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The measure of IL- 33 level in bacterial prostatitis and associated development men infertility in AL Najaf governorate, Iraq

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Abstract

Background: Interleukin -33 is a cytokine that has role pro- and anti-inflammatory effects engaged in the development of many inflammatory diseases. The current study tested the relationship between bacterial prostate inflammation and IL-33 serum levels in the development of infertility in male.

Aim: The current study aimed to estimate the part that bacterial prostate inflammation and IL-33 function in the development of infertility in male in Najaf governorate.

Method: The patients (120) were examined at the infertility unit in AL-Sadder Medical City, Al-Najaf governorate during the period from January to May of 2022. The patients were divided into categories: 60 prostatitis-related infertile men, 30 prostatitis-fertile men, and 30 infertile men compared with 30 healthy fertile men. Taken blood to measure IL-33 concentration by ELISA and semen samples were to identify the bacterial etiology as well as liquefaction of semen, appearance, volume, and basic sperm properties in the remaining semen (motility, viability, density, and morphology).

Result: The current study saw that patients with Prostatitis had greatly higher serum concentrations of IL-33 than infertile patients, the results were statistically significant ($p < 0.05$). In addition, IL-33 concentration increased with the severity of the disease.

Conclusion: The Present study establishes a connection between the infection with prostatitis and infertility, which is reflected in the immune response of the body at a higher level of IL-33.

Keywords: IL-33, prostatitis, men, infertility, Najaf

Introduction

Cytokines are Small proteins secreted by cells in the body and play a role in communication and interaction between cells. They have many names of which interleukin (Made by one white blood cell and act on another white blood cell) [1]. Cytokines may be Pro-inflammatory cytokines are resulted by macrophages activation and are shared in regulated of inflammatory or anti-inflammatory cytokines that rule the response of pro-inflammatory cytokine [2]. Cytokines, which may result in male infertility [3].

Interleukin 33 belongs to the IL-1 family of cytokines that has the ability to stimulate a number of cells in the body such as mast cells and Th2 cells, and basically expressed in lining and structural cells involving epithelial, endothelial, and fibroblasts cells of lungs, gastrointestinal tract, and skin [5]. Interleukin33 is released from nucleus of epithelial and endothelial cells in response to cellular stress and have an important role in the innate immunity of the intestinal mucosa and lungs [5, 6] it was primarily identified as NF-HEV "nuclear factor from high endothelial venules" [7] and acts by binding to its plasma membrane receptors and recruiting the IL-1RAP receptor extra protein by pathways similar to those of family [8]. Also IL33 / st2 pathway plays a protective role in metabolism and glucose balance, but it may cause tissue damage, so it is either anti-inflammatory or a stimulant, depending on the disease [9] in inactive cases, IL-33 is bear in the nuclei of cells and linked to chromatin [10]. Various from other cytokines, where IL-33 is released passively in its full-length shape through necrosis of cells, or activation of cells via ATP signaling without the death of cells or destruction of tissues, which suggests it may role as an alarmings for the immune system following the destruction of an endothelial or epithelial cell through infection, shock or somatic tension [11].

Infertility, which is defined as the inability to conceive after trying for a while without using birth control, has increased in prevalence during the past several decades. Worldwide, millions of people of reproductive age experience infertility, which has an impact on their families and communities [12]. More than 186 million individuals worldwide, mostly in developing nations, suffer with infertility [13].

Prostate gland has important role in reproduction of the male, and prostatitis is a correctable reason in infertility of men [14]. It is a common problem where do not conceive after a year of marriage, even though they do not use contraceptive (WHO). 5% from cases of infertility have part of the male factor and 12% of men infertility etiology result from infections of genital tract including inflammation of prostate gland [15]. Bacterial prostatitis is a common disease in (8-16) % of young to middle – aged gland being exposed to a bacterial infection, which can be acute or chronic infection. It is caused by infection with a member of family of Enterobacteriaceae, especially *E. coli* in addition *proteus* and *pseudomonas* and some gram – positive bacteria (14). The current study aimed to measure the level of interleukin-33 among patients with bacterial prostatitis and its association with the development of infertility in men in Najaf Governorate.

Method

The current study included 120 patients samples Who they came to Al sadder medical city/AL Najaf governorate for period January to May of 2022 the patients divided into categories: 60 prostatitis – related infertile men, 30 prostatitis fertile men, and 30 infertile men and compare with 30 healthy fertile men. IL-33 evaluated by used ELISA technique [Elab science@ company, China]. Taken (3 ml) of patient blood and placed in test tube for get serum and kept at -20 °C. Examined the semen to identify viability, motility, density and morphology, know bacterial agents caused infection [16].

Inclusion criteria

Any patients sever from acute or chronic prostate inflammation.

Exclusion criteria

Any patient who take treatment or had prostate cancer, chronic orchitis/epididymitis.

The participants agreed before sharing in this investigation, agreeing that their samples and the clinical information they supplied might be used for scientific aims.

Statistical analysis

The results of the current study were analyzed using the statistical program SPSS version 2022, where the results were compared with the control group based on the p-value $P \leq 0.05$.

Result

The current study included three categories of patients, the first category includes 60 (50%) prostatitis – related infertile men, the second category includes 30 (25%) prostatitis fertile men, The third 30 (25%) infertile men and compared with 30 healthy fertile men. The ages of the study samples ranged between (20 - 50) years where the age category (31-40) years more infection and as shown in and as shown in

(Table 1) and they were classified according to grade, (Table 1).

The study sample was subdivided into oligozoospermia, asthenozoospermia and teratozoospermia. Asthenozoospermia was 38 (63.3%), oligozoospermia was 14(23.3%), and teratozoospermia was 8(12.9%). 30 healthy people were used as the control group, as seen in Table (2).

Three infertility grades among patients of infertile, grades 1, 2, and 3, in infertile prostatitis patients was notable at 6.67%, 46.67%, and 46.67%, respectively. However, infertile patients were noted at 23.33%, 60.0%, and 16.67% respectively. The majority of infertile prostatitis patients with asthenozoospermia are present in large numbers within the 2nd and 3rd degree (45.95%, 48.64%), respectively, while the infertile patients who suffer from asthenozoospermia are mostly of the second degree (88.89%), while the first grade in patients suffering from oligozoospermia is high in infertile patients and patients with prostate infertility (41.18%, 13.33%) respectively. Table (3). Patients with prostatitis, prostatitis-related infertility, and infertility recorded a significant increase in the level of interleukin-33 compared to the healthy group ($p < 0.05$). Figure (1). Mean, Std. Deviation and Range were calculated for the criteria of the study sample. Table (4).

Discussion

The prostate gland, which plays a role in the process of ejaculation that ends with the fertilization of the egg, is the target of a number of diseases that affect male fertility through its effect on the performance of sperm, including bacterial prostatitis [17]. Which plays a hidden role in generative failure in men, due to its ability to intervene with function the reproductive for males and females, causing infertility. Despite the existence of a lot of research that revealed the negative impact of these bacteria on male fertility, there is still a need to understand the molecular system for bacterial effect on the reproductive system of males [18].

Our study showed that the majority of people with prostatitis are in the age group of (31-50) years, and this was confirmed by previous studies, In the report by [19], people with prostatitis had a range of 30-55. Also [20] saw that fertility is lot impacted by prostate inflammation, with a peak between (36-50) years. According to [21], inflammation of the prostate was shown to rise in old more than 40 years. This is associated with the change that occurs in the movement of the sperm and the abnormalities that occur in the sperm. It is also associated with an increase in the destruction of the genetic material of the sperm, which all play a role in male fertility. In addition, according to what was confirmed by the World Health Organization [16] that distortions of the external appearance of the sperm, lack of sperm concentration, and low movement of sperm are among the most causes of infertility in men. This is proven by our current study, where oligospermia and asthenospermia were among the most common causes of infertility in the sample of patients studied, and this is consistent with what was recorded by [22], which proved that males who suffer from asthenospermia have higher levels of infertility, as well as Study [23], which confirmed that asthenospermia A cause of infertility, especially in the ages (30-50) years. And [24], which proved that asthenospermia constitutes 20% of the causes of male infertility, This may contradict somewhat [25] who found that oligospermia is the

most common cause, followed by asthenospermia and then teratozoospermia.

The results of our current study proved that interleukin-33 is important in regulating the immune response as it is an indicator of proinflammatory and anti-inflammatory, as it was seen that the high level of interleukin-33 was associated with infertility in males, as its level was high in infertile people and those with infertility and inflammation of the prostate gland compared to healthy men. This can be explained where cytokines are a portion of the natural factors in the plasma of semen and are necessary for the natural physiology of men's reproductive. However, in numerous pathological cases, their levels rise and negatively affect the function of sperm (1). Due to the negative effect of cytokines on sperm functions and its presence in some pathological conditions, such as Interleukin 33 which a role in the process of regulating immune cells and tissue response in many diseases that affect humans, but there is still little information about biologically active forms of them in the human body [26] So the level of interleukin. 33

was measured to find out relationship between infertility and prostatitis in human [27].

When any tissue damage, infection, or inflammation occurs, interleukin-33 will be released as an alarm signal for the purpose of response, which is a multidirectional cytokine that regulates pathological and physiological responses [28]. The researcher predictor in etiology of the no capability of sperm to fertilizing in prostate inflammation is resulting from imbalance of TGF-B and IL-18 as regulators of immune cases of the system of reproductive, where found a significant raise in the IL-18 and IFN-y against significant lack in the TGF-B and IL-7 [29]. Lately Chatrabnous *et al.*, [30] found rise levels of IL-33 in the serum of patients smitten by cancer of prostate. An good discovery interesting the found of IL-33 and its receptor ST2 in fluid of human follicular [31]; yet, then studies are needful to scout the turn of IL-33 in male and female system of reproductive.so studies are required to find the role of IL-33 in women's and men's genital systems.

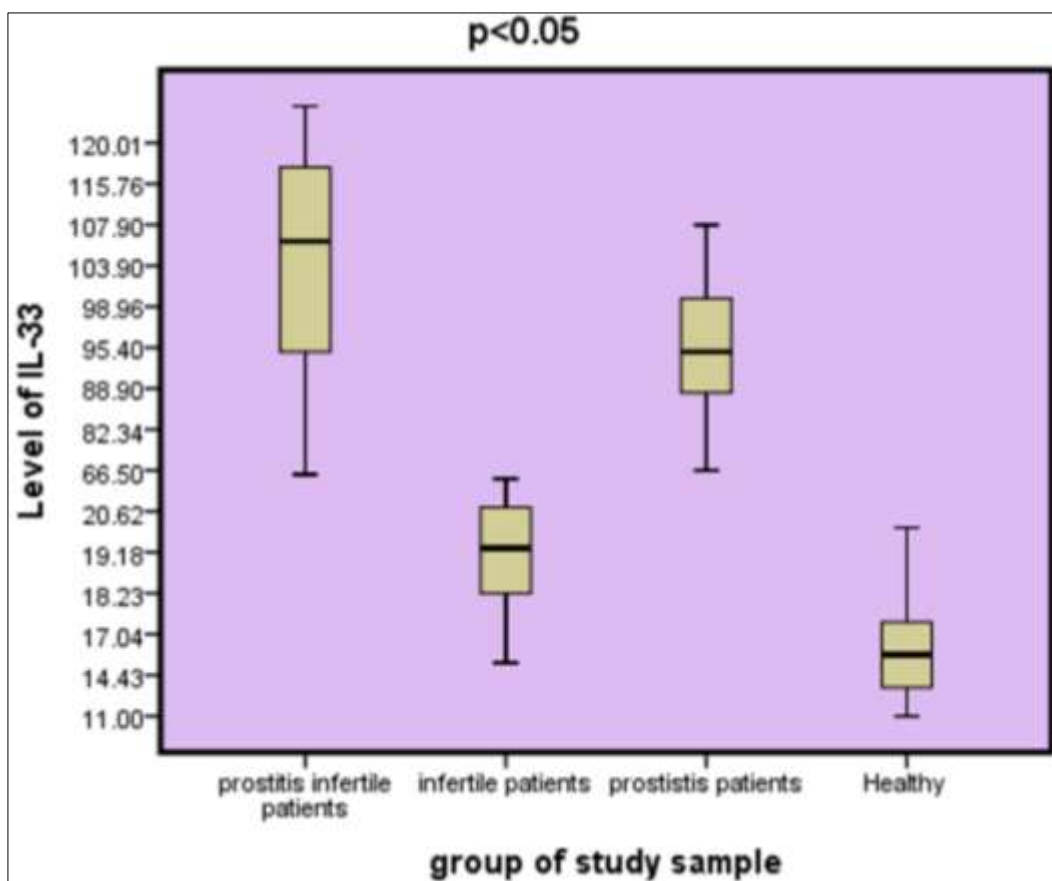


Fig 1: IL-33 concentration in patients of prostatitis infertile, infertile, prostatitis compared with healthy group

Table 1: Distribution of patients on base of age

Age	Prostatitis infertile N=60	Prostatitis fertile N=30	Infertile N=30	Healthy N=30
20-30	22(36.67)	3(10.0)	13(42.33)	18(60.0)
31-40	27(45.0)	14(46.67)	13(43.33)	12(40.0)
41-50	11(18.33)	13(43.33)	4(13.34)	-
Total	60	30	30	30

Table 2: Distribution of abnormality of sperm of patients

Abnormality of sperm	Prostatitis infertile N=60	Infertile N=30	Prostatitis fertile N=30	Healthy N=30
oligozoospermia	23.3%)(14	17(58.1%)	Nil	Nil
Asthenozoospermia	38(63.3%)	9(29%)	Nil	Nil
Teratozoospermia	8(12.9%)	4(12.9%)	Nil	Nil

Table 3: Distribution of Type and infertility grade of patients

		Grade			Total	Percent%
		Grade 1	Grade2	Grade3		
Prostatitis infertile	Oligozoospermia	2	7	6	15	25%
	Asthenozoospermia	2	17	18	37	61.67%
	Teratozoospermia	0	4	4	8	13.33
	Total	4	28	28	60	100%
Infertile patients						
Oligozoospermia		7	6	4	17	56.67%
Asthenozoospermia		0	8	1	9	30%
Teratozoospermia		0	4	0	4	13.33
Total		7	18	5	30	100%

Table 4: Show some statistical processes of IL-33 Level in the study sample

	level of IL-33 in prostatitis infertile patients	level of IL-33 in infertile	level of IL-33 in prostatitis	level of IL-33 in healthy
Mean	105.4425	19.5687	93.1233	15.8135
Std. Deviation	19.41417	2.22943	9.61657	2.32987
Minimum	66.08	15.13	66.50	11.00
Maximum	173.34	25.14	107.90	20.13
Range	107.27	10.01	41.40	9.12

Conclusion: The Present study establishes a connection between the infection with prostatitis and infertility, which is reflected in the immune response of the body at a higher level of IL-33.

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