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Study the Level of Cytokine in Unexplained and Idiopathic Infertile Men

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Abstract

Fertility in the male is dependent on the proper production of sperm cells. This process, called spermatogenesis is very complex and involves the synchronization of numerous factors. The presence of pro–inflammatory cytokines play important role in male infertility . Data analysis from unexplained infertility (n=50), idiopathic infertile men (Asthenozoospermia (n=50), Oligozoospermia (n=50)), and Normospermia fertile men as a control (n=26). Show a significant interleukin 17 level was reduced in unexplained infertility (mean± Std. Error 351.23±8.92 also reduced in Asthenozoospermia 286.76±18.61and Oligozoospermia 271.71±18.32 while significant increase was observed in Normospermia fertile men 390.74±5.43.

A negative correlation was found between interleukin 17 level, And the sperms concentration, Sperm Progressive motility percent and sperm normal morphology present in idiopathic infertile men respectively (r= -0.589, r = -0.584 and r = -0.544). And A negative correlation was found between interleukin 17 level and the sperms concentration , Sperm Progressive motility percent and sperm normal morphology present in unexplained infertile men Respectively (r= -0.467 , r = -0.324 and r = -0.307).

The result showed a significant TGFb1 level was reduced in unexplained infertility (mean± Std. Error 71.24± 1.19 also reduced in Asthenozoospermia 109.54±6.31and Oligozoospermia 202.22± 5.83 while significant increase was observed in Normospermia fertile men 68.3±0.52.

A negative correlation was found between TGFb1 level, And the sperms concentration, Sperm Progressive motility percent and sperm normal morphology present in idiopathic infertile men respectively (r= -0.444, r = -0.462 and r = -0.464). And A negative correlation was found between TGFb1 level and the sperms concentration , Sperm Progressive motility percent and sperm normal morphology present in unexplained infertile men Respectively (r= -0.693 , r = -0.234 and r = -0.399). The present study conclude that importance role of cytokines in infertile men and it had a negative correlation with sperm parameter.

Keywords -Cytokine, Interleukin 17, TGF-β1, unexplained male infertility, idiopathic male infertility.

INTRODUCTION

Sperm functions are an important factor for successful fertility, Sperm dysfunction is the most common cause of male infertility [1]. More importantly, it has been reported that sperm function is associated with the quality of the sperm genome apparatus, show high DNA fragmentation [2] Cytokines are secrete by several cells, Cytokines are small peptides are involved in different immune activities [3]. They bind to receptors of target cells and induce a signal transduction, Signal transduction induced by cytokines, which regulate cell growth, proliferation, differentiation and other functions [4]. Cytokines produced by the testes immune cells, interstitial cells, sertoli cells and spermatogonia cells all regulate growth and differentiation of germ cells, reproductive neuroendocrine and spermatogenesis [5]. Impaired cytokine secretion can affect function of the reproductive system and may lead to infertility [6].

Numerous immune regulatory functions have been reported for the IL-17 of cytokines, presumably due to their induction of many immune signaling molecules. The most notable role of IL-17 is its involvement in inducing and mediating proinflammatory responses. IL-17 is commonly associated with allergic responses. IL-17 induces the production of many other cytokines, chemokines and prostaglandins from many cell types. IL-17 acts with IL-22 (produced by T helper 17 cells) to induce expression of antimicrobial peptide by keratinocytes.[7]

The release of cytokines causes many functions, such as airway remodeling, a characteristic of IL-17 responses. The increased expression of chemokines attracts other cells including neutrophils [8]. IL-17 function is also essential to a subset of CD4+ T-Cells called T helper 17 (Th17) cells. As a result of these roles, the IL-17 has been linked to many immune/autoimmune related diseases including rheumatoid arthritis, asthma, lupus, allograft rejection, anti-tumour immunity and recently psoriasis [9].

Transforming growth factor beta 1 or TGF-β1 is a polypeptide member of the transforming growth factor beta superfamily of cytokines. TGF b1 performs many cellular functions, including the control of cell growth, cell proliferation, cell differentiation and apoptosis. In humans, it is s encoded by the TGFB1 gene [10].

TGF-β is a set of peptides with multifunctional properties that controls proliferation, differentiation, and other functions in many cell types [11].TGF-β acts with TGFA in inducing transformation. It also acts as a negative autocrine growth factor. Dysregulation of TGF-β activation and signaling can result in apoptosis [12]. Many cells synthesize TGF-β and almost all of them cells carry a specific receptors for this peptide. TGF-β1, TGF-β2, and TGF-β3 all function through the same receptor signaling systems [13].

The TGF b1 secretion from the testis, which have many cellular functions Such as lyding cells testis development and spermatogenesis, these TGFb1 cells that are found in the somatic cells and germs cells in the testis [14].The tgfb1 Play an important role in male reproductive system by providing physiological characteristics of the testes.[15].

In a study conducted by Sarmistha et.al., 2004 on male subjects with spinal cord injury these study include 31 male in a good healthy after the injury , semen was collected from the patients 4 weeks after their injury. Blood was also collected for concentration of TGFb1. The study found a decrease in TGFb1 concentration compared with other healthy male as a control group, Promise reason the TGFb1 decrease with inflammatory, The study was found an abnormal increase in Sperm morphology with increase with White blood cells.

In another study conducted on males with varicocele to examine the concentration of TGFb1. These study included 100 males with varicocele and was divided into two groups oligoasthenozoospermia and normospermia. In addition 100 male subjects were included as control groups. Semen and blood samples were collected after 3-5 days of sexual abstains. The results show a significant increase between the two groups As well as significant difference between the affected and control group. The study concluded that this increase is associated with a decrease sperm and semen parameter [17].

MATERIALS AND METHODS

Semen and serum specimens were collected from infertile normospermic patients (unexplained infertile male), idiopathic

unfertile men include (Asthenozoospermia and Oliegozoospermia)in addition to control group (Fertile Normozoospermia) that attended to fertility center. The average age of infertile patients was (32.99±32) years, the samples were collected are 521 and sample which tested are 176 samples, the sample which obtained from control group (fertile) was 26 samples (Normozoospermia), and 50 samples from Asthenozoospermia , 50 sample from Oliegozoospermia and 50 samples from unexplained infertile male. A biochemical test was performed on (176) samples had been measured IL 17 by immunological method (Enzyme-Linked-Imuno-Sorbent- Assay) by using ELISA reader (Huma Germany origin). All specimens and reagents must be allowed to come to room temperature before use. All reagents must be mixed softly without foaming. Once the procedure has started, all steps must be completed without interruption, and biochemical tests were conducted in the laboratories of Biology Department/ faculty of Sciences/ University of Kufa. The ELISA kits used in this study was (IL 17) (E-EL-H0105) and TGFb1 (DE1864) Elabscience Company USA in Origin).

RESULTS

The result showed a significant interleukin 17 level was reduced in unexplained infertility (mean± Std. Error 351.23±8.92 also reduced in Asthenozoospermia 286.76±18.61and Oligozoospermia 271.71±18.32 while significant increase was observed in Normospermia fertile men 390.74±5.43.

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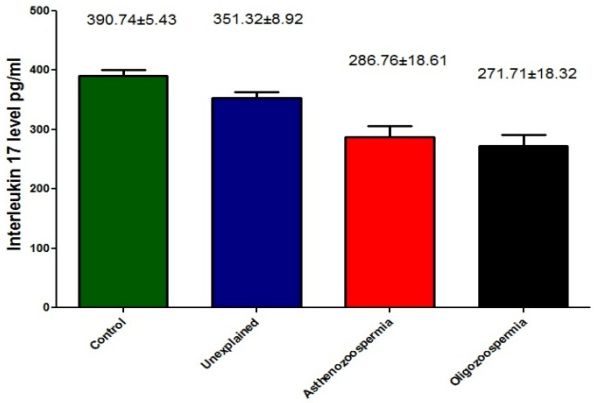

Figure (1): The comparison of IL17 level in the serum between Asthenozoospermia, Oligozoospermia, Unexplained infertile men with fertile men (control). b. This mean significant decrease ($p<0.05$)

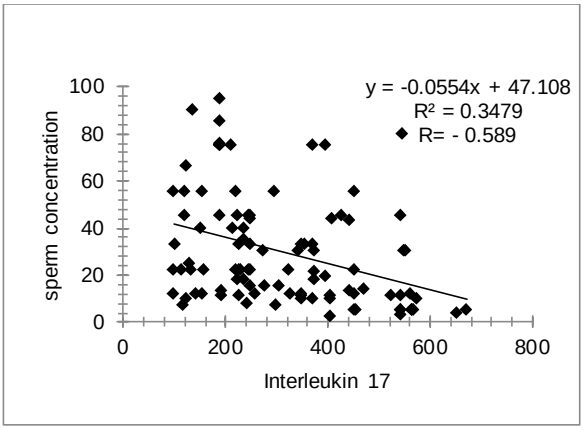

Figure (2): The correlation between Interleukin 17 with sperm concentration in idiopathic infertile male.

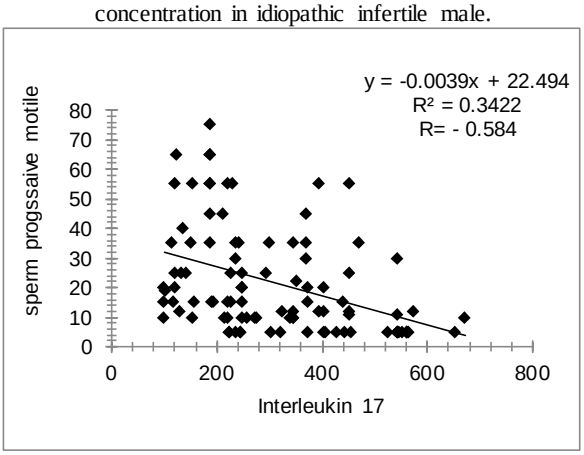

Figure (3): The correlation between Interleukin 17 with Sperm Progressive Motility in idiopathic infertile male.

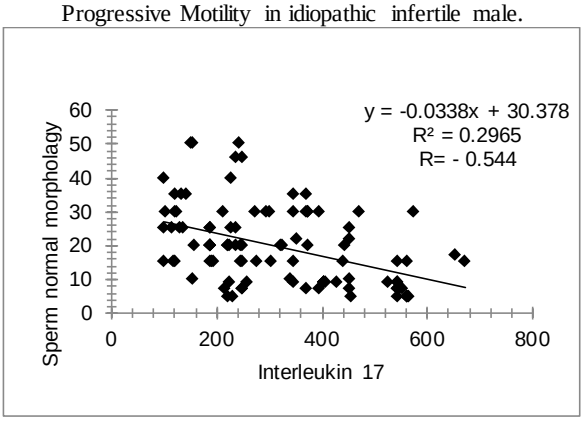

Figure (4): The correlation between Interleukin 17 with sperm normal morphology in idiopathic infertile male.

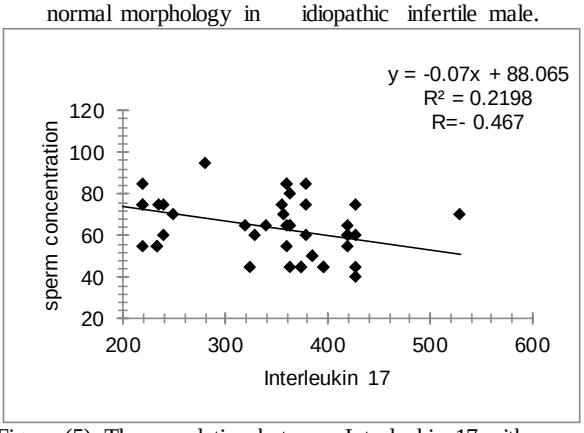

Figure (5): The correlation between Interleukin 17 with sperm concentration in unexplained infertile male.

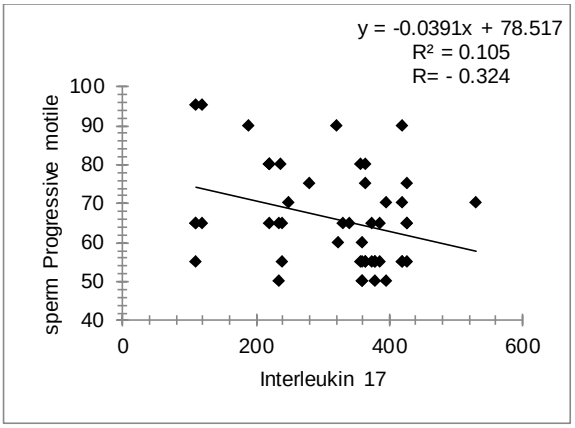

Figure (6): The correlation between interleukin 17 with Sperm Progressive motility percent in unexplained infertile male.

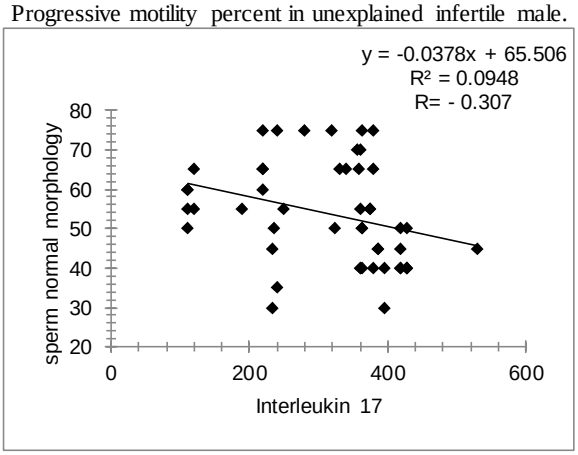

Figure (7): The correlation between interleukin 17 with sperm normal morphology in unexplained infertile male.

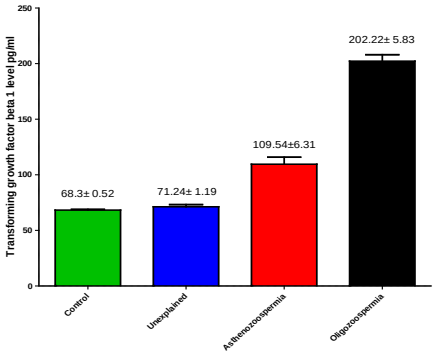

Figure (8): The comparison of TGFb1 level in the serum between Asthenozoospermia, Oligozoospermia, Unexplained infertile men with fertile men (control). b. This mean significant decrease ($p<0.05$)

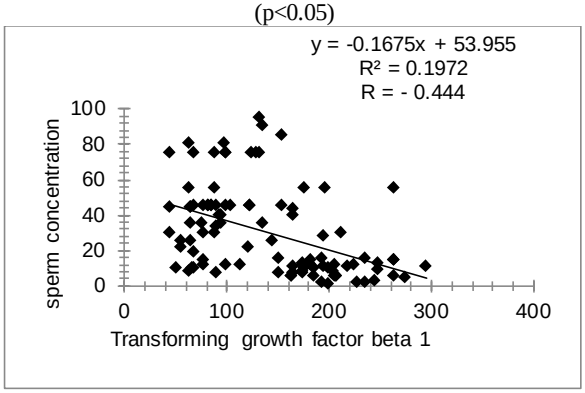

Figure (9): The correlation between transforming growth factor beta 1 with sperm concentration in idiopathic infertile male

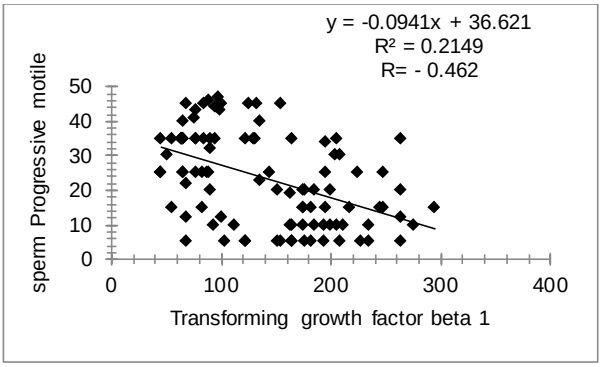

Figure (10): The correlation between transforming growth factor beta 1 with sperm Progressive motile in idiopathic infertile male

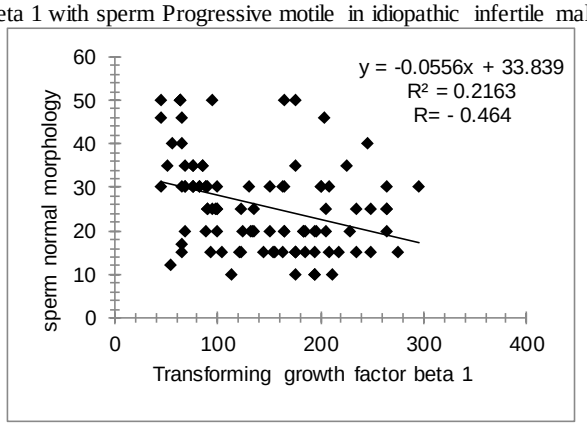

Figure (11): The correlation between transforming growth factor beta 1 with sperm normal morphology in idiopathic infertile male

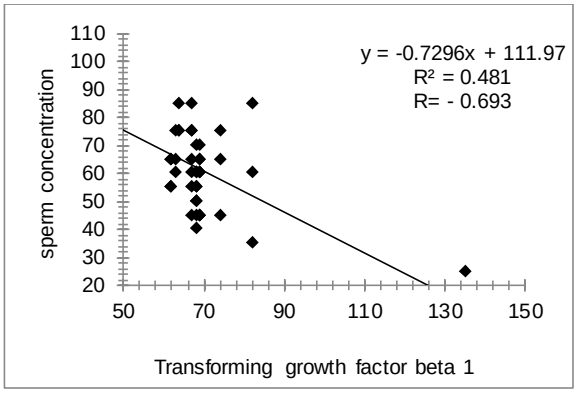

Figure (12): The correlation between transforming growth factor beta 1 with sperm concentration in unexplained infertile male.

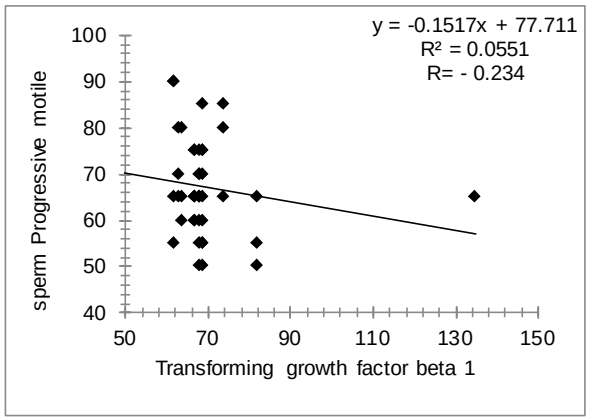

Figure (13): The correlation between transforming growth factor beta 1 with sperm Progressive motile in unexplained infertile male.

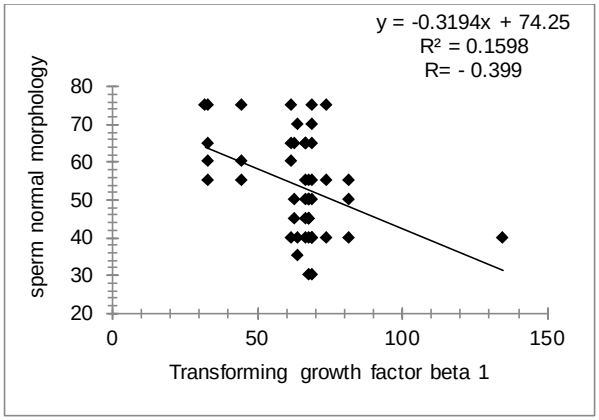

Figure (14): The correlation between transforming growth factor beta 1 with sperm normal morphology in unexplained infertile male.

DISCUSSION

The present study Show cytokine level (interleukin 17 and TGFb1) was significant decrease in unexplained infertility, Asthenozoospermia and Oligozoospermia compare with Normospermia fertile men may be due to increase evidence that sperm necrosis can adversely affect spermatogenesis [18]. The present study also show that cytokine level a negative correlation was found between cytokine level, with sperms concentration, Sperm Progressive motility and sperm normal morphology in idiopathic and unexplained infertile men, these result agree with study that show negative correlation was found between cytokine level, with sperms concentration, Sperm Progressive motility and sperm normal morphology (19). The cytokine level that effect by accompanying with spermatogenesis cause by increase free radicals (20).

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