provide an accurate picture of a male's fertility potential and help guide the treatment of both the individual and the couple seeking relief from their fertility.

KEYWORDS: Human infertility, Process of sperm production, Spermatogenesis, Lifestyle modification, Human semen, Semen analysis

How to cite this paper: Prof. Rahul Jagadale | Amol Khairnar | Laxmi Pardeshi | Yash Dhikale "A Prospective, Single Centre, Observational Study for the Impact of Lifestyle Modifications on Semen Parameters in Patients Diagnosed with Abnormal Semen Analysis" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-8 | Issue-1, February 2024, pp.191-197, URL: www.ijtsrd.com/papers/ijtsrd61263.pdf



Copyright © 2024 by author (s) and International Journal of Trend in Scientific Research and Development Journal. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0) (<http://creativecommons.org/licenses/by/4.0>)



INTRODUCTION

Background

Human Infertility

A sexually mature adult's inability to reproduce naturally is referred to as infertility. For scientific and medical purposes, infertility is typically characterized as the inability to conceive a healthy child following at least a year of regular, unprotected sexual activity. Primary or secondary infertility is possible. When a person has never experienced a successful pregnancy, it is said that they have primary infertility. When a woman has at least one successful pregnancy under her belt but is unable to get pregnant again despite trying for at least a year, the situation is referred to as secondary infertility. A prevalent issue is infertility. Infertility affects 16% of Canadian couples in 2019, according to the Canadian government, a number that has increased since the 1980s. If you take a look at the couples you know, you'll see that approximately one in six of them struggle with conception.

TYPES OF INFERTILITY

- Primary infertility, which is the inability to conceive in those who have never previously given birth.
- Secondary infertility is the inability to conceive after one or more previous pregnancies.[1]

MALE INFERTILITY

Male infertility is defined as the inability of a male to make a fertile female pregnant, also for a minimum of at least one year of unprotected intercourse. The male is solely responsible for about 20% and is a contributing factor in another 30% to 40% of all infertility cases.[2] As male and female causes often co-exist, it is important that both partners are investigated for infertility and managed together. Overall, the male factor is substantially contributory in about 50% of all cases of infertility.

Male fertility can arise for a variety of reasons, including both reversible and irreversible diseases.

Each partner's age, use of drugs, surgical history, exposure to chemicals in the environment, genetic issues, and systemic disorders are other variables that might have an impact. The main goal of a male's infertility evaluation is to identify his contributing causes, treat those that are reversible, decide if he qualifies for assisted reproductive techniques (ART), and provide counseling for issues that are irreversible and untreatable.[3] Male infertility occasionally may be a sign of a more serious ailment. This is yet another justification for doing a thorough evaluation of the male members of infertile couples, in order to detect and treat any serious underlying medical issues. [4]

Effect of age factor on Reproductive System:-

Despite individual variations, one of the impacts of aging on the male reproductive system is testicular morphology. Between the ages of 11 and 30, the average testicular volume tends to rise, between the ages of 30 and 60, it stays constant, and after the age of 60, it steadily declines each year [5]. Men over 75 years old have reported having 31% smaller mean testicular volumes than men between the ages of 18 and 40. This discrepancy is accompanied by significantly lower mean serum free testosterone levels and higher mean serum levels of gonadotropins. A decrease in semen volume, motility, and daily sperm production per testis are further patterns that can be seen. The idea that sperm concentration likewise decreases with age is unsupported by reliable research. [6]

PHYSIOLOGY OF MALE REPRODUCTION

The anatomy and development of the male genital and ductal system, the physiology of the testis, the hormonal control of the testis, as well as the procedures involved in the deposition of seminal fluid within the female genital tract, must all be understood properly in order to comprehend male reproductive physiology and related pathology. [7]

Process of Sperm production

The primary job of the male reproductive system is to produce sperm. Spermatogenesis is the medical or scientific word for the process through which your body produces sperm. Your body must first produce the required hormones in order to begin the process of spermatogenesis. Follicle-stimulating hormone (FSH) is one of the three primary hormones required.

Testosterone and luteinizing hormone (LH) Your pituitary gland, which is found in the base of your brain, produces both FSH and LH. FSH boosts testicular growth and aids in sperm maturation, whereas LH encourages the creation of testosterone in the testicles. Your testicles produce the hormone testosterone, which is in charge of creating and

maintaining male traits. The testosterone that men produce is a major contributing factor to their deeper voices and facial hair.

Your body produces sperm continually with the aid of FSH, LH, and testosterone working in concert. Sperm begin to form in a network of microscopic tubes inside your testicles known as seminiferous tubules once your body has produced enough hormones. Sperm begin as basic round cells that must develop and change into their characteristic tadpole shape. The sperm go to the epididymis, a different area of the male reproductive system, to continue developing once they have started to change. In your scrotum, next to your testicles, is another lengthy tube-like structure called the epididymis. Until ejaculation, mature sperm will remain in the epididymis.

From beginning to end, sperm maturation takes little over 70 days. [8]

Harmonal Control of Spermatogenesis

Several hormones, principally follicle-stimulating hormone (FSH) and luteinizing hormone (LH), regulate the hormonal activity of spermatogenesis. These hormones, which the anterior pituitary gland produces, are extremely important for controlling the spermatogenesis process.[9]

Spermatogenesis-

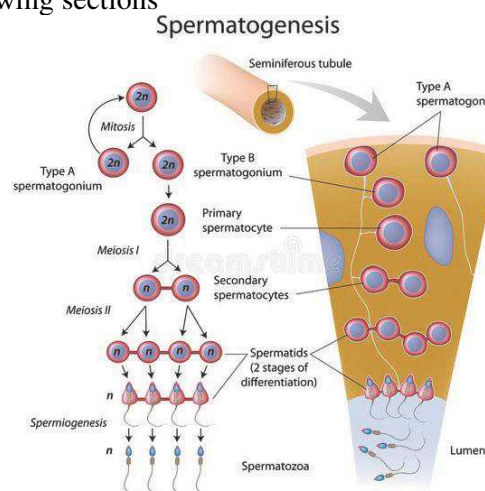
It is the process of creating male gametes (sperm) or spermatozoa from the testicular germinal epithelium.

Developmental stages of spermatogenesis

In the course of spermatogenesis the germ cells move the lumen as they mature. The following developmental stages are thereby passed through:

1. Primary spermatocytes (=spermatocytes order I)
2. Secondary spermatocytes (= spermatocytes order II)
3. Spermatids
4. Sperm cell (= spermatozoon)

The spermatogenesis can be subdivided into two following sections



Spermatogenesis diagram

The first includes cells from spermatozoa to secondary and inclusion cells in spermatocytes and is called spermatocytogenesis. The second involves sperm differentiation to maturation and from spermatid stage and is called spermatogenesis [10]

Patients and physicians are often curious if there are lifestyle modifications to improve their fertility. This is common lifestyle factors such as weight, exercise, substance use, diet, vitamin and antioxidant supplementation, and stress and their effects on fertility.

Weight: -

Being overweight does not seem to have the same effect on male fertility. BMI was not associated with sperm concentration, motility or morphology. Several studies have shown that overweight and obese women have decreased fertility. Similarly, obesity may play a role in male fertility. A study of farmers and their wives in the United States found that a 10 kg weight gain can reduce fertility by almost 10% and a large effect on men with a body mass index (BMI) above 32. A significant reduction in the number of normal motile spermatozoa was observed in men with BMI over 25 years of age, men with excess fat in the thighs and suprapubic region have also been found to have poor sperm quality. [11]

Exercise:-

Different amounts and frequencies of exercise have different effects on the fertility of men and women. The complicated relationship between exercise and the reproductive potential is most likely due to changes in the hypothalamic and pituitary axis. On the other hand, regular exercise does not seem to affect the sperm parameters. There are numerous health benefits of exercise. However, there are conflicting results regarding the effects of exercise on the reproductive function of men. [12]

Substance Use:-

When looking at substance use studies, it's important to keep in mind that substances can be used in different ways (e.g. smoking and alcohol) and it can be hard to determine the impact of each. Lifestyle factors and consumption can also change over time, and many studies only look at a snapshot of a specific lifestyle. [13]

Diet and nutrition:-

An optimal fertility diet has not yet been developed and the effect of dietary factors on fertility is largely unknown. However, dietary changes have been shown to improve ovulatory infertility.

Example of boost of fertility –

1. Beans and Lentils
2. Egg yolks

3. Sunflower seeds

4. Fruit and vegetables, etc .[14]

Vitamins & Supplements:-

Antioxidants:-

Antioxidants reduce or reduce the amount of reactive oxygen species, including hydroxyl radicals, superoxide anions, and also hydrogen peroxide [15]. Reactive oxygen balance can increase damage to sperm DNA structure, also with unclear association with female fertility [16].

Psychological Stress:-

Stress can manifest itself physically, mentally, and emotionally. Significant physical and psychological stress; changes in reproductive function, such as anorexia nervosa; However, evidence regarding the effects of moderate stress is mixed [17]

Smoking:-

Cigarette smoking is widely recognized to be a health risk and a leading cause of death, with approximately 20% of the adult population worldwide being smokers. Smoking-related DNA damage and methylation patterns have been observed in several human tissues, including those not directly exposed to smoking through indirect systemic exposure [18]. DNA adducts and DNA damage are inversely correlated with sperm parameters, especially concentration and motility, and both are transmitted to the fertilized egg with little possibility of repair by the oocyte [19]. Smoking is a risk factor for more than 60% of non-communicable diseases, and more than 6 million people die each year from tobacco use and second-hand smoke. Smoking is a risk factor for semen quality and reduces semen quality [20]

Tabacco:-

In the United States, about 30% of women of childbearing age and 35% of men of childbearing age smoke cigarettes. (21)

Caffeine:-

As a result, sperm concentration and number decreased slightly a man who consumes large amounts of caffeine and carbonated drinks. Inside a large complex European retrospective study, high-grade consumption Caffeine levels were [5 or more cups of coffee or 500 mg or more per day]. Associated with increased risk of infertility (as defined). 9.5 months or more until pregnancy) [22]

Alcohol:-

Alcohol and tobacco on adverse effects on male fertility and reproductive health. Numerous studies conducted around the world have revealed that these modifiable lifestyle factors negatively impact not only sperm count, but also sperm structure, morphology, vitality, and motility. [23] High and frequent alcohol

consumption has a negative effect on sperm count. Induction of sperm concentration. Normal sperm morphology. Decreased total sperm count, testosterone and SHBG, and increased serum testosterone levels [24, 25].

Human semen

Human sperm consists mainly of sperm secreted by several different accessory glands and spermatozoa that are produced in the testicle.

Semen can be divided into 4 fractions:-

1. Pre-ejaculatory-secretion from urethral and bulb urethral gland (no sperms)
2. Dilute fluid from prostate gland (no sperm)
3. Major portion of sperm from vas deferens and distal epididymis (Volume 5%)
4. Seminal vesicle secretion (few sperm) Fraction 1, 2, 3 make up the first portion of the ejaculate (30% of total Volume). Therefore it is important to ensure the first portion is collected.

IMPORTANT

Mix semen well before analysis.

The average ejaculation is between 2 and 5 ml, depending on the sperm concentration, and is usually gray opalescent. It is known that human sperm varies greatly in the ejaculate of different men, and it can also vary in the ejaculate of the same man at different times. From a biological perspective, such variations are caused by many things various factors, including the composition of the sperm, the source of these components and related secretions. The main task of sperm is to deliver the genetic material of the father during fertilization of the egg, sperm does not play a direct role in fertilization, because they are all complex biological fluids consisting of inorganic and organic components that allow it to perform many different functions. Sperm selection works a transport medium for sperm, actively participates in the sperm maturation process and provides an energy source thanks to fructose and its prostaglandins. Level, protects sperm from the acidity of vaginal fluids. In addition to these functions, antioxidant enzymes in seminal plasma have been shown to play a protective role against lipid oxidation when sperm chromatin is stabilized due to zinc content. [26]

Semen analysis

- This section begins with an overview of the process of semen analysis and points out that fertility or sperm production cannot be assessed on the basis of a single sample of semen. However, it fails to acknowledge that the cause of the changes in an abnormal semen analysis such as the impairment of sperm function or a reduction in sperm numbers cannot be determined

from the examination of a semen sample 1 and therefore medical laboratory scientists should refrain from giving advice on treatment.

- What the clinician needs for the correct management of infertility in the male is a diagnosis. Infertility is not a diagnosis: it is only a symptom. The analysis of semen only occasionally gives the clinician a diagnosis, as for the most part, the changes that take place in semen are largely non-specific. However, in conditions such as globozoospermia, only a semen analysis can provide a diagnosis but this situation is not common. Thus at best a semen analysis can usually only be a measure of the severity of a condition and will only rarely indicate the pathology that is causing that infertility. As infertility has no other presenting symptom, the main value of a semen analysis is in the identification of the infertility, i.e. it is simply a screening test for infertility in the male.
- There are other reasons why a semen analysis is only of limited value in the determination of infertility. Over time it has become clear that the relationship between infertility and sperm numbers, sperm movement and sperm morphology is not a simple one. Low sperm counts may be found among previously fertile men seeking vasectomy for fertility control

Semen analysis and infertility

Semen analysis, laboratory examination of a sample of seminal fluid, usually consisting of the determination of semen volume, alkalinity or acidity (pH), sperm number (or sperm count), and the motility, shape, and viability of sperm. An examination of seminal fluid is usually undertaken to check for possible male infertility. In addition to obtaining a complete history, performing a physical examination of both partners, and verifying that ovulation does occur in the woman, the physician will perform a semen analysis. Normal semen contains more than 60 million sperm per millilitre. More than 60 percent of the sperm are motile two hours after ejaculation, and 80–90 percent will have normal form and structure. Possible causes of infertility are a low sperm count, low motility, or a low percentage of normal forms. Rarely, a sperm analysis may be required in a case of suspected rape.

Collection of semen sample

The semen sample collection rooms were equipped with a clothes hanger and a hand basin. The patient was provided with a specimen cup for semen collection and asked to ejaculate using only masturbation. All incomplete collection was excluded in this study. Specimen information including the day

of masturbation and the time required for semen collection (time spent in the semen collection room) was recorded. However, for the privacy of the participants in this study, it was not possible to record the actual semen collection time.

Shaheed A. Abdulhaqq, Melween Martinez, Guobin Kang, Idia V. Rodriguez, Stephanie M. Nichols, David Beaumont, Jocelin Joseph, Livio Azzoni, Xiangfan Yin, Megan Wise, David Weiner, Qin Liu, Andrea Foulkes, Jan Münch, Frank Kirchoff, Christos Coutifaris, Georgia D. Tomaras, Carlos Sariol, Preston A. Marx, Qingsheng Li, Edmundo N. Kraiselburd, Luis J. Montaner

Macroscopic analysis of semen

Macroscopic Evaluation

Macroscopic semen analysis should begin with the examination of liquefaction, preferably within 30 min to 1 h after collection. Delay in processing may lead to dehydration or Alterations in semen quality due to temperature and environ-Mental changes since the specimen is being deposited in a Non-natural environment. Routine macroscopic evaluation Includes a quick examination of liquefaction, semen age, Appearance, color, viscosity, volume, and pH

Results, Reporting, and Critical Findings

The WHO has provided normal limits of reference for semen analysis. The values mentioned in the chart below represent the accepted 5th percentile for the parameters measured. [27]

Volume = >1.5 ml

pH = >7.2

Total sperm number = 39 million sperm per ejaculate or more

Morphology = >4 percent normal forms using the tygerberg method

Vitality = >58% live sperm

Progressive motility = >32%

Total (progressive motility and non-progressive motility) = >40%

No sperm agglutination

Viscosity = <2 cm after liquefaction

Optional investigations

Mixed antiglobulin reaction test with <50% motile spermatozoa with bound particles

Immunobead test with <50% motile spermatozoa with bound beads

Seminal fructose =>13 mcmol/ejaculate

Seminal zinc = >2.4 mcmol/ejaculate

Seminal neutral glucosidase = <20 milliunits /ejaculate

Go to:

Clinical Significance

Semen analyses are performed as part of the assessment of male factor infertility. It is imperative to take a complete medical and sexual history as well as perform a thorough physical examination in addition to the semen analysis to provide a complete diagnostic assessment. [27][28] If the semen analysis is normal per the WHO criteria, a single semen specimen may be sufficient, but two separate specimens are still recommended by some experts. If the semen analyses are abnormal, then the analysis can be repeated 3 months after completion of another complete spermatogenesis cycle. It can be repeated earlier if the sperm count is low or absent. A more comprehensive and detailed review of male infertility diagnosis and treatment can be found in our review article on the subject. [29]

Sperm Morphology

Abnormal sperm morphology is suggestive of a spermatogenesis problem. Assisted reproduction, such as intracytoplasmic sperm injection (ICSI). Whether the morphologic assessment of sperm has a significant impact on pregnancy rates after IVF or not is controversial. [30]

Cells in the Ejaculate

The presence of round cells in the ejaculate must be assessed with peroxidase activity and leukocyte markers. Men with >1 million leukocytes/ml (pyospermia) must be evaluated to rule out genital tract inflammation or infection. [31]

Go to:

Enhancing Healthcare Team Outcomes

Lifestyle measures including smoking cessation, reducing alcohol intake, healthy eating, exercise, weight loss if obese, avoiding toxic lubricants during intercourse, and ensuring the scrotal temperature is not increased can improve male factor fertility.[32][33] Low or absent sperm count in the semen may be due to hypothalamic-pituitary failure, primary testicular failure, or obstruction of the genital tract. Gonadotropin drugs can improve fertility in patients with hypogonadotropic hypogonadism. [33][34]

Genetic counseling should be offered to individuals with karyotypic abnormalities, including Klinefelter's syndrome, Y chromosome deletion, CBAVD, and CFTR gene mutation. [35] Surgical treatment of ejaculatory duct obstruction can help improve fertility. This is an alternative treatment to assisted reproductive procedures like intracytoplasmic sperm injection (ICSI) and in-vitro fertilization (IVF).

Semen analysis, when performed along with a detailed medical and sexual history together with a thorough physical examination, can help provide an accurate picture of a male's fertility potential and help guide the treatment of both the individual and the couple seeking relief from their infertility. [37]

Conclusion

A sexually mature adult's inability to reproduce naturally is referred to as infertility. For scientific and medical purposes, infertility is typically characterized as the inability to conceive a healthy child following at least a year of regular, unprotected sexual activity. When a woman has at least one successful pregnancy under her belt but is unable to get pregnant again despite trying for at least a year, the situation is referred to as secondary infertility. Primary infertility, which is the inability to conceive in those who have never previously given birth. Secondary infertility is the inability to conceive after one or more previous pregnancies. Male infertility is defined as the inability of a male to make a fertile female pregnant, also for a minimum of at least one year of unprotected intercourse. Overall, the male factor is substantially contributory in about 50% of all cases of infertility. This is yet another justification for doing a thorough evaluation of the male members of infertile couples, in order to detect and treat any serious underlying medical issues.

Reference

- [1] Thompson Rivers University Public university in Kamloops, British Columbia.
- [2] Hull MG, Glazener CM, Kelly NJ, Conway DI, Foster PA, Hinton RA, Coulson C, Lambert PA, Watt EM, Desai KM. Population study of causes, treatment, and outcome of infertility. *Br Med J (Clin Res Ed)*. 1985 Dec 14; 291 (6510):1693-7.
- [3] Shih KW, Shen PY, Wu CC, Kang YN. Testicular versus percutaneous epididymal sperm aspiration for patients with obstructive azoospermia: a systematic review and meta-analysis. *Transl Androl Urol*. 2019 Dec; 8(6):631-640.
- [4] Honig SC, Lipshultz LI, Jarow J. Significant medical pathology uncovered by a comprehensive male infertility evaluation. *Fertil Steril*. 1994 Nov; 62(5):1028-34.
- [5] Yang H, et al. The effects of aging on testicular volume and glucose metabolism: an investigation with ultrasonography and FDG-PET. *Mol Imaging Biol*. 2011; 13(2):391-8. Doi: 10.1007/s11307-010-0341-x.
- [6] Mahmoud AM, et al. Testicular volume in relation to hormonal indices of gonadal function in community-dwelling elderly men. *J Clin Endocrinol Metab*. 2003; 88(1):179-84. doi: 10.1210/jc.2002-020408.
- [7] Harvard-MIT Division of Health Sciences and Technology HST.071: Human Reproductive Biology.
- [8] Medically Reviewed by Dany Paul Baby, MD on November 11, 2022
- [9] principal of anatomy and physiology by Bryan H. Derrickson and Gerard J. Tortora
- [10] chapter 2 reproduction in lower and higher animals, std.xii sci: perfect biology (vol. 1), page no.30 to 46
- [11] Comstock IA, Kim S, Behr B, Lathi RB. Increased body mass index negatively impacts blastocyst formation rate in normal responders undergoing in vitro fertilization. *J Assist Reprod Genet*. 2015; 25.
- [12] Gudmundsdottir SL, Flanders WD, Augestad LB. Physical activity and fertility in women: the North-Trondelag Health Study. *Hum Reprod*. 2009; 24(12): 3196 – 204.
- [13] Practice Committee of the American Society for Reproductive Medicine. Smoking and infertility: a committee opinion. *Fertil Steril*. 2012; 98(6):1400-6.
- [14] Stamets K, Taylor DS, Kunselman A, Demers LM, Pelkman CL, Legro RS. A randomized trial of the effects of two types of short-term hypocaloric diets on weight loss in women with polycystic ovary syndrome. *Fertil Steril*. 2004; 81(3):630-7.
- [15] Combelles CM, Gupta S, Agarwal A. Could oxidative stress influence the in-vitro maturation of oocytes? *Reprod Biomed Online*. 2009; 18(6):864-80.
- [16] Zareba P, Colaci DS, Afeiche M, Gaskins AJ, Jorgensen N, Mendiola J, et al. Semen quality in relation to antioxidant intake in a healthy male population. *Fertil Steril*. 2013; 100(6):1572-9.
- [17] 2014; 4(10), e005767. -2014-005767. 80. Catherino WH. Stress relief to augment fertility: the pressure mounts. *Fertil Steril*. 2011; 95(8):2462-3.
- [18] Cui X, Jing X, Wu X, Wang Z, Li Q. Potential effect of smoking on semen quality through DNA damage and the down regulation of Chk1 in sperm. *Mol Med Rep*. 2016; 14(1):753-61.

- [19] Harlev A, Agarwal A, Gunes SO, Shetty A, du Plessis SS. Smoking and male infertility: an evidence-based review. *The world journal of men's health*. 2015; 33(3):143–60.
- [20] Yao DF, Mills JN. Male infertility: lifestyle factors and holistic, complementary, and alternative therapies. *Asian J Androl*. 2016; 18(3):410–8.
- [21] Jick H, Porter J. Relation between smoking and age of natural menopause. Report from the Boston Collaborative Drug Surveillance Program, Boston University Medical Center. *Lancet*. 1977; 1(8026):1354–5.
- [22] Bolumar F, Olsen J, Rebagliato M, Bisanti L. Caffeine intake and delayed conception: a European multicenter study on infertility and subfecundity. European Study Group on Infertility Subfecundity. *Am J Epidemiol*. 1997; 145(4):324–34.
- [23] Brugo-Olmedo S, Chillik C, Kopelman S. Definition and causes of infertility *Reprod Biomed Online*. 2001; 2:41–53
- [24] Habitual alcohol consumption associated with reduced semen quality and changes in reproductive hormones; a cross-sectional study among 1221 young Danish men
- [25] Alcohol and male reproductive health: a cross-sectional study of 8344 healthy men from Europe and the USA
- [26] world health organisation laboratory manual for the examination and process of human semen, 5th edition
- [27] Anne M. Jequier , Semen analysis: a new manual and its application *Asian J Androl*. 2010 Jan; 12(1): 11–13. Published [2] online [3] 2010 [4] Jan [5] 29. doi:10.1038/aja.2009.12
- [28] Helena Chmura Kraemer, Ph.D., George A. Morgan, Ph.D., Nancy L. Leech, Ph.D., Jeffrey A. Gliner, Ph.D., Jerry J. Vaske, Ph.D., And Robert J. Harmon, M.D. Measures Of Clinical Significance *J. Am. Acad. Childadolesc.Psychiatry*,42:12,Decembr 2003
- [29] LucaBoeri, GiuseppeFallara, EdoardoPozzi, FedericoBelladelli, ChristianCorsini, MassimilianoRaff o, NicolòSchifano, PaoloCapogrosso, Alessiad'Arma, FrancescoMontorsi, AndreaSalonia The impact of different WHO reference criteria for semen analysis in clinical practice Received:22March2022,
- Revised:18May2022,Accepted:25May2022 DOI:10.1111/andr.13213
- [30] Roelof Menkveld, 1Cas AG Holleboom,2 and Johann PT Rhemrev2 Measurement and significance of sperm morphology *Asian J Androl*. 2011 Jan; 13(1): 59–68. Published online 2010 Nov 15. doi: 10.1038/aja.2010.67 Volume 13(1); 2011 Jan
- [31] Lique M. Coolen, Julien Allard, William A. Truitt, Kevin E. McKenna Central regulation of ejaculation *Physiology & Behavior* Volume 83, Issue 2, 15 November 2004, Pages 203-215 <https://doi.org/10.1016/j.physbeh.2004.08.023>
- [32] John A. Owen, Valentina L. Brashers, Keith E. Littlewood, Elisabeth Wright, Reba Moyer Childress & Shannon Thomas enhancing healthcare team collaboration Pages 212-217 | Received 28 Jan 2013, Accepted 29 Jan 2014, Published online: 04 Mar 2014 <https://doi.org/10.3109/13561820.2014.890581>
- [33] Jason Gandhi, Rafael J. Hernandez, Andrew Chen, Noel L. Smith, Yefim R. Sheynkin, Gargi Joshi and Sardar Ali Khan Impaired hypothalamic-pituitary-testicular axis activity, spermatogenesis Published online by Cambridge University Press: 10 February 2017 Volume 25 Issue 2
- [34] Boeri, Luca; Capogrosso, Paolo; Salonia, Andrea Source: *Current Pharmaceutical Design, Gonadotropin Treatment for the Male Hypogonadotropic Hypogonadism* Volume 27, Number 24, 2021, 2775-2783(9) Publisher: Bentham Science Publishers DOI: <https://doi.org/10.2174/1381612826666200523175806>
- [35] Inge Liebaers, André Van Steirteghem, Willy Lissens *Book Textbook of Assisted Reproductive Techniques* Edition 2nd Edition, First Published 2005 Pages14
- [36] Randall B. Meacham M.D., Daniel K. Hellerstein M.D, Larry I. Lipshultz M.D. Evaluation and treatment of ejaculatory duct obstruction in the infertile male Received 10 June 1991, Revised 13 October 1992, Accepted 13 October 1992, Available online 6 May 2016, Version of Record 6 May 2016. *Fertility andSterility* Volume 59, Issue 2, February 1993, Pages 393-397
- [37] Fernando Tadeu Andrade-Rocha On the Origins of the Semen Analysis: A Close Relationship with the History of the *Reproductive Medicine* Volume 10(4) Oct-Dec 2017