

# Trends of male factor infertility, an important cause of infertility: A review of literature

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## ABSTRACT

Infertility and problems of impaired fecundity have been a concern through ages and is also a significant clinical problem today, which affects 8–12% of couples worldwide. Of all infertility cases, approximately 40–50% is due to “male factor” infertility and as many as 2% of all men will exhibit suboptimal sperm parameters. It may be one or a combination of low sperm concentration, poor sperm motility, or abnormal morphology. The rates of infertility in less industrialized nations are markedly higher and infectious diseases are responsible for a greater proportion of infertility. The present literature will help in knowing the trends of male factor infertility in developing nations like India and to find out in future, various factors that may be responsible for male infertility.

**KEY WORDS:** Infertility, semen, sperm

## INTRODUCTION

Infertility is a condition with psychological, economic, medical implications resulting in trauma, stress, particularly in a social set-up like ours, with a strong emphasis on child-bearing. According to the International Committee for Monitoring Assisted Reproductive Technology, World Health Organization (WHO), infertility is a disease of reproductive system defined by failure to achieve the clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.<sup>[1]</sup> It can also be defined as failure of couple to conceive after 12 months of regular intercourse without the use of contraception in women <35 years; and after 6 months of regular intercourse without the use of contraception in women ≥35 years.<sup>[2]</sup>

## GLOBAL INCIDENCE OF INFERTILITY

There are no reliable figures for global prevalence of infertility,<sup>[3]</sup> but estimates suggest that nearly 72.4 million couples globally experience fertility problems.<sup>[4]</sup> As per the WHO estimates 60–80 million couples worldwide currently suffer from infertility.<sup>[5]</sup> It varies across regions of the world and is estimated to affect 8–12% of couples worldwide.<sup>[6,7]</sup> It tends to be the

highest in countries with high fertility rates; an occurrence termed “barrenness amid plenty.”<sup>[8]</sup> In recent decades, infertility has impacted an increasing number of couples. Approximately, 10% of couples in the United States are defined as infertile based on the inability to conceive after 12 months of unprotected intercourse.<sup>[9,10]</sup> According to National Center for Health Statistics, the absolute numbers of impaired fecundity increased by about 2.7 million women, from 4.56 million in 1982 to 7.26 million in 2002, then fell slightly to 6.71 million in 2006–2010.<sup>[11]</sup> Moreover, the fertility rate in men younger than age 30 years has also decreased worldwide by 15%.<sup>[12]</sup>

## INFERTILITY IN INDIA

As per the WHO, the overall prevalence of primary infertility ranges between 3.9%

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and 16.8%.<sup>[5]</sup> Also, the estimates of infertility vary widely among Indian states from 3.7% in Uttar Pradesh, Himachal Pradesh, and Maharashtra,<sup>[13]</sup> to 5% in Andhra Pradesh,<sup>[14]</sup> and 15% in Kashmir.<sup>[15]</sup> Moreover, the prevalence of primary infertility has also been shown to vary across the tribes and castes within the same region in India.<sup>[13,16]</sup>

It was reported that 40% of infertility cases were related to men, 40% of women and 20% of both sexes.<sup>[17]</sup> According to a multicentric study conducted by WHO from 1982 to 1985, 20% of cases were attributed to male factors, 38% to female factors, 27% had causal factors identified in both partners, and 15% could not be satisfactorily attributed to either partner.<sup>[18]</sup> In Indian couples seeking treatment, the male factor is the cause in approximately 23%.<sup>[15]</sup> A recent report on the status of infertility in India, states that nearly 50% of infertility is related to the reproductive anomalies or disorders in the male.<sup>[19]</sup> In addition, over 25% of infertility cases, no detectable cause can be traced after routine tests, which leaves the case as unexplained infertility.<sup>[19]</sup>

## MALE INFERTILITY: AN IMPORTANT FACTOR

Male infertility refers to a male's inability to result pregnancy in a fertile female. "Male factor" infertility is seen as an alteration in sperm concentration and/or motility and/or morphology in at least one sample of two sperm analyzes, collected 1 and 4 weeks apart.<sup>[20]</sup> In humans, it accounts for 40–50% of infertility<sup>[21-23]</sup> and affects approximately 7% of all men.<sup>[24]</sup> Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fecundity.<sup>[25]</sup>

Males with sperm parameters below the WHO normal values are considered to have male factor infertility.<sup>[26]</sup> The most significant of these are low sperm concentration (oligospermia), poor sperm motility (asthenospermia), and abnormal sperm morphology (teratospermia). Other factors less well associated with infertility include semen volume and other seminal markers of epididymal, prostatic, and seminal vesicle function.<sup>[27]</sup> As high as 90% of male infertility problems are related to count and there is a positive association between the abnormal semen parameters and sperm count.<sup>[28]</sup> The problem with sperm count, motility, and morphology stems from disarray in control mechanism, including pre-testicular, testicular, and post-testicular factors.<sup>[29]</sup>

Hence, semen analysis remains the single most useful and fundamental investigation with a sensitivity of 89.6%, that it is able to detect 9 out of 10 men with a genuine problem of male infertility.<sup>[30]</sup> It is a simple test that assesses the formation and maturity of sperm as well as how the sperm

interacts in the seminal fluid. It also provides insight not only on sperm production (count), but the sperm quality (motility, morphology) as well.<sup>[31]</sup>

## NORMAL SEMINAL PARAMETERS

Semen analysis is an imperfect tool but remains the cornerstone to investigate male infertility.<sup>[32]</sup> It must be performed to a consistently high standard in order to evaluate the descriptive parameters of the ejaculate.<sup>[20,33]</sup> Although this assay reveals a useful information for the initial evaluation of the infertile male, it is not a test of fertility.<sup>[34]</sup> It provides no insights into the functional potential of the spermatozoon to undergo subsequent maturation processes required to achieve fertilization. It is important that while the results may correlate with "fertility," the assay is not a direct measure of fertility.<sup>[35-37]</sup>

The WHO has revised lower reference limits for semen analyses: The following parameters represent the accepted 5<sup>th</sup> percentile (lower reference limits and 95% confidence intervals [CIs] in parentheses), derived from a study of over 1900 men whose partners had a time-to-pregnancy of ≤12 months.<sup>[25]</sup>

- Volume: 1.5 mL (95% CI: 1.4–1.7)
- Sperm concentration: 15 million spermatozoa/mL (95% CI: 12–16)
- Total sperm number: 39 million spermatozoa per ejaculate (95% CI: 33–46)
- Morphology: 4% normal forms (95% CI: 3–4), using "strict" Tygerberg method<sup>[33]</sup>
- Vitality: 58% live (95% CI: 55–63)
- Progressive motility: 32% (95% CI: 31–34)
- Total (progressive + nonprogressive motility): 40% (95% CI: 38–42).

## ABNORMALITIES OF SPERM COUNT AND MORPHOLOGY

Sperm abnormalities are a critical factor in male infertility. These abnormalities include:

### Abnormalities related to sperm count

- Azoospermia: Absence of sperm in seminal plasma
- Low sperm count (oligozoospermia: <15 million sperms/mL).<sup>[25]</sup>

### Abnormalities related to sperm motility

The efficient passage of spermatozoa through the cervical mucus depends on rapid progressive motility,<sup>[38,39]</sup> that is, spermatozoa with a forward progression of at least 25 μm/s. A normal semen analysis must contain at least 50% grade A and B, progressively motile spermatozoa. Persistent poor motility is a predictor of failure in fertilization.<sup>[40]</sup>

### Abnormal sperm structure and shape (teratozoospermia)

For morphology of sperms, smears can be scored using the WHO classification, or by Kruger's strict criteria classification.<sup>[44]</sup> Morphology should be used along with other parameters, and not as an isolated parameter when determining clinical implications.<sup>[42,43]</sup>

### MALE INFERTILITY ON THE RISE?

Time and again, various studies have been published supporting a decline in sperm quality or dismissing the same.<sup>[44-48]</sup> Analysis of retrospective data indicates that sperm counts may have declined in some parts of the world, but there seems to be geographical variations in the semen quality.<sup>[49-51]</sup> The reason for geographic variations in semen characteristics is not clear, but it may be due to environmental, nutritional, socioeconomic, or other unknown causes.<sup>[52]</sup> The decline in the semen quality coincides with an increasing incidence of abnormalities of the male genital tract including testicular cancer and cryptorchidism in various countries.<sup>[53,54]</sup>

### GLOBAL TRENDS OF MALE INFERTILITY

As early as in the 1980s, many scientists/clinicians reported an emerging concern about deteriorating semen quality.<sup>[55-57]</sup> To better elucidate this problem, a study was done in 1992, which included the meta-analysis of, which had 61 articles 14,947 men with no previous history of infertility. This study concluded that the mean sperm count of healthy men declined by 1% per year between 1938 and 1990.<sup>[44]</sup> Furthermore, they reported a statistically significant 50% reduction in the mean sperm count from  $113 \times 10^6 \text{ mL}^{-1}$  in 1940 to  $66 \times 10^6 \text{ mL}^{-1}$  in 1990 and in the seminal volume from 3.40 to 2.75 mL, using linear regression data weighted by the number of men in each study.<sup>[44]</sup> In 2000, an updated comprehensive meta-analysis was done, which also confirmed the falling trend in sperm count.<sup>[58]</sup> Also, an another meta-analysis reported that sperm density has decreased globally by about 50% over the past 50–60 years.<sup>[31,44]</sup> A study in Finland found a temporal decrease in semen quality in the general population over a period of 1998 to 2006.<sup>[59]</sup> Another study between 1996 and 2007 in the Sfax area of Southern Tunisia in a sample of 2940 men in infertile relationships concluded the decline in semen quality over a period of 12 years.<sup>[60]</sup> A retrospective study of 9168 cases (men ages 20 to 77) obtained from Andrology and Reproduction Laboratory in Cordoba, Argentina for 10 years (1995–2004) showed a significant decrease in seminal volume, sperm count, motility, viability and normal morphology, and a reduction in alpha-glucosidase and fructose levels in relation to age.<sup>[61]</sup> Furthermore, a study at the Reproduction Biology Laboratory of the University Hospital of Marseille (France) between 1988 and 2007, which

included semen analysis of 10,932 male partners of infertile couples concluded that the whole population demonstrated the declining trends in sperm concentration (1.5%/year), total sperm count (1.6%/year), total motility (0.4%/year), rapid motility (5.5%/year), and normal morphology (2.2%/year). Also, in the group of selected samples with total normal sperm count, the same trends of sperm quality deterioration with time were observed.<sup>[62]</sup>

On contrary to this many studies have demonstrated no change in seminal parameters over the time. For example, a cross-sectional study of 4867 men from the general Danish population between 1996 and 2010 concluded that over 15 years, median sperm concentration increased from 43 to 48 million/ml and the total sperm count from 132 to 151 million. The median percentage of motile spermatozoa and abnormal spermatozoa were 68% and 93% and did not change during the study period.<sup>[63]</sup> Another similar study conducted between 2000 and 2010 among young Swedish men from the general population concluded that there is no evidence of time-related deterioration of semen parameters.<sup>[64]</sup>

### TRENDS OF MALE INFERTILITY IN INDIA

Although, the baseline semen quality and sperm functional parameters in fertile Indian men have been documented,<sup>[65]</sup> the data on declining sperm count in Indian males is limited. According to a study conducted in South India over a period of 13 years, it was found that the decline in sperm count was 30.31% whereas, sperm motility and morphology was reduced by 22.92% and 51.25%, respectively.<sup>[66]</sup> More importantly, the increase in the incidence of sperm morphological abnormalities in addition to the low sperm count observed in this study indicates the qualitative impairment of spermatogenesis and perhaps of the sertoli cells.<sup>[67]</sup>

Also, the Doctors from the All India Institute of Medical Sciences reported that over 12–18 million couples in India are diagnosed with infertility every year.<sup>[68]</sup> They have reported that while the sperm count of a normal Indian adult male used to be 60 million/ml three decades ago, it now stands at around 20 million/ml.<sup>[69]</sup> It was found that majority of men who were exposed to high temperature at their workplace - welders, dyers, blast furnace workers and those employed in cement and steel factories - were more prone to infertility. This is due to excess environmental heat which increases the temperature of the scrotum, causing a negative effect on sperm production. A 1° elevation in testicular temperature leads to 14% depression of spermatogenesis.<sup>[68]</sup> Not only has quantity of sperm production declined in males across the world, but there has also been a decrease in motility and morphology of the sperms. There has been

a 2% decrease in quality of male sperm annually.<sup>[69]</sup> About 40% men in the reproductive age group are presently recording a quantitative and qualitative decline in sperm quality.<sup>[70]</sup> According to a 10-year comparison study on sperm quality and quantity (2000–2001 to 2010–2011), the percentage of semen ejaculation, which is considered less than normal (below 4 ml), increased from 34% to 65% and the most suitable ejaculation volume (more than 4 ml) went down from 15% to 3%.<sup>[69]</sup> As far as the morphology of sperm was concerned, in 2000–2001, 26% of the sperms showed above 60% normality, whereas in 2000–2011 this was reduced to 7%.<sup>[69]</sup> However, a similar study in Calcutta, which included semen analysis of 3729 men presenting with infertility problems in two distinct decades, that is, between 1981–1985 and 2000–2006 concluded a significant decline in the sperm motility parameters and seminal volume in the present decade, but no change in overall sperm concentration. A decline was seen in sperm motility with increasing age in both decades.<sup>[71]</sup>

The exact reason for the decline in semen quality is not clear, but it may be due to environmental, nutritional, socioeconomic or other unknown causes.<sup>[43,44,50,72]</sup> Aging is an important factor responsible for the decline in semen quality, as first described in 1969 by Sasano and Ichijo, that the sperm concentration decreases as men age. They reported that 90% of seminiferous tubules in men in their 20s and 30s contained spermatids, whereas men in their 40s and 50s had spermatids in 50% of their seminiferous tubules. Only 10% of seminiferous tubules from men aged >80 years contained spermatids.<sup>[73]</sup> In contrast to concentration, evidence consistently indicates that sperm motility decreases with advancing age.<sup>[27]</sup> Various studies revealed statistically significant decreases in motility of 0.17–0.6% per year of age<sup>[44,48]</sup> resulting in a 3–12% decline in motility over 20 years. Similar to motility, morphology appears to decrease with advancing male age.<sup>[27]</sup> Studies indicate a decline in normal sperm morphology of 0.2–0.9% per year of age,<sup>[27]</sup> resulting in a 4–18% decrease in normal morphology over a 20-year period.<sup>[45,74]</sup>

Also, *in utero* exposures to exogenous estrogenic compounds are capable of altering neonatal testicular development and reducing sperm production in adult men.<sup>[67,75]</sup> Diethylstilbestrol is thought to be responsible for an increase in abnormalities of the reproductive tract and for a reduction in the output and fertilizing potential of sperm of male offspring.<sup>[76]</sup>

## CONCLUSION

Hence, male infertility is an important cause of infertility with a strong impact on the psychology and physiology of couple. It can be due to several reasons. Also, the present

literature reveals that its trend is increasing in India. Therefore, it's the need of the hour to look into the factors which are causing such a rise in male infertility and attempts should be made to control such factors in near future.

## WAY FORWARD

Male infertility is an alarming global health issue that has not been researched or studied to truly understand its magnitude and prevalence. There is still a great need for further research into underlying etiology and treatment of male infertility. In future, we can work together in this field to achieve certain goals like:

- Attempts should be made to reduce the barriers from stigmas associated with infertility due to religious and cultural beliefs so that patients open up and share their problems
- Create a globally accepted population-based calculation in order to understand the prevalence and magnitude of male infertility
- To create awareness about male infertility in society.

The present study is only a review of various studies conducted all over the world. The exact rates of male infertility from developing countries like ours are difficult to find because of the problem with the definition of male infertility and lack of accurate reporting rather than a true reflection of male infertility. But still in future, we can conduct various research studies to find out the major causes of male infertility and can work in that direction to reduce such factors which can affect the future fertility of males.

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## REFERENCES

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, *et al.* International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. *Fertil Steril* 2009;92:1520-4.
2. Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss. *Fertil Steril* 2008;90 5 Suppl: S60.
3. Mascarenhas MN, Cheung H, Mathers CD, Stevens GA. Measuring infertility in populations: Constructing a standard definition for use with demographic and reproductive health surveys. *Popul Health Metr* 2012;10:17.



4. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care. *Hum Reprod* 2007;22:1506-12.
5. World Health Organization. Infecundity, Infertility, and Childlessness in Developing Countries. DHS Comparative Reports No 9. Calverton, Maryland, USA: ORC Macro and the World Health Organization; 2004.
6. Sciarra J. Infertility: An international health problem. *Int J Gynaecol Obstet* 1994;46:155-63.
7. Population Council. Infertility. Looking Back, Looking Forward: A Profile of Sexual and Reproductive Health in India. New Delhi: Population Council; 2004. p. 67-72.
8. van Balen F, Gerrits T. Quality of infertility care in poor-resource areas and the introduction of new reproductive technologies. *Hum Reprod* 2001;16:215-9.
9. Stephen EH, Chandra A. Declining estimates of infertility in the United States: 1982-2002. *Fertil Steril* 2006;86:516-23.
10. Stephen EH, Chandra A. Updated projections of infertility in the United States: 1995-2025. *Fertil Steril* 1998;70:30-4.
11. Chandra A, Copen CE, Stephen EH. Infertility and impaired fecundity in the United States, 1982-2010: Data from the National Survey of Family Growth. National Health Statistics Reports; No 67. Hyattsville, MD: National Center for Health Statistics; 2013. Available from: <http://www.cdc.gov/nchs/data/nhsr/nhsr067.pdf>. [Last accessed on 2015 Sep 15].
12. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S. Births: Final data for 2004. *Natl Vital Stat Rep* 2006;55:1-101.
13. Talwar PP, Go OP, Murali IN. Prevalence of infertility in different population groups in India and its determinants. *Statistics and Demography*. New Delhi: National Institute of Health and Family Welfare and Indian Council of Medical Research; 1986.
14. Unisa S. Childlessness in Andhra Pradesh, India: Treatment-seeking and consequences. *Reprod Health Matters* 1999;7:54-64.
15. Zargar AH, Wani AI, Masoodi SR, Laway BA, Salahuddin M. Epidemiologic and etiologic aspects of primary infertility in the Kashmir region of India. *Fertil Steril* 1997;68:637-43.
16. Kumar D. Prevalence of female infertility and its socio-economic factors in tribal communities of Central India. *Rural Remote Health* 2007;7:456.
17. Sadock BJ, Sadock VA. *Kaplans and Sadocks Symptoms of Psychiatry Behavioral Sciences Clinical Psychiatry*. 9<sup>th</sup> ed. Philadelphia: Lippincott Williams and Wilkins; 2003. p. 872-4.
18. World Health Organization. Towards more objectivity in diagnosis and management of male infertility. *Int J Androl* 1987;7:1-53.
19. Kumar TCA. Fertility and *in-vitro* fertilization in India. *Curr Sci* 2004;86:254-6.
20. World Health Organization. WHO Laboratory Manual for the Examination of Human Semen and Semen-Cervical Mucus Interaction. 4<sup>th</sup> ed. Cambridge: Cambridge University Press; 1999. p. 1-86.
21. Men's Health – Male Factor Infertility. University of Utah Health Sciences Center. 04 January, 2003. Archived from the Original on 04 July 2007. Available from: <http://web.archive.org/web/20080620064743/http://healthcare.utah.edu/healthinfo/adult/men/infertil.htm>. [Last retrieved on 2007 Nov 11].
22. Brugh VM 3<sup>rd</sup>, Lipshultz LI. Male factor infertility: Evaluation and management. *Med Clin North Am* 2004;88:367-85.
23. Hirsh A. Male subfertility. *BMJ* 2003;327:669-72.
24. Lotti F, Maggi M. Ultrasound of the male genital tract in relation to male reproductive health. *Hum Reprod Update* 2015;21:56-83.
25. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, Behre HM, *et al*. World Health Organization reference values for human semen characteristics. *Hum Reprod Update* 2010;16:231-45.
26. Plachot M, Belaisch-Allart J, Mayenga JM, Chouraqi A, Tesquier L, Serkine AM. Outcome of conventional IVF and ICSI on sibling oocytes in mild male factor infertility. *Hum Reprod* 2002;17:362-9.
27. Harris ID, Fronczak C, Roth L, Meacham RB. Fertility and the aging male. *Rev Urol* 2011;13:e184-90.
28. Sabra SM, Al-Harbi MS. An influential relationship of seminal fluid microbial infections and infertility, Taif Region, KSA. *World J Med Sci* 2014;10:32-7.
29. Wamoto TI, Nozawa S, Yoshiike M. Semen quality of Asian men. *Reprod Med Biol* 2007;6:185-93.
30. Butt F, Akram N. Semen analysis parameters: Experiences and insight into male infertility at a tertiary care hospital in Punjab. *J Pak Med Assoc* 2013;63:558-62.
31. Fisch H. Declining worldwide sperm counts: Disproving a myth. *Urol Clin North Am* 2008;35:137-46, vii.
32. Barratt CL. Semen analysis is the cornerstone of investigation for male infertility. *Practitioner* 2007;251:8-10, 12, 15-7.
33. World Health Organization Department of Reproductive Health and Research. *World Health Organization Laboratory Manual for the Examination and Processing of Human Semen*. 5<sup>th</sup> ed. Geneva, Switzerland: World Health Organization; 2010.
34. Jequier AM. Semen analysis: A new manual and its application to the understanding of semen and its pathology. *Asian J Androl* 2010;12:11-3.
35. Guzick DS, Overstreet JW, Factor-Litvak P, Brazil CK, Nakajima ST, Coutifaris C, *et al*. Sperm morphology, motility, and concentration in fertile and infertile men. *N Engl J Med* 2001;345:1388-93.
36. Smith KD, Rodriguez-Rigau LJ, Steinberger E. Relation between indices of semen analysis and pregnancy rate in infertile couples. *Fertil Steril* 1977;28:1314-9.
37. Brazil C. Practical semen analysis: From A to Z. *Asian J Androl* 2010;12:14-20.
38. Björndahl L. The usefulness and significance of assessing rapidly progressive spermatozoa. *Asian J Androl* 2010;12:33-5.
39. Lindholmer C. The importance of seminal plasma for human sperm motility. *Biol Reprod* 1974;10:533-42.
40. Aitken RJ, Sutton M, Warner P, Richardson DW. Relationship between the movement characteristics of human spermatozoa and their ability to penetrate cervical mucus and zona-free hamster oocytes. *J Reprod Fertil* 1985;73:441-9.
41. Menkveld R, Stander FS, Kotze TJ, Kruger TF, van Zyl JA. The evaluation of morphological characteristics of human spermatozoa according to stricter criteria. *Hum Reprod* 1990;5:586-92.
42. Van Waart J, Kruger TF, Lombard CJ, Ombelet W. Predictive value of normal sperm morphology in intrauterine insemination (IUI): A structured literature review. *Hum Reprod Update* 2001;7:495-500.
43. Keegan BR, Barton S, Sanchez X, Berkeley AS, Krey LC, Grifo J. Isolated teratozoospermia does not affect *in vitro* fertilization outcome and is not an indication for intracytoplasmic sperm injection. *Fertil Steril* 2007;88:1583-8.
44. Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.
45. Auger J, Kunstmann JM, Czyglik F, Jouannet P. Decline in semen quality among fertile men in Paris during the past 20 years. *N Engl J Med* 1995;332:281-5.
46. Lackner J, Schatzl G, Waldhör T, Resch K, Kratzik C, Marberger M. Constant decline in sperm concentration in infertile males in an urban population: Experience over 18 years. *Fertil Steril* 2005;84:1657-61.
47. Marimuthu P, Kapilashrami MC, Misro MM, Singh G. Evaluation of trend in semen analysis for 11 years in subjects attending a fertility clinic in India. *Asian J Androl* 2003;5:221-5.
48. Fisch H, Goluboff ET, Olson JH, Feldshuh J, Broder SJ, Barad DH. Semen analyses in 1,283 men from the United States over a 25-year period: No decline in quality. *Fertil Steril* 1996;65:1009-14.
49. Auger J, Jouannet P. Evidence for regional differences of semen quality among fertile French men. *Fédération Française des Centres d'Etude et de Conservation des Oeufs et du Sperme humains*. *Hum Reprod* 1997;12:740-5.
50. Jørgensen N, Andersen AG, Eustache F, Irvine DS, Suominen J, Petersen JH, *et al*. Regional differences in semen quality in Europe.

- Hum Reprod 2001;16:1012-9.
51. Swan SH. Semen quality in fertile US men in relation to geographical area and pesticide exposure. *Int J Androl* 2006;29:62-8.
  52. Fisch H, Goluboff ET. Geographic variations in sperm counts: A potential cause of bias in studies of semen quality. *Fertil Steril* 1996;65:1044-6.
  53. Giwercman A, Skakkebaek NE. The human testis – An organ at risk? *Int J Androl* 1992;15:373-5.
  54. Bussen S, Sütterlin M, Steck T, Dietl J. Semen parameters in patients with unilateral testicular cancer compared to patients with other malignancies. *Arch Gynecol Obstet* 2004;269:196-8.
  55. Menkveld R, Van Zyl JA, Kotze TJ, Joubert G. Possible changes in male fertility over a 15-year period. *Arch Androl* 1986;17:143-4.
  56. Murature DA, Tang SY, Steinhardt G, Dougherty RC. Phthalate esters and semen quality parameters. *Biomed Environ Mass Spectrom* 1987;14:473-7.
  57. Osser S, Liedholm P, Ranstam J. Depressed semen quality: A study over two decades. *Arch Androl* 1984;12:113-6.
  58. Swan SH, Elkin EP, Fenster L. The question of declining sperm density revisited: An analysis of 101 studies published 1934-1996. *Environ Health Perspect* 2000;108:961-6.
  59. Jørgensen N, Vierula M, Jacobsen R, Pukkala E, Perheentupa A, Virtanen HE, *et al.* Recent adverse trends in semen quality and testis cancer incidence among Finnish men. *Int J Androl* 2011;34 (4 Pt 2):e37-48.
  60. Feki NC, Abid N, Rebai A, Sellami A, Ayed BB, Guermazi M, *et al.* Semen quality decline among men in infertile relationships: Experience over 12 years in the South of Tunisia. *J Androl* 2009;30:541-7.
  61. Molina RI, Martini AC, Tissera A, Olmedo J, Senestrari D, de Cuneo MF, *et al.* Semen quality and aging: Analysis of 9.168 samples in Cordoba, Argentina. *Arch Esp Urol* 2010;63:214-22.
  62. Geoffroy-Siraudin C, Loundou AD, Romain F, Achard V, Courbière B, Perrard MH, *et al.* Decline of semen quality among 10 932 males consulting for couple infertility over a 20-year period in Marseille, France. *Asian J Androl* 2012;14:584-90.
  63. Jørgensen N, Joensen UN, Jensen TK, Jensen MB, Almstrup K, Olesen IA, *et al.* Human semen quality in the new millennium: A prospective cross-sectional population-based study of 4867 men. *BMJ Open* 2012;2. pii: E000990.
  64. Axelsson J, Rylander L, Rignell-Hydbom A, Giwercman A. No secular trend over the last decade in sperm counts among Swedish men from the general population. *Hum Reprod* 2011;26:1012-6.
  65. Pal PC, Rajalakshmi M, Manocha M, Sharma RS, Mittal S, Rao DN. Semen quality and sperm functional parameters in fertile Indian men. *Andrologia* 2006;38:20-5.
  66. Adiga SK, Jayaraman V, Kalthur G, Upadhy D, Kumar P. Declining semen quality among South Indian infertile men: A retrospective study. *J Hum Reprod Sci* 2008;1:15-8.
  67. Sharpe RM. Declining sperm counts in men – Is there an endocrine cause? *J Endocrinol* 1993;136:357-60.
  68. Available from: <http://www.newindianexpress.com/cities/chennai/Male-and-Female-Infertility-Just-Keeps-on-Rising/2014/01/27/article2021526.ece1>. [Last updated on 2014 Jan 27].
  69. Sengupta P. Challenge of infertility: How protective the yoga therapy is? *Anc Sci Life* 2012;32:61-2.
  70. Sengupta P. Environmental and occupational exposure of metals and their role in male reproductive functions. *Drug Chem Toxicol* 2013;36:353-68.
  71. Mukhopadhyay D, Varghese AC, Pal M, Banerjee SK, Bhattacharyya AK, Sharma RK, *et al.* Semen quality and age-specific changes: A study between two decades on 3,729 male partners of couples with normal sperm count and attending an andrology laboratory for infertility-related problems in an Indian city. *Fertil Steril* 2010;93:2247-54.
  72. Magnúsdóttir EV, Thorsteinsson T, Thorsteinsdóttir S, Heimisdóttir M, Ólafsdóttir K. Persistent organochlorines, sedentary occupation, obesity and human male subfertility. *Hum Reprod* 2005;20:208-15.
  73. Sasano N, Ichijo S. Vascular patterns of the human testis with special reference to its senile changes. *Tohoku J Exp Med* 1969;99:269-80.
  74. Andolz P, Bielsa MA, Vila J. Evolution of semen quality in North-Eastern Spain: A study in 22,759 infertile men over a 36 year period. *Hum Reprod* 1999;14:731-5.
  75. Delbès G, Levacher C, Habert R. Estrogen effects on fetal and neonatal testicular development. *Reproduction* 2006;132:527-38.
  76. Fielden MR, Halgren RG, Fong CJ, Staub C, Johnson L, Chou K, *et al.* Gestational and lactational exposure of male mice to diethylstilbestrol causes long-term effects on the testis, sperm fertilizing ability *in vitro*, and testicular gene expression. *Endocrinology* 2002;143:3044-59.