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The Impact Of Tnf- A , Il17 , Fsh And Lh On Male Infertility In Al-Najaf Province

Muntadher Jihad Jahil[1], Mohamed Abdulrazzaq Assi[2,3]
[1]Department of Medical Analytical Techniques , College of Health and Medical Techniques / Kufa,-Al_Furat Al_Awsat Technical Unuversity, 31003 Al-Kufa, Iraq .[1]
[2]Department of Anesthesia Techniques Techniques, College of Health and Medical Techniques/ Baghdad, Middle Technical University, Iraq.
[3]Department of Medical Laboratory Techniques, Institute of Medical Technology Al-Mansour, Middle Technical University, Iraq.

Abstract *:*
Male infertility is one of more common disease around the world , there are many factor affect on infertility or subfertility such as hormonal imbalance , inflamatory and proinflamatory cytokine , tumor necrosis factor alpha , Interleukin -17, FSH and LH associated with impaired spermatogenesis . the aim of this study to investigation TNF-α , IL-17,FSH and LH in serum for male infertility and compare with fertility as well as the association with semen parameter . A case control study involved 60 infertility group and 30 fertility group the blood serum was collected and measured using ELIZA device while semen parameter measuring according to WHO 2021 guide line . The infertility men show high level in proinflamatory cytokine TNF-α and IL-17 compared to fertility group and decrees the level of gonadotropic hormone in infertility group compared with fertility group , age ,ejaculate volume ,concentration ,motility and morphology found associated with elevated of inflammatory cytokine as well as hormonal imbalance. In conclusion chronic immunity inflammation and hormonal disturbance affect on fertility so the TNF-α , IL-17,LH and FSH can regard as a biomarker for monitor and treatment male infertility.
Keyword *: Male infertility , TNF-α , IL-17, LH,FSH, Inflammation*

INTRODUCTION

male infertility is on of the more common issue around the world (1). in Iraq the rate of male infertility begin increases , there are many factors affect on this rate such as hormonal imbalance , environmental condition ,life style also another factor contribute in disturbance or impaired in immune system , tumor necrosis factor alpha and interlukin 17 is inflammatory cytokine that affect directly on testes that play critical role in immune response and inflammation ,increase the level of this cytokine associated with impaired sperm and inflammation in reproductive tract that contribute in male infertility , tumor necrosis factor alpha stimulus apoptotic sperm cell (2).TNF-α found in reproductive organ in few amount and responsible for regulation and development sperm cell , maintained immunity homeostasis inside the testes and support leyding cell and sertolly cell , elevated the level of TNF - α during inflammation lead to impaired spermatogenesis and increase reactive oxygen species (ROS) (3). On the other hand interlukin – 17 responsible for response to inflammatory cell and critical role in blood testes barrier ,elevated of this cytokine lead to enter inflammatory cell inside the testes , new research found elevated in the IL-17 associated with increase oxidative and destroy cell membrane for the sperm lead to decrease fertility rate (4) in Iraq study found IL- 17 elevated in infertility group compared with fertility group ,this indicate that there are association between IL-17 impaired in sperm production (5). Also many study indicate association between the inflammatory cytokine with abnormal sperm as well as with sperm concentration , sperm motility and sperm morphology in al-najaf province in the last years become suitable environment for recurrent inflammation so the association study between this cytokine with male infertility become essential for identify this disease in a curase form . The Follicular stimulating Hormone (FSH) secreted from anterior pituitary gland regulated by hypothalamic pituitary gonadal axis (HPG), in the male FSH play supporting role in testes to activation sertoli cell for activation and maintain germ cell , this hormone performed three important function , first stimulating sertoli cell for secretion Androgen Binding Protein (ABP) that maintained testosterone concentration inside the semeinefural tubal , second function maintained optimal environment for complete

mature sperm cell , third stimulate production inhibin B act as ngative feedback mechanism for suppression elevated FSH (6). Elevated in this hormone indicate primary testicular failure explain for this phenomena when increase the level of FSH the body meaning that testes not produced sufficient amount from sperm cell , acompensetory response this hormone begin increase , while decrease the level of this hormone indicate for hypogonadism causes inhibition formation germ cell and causes infertility (7). The Leutinizing Hormone (LH) Hormone secreted from anterior pituitary gland work together with FSH hormone within HPG for regulation the function of reproductive gland in the male , LH play important function for stimulating leyding cell for secretion testosterone hormone within seminiferous tube, LH control the level of testosterone inside the testes and the blood , with the same function for FSH elevated the level of LH lead to primary testicular failure while decrease the level lead to hypogonadism because both hormone controlled from (GnRH) under the influencing hypothalamus gland any disturbance in (GnRH) lead to decrease in FSH , LH , testosterone and decrease sperm production (8). So the aim of this study investigation the level of proinflamatory cytokine (TNF –α IL- 17) and Gonadotropin hormone (FSH and LH) between male infertility and fertility group additionalley study the association between TNF –α , IL- 17 FSH and LH with age and semen parameter such as concentration , motility and morphology .

METHODOLOGY

The current study was conducted as case control for the evolution the pro-inflammatory cytokine (TNF-α and IL-17) with semen quality in alnajaf province , Iraq . the study were conducted in fertility and infertility center Al-Sadr hospital, this research carry out in alforat al-Awsat for cancer research in corporation with al-amen center for research . The participated of patient that attenuated at this center divided into two group , first fertility (control) and the infertility (patient) the sample collection continues six month from (may 2024 to November 2024) . 90 sample was collected classified into two group 30 sample control group and 60 sample infertility group inclusion in this criteria age between 20 to 45years without any anatomical and genetic abnormality. Exclusion in this criteria male with chronic disease such as diabetic , hypertension and thyroid disease also without any medication and hormonal treatment at lest three months . blood collected from participant patient and put on plane tube thein separate by centrifuge at 3000 rpm and stored in deep freeze until cytokine analyze while semen sample was conducted after at least three day abstinence , the semn examining immediately according to world health organization WHO 2021 the semen exame involved concentration , motility and morphology , thein sample classify into three group (normozooospermia ,oloigozoospermia and asthenozoospermia). the level for proinflamatory cytokine (TNF –α IL- 17) and Gonadotropin hormone (FSH and LH) in serum sample were determine by ELIZA reader using the sandwich method according to manufacture instructional for Bio assay . finally the result descriptive statistic in SBSS version 26 and using T-test ,mann – wittney T test and person correlation test.

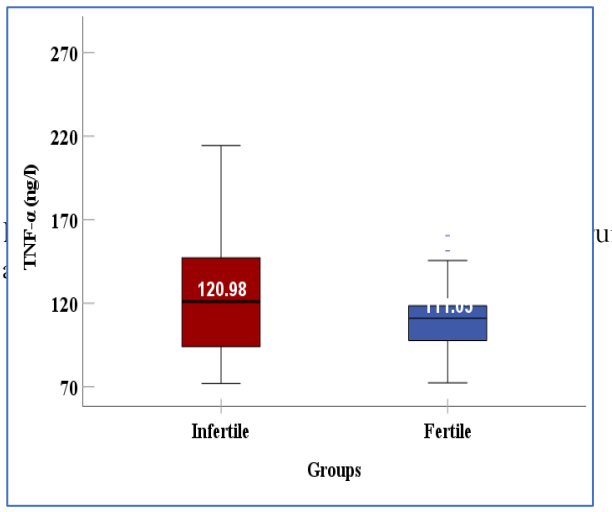
RESULT

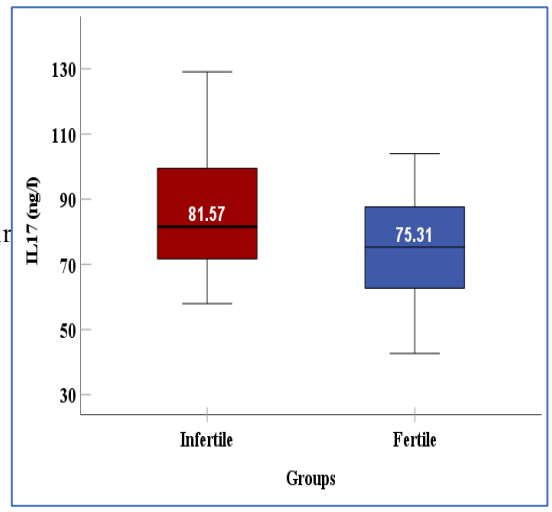
According to the present study the mean for the cytokine level was found higher in infertility group compared to fertility group as illustrated in table the study clarify the significant difference in TNF –α P value (< 0.001) and mean for infertility and fertility group (136.37±61.63, 111.13±20.2) respectively, higher IL17 in infertility group mean (85.95± 18.33) compared with fertility(74.53±18.54) P value =< 0.001. Also the gonadotropin Hormone appear highly statistically differences between two group where the mean for infertility group for FSH hormone 11.65±5.42 and the mean for LH 16.6±6.59 while the mean for fertility group is 8.4 ±4.43 , 21.61±11.06 respectively , P value =< 0.001.as illustrated in table (1) and figure (1,2,3 and 4)

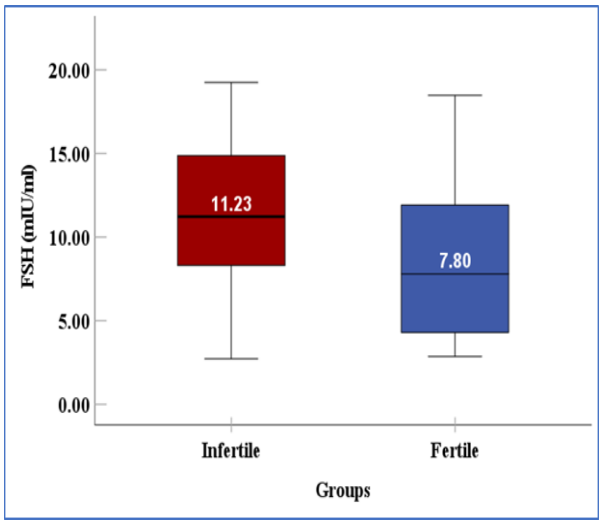
Table (1): Compression of hormone and inflammatory marker between infertility and fertility male

Parameter	Infertility group (Mean ± SD)	Control fertility group (Mean ± SD)	P- value
TNF-α	136.37±61.63	111.13±20.2	< 0.001

IL-17	85.95± 18.33	74.53±18.54	< 0.001
FSH	11.65±5.42	8.4 ±4.43	< 0.001
LH	16.6±6.59	21.61± 11.06	< 0.001







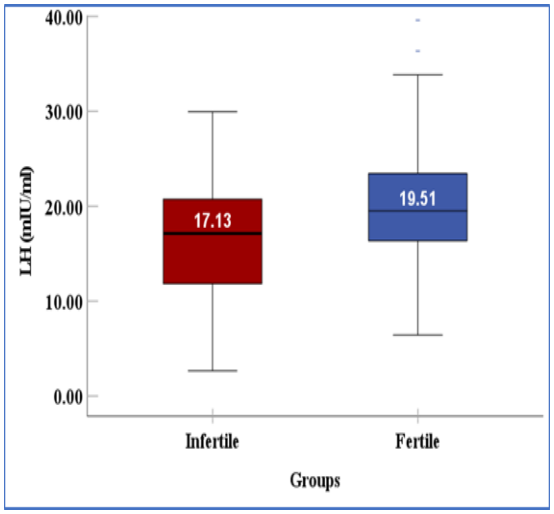


Figure (3) : level of FSH(ng/l) in infertility and fertility

figure (4): level of LH (ng/l) in infertility and fertility

According to seminal classification into three group the majority of sperm sample is Normozoospermia 60% and 22% for Oligozoospermia and 3% Asthenozoospermia as seen in figure (5) . Tumor necrosis factor alpha highest level in Oligozoospermia 175.89±83.13 fallowed by Asthenozoospermia 150.12± 7.83 and Normozoospermia 111.47 ± 24.99 . While Interleukin 17 did not differ significantly between two group p value 0.130 the mean IL17 84.74±31.39 Asthenoaoospermia , 96.77±21.01 Oligozoospermia and 79.41±12.47 Normozoospermia . Also follicular stimulating hormone statistically significant in Asthenozoospermia the mean 12.69 ±2.58 compared with Oligozoospermia 9.22 ± 4.17 and 13.08 for Normozoospermia . at last the Leutinizing hormone high significant 8.91 ± 8.81, 9.22 ±4.17 and 19.1± 6.08 for Asthenoaoospermia, Oligozoospermia and Normozoospermia respectively as seen in table (2)

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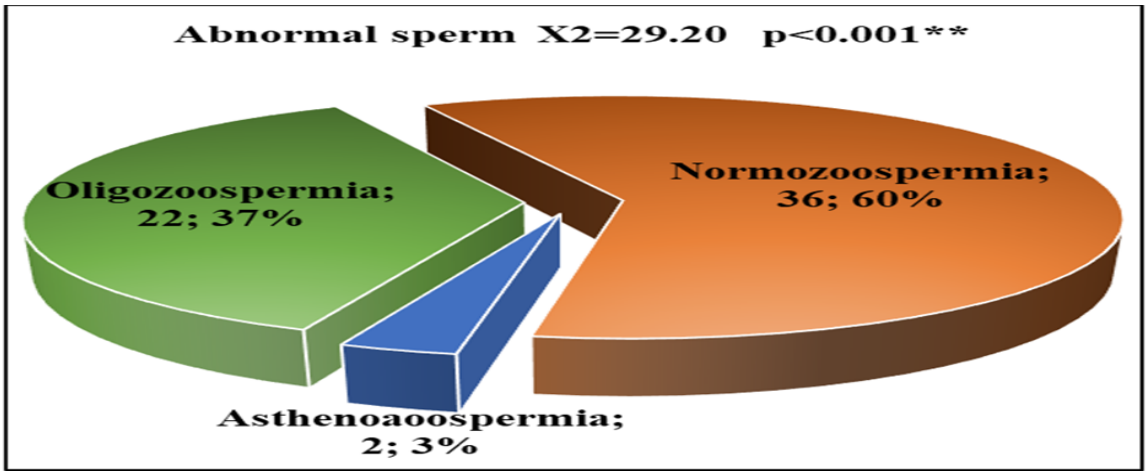

Figure (5) : classification of sperm sample in infertility group

Table (2):Association of Abnormal Sperm Classification with serum markers levels in infertile patients

Semen parameter	Abnormal sperm classification	(Mean ± SD)	P- value
TNF-α	Asthenoaoospermia Oligozoospermia Normozoospermia	150.12 ± 7.83 175.89 ±83.13 111.47±24.99	< 0.001
IL-17	Asthenoaoospermia Oligozoospermia Normozoospermia	84.74 ±31.39 96.77 ±21.01 79.41±12.47	0.130
FSH	Asthenoaoospermia Oligozoospermia Normozoospermia	12.69 ± 2.58 9.22 ± 4.17 13.08 ± 5.75	0.027
LH	Asthenoaoospermia Oligozoospermia Normozoospermia	8.91 ± 8.81 9.22 ±4.17 19.1 ± 6.08	0.0001

Also The current study show significant statistically appear between hormonal and semen parameter in infertile man , the sperm concentration appear strong positive correlation (0.539**) with LH and strong positive association between FSH hormone and sperm concentration (0.347**) both hormone appear no statesticalley variation with age , motility and ejaculate volume .The both inflammatory hormone (IL-17 and TNF- α show strong negative association with sperm concentration (-0.386** and -0.408**) for IL-17 and TNF –α respectively the proinflamatory hormone similar to gonadotropic hormone appear no statistically correlation with age , motility and ejaculate volume.

		LH (mIU/ml)	FSH (mIU/ml)	IL17 (ng/l)	TNF-α (ng/l)
Age (year)	R	-0.286*	-0.236	0.134	0.155
	P	0.027	0.070	0.309	0.237
Ejaculate volume (ml)	R	-0.149	-0.188	0.143	0.082
	P	0.254	0.151	0.277	0.532
Sperm Conc. (10^6/ml)	R	0.539**	0.347**	-0.386**	-0.408**
	P	0.0001	0.007	0.002	0.001

All progressive %	R	0.179	0.234	-0.248	-0.204
	P	0.171	0.072	0.056	0.118
Non progressive	R	0.089	0.060	0.052	0.032
	P	0.498	0.649	0.691	0.808
Immotile	R	-0.140	-0.249	0.249	0.224
	P	0.288	0.055	0.055	0.086
Total motility %	R	0.138	0.246	-0.249	-0.221
	P	0.292	0.058	0.055	0.089
Grade activity	R	0.065	0.115	-0.258*	-0.259*
	P	0.623	0.383	0.046	0.046
Normal morphology %	R	0.172	0.200	-0.136	-0.226
	P	0.188	0.126	0.301	0.082
Abnormal morphology %	R	-0.172	-0.200	0.136	0.226
	P	0.188	0.126	0.301	0.082

DISCUSSION

Inflammation in orchitis , prostate and epididymis are affect on male infertility causes leukocytospermia causes impaired in sperm motility , leukocytospermia work to activate leukocyte and active cytokine in male reproductive tract , these cytokine elevated in male infertility and causes clinical symptoms such as genitourinary inflammation , previous study on effect of TNF- α and IL-17 with semen parameter remind controversial , some study appear negative association with semen parameter (9) while other show positive correlation with semen parameter .TNF- α is proinflamatory cytokine produced mainly from macrophage in response to inflammation or infection , in natural condition TNF- α present in testes in low level and performed critical role in regulatory spermatogenesis , howover high level of this cytokine was associated with apoptosis of germ cell , blood testes barrier through affect on testicular tissue (10). The current study appear elevated the level of TNF- α associated with concentration , motility and morphology , these result agreement with previous study the possible explanation when this cytokine elevated above normal level lead to impaired sperm function by affect on mitochondria causes DNA damage (11). On the other side in present study show elevated the level of IL-17 that produced from T- helper cell play role in autoimmune response and chronic inflammation , IL-17 increase in male infertility in compared with fertility group while the result no association with semen parameter , IL-17 recurrent neutrophil by inducing TNF- α and IL-6 and other chemokine causes testicular damage especially when inflammatory become chronic , as well as elevated the IL-17 faciliting autoimmunity and damage for development of spermatozoa . Chronic elevation of both cytokine affect on both sertoliy cell and leyding cell causes imbalance in hormonal secretion required in male infertility or subfertility (12). Another an important finding is that measurement the expression of LH show lower significant in infertility male than fertility male, LH produced testosterone through stimulating leyding cells in the testes which play important role in spermatogenesis ,Male with low LH level may have dysfunction in the pituitary gland axis , so male with high level LH and low level testosterone causes testicular failure new research support this result observed hormonal abnormality especially LH have major role in productive outcome (13). The current study show the increase the level of FSH in male infertility compare with fertility male the present study confirming with the present finding(14). On of hypothesis to explain this question is that the elevated the level of FSH causes testicular dysfunction particularly sertoli cell axis , damage in semenifural tube and low inhipin –B that lead to impaired or poor in spermatogenesis causes increase the level of FSH by pituitary gland (15).

In conclusion elevated the level of proinflamatory cytokine and hormonal disturbance affect on fertility and strong associated with semen parameter so can regarded this marker in monitor and treatment of infertility .

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