HOSTED BY
ELSEVIER

Contents lists available at ScienceDirect

Asian Pacific Journal of Reproduction

journal homepage: www.apjr.net

Original research http://dx.doi.org/10.1016/j.apjr.2015.06.010

Reviewing reports of semen volume and male aging of last 33 years: From 1980 through 2013

Pallav Sengupta*

Department of Physiology, Vidyasagar College for Women, University of Calcutta, Kolkata, West Bengal, India

ARTICLE INFO

Article history:
Received 27 Feb 2015
Received in revised form 10 Apr 2015
Accepted 15 Apr 2015
Available online 24 July 2015

Keywords:
Age
Infertility
Semen
Sperm
Volume

ABSTRACT

Since several decades numerous experimental and epidemiological experiments tend to establish that in humans the semen volume declines with progression of age. This literature review is intended to report the association between male age and semen volume. Review of English language-published research over the last 33 years, from January 1, 1980, up to December 31, 2013, has been conveniently constructed using MEDLINE database. Studies with inadequate numbers of subjects and case reports were excluded. Among the methodologically stronger studies, declines in semen volume of 3%–22% were likely when comparing 30-year-old men to 50-year-old men. The report suggests that increased male age is associated with a decline in semen volume, *i.e.* there has been a genuine diminution in semen volume over the past 33 years. As male fertility is to some extent correlated with semen volume the results may reflect an overall reduction in male fertility.

1. Introduction

During the last few decades there has been uprising debate regarding the issue of declining semen parameters which are generally considered to be a proxy measure of male fertility. Changes in semen quality can occur after occupational and environmental exposure to toxic agents [1] or from the predictor factors of the host, such as age [2]. The weight of evidences primarily from the clinical studies suggest that age is associated with diminished semen volume [3]. Also, men at older ages (e.g. ≥50 years) were under-represented in many clinical studies, which restricted statistical strength and prevented unveiling of the exact form of relationship between age and semen volume. In addition, potential confounders that might explain changes with age, such as smoking history or duration of abstinence, were hardly ever taken under consideration [4]. The deterioration of semen qualities was first reported in 1974 by Nelson and Bunge [5]. In 1992, Carlsen *et al.* [6] reported a global decline in semen qualities between 1938 and 1990. Swan *et al.* [7] published a reanalysis of the studies included by Carlsen *et al.* [6] In that investigation, they have found significant declines in semen quality in the United States, Europe, and Australia, but no such decline in non-Western countries. The similar declines were also proclaimed by numerous other studies [7,8]. A thorough dive into diverse studies from specific cites reveals evidences of declines in semen volume but a worldwide decline has not been demonstrated. It is definitely arduous to execute a systematic, scientific study regarding the decline in human semen quality. Thus, this review has been intended to build-up a substantial idea regarding alterations in semen volume in human with increase in age by picking the scattered reports of last 33 years.

2. Methods of literature review

Research articles on humans published in English from January 1, 1980, through December 31, 2013 have been included in this report. The data for this review were obtained from extensive search using Medical Subject Headings (MeSH) of electronic databases which included Medline, Elsevier, Medscape, and PubMed. Relevant literature on the effect of age on the semen volume and its impact on future natural and assisted conception cycles were retrieved. Data of the subjects with normal semen analysis or clinical problems have been excluded. Studies with insufficient numbers of subjects ($n < 20$), case reports, case series, and anecdotal data were excluded. In each case sperm volume and its outcome were evaluated. Analytic epidemiological studies were emphasized. In results section the relative changes in the outcome with age were represented.

*Pallav Sengupta, Lecturer, Department of Physiology, Vidyasagar College for Women, University of Calcutta, 39, Sankar Ghosh Lane, Kolkata 700 006, West Bengal, India.
Tel: +91 33 22418887
E-mail: sunny_pallav_1984@yahoo.co.in
Peer review under responsibility of Hainan Medical College.

Table 1

Male age and semen volume (data from 1980 to 2013).

Country	Population	Sample size	Male age definition (range/mean/group)	Semen volume, mL	Direction of effect with increasing age	Ref no.	Year
Israel	Infertility clinic	555	A. 31 (0.2); B. 54 (4.2)	30% decrease from A to B	↓ ($P < 0.0005$)	[9]	1982
Germany	Volunteers responding to advertisement	43	A. 29 (3.2); B. 67 (7.8)	A. 4.0 (1.7); B. 3.2 (1.9)	↓ (NS)	[10]	1982
Paris	Semen donors	809	A. 21–25; B. 26–30; C. 31–35 D. 36–40; E. 41–45; F. 46–50	A. 3.2 (1.6); B. 3.7 (1.2); C. 3.6 (1.3) D. 3.6 (2.1); E. 3.6 (1.7); F. 3.1 (2.1)	↔ (NS)	[11]	1983
Italy	Volunteers	445	A.<40; B. 40–60; C. >60	Gradual decrease after age 40	↓	[12]	1985
China	Family planning clinic	1239	19–53	No correlation with age	↔	[13]	1985
Israel	Sperm donors with counts >200 × 10^6/mL	1299	A. 34.6 (6.4); B.35.2 (9.4); C. 38.4 (12.5)	A. ≥6; B. 1–5; C. <1	↓	[14]	1990
U.S.A.	Sperm donors	1283	34.3 (0.2)	0.15% decrease per year of age	↓ ($P < 0.001$)	[15]	1996
Spain	Assisted conception	345	A. ≤30; B. 31–40 C. 41–50; D. 51–64	A. 3.1 (0.6); B. 2.6 (1.4) C. 2.3 (2.0); D. 2.2 (0.9)	↓ (NS)	[16]	1996
Germany	Infertility clinic	78	A. <30 (matched by year of attendance) B. <30 (matched by wives' ages) C. >50	A. 4.1 (1.6) C. 3.2 (1.9)	↓ (NS)	[17]	1996
Germany	Older men planning further children	64	A. 32.2; B. 50.3	A. 3.2 (1.5); B. 3.2 (1.7)	↔ (NS)	[18]	1996
U.K.	Sperm donors	577	18–53	0.01% increase per year of age	↑ (NS)	[19]	1996
Belgium	Sperm donors	416	No age data	Volume increased slightly	↑ (NS)	[20]	1996
Greece	Infertility clinic	2385	25–59	No significant drop in semen volume	↔	[21]	1996
U.S.A.	Tertiary University centre	510	No age data	No change in semen volume	↔	[22]	1996
Australia	Volunteers	689	No age data	No decrease in semen volume	↔	[23]	1997
Denmark	Fertility clinic	1055	No age data	No decrease in semen volume	↔	[24]	1997
Denmark	Fertility clinic	8608	No age data	No decrease in semen volume	↔	[25]	1997
Sweden	Infertility clinic	718	21–54	Age correlation with volume (r = 0.06)	↔	[26]	1997
Italy	Infertility clinic	3203	25–50	No alteration with age	↔	[27]	1998
U.S.A.	Assisted conception	821	A. ≤39; B. 40–49; C. ≥50	A. 2.7 (0.1); B. 2.5 (0.1); C. 2.1 (0.2)	↓ ($P < 0.05$)	[3]	1998
Spain	Infertility clinic	20411	31.9 (5.4); 15-74	0.5% decrease per year of age	↓ ($P < 0.001$)	[28]	1999
U.S.A.	Andrology lab	2065	33.6 (5.8); 19–67	Age correlation with volume (r = 0.04)	↓ (NS)	[29]	1999
Germany	Infertility clinic	3437	19–63	Age-dependent decrease in semen volume	↓	[30]	1999
Norway	Volunteers	5180	No age data	Decline in semen volume	↓	[31]	1999
Slovenia	Volunteers	2343	No age data	No decrease in semen volume	↔	[32]	1999
Denmark & Finland	Comparative clinical study	632	A. 20–35 (Danish); B. 22–47 (Finnish)	High volume was observed in B than A	↑ ($P < 0.01$)	[33]	2000
Korea	Andrology lab	22,249	21–40	No decrease in semen volume	↔	[34]	2000
Japan	Andrology lab	711	>20	No decrease in semen volume	↔	[35]	2001
Germany	Infertility clinic	3698	19–63	Age-dependent decrease in semen volume	↓ ($P < 0.001$)	[36]	2002
Germany	Infertility lab	200	A. 21–25; B. >50	29% decrease in Group B than A	↓ ($P < 0.0005$)	[37]	2002
U.S.A.	Cohort study	97	22–80	0.03 mL decrease per year of age	↓ ($P < 0.01$)	[38]	2003
Australia	Prostate cancer project	567	52–79	Age-dependent decrease in semen volume	↓ ($P < 0.001$)	[39]	2004
Brazil	Infertility patients	889	A.≤45; B. >45	0.01 mL decrease per year of age	↓	[40]	2005
U.S.A.	Andrology lab	1174	>45	Age-dependent decrease in semen volume	↓	[41]	2006
India	Andrology lab	368	25–59	Age-dependent decrease	↓	[42]	2006
U.S.A.	Infertility clinic	388	>45	Age-dependent decrease in semen volume	↓	[43]	2007
Australia	Infertility clinic	225	>30	Decreased volume with low sperm count	↓	[44]	2009
Germany	Fertility centre	320	A. <30; B. 30–35; C. 36–39; D. >40	No alteration observed	↔ (NS)	[45]	2009
Korea	Andrology lab	1139	A. 19–27; B. >54	Age-dependent decrease in semen volume	↓	[46]	2010

(*continued on next page*)

Table 1 (*continued*)

Country	Population	Sample size	Male age definition (range/mean/group)	Semen volume, mL	Direction of effect with increasing age	Ref no.	Year
Netherlands	Periconceptional prospective cohort study	227	26–59	Age-dependent decrease	↓ ($P < 0.01$)	[47]	2011
Poland	Andrology lab	224	A.≤35; B. >35	Age-dependent decrease	↓	[48]	2011
China	Andrology lab	90	25–40	Age-dependent decrease in semen volume	↓	[49]	2012
China	Andrology lab	104	A.<35; B. 35–39; C. ≥40	A. 2.87 (0.89); B.2.98 (1.09); C. 2.65 (0.95)	↔ (NS)	[50]	2012
Denmark	Danish one-centre study	4867	A. 18–19; B. >54	Increase per year of age	↑	[51]	2012
India	Andrology lab	3729	33–35	Age-dependent decrease in semen volume	↓ ($P < 0.05$)	[52]	2013
China	Infertility clinic	201	A.20–40; B. 40–60; C. >60	Age-dependent decrease in sperm volume	↓	[53]	2013
U.S.A.	Infertility clinic	5081	16.5–72.3	Volume decreases after 45 years of age	↓	[54]	2013
India	Infertility clinic	100	A.≤30; B. >30	Decrease with age	↓	[55]	2013

Data are represented as Mean(SD); ↓ = decrease; ↑ = increase; ↔ = no change; NS = not significant at $P < 0.05$, no P value indicates that no statistical testing was done.

For example, if semen volume decreased from 4.2 mL in the younger age group to 3.6 mL in the older age group, then the relative decrease was 0.6/4.2, a 14% decrease in volume with increased age. Whenever possible, the differences between younger men (*i.e.*, ages ≤30 years) and older men (*i.e.*, ages ≥50 years) were summarized.

3. Discussion: scenario of last 33 years

During the retrieval of relevant documents, it has been found a total of forty eight studies have evaluated the relationship between male age and semen volume in the last 33 years. The outcome of these studies are represented in Table 1. Most of the reports are based on infertility clinic (37.5%), andrology laboratories or assisted conception populations (25%), while the others used volunteers recruited from sperm banks or advertisements (20.8%) and epidemiological studies (16.7%). Among the 48 published research works discussed in this article from 1980 through 2013, most are carried out in U.S.A., Germany and China, while others include Australia, India, Korea, Demark and so on. Most of the studies have used sample size ≥1000 (39.5%), a few used sample size between 500 and 1000 subjects (22.9%) and 18 studies have used sample size less than 500 men (37.6%). Two reports from Spain [28] and Korea [34] have used an extraordinarily large sample size (20 411 and 22 249 respectively). Out of 48 reports, 41 studies (85.4%) have provided data about the age of subjects. Most of the reports revolve around comparative study between younger and aged subjects, while some reports generally described the change in semen volume with increasing age. Although most of the studies have reported declines in semen volume with increased age; but, the number of reports with no alterations are also not negligible (31.2%). But most the reports are not ambiguous. Out of the 48 published articles, 29 have reported (60.4%) about decline in semen volume with male age, out of which again 10 reports depicted strong correlation with age [3,9,15,28,36,37,38,39,47,52]. Two of them [15,28], those examined age as a continuous variable, showed a decrease of 0.15% [15] to 0.5% [28] for increase in age by each year, even after adjustment for potential confounding by duration of abstinence. Several of the remaining studies claiming decline in semen volume with increasing age found large differences in semen volume (ranging from 0.6 to 0.9 mL) between the youngest and the oldest age group(s) [3,10,16,17]. However, only one of these studies adjusted for potential confounding by duration of abstinence. Among the four studies that found no relationship between age and volume [11,13,18,26], only one adjusted for duration of abstinence, by restricting analyses to less than ≤5 days of abstinence [11]. The one study [19] that reported a slight increase (0.01 mL/year) in volume with increased age, suggests that factor(s) related to time, other than aging, may also be responsible for the findings. Most of the studies listed in the following table did not adjust for potential confounding (e.g., smoking, type of infertility among clinic patients). Few studies adjusted are for abstinence, although there is good evidence in the literature that an increased duration of abstinence increases volume in a time-dependent fashion. A longer duration of abstinence among older men would likely to be bias towards finding no association or a positive association (an increase in volume with an increase in age). Overall, this may have contributed to a bias towards the null in results across studies. Four [15,17,28,30] of the five

[11,15,17,28,30] studies that did control for duration of abstinence showed a decrease in volume with increased age. The weight of the evidence suggests that there is a decrease in semen volume with increasing age, most notably among men over 50 years of age. In those studies that report a decrease, the relative decrease ranges between 3% and 30% for men less than 30 years old compared with men ≥50 years old, with most of these studies reporting a change of approximately 20%–30%. The methodologically stronger studies [15,17,28] found more modest decreases of 3%–22% comparing men in these age groups.

This review may strongly evince that the trend of fathering in older age may come with risks for diminished sperm volume which is also attributed to environmental, occupational and other lifestyle factors [56–61]. Future studies examining the relationship between male age and semen volume could improve the methodological quality of the existing studies by controlling the effects of potential confounding factors. As better biomarkers are now developed and are being used in epidemiological study designs, more knowledge may be gained regarding associations of age with semen volume and fertility in the future reports.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Sengupta P, Banerjee R. Environmental toxins: alarming impacts of pesticides on male fertility. *Hum Exp Toxicol* 2014; **33**(10): 1017-1039.

[2] Kidd SA, Eskenazi B, Wyrobek AJ. Effects of male age on semen quality and fertility: a review of the literature. *Fertil Steril* 2001; **75**: 237-248.

[3] Spandorfer SD, Avrech OM, Colombero LT, Palermo GD, Rosenwaks Z. Effect of parental age on fertilization and pregnancy characteristics in couples treated by intracytoplasmic sperm injection. *Hum Reprod* 1998; **13**: 334-338.

[4] Wyrobek AJ, Gordon LA, Burkhart JG, Francis MW, Kapp RW, Letz G, et al. An evaluation of human sperm as indicators of chemically induced alterations of spermatogenic function. A report of the U.S. Environmental Protection Agency Gene-Tox Program. *Mutat Res* 1983; **115**: 73-148.

[5] Nelson CMK, Bunge RG. Semen analysis-evidence of changing parameters of male fertility potential. *Fertil Steril* 1974; **25**: 503-507.

[6] Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *Br Med J* 1992; **305**: 609-613.

[7] Swan SH, Elkin EP, Fenster L. Have sperm densities declined? A reanalysis of global trend data. *Environ Health Persp* 1997; **105**: 1228-1232.

[8] Auger J, Kunstmann JM, Czyglik F, Jouannet P. Decline in semen quality among fertile men in Paris during the past 20 years. *New Eng J Med* 1995; **332**: 281-285.

[9] Homonnai ZT, Fainman N, David MP, Paz GF. Semen quality and sex hormone pattern of 29 middle aged men. *Andrologia* 1982; **14**: 164-170.

[10] Nieschlag E, Lammers U, Freischem C, Langer K, Wickings E. Reproductive functions in young fathers and grandfathers. *J Clin Endocrinol Metab* 1982; **55**: 676-681.

[11] Schwartz D, Mayaux MJ, Spira A, Moscato ML, Jouannet P, Czyglik F, et al. Semen characteristics as a function of age in 833 fertile men. *Fertil Steril* 1983; **39**: 530-535.

[12] Dondero F, Mazzilli F, Giovenco P, Lenzi A, Cerasaro M. Fertility in older men. *J Endocrinol Invest* 1985; **8**(2): 87-91.

[13] Wang C, Chan SYW, Leung A, Ng RP, Ng M, Tang LCH, et al. Cross-sectional study of semen parameters in a large group of normal Chinese men. *Int J Androl* 1985; **8**: 257-274.

[14] Singer R, Sagiv M, Levinsky H, Allalouf D. Andrological parameters in men with high sperm counts and possible correlation with age. *Arch Androl* 1990; **24**: 107-111.

[15] Fisch H, Goluboff E, Olson J, Feldshuh J, Broder S, Barad D. Semen analyses in 1283 men from the United States over a 25-year period: no decline in quality. *Fertil Steril* 1996; **65**: 1009-1014.

[16] Gallardo E, Simon C, Levy M, Guanes P, Remohi J, Pellicer A. Effect of age on sperm fertility potential: oocyte donation as a model. *Fertil Steril* 1996; **66**: 260-264.

[17] Rolf C, Behre H, Nieschlag E. Reproductive parameters of older compared to younger men of infertile couples. *Int J Androl* 1996; **19**: 135-142.

[18] Haidl G, Jung A, Schill WB. Aging and sperm function. *Hum Reprod* 1996; **11**: 558-560.

[19] Irvine S, Carwood E, Richardson D, MacDonald E, Aitken J. Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years. *BMJ* 1996; **312**: 467-471.

[20] Van Waeleghem K, De Clercq N, Vermeulen L, Schoonjans F, Comhaire F. Deterioration of sperm quality in young healthy Belgian men. *Hum Reprod* 1996; **11**: 325-329.

[21] Adamopoulos DA, Pappa A, Nicopoulou S, Anderou E, Karamertzanis M, Michopoulos J, et al. Seminal volume and total sperm number trends in men attending subfertility clinics in the Greater Athens area during the period 1977-1993. *Hum Reprod* 1996; **11**: 1936-1941.

[22] Paulsen CA, Berman NG, Wang C. Data from men in greater Seattle area reveals no downward trend in semen quality: further evidence that deterioration of semen quality is not geographically uniform. *Fertil Steril* 1996; **65**: 1015-1020.

[23] Handelsman DJ. Sperm output of healthy men in Australia: magnitude of bias due to self-selected volunteers. *Hum Reprod* 1997; **12**: 2701-2705.

[24] Rasmussen PE, Erb K, Westergaard L, Laursen Steen B. No evidence for decreasing semen quality in four birth cohorts of 1,055 Danish men born between 1950 and 1970. *Fertil Steril* 1997; **68**: 1059-1064.

[25] Zheng Y, Bonde JPE, Ernst E, Mortensen JT, Egense J. Is semen quality related to the year of birth among Danish infertility clients? *Int J Epidemiol* 1997; **26**(6): 1289-1297.

[26] Berling S, Wolner-Hanssen P. No evidence of deteriorating semen quality among men in infertile relationships during the last decade: a study of males from southern Sweden. *Hum Reprod* 1997; **12**: 1002-1005.

[27] Mita P, Piatti E, Romano A, Magro B. Epidemiology of male infertility. *Arch Ital Urol Androl* 1998; **70**(2): 85-91.

[28] Andolz P, Bielsa MA, Vila J. Evolution of semen quality in northeastern Spain: a study in 22,759 infertile men over a 36 year period. *Hum Reprod* 1999; **14**: 731-735.

[29] Centola GM, Eberly S. Seasonal variations and age-related changes in human sperm count, motility, motion parameters, morphology, and white blood cell concentration. *Fertil Steril* 1999; **72**: 803-808.

[30] Rolf C, Kenkel S, Nieschlag E. Age-dependent changes in semen characteristics of patients attending a tertiary infertility clinic [abstract R-022]. In: *Abstracts of the 15th Annual Meeting of the European Society of human Reproduction and Embryology. Tours, France. Hum Reprod*; 1999, p. 288-289.

[31] Ulstein M, Irgens Å Irgens LM. Secular trends in sperm variables for groups of men in fertile and infertile couples. *Acta Obstet Gynecol Scand* 1999; **78**: 332-335.

[32] Zorn B, Virant-Klun I, Verdenik I, Meden-Vrtovec H. Semen quality changes among 2343 healthy Slovenian men included in an IVF-ET programme from 1983 to 1996. *Int J Androl* 1999; **22**: 178-183.

[33] Jensen TK, Vierula M, Hjollund NHI, Saaranen M, Scheike T, Saarikoski S, et al. Semen quality among Danish and Finnish men attempting to conceive. *Eur J Endocrinol* 2000; **142**: 47-52.

[34] Seo JT, Rha KH, Park YS, Lee MS. Semen quality over a 10-year period in 22,249 men in Korea. *Int J Androl* 2000; **23**: 194-198.

[35] Itoh N, Kayama F, Tatsuki TJ, Tsukamoto T. Have sperm counts deteriorated over the past 20 years in healthy, young Japanese men? results from the Sapporo area. *J Androl* 2001; **22**(1): 40-44.
[36] Rolf C, Kenkel S, Nieschlag E. Age-related disease pattern in infertile men: increasing incidence of infections in older patients. *Andrologia* 2002; **34**: 209-217.
[37] Jung A, Schuppe HC, Schill WB. Comparison of semen quality in older and younger men attending an andrology clinic. *Andrologia* 2002; **34**(2): 116-122.
[38] Eskenazi E, Bradman A, Gladstone E, Jaramillo S, Birch K, Holland N. CHAMACOS, a longitudinal birth cohort study: lessons from the fields. *J Children's Health* 2003; **1**: 3-27.
[39] Ng KK, Donat R, Chan L, Lalak A, Di Pierro I, Handelsman DJ. Sperm output of older men. *Hum Reprod* 2004; **19**(8): 1811-1815.
[40] Pasqualotto FF, Sobreiro BP, Hallak J, Pasqualotto EB, Lucon AM. Sperm concentration and normal sperm morphology decrease and follicle-stimulating hormone level increases with age. *BJU Int* 2005; **96**(7): 1087-1091.
[41] 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): 421-428.
[42] 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**(1): 20-25.
[43] Meeker JD, Godfrey-Bailey L, Hauser R. Relationships between serum hormone levels and semen quality among men from an infertility clinic. *J Androl* 2007; **28**(3): 397-406.
[44] Stewart TM, Liu DY, Garrett C, Jørgensen N, Brown EH, Baker HW. Associations between andrological measures, hormones and semen quality in fertile Australian men: inverse relationship between obesity and sperm output. *Hum Reprod* 2009; **24**(7): 1561-1568.
[45] Winkle T, Rosenbusch B, Gagsteiger F, Paiss T, Zoller Nicole. The correlation between male age, sperm quality and sperm DNA fragmentation in 320 men attending a fertility center. *J Assist Reprod Genet* 2009; **26**: 41-46.
[46] Bahk JY, Jung JH, Jin LM, Min SK. Cut-off value of testes volume in young adults and correlation among testes volume, body mass index, hormonal level, and seminal profiles. *Urology* 2010; **75**(6): 1318-1323.
[47] Hammiche F, Laven JSE, Boxmeer JC, Dohle GR, Steegers EAP, Steegers-Theunissen RPM. Sperm quality decline among men below 60 Years of age undergoing IVF or ICSI treatment. *J Androl* 2011; **32**(1): 70-76.
[48] Łepecka-Klusek C, Wdowiak A, Pilewska-Kozak AB, Syty K, Jakiel G. The role of age, environmental and occupational factors on semen density. *Ann Agri Env Med* 2011; **18**: 437-440.
[49] Tang WH, Jiang H, Ma LL, Hong K, Zhong Q, Yang CS, et al. Relationship of sperm morphology with reproductive hormone levels in infertile men. *Zhonghua Nan Ke Xue* 2012; **18**(3): 243-247.
[50] Nie ZY, Wu HF, Zhang N, Guo LN, Zhao SY, Zhen XL, et al. Effects of males' age on sperm apoptosis and DNA integrity. *Zhonghua Nan Ke Xue* 2012; **18**(11): 1004-1008.
[51] Jørgensen N, Joensen UN, Jensen TK, Jensen MB, Almstrup K, Olesen IA, et al. Human semen quality in the new millennium: a prospective crosssectional population-based study of 4867 men. *BMJ Open* 2012; **2**: e000990-1003.
[52] 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 3729 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**(7): 2247-2254.
[53] Diao R, Fok KL, Zhao L, Chen H, Tang H, Chen J, et al. Decreased expression of cystic fibrosis transmembrane conductance regulator impairs sperm quality in aged men. *Reproduction* 2013; **146**(6): 637-645.
[54] Stone BA, Alex A, Werlin LB, Marrs RP. Age thresholds for changes in semen parameters in men. *Fertil Steril* 2013; **100**(4): 952-958.
[55] Jajoo S, Kalyani KR. Prevalence of abnormal semen analysis in patients of infertility at a rural setup in Central India. *Int J Reprod Contracept Obstet Gynecol* 2013; **2**(2): 161-164.
[56] Dutta S, Joshi KR, Sengupta P, Bhattacharya K. Unilateral and bilateral cryptorchidism and its effect on the testicular morphology, histology, accessory sex organs and sperm count in laboratory mice. *J Hum Repro Sci* 2013; **6**(2): 106-110.
[57] Bhattrai T, Bhattacharya K, Chaudhuri P, Sengupta P. Correlation of common biochemical markers for bone turnover, serum calcium and alkaline phosphatase, in post-menopausal women. *Malays J Med Sci* 2014; **21**(1): 58-61.
[58] Bhattarai T, Chaudhuri P, Bhattacharya K, Sengupta P. Effect of progesterone supplementation on post-coital unilaterally ovariectomized superovulated mice in relation to implantation and pregnancy. *Asian J Pharm Clin Res* 2014; **7**(1): 29-31.
[59] Krajewska-Kulak E, Sengupta P. Thyroid function in male infertility. *Front Endocrinol* 2013; **4**: 1-2.
[60] Sengupta P. Current trends of male reproductive health disorders and the changing semen quality. *Int J Prev Med* 2014; **5**(1): 1-5.
[61] Sengupta P. Recent trends in male reproductive health problems. *Asian J Pharm Clin Res* 2014; **7**(2): 1-5.