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Impact of Male Aging on Semen Parameters

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ABSTRACT

Aim: *To investigate the effect of increasing male age on the semen parameters including semen volume, sperm concentration, and progressive sperm motility.*

Materials and Methods: *1038 patients who applied to our IVF clinic for semen analysis or for infertility treatment were included in the study. The participants were divided into three age categories as follows: 680 participants (65.5%) aged 22-30, 139 participants (13.4%) aged 31-45 years, and 219 participants (21.1%) aged ≥45 years. Demographic and baseline clinical characteristics were recorded. The variables considered in this study were age and the following semen parameters: volume (ml); sperm concentration (millions/ml); and progressive sperm motility A+B (%). Normal semen values were defined based on the WHO criteria (World Health Organization, 2010).*

Results: *The mean age of the participants was 33.1(± 4.8). The mean BMI of the participants was 24.1(± 2.8). The mean semen volume was 3.3 (± 1.5), the mean semen concentration was 43.6 (± 31.7), and the mean progressive sperm motility was 43.6 (± 10.1). There was a moderate negative correlation between paternal age and semen volume (r=-0.13) and sperm motility (r=-0.32), while there was a moderate positive correlation between paternal age and sperm concentration (r=0.24). The proportion of likelihood ratio measured between semen volume, sperm concentration, sperm motility and age was found to be 1 in patients between the ages of 22-30. The 22-30 age group does not have a decreasing or increasing effect on semen volume (OR: 1), sperm concentration (OR: 1) and motility (OR: 1). Regression analysis of patients in the 31-45 age group revealed no change in semen volume (OR: 0.99, 95% CI: 0.43-2.3, p <0.9), but an increase in sperm concentration (OR: 1.74, 95% CI: 1.13-2.7, p <0.01), and decreased sperm motility (OR: 0.28, 95% CI: 0.16-0.47, p <0.00). In the regression analysis of participants over the age of 45, semen volume (OR: 0.31, 95% CI: 0.19-0.53, p <0.00) and sperm motility (OR: 0.05, 95% CI: 0.03-0.08, p <0.00) decreased with age. No change was detected in the concentration (OR: 0.87, 95% CI: 0.63-1.2, p <0.3).*

Conclusion: *With increasing male age, semen volume and sperm motility begin to decrease. However, a significant decrease in sperm concentration does not occur until the age of 45.*

Keywords

Paternal age, Progressive sperm motility, Sperm concentration, Semen volume.

Introduction

Somatic cell aging occurs similarly in many organs. Although testicular cells are responsible for germ cell production, they are somatic cells themselves. Unlike other somatic cells, testicular cells have an intense antioxidant protection capacity. In addition, the blood testicular barrier provides an extra protection to the testicular cells. With age, decreasing antioxidant capacity, increase in reactive oxygen derivatives and decrease in DNA repair enzymes because some defects in sperm production in testicular cells [1]. Age-related changes in sperm parameters become apparent at later

ages, unlike women. In the last two decades, couples have been delaying their marriage age due to varying economic and social factors as well as prolonged life expectancy. The rapid development in assisted reproductive techniques and the easy access to these techniques have also provided the couples with the opportunity to move forward the age of marriage and the conception process. In the last decade, there has been an increase of approximately 15% in the age of fatherhood of male partners in western societies [2].

Despite the advancing age of male partners, even if the chances of paternity continue, deviations in sperm parameters that will occur if this process is not managed well may cause them to lose their hope of paternity [3]. High paternal age has adverse effect on reproductive hormones [4], epigenetic factors [5], testicular function [6], and semen parameters [7,8], which negatively affect the fertility outcomes in older couples [9,10]. Studies demonstrated that with the advancing male age sperm motility, semen volume, and sperm morphology decreases [7,8]. The men aged 60 and over may exhibit significant changes in sperm characteristics, hormonal futures, and histological alteration in testicular structures [11-13]. It is a known fact that semen parameters are affected negatively with age [14]. With increasing age, seminal vesicle and prostate functions deteriorate, as well as a decrease in daily sperm production [1]. There are reports that age also negatively affects sperm viability and morphology to some extent [15,16]. Although some improvement in semen parameters was reported between the ages of 30 and 45 years, most studies reported a decrease in sperm motility and semen volume with advancing age. Morphological sperm anomalies are more common in elderly patients [17,18]. The aim of this study was to investigate possible correlations between male age and different semen parameters including semen volume, sperm concentration ans sperm motility. Possible correlation between demographic, preproductive parameters and semen characteristics were also analysed.

Materials and Methods

This cross-sectional retrospective study examined the data from the medical records of patients aged 22 years or older submitted to semen analysis at the Memorial Hospital IVF-Center between January 2019 and January 2020. Only the patient with more than one sample in the medical database were included the study. As a result, current study evaluated data from 1038 men seeking solutions to have a baby. The patients were divided into three groups based on age as follows: 22-30 years; 31-45 years; and more than 45 years. Demographic characteristics and baseline clinical characteristics, including age, BMI, infertility duration, total oocyte count, etc., were recorded. The paternal age and the semen parameters including semen volume (ml), sperm concentration (millions/ml), and progressive sperm motility A+B (%) were compared. Normal semen values were defined based on the WHO criteria (World Health Organization, 2010).

Semen samples from all participants were collected through masturbation after three days of abstinence. The reference range was 1.5 ml (1.4-1.7) for semen volume, 15 millions/ml (12-16) for sperm concentration and 40 (38-42) for progressive sperm motility. The value above this reference range was considered sufficient and the value below this reference range was considered insufficient. Participants in abstinence for less than three or more than 15 days prior to semen analysis were excluded. Participants presenting more than one millions round cells during semen analysis were not included study. The informed consent was received from all participants. This study was approved by the Ethics Committee of Kayseri Memorial Hospital. All procedures conducted in studies, including human participants, conformed to the national or institutional research committee's ethical standards and the 1964 Helsinki Declaration and its later amendments or other ethical standards.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 26.0 (SPSS Inc., Chicago, IL, USA) was used to perform statistics. Logistic regression analysis was used to assess the factors associated with semen volume (cut-off point=1.5), sperm concentration (cut-off point=14), and progressive sperm motility (cut-off point=40). Odds ratios (OR) and their respective *p* values were calculated based on these analyses. In the case of OR = 1, it was accepted that age had no effect on the measured parameters, in the case of OR <1, age had a probability-reducing effect on the measured parameters, and in the case of OR> 1, age had an increasing effect on the measured parameters. Men with ages between 22 and 30 years were accepted as the reference group. Age was considered both a quantitative and a categorical variable. The results of the Kolmogorov test show that not all quantitative variables have a normal distribution. The relationship between semen parameters and independent variables was examined using Spearman correlation analysis. Statistical significance was defined as a p value $\leq .05$, and confidence intervals were adjusted at 95%.

Results

As shown in Table 1, 1038 subjects were participated in the study. 680 of them (65.5%) were aged 22-30, 139 (13.4%) were aged 31-45 years, and the remaining 219 participants (21.1%) were aged ≥45 years. The mean age of the all participants is 33.1(± 4.8). The mean BMI of the participants is 24.1(± 2.8). The mean infertility duration is 7.5(± 4.5). The mean number of IVF-ET attempts is 1.9(± 1.2). The mean E2 concentration on the day of hCG is 2482.3(± 1258.4), the mean endometrium thickness on the day of hCG is 11.07(± 2.1). The total mean rFSH dose is 2675.7(± 1205.5). The mean induction duration is 9.2(± 1.7). The number of mean total oocyte is 13.1(± 6.3). The number of mean M II oocyte and 2 PN embryo are 10.2(± 5.5) and 7.9(± 4.3) respectively. The mean number of transferred embryo is 2.9(± 0.9). While the mean semen volume is 3.3(± 1.5), the mean sperm concentration and progressive sperm motility are 43.6(± 31.7) are 43.6(± 10.1) respectively. A negative and significant correlation was found between patient age and semen volume ($r = -0.13$, $p < 0.00$) and sperm motility ($r = -0.32$, $p < 0.00$). To be clear, as the age increased, there was a significant decrease in both semen volume and sperm motility. However, the correlation coefficient for both

Table 1: Demographic and reproductive parameters of participants.

Variables	N	Minimum	Maximum	Mean	Sd
Age of women (yrs)	1038	19	39	32.5	4.1
Age of men (yrs)	1038	22	55	39.1	4.8
BMI (kg/m2)	1038	16.9	29.9	24.1	2.8
Infertility time (yrs)	1038	1	22	7.5	4.5
Total number of IVF-ET attempts	1038	1	8	1.9	1.2
E2 on the day of hCG (pg/mL)	1038	225	7409	2482.3	1258.4
Endometrium thickness (mm)	1038	7	18.5	11.07	2.1
Total rFSH dose	1038	450	7200	2675.7	1205.5
Induction duration (day)	1038	2	16	9.2	1.7
Total oocyte	1038	5	37	13.1	6.3
MII oocyte	1038	4	34	10.2	5.5
2 PN	1038	1	28	7.9	4.3
The number of transferred embryo	1038	1	2	1.4	0.9
ET day	1038	2	6	3.6	0.9
Semen volume (ml)*	1038	0.3	11	3.3	1.5
Sperm concentration (millions/ml)*	1038	1	130	43.6	31.7
Progressive sperm motility A+B (%)*	1038	0	80	43.6	10.1
		Frequency		Percent (%)	
Age distrubition of men					
22-30		680		65.5	
31-45		139		13.4	
45≥		219		21.1	

*:Normal semen values were defined based on the WHO criteria (World Health Organization, 2010).

Table 2: Correlation between semen parameters and independent variables.

Variable	Semen volume		Sperm concentration		Sperm motility	
	Correlation Coefficient (r)	P	Correlation Coefficient (r)	P	Correlation Coefficient (r)	P
Age of man	-0.13	0.000	0.24	0.000	-0.32	0.000
BMI	0.054	0.08	0.059	0.05	-0.04	0.2
Infertility duration	-0.001	0.9	0.03	0.3	-0.004	0.9
IVF attempt	-0.02	0.5	-0.02	0.4	-0.01	0.6
Estradiol	0.05	0.09	0.03	0.3	0.05	0.09
Endometrium thickness	003	0.2	-0.01	0.6	0.066	0.03
rFHS dose	-0.04	0.1	0.04	0.2	-0.002	0.9
Induction duration	-0.02	0.4	0.097	0.002	0.03	0.3
Total oocyte number	0.06	0.03	0.04	0.1	0.1	0.002
M II oocyte	0.06	0.06	0.07	0.03	0.12	0.000
2 PN	0.065	0.03	0.04	02	0.059	0.05
The number of transferred embryo	0.03	0.3	0.04	0.1	0.07	0.02
Transfer day	-0.01	0.7	-0.004	0.9	0.003	0.9

parameters was recorded as quite weak. A weak but positive and significant correlation (r = 0.24, p <0.00) was found between age and sperm count. That is, a slightly significant increase in sperm count was detected with increasing age.

The relationship between age groups and semen volume, sperm concentration and sperm motility was analyzed using the logistic regression method (Table 3). With the help of the odds ratio (likelihood) we obtained through this method, it was possible to reveal whether age has an increasing or decreasing effect on the probability of sperm parameters. The proportion of likelihood ratio measured between semen volume, sperm concentration, sperm motility and age was found to be 1 in patients between the ages of 22-30. In other words, the 22-30 age group does not have a decreasing or increasing effect on semen volume (OR: 1), sperm concentration (OR: 1) and motility (OR: 1). Regression analysis of patients in the 31-45 age group revealed no change in semen volume (OR: 0.99, 95% CI: 0.43-2.3, p <0.9), but an increase in sperm concentration (OR: 1.74, 95% CI: 1.13-2.7, p <0.01), and decreased sperm motility (OR: 0.28, 95% CI: 0.16-0.47, p <0.00). In the regression analysis of participants over the age of 45, semen volume (OR: 0.31, 95% CI: 0.19-0.53, p <0.00) and sperm motility (OR: 0.05, 95% CI: 0.03-0.08, p <0.00) decreased with age. No change was detected in the concentration (OR: 0.87, 95% CI: 0.63-1.2, p <0.3).

Table 3: Logistic regression analysis of participants.

Variables	Semen volume (ml)		Sperm concentration (millions/ml)		Progressive sperm motility A+B (%)	
	OR (95%CI)	p-value	OR (95%CI)	p-value	OR (95%CI)	p-value
Age of man						
22-30	1		1		1	
31-45	0.99 (0.43-2.3)	0.9	1.74 (1.13-2.7)	0.01	0.28(0.16-0.47)	0.000
45≥	0.31 (0.19-0.53)	0.000	0.87 (0.63-1.2)	0.3	0.05(0.03-0.08)	0.000
BMI	1.08 (0.99-1.18)	0.05	1.04 (0.99-1.09)	0.07	1.01(0.96-1.07)	0.4
Infertility duration	1.01 (0.96-1.07)	0.5	1 (0.97-1.03)	0.6	0.99 (0.96-1.03)	0.9
Total number of IVF attempts	0.85 (0.72-1)	0.05	0.98 (0.89-1.09)	0.7	0.89 (0.79-1)	0.05
E2	1 (0.99-1)	0.2	0.99 (0.99-1)	0.8	0.99 (0.99-1)	0.5
Endometrium thickness	1.05 (0.94-1.18)	0.3	0.95 (0.89-1)	0.1	1.02 (0.95-1.09)	0.5
Total rFSH dose	1 (0.99-1)	0.1	1 (1.000-1.00)	0.01	1 (0.99-1)	0.7
Induction duration	1.18 (1.03-1.36)	0.01	1.14 (1.05-1.23)	0.001	1.03 (0.94-1.13)	0.4
Total oocyte number	1.03 (0.99-1.07)	0.1	1 (0.98-1.02)	0.5	1.01 (0.98-1.04)	0.3
M II oocyte	1.04 (0.99-1.09)	0.07	1.01 (0.98-1.03)	0.3	1.02 (0.99-1.05)	0.1
2 PN	1.02 (0.96-1.08)	0.4	0.98 (0.96-1.01)	0.4	1.01 (0.97-1.04)	0.6
Transferred embryo	1.34 (1.3-1.74)	0.02	1.05 (0.91-1.2)	0.4	0.92 (0.77-1.09)	0.3
ET day	0.95 (0.74-1.23)	0.7	0.95 (0.83-1.09)	0.5	1.04 (0.88-1.23)	0.6

Discussion

The present study aimed to investigate the effect of paternal age on the semen parameters such as sperm concentration, semen volume, and progressive sperm motility. We also investigated possible association between semen parameters, demographic and reproductive variables. Our study showed a moderate negative correlation between paternal age, semen volume and progressive sperm motility while there was a moderate positive correlation between paternal age and semen concentration. According to our results, the older participants had lower semen volume and sperm motility while increasing age enhanced the semen concentration. There is a significant decline in semen volume and sperm motility after the age of 45 years. We could not detect a significant decreasing or increasing effect of age on semen parameters in men aged between 22 and 30 years. The fact that likelihood ratio of 1 for all three parameters in the regression analysis supports no significant age-related changes in semen parameters between the ages of 22-30. Thanks to these data, the accuracy of taking patients in this age group as a reference has been revealed.

In male partners between the ages of 31-45, there was no change in semen volume, but a decrease in sperm motility started. The most striking effect of this age group is the increase in sperm count. Likelihood ratio greater than 1.7 indicates a significant increase in sperm production between the ages of 31 and 45 years. After the age of 45, the decrease in semen volume and motility becomes evident, but there is no significant change in sperm count. In the light of these data, there is a gradual decrease in semen volume and sperm motility while the sperm number increases until the paternal age reaches 45. A decrease in volume and motility may be associated with age, as well as other age-related factors. Decrease in fluid consumption, excessive use of alcohol and smoking, exposure to environmental toxins as well as weakening of the testicular blood barrier and a decrease in the antioxidant capacity of the testis may contribute to the decrease in semen volume and sperm motility. Age-related decrease in prostate functions may also contribute to the decrease in semen volume.

Our study results are compatible with most studies in the literature, and there are studies in which we are rarely incompatible with one parameter. Kidd et al. [15] reported a correlation between the higher age of men and reduced sperm motility, ejaculate volume, and morphology. They did not find any correlation between advancing paternal age and sperm concentration. Our study is similar to the work of Kidd et al. in terms of semen volume and decrease in sperm motility, but different in terms of sperm concentration. Our results are in line with a study by Hossain et al. who showed that advancing age of men was associated with reduced sperm count and semen volume [19]. Similarly, in a large prospective study, a significant decrease was reported in semen volume and motility with higher age of men [20].

According to our results, the decrease in sperm motility starts after the age of 30 and becomes evident after the age of 45. However, by the age of 45, we found a gradual increase in sperm count as opposed to a decrease. There was no decrease in sperm count after 45 years of age. Stone et al [21] reported that the decrease in sperm quality and quantity starting from the age of 35 decreases the chance of pregnancy and that decrease in volume and sperm motility started between the ages of 43-45. Similar to the above study, we detected a decrease in volume from the age of 45 years. Unlike our work, Brahem et al [7] reported that low male age increased sperm count, but there was no change in other parameters with increasing age. The results of most studies in the literature are similar to ours [22]. Gallo et al [23] demonstrated that male age had no significant effect on semen parameters. Many studies found that decreased progressive sperm motility, semen volume, and abnormal forms percentage were significantly associated with increasing age, which supports our findings [24-27].

Conclusion

With increasing male age, semen volume and sperm motility begin to decrease. However, a significant decrease in sperm concentration does not occur until the age of 45. With increasing age; increased DNA replication defects and oxidative DNA damage, deterioration of oxidant-antioxidant balance, decrease in testosterone and GnRH pulse frequency may be the most important reasons for the change in age-related smen parameters. The effect of male age on semen parameters should be investigated with more comprehensive studies.

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