



Nerve growth factor and infertility status among infertile males in Kerbala city, Iraq

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Abstract

Introduction: Nerve growth factor (NGF) is known to share a mutual effect regulating neuronal and reproduction functions.

Aim: To estimate the correlation of NGF with semen parameters, age, Body Mass Index, smoking and infertility duration.

Materials and Methods: Semen samples from 121 infertile males (40 asthenozoospermia, 41 oligoasthenozoospermia) and 40 normospermia (controls) were analyzed for NGF by ELIZA assay. Sperm parameters were assessed using the World Health Organization guidelines.

Results: The serum content of NGF positively correlated with age ($r= 0.0367$; $p<0.018$) in oligoasthenozoospermic subjects; yet the correlation did not reach a significant level in total infertile males (asthenozoospermic and oligoasthenozoospermic). No correlation was found between NGF in serum and seminal plasma and BMI, smoking status and infertility duration.

Conclusion: The study showed that Serum NGF positively correlated with age. Additional study using a large sample size is required to confirm these results.

Keywords: age, BMI, infertility duration, smoking

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INTRODUCTION

Infertility is an increasing concern that affects as many as 186 million people wide-reaching (Inhorn, & Patrizio, 2015). Male infertility may be initiated by several factors including medical, environmental contact to diverse agents (chemotherapeutic agents, chemicals, radiations, and pollution) and lifestyle behaviours (smoking, alcohol use, banned recreational drugs use) or other unidentified causes. Likewise, there are lifestyle associations between male infertility and a consistent rise in obesity, which frequently exist with an inactive lifestyle or overall shortage of exercise. It has been acknowledged that obesity is associated with male fertility. Obesity affects male reproductive ability not only by decreasing sperm features but by changing the structure of germ cells in the testes, which eventually affects the maturity and function of sperm cells (Shukla, et al. 2014; Kozyreva et al., 2019).

Nerve Growth Factor (NGF) is a polypeptide member of the neurotrophin protein family that plays an essential role in the differentiation and regulation of neuronal survival, mediated through tyrosine kinase receptors (Barbacid, 1994). Evidence added over the past few years displays the existence of NGF and its receptors

outside the nervous system, mainly in the male reproductive organs (Artico, et al. 2007. Perrard, 2007. Li, et al. 2010.), which directs the possible role of NGF in the reproductive system.

Our previous study showed that the NGF content in seminal plasma and serum was significantly higher in normozoospermia compared with asthenozoospermia and oligoasthenozoospermia samples (Abdulrahman, et al. 2019); the present study was a continuum to assess the correlation of between NGF, Body Mass Index, age, infertility duration and smoking with sperm parameters abnormalities of the infertile male population from Iraq.

MATERIALS AND METHODS

Subjects

The study included 121 men who were enrolled in this study from December 2017 to March 2018. The semen and blood samples were collected from the infertility clinic, at Kamal Al- Samurai Specialist Hospital. The study was approved by the local Ethics committee

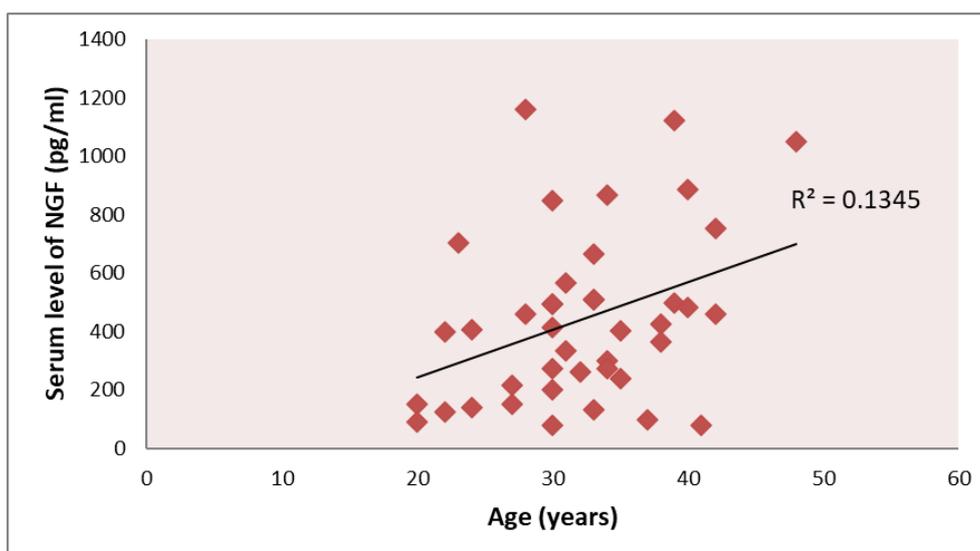
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Table 1. Characteristics of the study population of infertile males

Factors	Characteristics	Numbers	Percentage
Age (years)	20-29	24	29.62963 %
	30-39	43	53.08642 %
	40-49	14	17.28395 %
Body Mass Index (kg/ cm ²)	18.5- 24.9	29	36.70886 %
	25- 29.9	29	36.70886 %
	> 30	21	26.58228 %
Smoking	yes	60	74 %
	no	21	26%
Infertility Duration (years)	2-5 years	42	52 %
	More than 5 years	39	48%

**Fig. 1.** The correlation between serum level of NGF and age in patients with oligoasthenozoospermia

of the Hospital. Information about the participation, including age, height, weight, body mass index (BMI), alcohol status, smoking status, fertility history, and occupation was obtained.

Collecting and Analyzing Samples

Semen samples were collected and examined according to the 2010 guidelines by the WHO.

Measurement of NGF in blood and seminal fluid

NGF calculation was assessed using an enzyme-linked immunosorbent assay (ELISA) kit (E-EL-H1205, USA) as described in our previous study. (Abdulrahman, et al. 2019)

Statistical analysis

Statistical analysis was accomplished with Statistical Package for Social Sciences (SPSS) (version 23.0, SPSS Inc., Chicago, IL, USA). The independent correlation of NGF and (age, BMI, smoking and infertility duration) with semen parameters was tested by linear regression analysis with Pearson's correlation test.

RESULTS

Characteristics of the study population of infertile males

Mean values for age and Body mass index did not significantly different between studied groups. The mean

age range of the infertile men was (32.4±1.0971) years in asthenozoospermic males and (31.122±1.005) years in oligoasthenozoospermic males.

Age

The infertile males were classified into three groups according to their age (Table 1). Although, there was no significant difference in age of infertile men, the serum level of NGF had positive correlation coefficients with age ($r= 0.0367$; $p<0.018$) (Fig. 1) in oligoasthenozoospermic subjects; yet the correlation does not reach a significant level in total infertile males (asthenozoospermic and oligoasthenozoospermic). Age positively correlated with the seminal level of NGF, although the correlation was not significant; it is still applicable to keep it in the comparison.

We found that there was no significant correlation between age and semen parameters, but age negatively correlated with sperm concentration, the percentage of normal sperm morphology and ejaculate volume.

Body Mass Index (BMI) factor

Based on BMI and the cataloguing and assessment standards of the WHO, the infertile males were divided into three groups. The percentage of these groups is shown in Table 1. No statistically significant relationships were found between BMI and sperm parameters. Correlation analysis showed no significant

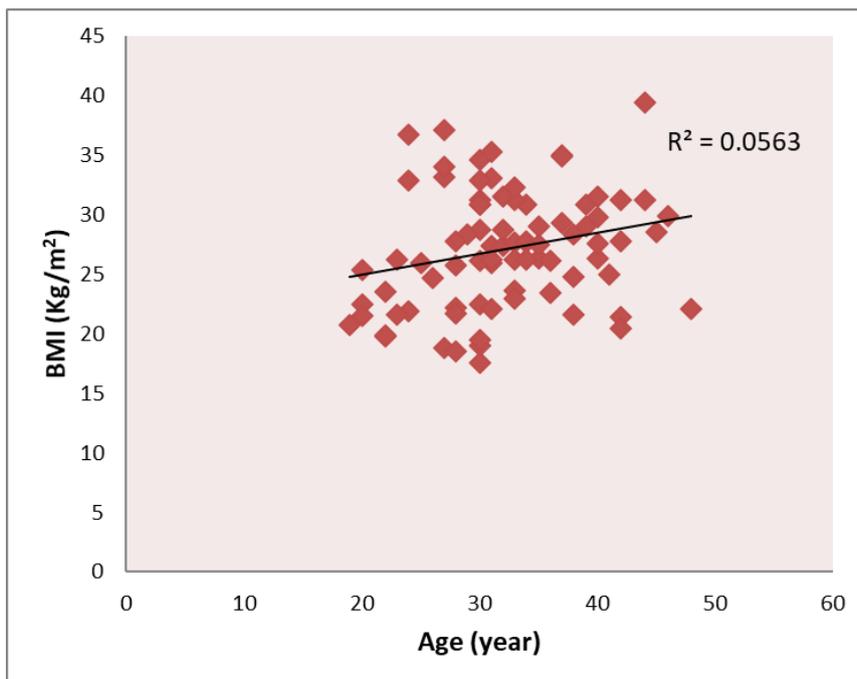


Fig. 2. The correlation between serum level of BMI and age in patients with asthenozoospermia and oligoasthenozoospermia

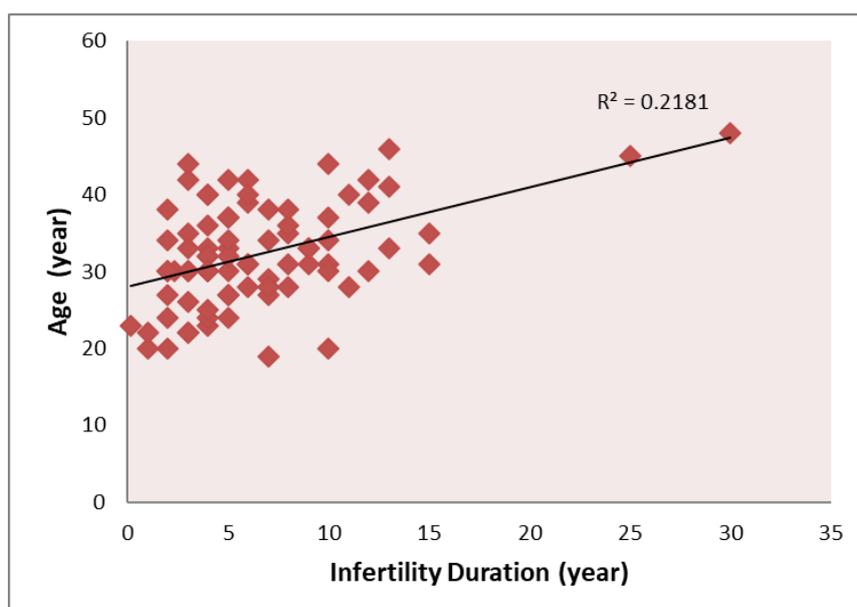


Fig. 3. The correlation between age and infertility duration in patients with asthenozoospermia and oligoasthenozoospermia

relationship between BMI serum and seminal plasma NGF levels. However, BMI positively correlated with age ($r=0.237$; $p<0.033$) (**Fig. 2**).

Smoking

Among the 81 patients studied, 74% of subjects were a smoker, and 26 % of subjects were non- smoker (**Table 1**). There was no statistically significant difference in any of the semen parameters or the

concentration of NGF in serum or seminal plasma between smoking or non-smoking patients.

Infertility duration

The mean infertility duration was 6.2672 ± 0.429 years. The percentage of infertile males, according to their infertility duration, is shown in **Table 1**. The result of the current study analysis showed that infertility duration among men had a significantly positive correlation ($r=0.466$, $p< 0.01$) with age (**Fig. 3**).

DISCUSSION

The exact cause for decreasing semen parameters is not clear. However, it may be related to environmental, nutritional, and modifiable lifestyle factors or other unknown reasons (Carlsen, et al. 1992, Magnusdottir, et al. 2005). Aging contributes considerably to human infertility by a range of issues; most studies inspecting fertility status suggest a relationship between male age and semen quality. A decrease in semen volume, sperm morphology and sperm motility, but not with sperm concentration was correlated with increased male age (Kidd, 2001).

The previous study showed that the levels of NGF in human sera revealed no significant differences with age; although an inclination to a reduction appeared to occur over the age of 40 years. Correspondingly, no significant relationship existed between NGF levels in normal human sera and age (Serrano, Lorigados, & Armenteros, 1996).

Correlation analysis showed no significant relationship between BMI serum and seminal plasma NGF levels. The results of the index study are in contrast with the documented significant correlation between plasma levels of NGF with BMI in non-morbidly obese women (Bulló, et al. 2007). BMI positively correlated with age. There is still argument as to how body mass index affects male reproduction. Negative associations between BMI and sperm parameters, serum levels of anti-Müllerian hormone, serum levels of testosterone and sex hormone is well proven, et al. 2015) whereas LH and FSH appear to be unaffected by high BMI (Chavarro, et al. 2010).

Infertility duration is another reason that affects the feature of the life of infertile couples. This leads to failure in relationships and sexual activity of the couples. Studies have regularly revealed that increasing male age is related to an increased period of pregnancy and reduced pregnancy proportions. Studies showed that erectile dysfunction increases with age (Rosen, et al. 2005).). Subsequently, reduced sexual activity can weaken the probabilities of conception (Weinstein, & Stark, 1994).

The result of the current study analysis showed that infertility duration among men have a significantly positive correlation with age. The result of this study was in agreement with a study by Agustina D *et al.*, which found that age affected infertility among men, and it was statistically significant with age ≥ 40 years (Agustina, Budihastuti, & Murti, 2018). Another study reported that male age was associated with infertility duration (Liu, et al. 2017) ; that the prevalence of infertility increased after 35 years of age (Somigliana, et al. 2016).

CONCLUSION

The concentration of NGF in seminal plasma and serum has no significant correlation with smoking, BMI and infertility duration yet the concentration of NGF in serum was positively correlated with age.

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