

What is the optimum age of male fertility in infertile couples?

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Received: 2 February, 2019

Accepted: 26 February, 2019

ARTICLE INFO

Article type:

Original article

Keywords:

Infertility

Male

Semen Analysis

Age

Abstract

Background: The results of studies on the effects of age on sperm parameters are controversial. The aim of this study was to evaluate the association of age and semen parameters.

Methods: In this study 278 men (32.3±6.5 years, range 19 to 65 years) referred to a private medical laboratory to evaluate couple infertility were included from April 2016 to March 2017. Cases with azospermia were excluded from the current study. In some cases, the cause of the couple infertility was female factor, which is not addressed in this report. Semen samples were collected using standard methods. We analyzed semen parameters using computer-assisted sperm analysis.

Results: All semen parameters were deteriorating with increasing age; however, only the correlation of age with sperm motility was statistically significant. This correlation showed a quadratic model with an increasing trend up to a peak at 32 years and then decreasing ($R^2=0.024$, $P=0.03$). We divided cases into two age groups and repeated the analysis separately for patients younger than 31 years (median age of our population) or patients older than 31 years. We found that the semen parameters including count, volume, total motility and vitality showed a negative correlation with age in older patients, however, this correlation was significant only for the total motility ($P=0.02$).

Conclusion: Age has an insignificant impact on sperm count, whereas, Sperm motility showed an increasing trend up to a peak at 32 years and then decreasing significantly.

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Citation: Nazari A.R, Ketabchi A.A, Pakmanesh H, Rahnama A, Fard A, Kharazmi F. What is the optimum age of male fertility in infertile couples?. *Journal of Kerman University of Medical Sciences*, 2019; 26 (2): 161-168.

Introduction

Infertility is defined as the inability to conceive for one year without contraception and in 35 to 40 percent of cases male factor is responsible (1,2). Infertility is associated with important individual and social problems (3). Sperm quantity and quality are influenced by several factors including diseases such as varicocele (4), chemotherapy (5), radiotherapy (6), obesity (7), chemicals (8), environmental factors (9) and cigarette (10).

Several studies have evaluated the effect of maternal age on fertilization and reproduction. Women over 35 years of age are at higher risk for infertility, complications of pregnancy, spontaneous abortion and congenital malformations (11). However, the effect of the male age on the quality of semen and reproductive performance is not clear (12). An important factor in increasing the average age of fathers is the increase in life expectancy and the widespread use of contraceptive methods (13). There is no clear global definition for the father's age. Furthermore, the results of researches in the context of sperm indexes during aging are contradictory. Despite the fact that men retain their ability to reproduce even until they are aged, the testis size and sperm motility decreases with aging (14). The effect of age on sperms is not only related to the volume and shape but also the results of a study showed that the offspring of older fathers is more at risk for genetic abnormalities. At a higher age, the possibility of mutation in sperm DNA is higher (15). Natural mechanisms such as apoptosis that eliminates damaged sperms may be influenced by age (16).

The study of sperm parameters provides a comprehensive understanding of the various aspects of male infertility and its treatment (17). Such a study can be used as an inseparable part of infertility research and as one of the primary measures in

male infertility screening. (18) The spermogram provides useful information on the number of sperms, natural sperms and mobility (19). Based on the World Health Organization (WHO) guidelines, and given that the geographical area (20) and food habits (21,22) can affect sperm parameters, the determination of these indicators based on the age of males for each region is important. In addition, age, at which sperm motility can be significantly reduced, can help determine the risk of male infertility and its complications. For this purpose, the present study was conducted to determine the relationship between age and sperm parameters of men referred for evaluation of the couple infertility.

Materials and Methods

The population of this prospective descriptive study was 278 men referred to a private medical laboratory in Rafsanjan, Iran for the evaluation of couple infertility from April 2016 to March 2017. The inclusion criteria encompassed every man who was referred for semen analysis to evaluate the couple infertility. Cases with azospermia were excluded from the current study. In some cases, the cause of the couple infertility was female factor, which is not addressed in this report. We explained the purpose of the study to the patients and based on the obtained informed consent they were included in the study. The ethics committee of ... University of Medical Sciences approved the study (IR.RUMS.REC.1394.171). This study adheres to the principles of the Declaration of Helsinki.

Demographic data of the individuals was recorded. Semen samples were collected by the standard masturbation method in the laboratory following a period of 3 to 7 days of abstinence in the sterile containers. We analyzed data using computer-assisted sperm analysis (CASA) after 20 minutes of incubation

in 37 °C. Sperm parameters were evaluated according to the World Health Organization (WHO) guidelines. These included semen volume, sperm count, vitality, motility and the grade of motility (rapid progressive motility, slow progressive motility, non-progressive motility or immotile sperms).

Statistical analysis: Data were analyzed using SPSS software version 22 (IBM SPSS) and the significance level of the tests was considered at $P\text{-value} < 0.05$. We used Pearson correlation test to examine the correlation between age and spermogram findings. The difference of semen parameters between age groups was analyzed using ANOVA test. In addition, we divided patients in three age groups based on the age percentiles including younger than or equal to 28 years (27%), 28 to 35 years (48%) and older than 35 years (25%). In this regard, we compared semen parameters between these age

groups. Chi square test was used to evaluate the frequency of oligospermia as a categorical variable in different age groups.

Result

In this study, 278 men with the mean age of 32.35 ± 6.54 years were included. We used Pearson test to examine the correlation between age and spermogram findings. All semen parameters showed a deteriorating trend with increasing age; however, the linear correlation was not statistically significant. In addition, Curve estimation for the correlation between age and motility showed a Quadratic curve model ($R^2=0.024$, $P=0.03$) (Figure 1). This curve shows that sperm motility increases with age up to a peak at around 32 and then starts to decrease.

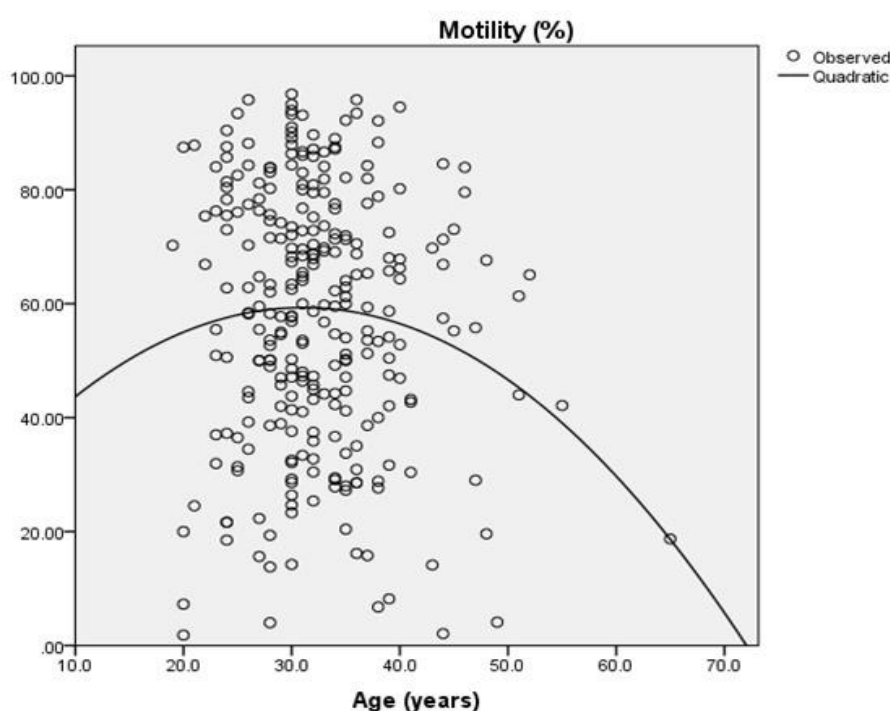


Figure 1. Correlation between age and total sperm motility, quadratic curve estimate

We repeated the analysis excluding young patients less than 31 years (median) and found that the semen parameters including volume, total motility and vitality showed a negative correlation with age in older patients. This correlation was especially significant regarding the total motility ($P=0.02$) and in non-progressive subgroup ($P=0.01$). In addition, sperm vitality showed a decreasing trend in the older subgroup, but the correlation was not significant ($P = 0.06$). Conversely, in younger men (less than 31 years) we did not observe a significant trend regarding semen parameters.

Finally, we compared the results of the semen parameters analysis between three groups based on age percentiles. Figure 2 depicts the results of semen motility grades in these three

groups. An interesting finding was that men in the median percentile (28-35 years old) showed a relatively better sperm quality regarding motility and vitality compared with older and younger groups, however, this difference was not significant (Table 1). The immotile sperms were observed to be higher in the older percentile; however, this difference was not significant ($P=0.1$). ANOVA test showed that the non-progressive motility rate was lower in the older percentile compared to the median percentile ($P=0.03$) (Table 1). Finally, the rate of oligospermia was 9.2% in the younger percentile, 17.3% in the median percentile and 21.7% in the older percentile ($P=0.11$).

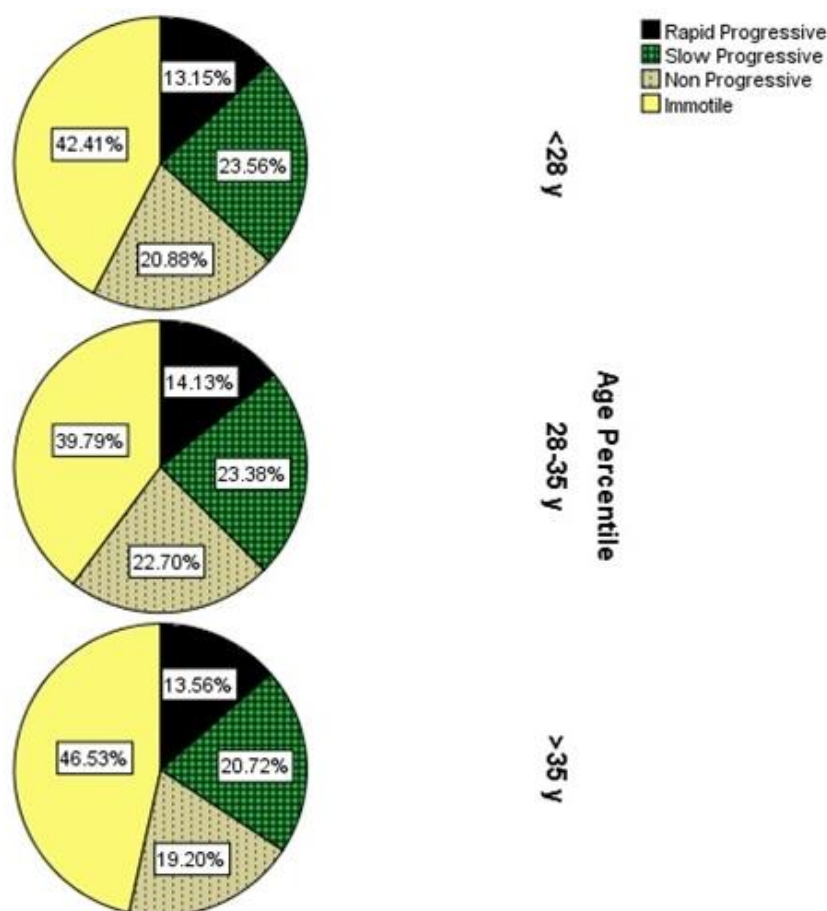


Figure 2. Sperm motility grades in three age groups

Table 1. Semen parameters in the three age groups

	Age Percentile						P-value
	≤ 28 years		28-35 years		>35 years		
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	
Volume (ml)	2.82	1.13	2.88	0.99	3.00	1.12	0.57
Sperm Concentration (per ml)	64.81	43.02	64.35	37.73	61.33	41.93	0.87
Vitality (%)	57.51	24.75	63.70	41.18	53.94	23.47	0.12
Motility (%)	57.51	24.75	60.14	20.38	53.41	24.18	0.13
Rapid Progressive (%)	13.18	10.26	14.16	10.62	13.58	11.71	0.80
Slow Progressive (%)	23.60	11.58	23.43	9.42	20.74	11.48	0.17
Non-Progressive (%)	20.92	8.73	22.74	10.25	19.22	8.44	0.03
Immotile (%)	42.49	24.75	39.86	20.38	46.59	24.18	0.13

Discussion

In the present study, all of the spermogram indexes showed a deteriorating trend with age; however, except for motility, other correlations were not statistically significant. In Johnson's study, no significant relationship was found between age and sperm count (23). Kidd also did not observe a significant correlation between age and sperm count in their review study (24). From this perspective, the results of the current study are in line with the above studies. Although we detected a higher rate of oligospermia in older patients, this finding was not significant.

Regarding the correlation between aging and sperm motility, Sheykhasan et al. indicated that with an increase in age, the sperm count will increase and sperm motility decreases (25). Levitas evaluated 6022 semen samples with the sperm concentration of more than 20 million per ml and found a decrease in motility by age with the greatest decrease after 55 years of age (26). In the study conducted by Harris, age had an adverse effect on male sexual function, sperm parameters, and reproductive capacity (27). Kumar et al. analyzed the data of infertile men during 10 years and found that all semen parameters including volume, count and motility decrease most

significantly after the age of 35. (28). Similar results were observed recently in a study including 11706 men from Argentina with a cut off age of 40 years (29). Likewise, we found a negative correlation between age and sperm motility in men older than 31 years but not in younger men. This finding is in accordance with the results of the study by Levitas (26). This study showed a negative effect for age in older population. An interesting finding of our study was that sperm motility reaches a peak in the age of 32 (Figure 1). This finding demonstrates an optimum sperm quality in the middle age compared with very young or old age groups. Similarly, Levitas et al. revealed that top sperm parameters is at the age of 30 to 35 years (26).

Some studies have shown reduction in the sperm vitality with aging (30,31). Rolf observed a significant difference in the volume of semen of young and older men (32). Fisch showed that the quality and quantity of some semen parameters will decrease from 0.15% to 0.5% for each year (33). Likewise, Stone showed that all spermogram parameters decrease significantly with age (34). Recently, Petersen et al. showed that DNA fragmentation worsens with age.(35) Zhu found that progressive sperm motility, survival rate, and normal sperm

motility decline after 20 years and the subgroup of rapid progressive sperm motility and sperm morphology percentage will decrease gradually after 30 years of age (36). In the current study we observed that vitality will decrease with age but this change was not significant in our study ($P=0.06$).

The advantage of this study was that data were collected prospectively. It is worth mentioning that this study was conducted on couples with infertility. To evaluate the effect of aging on semen parameters more precisely, we suggest sampling from normal population if ethically approved. In addition, age is one of the factors affecting sperm parameters. Other studies are needed to reveal the effects of other contributors such as inheritance, environmental and

geographical parameters, nutrition, and possibly psychological parameters on sperm and its indicators.

Conclusion

Age has an insignificant impact on sperm count, whereas, Sperm motility showed an increasing trend up to a peak at 32 years and then decreasing significantly.

Acknowledgments

All authors declare that they have no competing interests. We are grateful for the people who participated in this research. We thank the deputy of educational and research affairs of Rafsanjan University of Medical Sciences and the Rahnama laboratory staff.

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