

Estimation of the seminal fluid of subfertile patients of different age groups

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Summary:

Background: Among different lifestyle factors, aging process can adversely affect male semen parameters and hence male fertility in this study, semen parameters and reproductive hormonal profiles of subfertile young men were compared with subfertile middle and old age men

Objective: The Objective of the current study is to find the relationship of age on fertility in Iraqi sub fertile patients.

Patients and Methods: At the male infertility clinic of Al-yarmuk teaching hospital, Almustanseria medical college, Baghdad, Iraq from the 1st of October 2010 to the end of Aughest 2011, 100 men [81 young with mean ages (31.36 ± 5.18) and 19 middle or old age with mean ages (43.40 ± 6.08)] with history of subfertility for at least 1 year were evaluated by medical history, physical examination, semen analyses and reproductive hormonal profile namely serum FSH, LH, E2, Test. And PRL.

Results: there was a significant impairment of semen parameters namely sperm count and sperm motility in subfertile middle or old age men (means ± SD were 16.94 ± 19.25, and 9.88 ± 15.21 respectively as compared to subfertile young men in which means ± SD were 50.01 ± 25.69 and 26.53 ± 18.93 p value < 0.005 for both and with a non significant changes in sperm morphology and reproductive hormonal profile between the 2 groups.

Conclusion: Qualitative analysis of semen indicates that as men age, they produce fewer motile sperm, These findings may have fertility implications for men who choose to delay fatherhood.

Key words: male subfertility, age, semen, reproductive hormones.

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Introduction:

One in six couples of childbearing age is unable to conceive, and male factors contribute to >25% of cases (1). About 60% of male factor infertility may be due to genetic causes, but the contributions from environmental and host factors such as age and diet are poorly understood. Prior rodent and human studies have reported that certain aspects of semen quality decline with age (2, 3 and 4). Male fecundity also seems to decline with age, although spermatogenesis continues well and some men of advancing age can give birth to children (3). However, the risks for abnormal pregnancies and heritable effects associated with advancing paternal age are poorly understood. Until recently it has been widely thought that a man's reproductive capability was not affected by advancing age. There are many stories about men who have fathered children in their sixties and even as late as their nineties. Yet now figures show that men over 40 are making up nearly a quarter of fertility consultations. (2). Until recently there has been a poor understanding of the effect of age on male infertility. It is only now that the field of male infertility has become mainstream and full of new research, data and conclusions. The effects of aging are not as dramatic as those seen in women, subtly changes in the DNA quality could seriously affect a couple's ability to conceive, or could lead to miscarriage or even health problems in any child born.

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The aim of the study was to evaluate the effect of male age on different semen parameters and some reproductive hormones in a group of subfertile Iraqi subjects.

Patients and methods:

Patients who were evaluated at the infertility clinic of Al-Yarmok teaching hospital between October, 2010 and Aughest, 2011 with a history of subfertility for at least 1 year were included in this study, all of them had normal female partners regarding history, physical examination and investigations. Eligible men were mailed a questionnaire on medical and reproductive history, sociodemographic characteristics. Clinical evaluation of all participants included history, genital examination Scrotal Doppler ultrasound was performed, as needed, to exclude subclinical varicocele. History included data on smoking, alcohol, recreational drugs, fever, and exposure to gonadotoxins such as chemotherapy, radiotherapy, or pesticides. Patients with azospermia and those with a history of smoking, recreational drug use (i.e., marijuana use and/or narcotic agents) or alcohol consumption (including social drinking) within the past year were excluded. Also, patients were excluded if they had a history of a recent fever or exposure to gonadotoxins such as chemotherapy, radiotherapy, or pesticides. Patients who had abnormalities in their genital examination such as cryptorchidism, varicoceles and genital tract infections also patients with history of chronic diseases

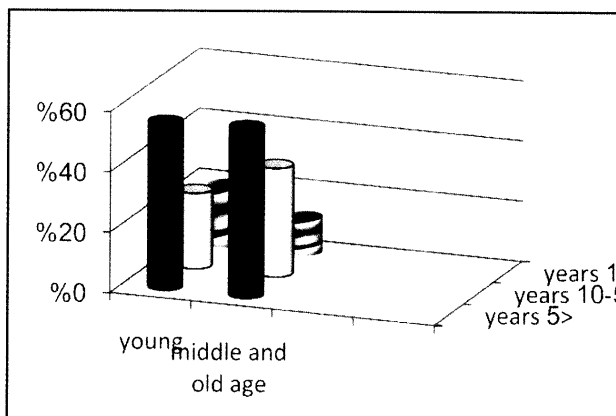
such as high blood pressure, heart problems or diabetes; history, were excluded. The patients ages were between 19 and 59 years (mean 34.47) were classified into 2 groups: group 1, young age (≤ 40 years) (n= 81) and group 2 middle and old age (>40 years) (n= 19). Semen Analysis: All subjects were required to collect semen specimens by masturbation in a private room near the laboratory after a period of 3 to 5 days of sexual abstinence. Following liquefaction at 37 °C a drop of 20 μ l of homogenized semen is placed by a micropipette on a warm clean microscopic glass slide and covered with a cover slip Examination was performed by light microscope under a magnification of 400X as stated by WHOM manual for human semen analysis (5). Hormonal assay: Venous blood was collected in plain tubes for the preparation of the serum by centrifugation then serum was collected and frozen at -20 degree centigrade in the freezer until hormonal analysis which was performed by using Addendum-Mini VIDAS apparatus (VIDAS) 12 model0, 1992, Biomerieux company, France, through an enzyme linked fluorescent assay (ELFA) technique.

Statistical Analysis: Using SPSS (statistical package of social sciences) V. 14 for Statistical Analysis. Independent sample T test was used to determine the effects of aging on standard semen variables and reproductive hormonal profiles P<0.05 was considered statistically significant.

Results:

The 100 subfertile men initially evaluated in this study were divided into 2 groups group 1(young age subjects (n=81) their mean age \pm SD was about (31.17 \pm 5.31) and group 2 middle and old age subjects (n=19), their mean age \pm SD was about (49.53 \pm 6.24). The mean duration of subfertility of group 1 was 4.95 years and 55% of them report history of less than 5 years subfertility as compared to 25% who report 5-10 years history and only 20% were having history of more than 10 years subfertility. The mean duration of subfertility of group 2 was 5.98 years and 52% of them report history of less than 5 years subfertility as compared to 36% who report 5-10 years history and only 12% were having history of more than 10 years subfertility (fig. 1). Regarding the type of subfertility 79% of group 1 was having primary subfertility whereas 21% were of secondary type as compared to group 2 in which 73% were having primary subfertility whereas 27% were of secondary type.

Fig-1; the distribution of patients according to their duration of subfertility



Standard Semen Parameters:

Mean sperm count \pm SD in group 1 was about 50.01 \pm 25.69 as compared to that of group 2 (16.94 \pm 19.25). On the other hand the mean percent of progressive motile sperms \pm SD was (26.45 \pm 18.93) in group 1 as compared to (9.88 \pm 15.21) in group 2. The mean percentage of normal sperm forms \pm SD in group 1 was (50.47 \pm 17.90) whereas that of group 2 was 39.71 \pm 26.72) these three parameters results were statistically significant (P values were <0.05) as in table 1.

Table 1: Mean semen parameters, SD and SEM of different semen parameters of group 1 and 2.

	Age	Mean	Std. Deviation	Std. Error Mean	P value
Count*	young	50.01	25.692	2.909	.000
	middle and old age	16.94	19.256	4.670	
% of progressive motile sperms*	young	26.54	18.938	2.144	.001
	middle and old age	9.88	15.215	3.690	
% of normal sperms morphology*	young	50.47	17.906	2.027	.059
	middle and old age	39.71	26.720	6.481	

*P value < 0.005 means statistically significant

Regarding hormonal profile mean serum FSH was lower in group 1 (6.72 \pm 6.71) mIU/l as compared to group 2 (8.08 \pm 9.36) mIU/l). Regarding mean serum LH level it was higher in group 1 (8.20 \pm 22.58) mIU/l) as compared to group 2 (4.74 \pm 3.24) mIU/l). Mean serum estradiol level was higher in group 1 (46.08 \pm 14.26) pg/ml. as compared to group 2 (45.35 \pm 15.68) pg/ml. Mean serum testosterone level was lower in group 1 (3.96 \pm 1.92) ng/ml. as compared to group 2 (6.68 \pm 9.32) ng/ml. Mean serum prolactin level was higher in group 1 (17.53 \pm 34.31) ng/ml. as compared to group 2 (8.25 \pm 5.30) ng/ml. However all these were statistically non significant as in table 2.

Table 2: Mean hormonal profile levels, SD and SEM of different reproductive hormones of group 1 and 2.

	age	Mean	Std. Deviation	Std. Error Mean	P value
FSH	young	6.727	6.7108	.8021	.477
	middle and old age	8.084	9.3619	2.1478	
LH	young	8.207	22.5836	2.6993	.509
	middle and old age	4.748	3.2432	.7440	
E⁺	Young	46.088	14.2632	1.7171	.852
	middle and old age	45.353	15.6844	3.8040	
Test.	Young	3.964	1.9229	.2298	.221
	middle and old age	6.689	9.3253	2.1394	
PRL.	Young	17.535	34.3154	6.1632	.428
	middle and old age	8.256	5.3012	1.7671	

All were statistically not significant P value > 0.005 means

Discussion:

Previous data suggest that, unlike fertility in women, there appears to be no evidence of an age threshold for sperm parameters for men, but rather a gradual decline with advancing age may occur. Our findings suggest impairment of conventional sperm parameters (count, motility and morphology) with advancing age and may have important implications for men who choose to delay fatherhood, because age may reduce their chance for success. Our findings are consistent with those of Kidd et al 2001, Schwatz et al 1983 Singh et al 2003, Wayne and Hellstrom 2006, who all report significant effect of male age on different semen parameters but not with Chen et al 2004, who did not found any effect of male age on the semen parameters. Age-related cellular or physiologic changes in the reproductive tract, hormonal changes or increased oxidative damage may be primary events leading to decreased motility in older men. Age effects on the prostate may contribute to changes in seminal plasma which may affect sperm motility (10). There may also be age-related changes in the epididymis, where sperm acquire the capacity for vigorous forward motility during transit (11). Ageing results in histological and biochemical changes in the epididymis that are suggestive of oxidative damage (12). Also increasing age correlated with increasing percentage of spermatozoa with highly damaged DNA (7). Other explanations include a decrease in the function and number of Leydig cells (13), reduced testicular perfusion (14), decreased Sertoli cell function (15), and increased testicular connective tissue deposition (16) have been suggested as age-related changes that might impair spermatogenesis and diminish feedback from the testes to the pituitary, resulting in elevated LH and FSH (17). However, decreased spermatogenesis does not necessarily imply a decrease in fertility potential. (18 and 19).

Deterioration of fertility in older men may also be confounded by the decrease in sexual activity with increasing age (20).

Conclusion:

Age does significantly affect male fertility by reducing sperm count and motility and can have a deleterious but non significant effect on reproductive hormones so middle and old age as a group may not experience reduced fertility, it is better for a male not to delay fatherhood.

References:

1. Templeton A. Infertility-epidemiology, aetiology and effective management. *Health Bull (Edinb)* 1995; 53(5), 294-298.
2. Kidd SA, Eskenazi B and Wyrobek AJ. Effects of male age on semen quality and fertility: a review of the literature. *Fertil Steril*; 2001; 75(2), 237-248.
3. Sloter E, Nath J, Eskenazi B and Wyrobek AJ. Effects of male age on the frequencies of germinal and heritable chromosomal abnormalities in humans and rodents. *Fertil Steril*. 2004; 81(4), 925-943.
4. Eskenazi B, Wyrobek AJ, Sloter E, Kidd SA, Moore L, Young S and Moore D. The association of age and semen quality in healthy men. *Hum Reprod*. 2003; 18(2), 447-454.
5. World Health Organization (WHO). *Laboratory manual for the examination and processing of human semen* 5th ed. New York: 2010.
6. Schwartz D, Mayaux MJ, Spira A, Moscato ML, Jouannet P, Czyglik F and David G (1983) Semen characteristics as a function of age in 833 fertile men. *Fertil Steril* 39(4), 530-535.
7. Singh NP, Muller CH and Berger RE. Effects of age on DNA double-strand breaks and apoptosis in human sperm. *Fertil Steril* 2003; 80(6), 1420-1430.
8. Wayne J. G. and Hellstrom W. Semen and Sperm Reference Ranges for Men 45 Years of Age and Older. *Journal of Andrology*. 2006; 27, 3, May/June (421-428).
9. Chen Z, Godfrey-Bailey L, Schiff I and Hauser R. Impact of seasonal variation, age and smoking status on human semen parameters: The Massachusetts General Hospital experience. *J Exp Clin Assist Reprod* 2004; 1(1), 2.
10. Schneider EL and Monticone RE. Aging and sister chromatid exchange. II. The effect of the in vitro passage level of human fetal lung fibroblasts on baseline and mutagen-induced sister chromatid exchange frequencies. *Exp Cell Res*. 1978; 115(2), 269-276.
11. Hamilton D and Naftolin F *Basic Reproductive Medicine*. MIT Press, Cambridge, MA. Hirano Y, Shibahara H, Obara H, Suzuki T, Takamizawa S, Yamaguchi C, Tsunoda H and Sato I (2001) Relationships between sperm motility characteristics assessed by the computer-aided sperm analysis (CASA) and fertilization rates in vitro. *J Assist Reprod Genet* 1981; 18(4), 213-218.
12. Robaire B and Hales BF. Mechanisms of action of cyclophosphamide as a male-mediated developmental toxicant. *Adv Exp Med Biol* 2003; 518, 169-180.
13. Neaves WB, Johnson L, Porter JC, Parker CR Jr, Petty

- C.S. Leydig cell numbers, daily sperm production, and serum gonadotropin levels in aging men. *J Clin Endocrinol Metab.* 1984;59:756-763.
14. Suoranta H. Changes in the small blood vessels of the adult human testis in relation to age and to some pathological conditions. *Virchows Arch A Pathol Pathol Anat.* 1971;352:165-181
15. Tenover JS, McLachlan RI, Dahl KD, Burger HG, de Kretser DM, Bremner WJ. Decreased serum inhibin levels in normal elderly men: evidence for a decline in Sertoli cell function with aging. *J Clin Endocrinol Metab.* 1988;67:455-459.
16. Plas E, Berger P, Hermann M, Pfluger H. Effects of aging on male fertility? *Exp Gerontol.* 2000;35:543-551.
17. Hermann M, Untergasser G, Rumpold H, Berger P. Aging of the male reproductive system. *Exp Gerontol.* 2000;35:1267-1279.
18. 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.
19. Paulson RJ, Milligan RC, Sokol RZ. The lack of influence of age on male fertility. *Am J Obstet Gynecol.* 2001;184:818-822.
20. Handelsman DJ. Male reproductive ageing: human fertility, androgens and hormone dependent disease. *Novartis Found Symp.* 2002; 242:66-77.