Online ISSN: 2588-3526

Journal of Wildlife and Biodiversity

Volume 7 (Special Issue): 478-498 (2023) (http://www.wildlife-biodiversity.com/)

Research Article

Insights into Male Infertility: A Clinical Examination of Hormonal and Adipokine Profiles in Mosul

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Received: 29 August 2023 / Revised: 28 September 2023 / Accepted: 29 October 2023/ Published online: 28 November 2023.

How to cite: Shahadha, K.M., Al-Bajari, S., Maher, F. (2023). A clinical study to evaluate levels of hormones and adipokines of infertility patients in Mosul City, Journal of Wildlife and Biodiversity, 7 (Special Issue), 478-498. **DOI**: https://doi.org/10.5281/zenodo.10251849

Abstract

Infertility is a global concern affecting numerous couples, with hormonal imbalances and adipokines contributing to approximately half of all cases. This study explores the impact of male hormones and adipokines on infertility, measuring various parameters in the blood serum of men with and without identified reasons for infertility, as well as fertile men. Findings reveal a significant decrease in testosterone and an increase in FSH, LH, PRL, and E2 in infertile men compared to the control group. While RETN and Visfatin showed no significant differences, CHEM exhibited variations among infertile and control groups. The study establishes positive connections between certain hormones and age, smoking, and periods of infertility. Identifying these variables could aid in diagnosing and treating infertility.

Keywords: Testosterone, Hormonal imbalance, Male reproductive health, Biomarkers

Introduction

Male infertility occurs when, a man despite engaging in regular, unprotected sexual intercourse with a woman for a year, is unable to make her pregnant (Mustafa et al., 2019). Between 30% and 50% of male infertility cases are caused by problems with sperm production (Barberán et al., 2020). Any case that prevents the sperm from making contact with the egg and fertilizing it results in infertility. Anomalies in the male reproductive system may also contribute to male infertility. Male infertility can also be caused by abnormality in the sperm cell's characteristics may result in a delay in conception, and may affect men for a variety of reasons. Male hormones have a significant part in controlling the functioning of the male reproductive system and preserving fertility. Additionally, certain drugs that alter male hormones may have a detrimental impact on fertility (Abdul-razzaq, 2023; Okonofua et al., 2022). For

instance, several chemotherapy therapies and anti-tumour medications may have an impact on sperm production. To investigate and diagnose infertility, it is crucial to comprehend how male hormones affect infertility. Unbalanced levels of male hormones can cause male infertility (Murgia et al., 2020).

Here are a few key hormones and their role in male fertility: 1)Testosterone: is a hormone responsible for the appearance of masculine characteristics in men. Is produced mainly from the testicles by cells called Leydig cells (Corradi et al., 2016). It contributes at the beginning of puberty to the appearance of masculine characteristics, and it also contributes to many different functions in the body, including building muscles and bones, maintaining the distribution of fat in the body, growing facial and body hair, maintaining the production of red blood cells, sexual desire, and sperm production The growth of the sexual organs in men and the roughness of the voice (Walker, 2011). 2)Follicle-stimulating hormone (FSH): is a hormone produced by the pituitary gland and is in charge of promoting sperm production in the testes. Elevated FSH levels might be a sign of sperm production issues or testicular dysfunction (Krishnan & Muthusami, 2017). 3) Luteinizing hormone (LH): the pituitary gland also produces LH, which contributes to the creation of testosterone. It encourages the production of testosterone by the testes' Leydig cells.

The synthesis of testosterone can be impacted by abnormal LH levels, which can have an effect on the quantity and quality of sperm (Johnson et al., 2019). 4) Prolactin (PRL): is a hormone produced by the pituitary gland, that fosters women to make more milk. Hyperprolactinemia, or excessive prolactin levels, can prevent testosterone from being produced normally in males, which can result in infertility (Al-bofkane & Al-bofkane, 2021; Lennartsson & Jonsdottir, 2011). 5) Estradiol(E2): despite being largely a hormone for women, males can also generate modest levels of estradiol. Increased estradiol levels in males can be brought on by diseases like obesity or drugs, and they can harm sperm quality and fertility. In addition, the relationship between metabolism and reproductive function is now well acknowledged (Kilicdag et al., 2004). Adipokines, which are cytokines involved in a variety of physiological processes, are secreted hormonally by adipose tissue, which is now thought of as an endocrine organ that may affect fertility (Suzuki et al., 2010). These physiologically active proteins are thought to be the primary controllers of overall energy balance in the body. The critical functions of leptin and adiponectin in several physiological processes, including reproduction, have already been characterized. These physiologically active proteins are thought to be the primary controllers of overall energy balance in the body. The critical functions of leptin and adiponectin in several physiological processes, including reproduction, have already been characterized and addressed in numerous reviews (Alghannam et al., 2021). Therefore, we concentrated on this study on four new adipokines are,

chemerin, visfatin, resistin, and apelin, which have also been recognized as crucial regulators of energy metabolism (Lhomme et al., 2021). In addition, the relationship between metabolism and reproductive function is now well acknowledged. Adipokines, which are cytokines involved in a variety of physiological processes, are secreted hormonally by adipose tissue, which is now thought of as an endocrine organ that may affect fertility (Suzuki et al., 2010).

These physiologically active proteins are thought to be the primary controllers of overall energy balance in the body. The critical functions of leptin and adiponectin in several physiological processes, including reproduction, have already been characterized. These physiologically active proteins are thought to be the primary controllers of overall energy balance in the body. The critical functions of leptin and adiponectin in several physiological processes, including reproduction, have already been characterized and addressed in numerous reviews (Alghannam et al., 2021). Therefore, we concentrated on this study on four new adipokines. 1) Apelin: apelin inhibits gonadotropin production, therefore indirectly regulating biological activities such as steroidogenesis, cell proliferation, and apoptosis in the gonads In addition, the expression of apelin was considerably higher in the varicocele group compared to the control group. and in endothelial, Sertoli, and spermatogonium cells found in interstitial connective tissue regions, but it may also cause infertility by inhibiting reproductive hormones (Rayalam et al., 2008). As a result, apelin may be a target protein that should be studied in reproductive diseases and infertility (Goazigo et al., 2007). 2) Chemerin: which is secreted as an inactive protein precursor (prochemerin) and activated by enzymatic cleavage at its C-terminus .is found in adipose tissue and regulates adipocyte metabolism. Chemerin has a sex dimorphic pattern of expression, with greater levels in males than in women, making it a possible novel candidate in the relationship between sex steroid regulation, and inhibiting Leydig cell steroidogenesis (Dubois-vedrenne et al., 2021). 3)Resistin: is a 108-amino acid propeptide that has a signal peptide, a variable region, and a conserved C-terminus. Resistin 12.5kDa is a dimeric protein that forms high- and low-molecular-weight complexes in the human blood (Malamitsi-Puchner et al., 2007). Resistin has been found to be depicted in the testis and seminiferous tubules of rats, especially in Sertoli and Leydig cells (Maillard et al., 2017). 4) Visfatin: is an adipokine that has been investigated in relation to a number of physiological processes, including its possible interactions with hormones like luteinizing hormone (LH). Visfatin is mostly secreted by adipose tissue and functions as a regulator at the hypothalamic-pituitary level, which was identified by immunohistochemistry in the anterior and intermediate lobes of the pituitary (Estienne et al., n.d.; Malamitsi-Puchner et al., 2007).

The study aims to examine the male infertility effect of Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2) and its relationships to men's Infertility without reason, evaluating the role of APLN (Apelin), CHEM (Chemerin), RETN (Resistin), and Visfatin in the blood serum in order to determine the functional ability of those who have male infertility, and knowledge the relationship between biochemical parameters and the effect on some factors such as Age, Smoking, and period of Infertility in infertility patients and a control group

Martial and methods

Sample Collection

Blood samples were collected from 180 male divided into three groups 50 control 65 had Infertility with reason and 65 had Infertility without reason. Their ages ranged between 20-50 years, and periods of infertility ranged between two and fourteen years, noting that their wives were healthy (fertile females) after conducting all examinations by specialized doctors all the men participating in this study were residents of Mosul City, in the morning between eight and ten o'clock collected 5mL of blood was drawn from the antecubital vein with sterile single-use syringes, blood samples were placed in a test Jel tube that contained a substance clot activator that aids rapid blood clotting for the purpose of separating the blood and obtaining the serum, followed by centrifugation at a speed of 3000 Cycles/Min. for 5Min.

Determination of Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol (E2) in Blood Serum by Cobas®6000 Analyzer

A. Principle: Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2) were measured in the blood serum of men in Infertility with reason, men Infertility without reason, and men fertile, by using the ready-made Elecsys measuring kit manufactured by Roche Diagnostics, Germany, and using the Communauté d'agglomération du Bassin d'Arcachon Sud (COBAS) is a completely automatic device that is programmed on the computer to carry out a large number of analyses at once, with the capability of repeating the analyses automatically. It is known by the abbreviation Cobas. Testosterone, FSH, LH, PRL., and E2 testes operate under the immunoassay principle, especially the electrochemiluminescence immunoassay (ECLIA) basis. ECLIA is a commonly utilized technology, used for the quantitative determination of numerous analytes in clinical diagnostics (Zolotykh & Karantysh, 2022).

B. Procedure: Testosterone, FSH, LH, PRL., and E2 levels in the sample are measured by the Cobas® 6000 analyzer using an immunoassay approach, such as an enzyme-linked immunosorbent assay (ELISA). This includes the samples of each Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2) interacting with certain antibodies or

antigens. Signals produced during the immunoassay, such as variations in color or fluorescence, are picked up by the Cobas®6000 analyzer. The calibration curve created during setup is used by the equipment to measure these signals and translate them into each Testosterone, FSH, LH, PRL, and E2 concentration. Then Cobas®6000 analyzer generates a report with each of testosterone, FSH, LH, PRL., and E2 concentration in the patient's blood serum after the analysis is finished, this result shown on the analyzer's screen was forwarded to a laboratory information system to be printed (Analytics et al., 2019; Analytics & Analytics, 2018, 2019; Cobas 8000, 2020).

C. Calculation: The Cobas®6000 analyzer automatically calculates the concentrations of each of the Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2). After the analysis, the result appears on the screen of the analyzer and then it will be sent to the laboratory information system to be printed in either unit of each of the units hormones Testosterone in either unit ng/mL, ng/dL, or nmol/L, FSH and LH in either unit mIU/mL or IU/L (Analytics & Analytics, 2018, 2019), PRL in either unit μIU/mL, ng/mL or in mIU/L (Analytics et al., 2019), E2 in either unit pmol/L, pg/mL, ng/L, or nmol/L (Analytics et al., 2019).

Units conversion factors:

- ng/mL x 3.47 = nmol/L, ng/mL x 21.2 = μIU/mL (mIU/L), ng/mL x 100 = ng/dL
- pg/mL x 0.00367 = nmol/L, pg/mL x 3.67 = pmol/L, pmol/L x 0.272 = pg/mL (ng/L)
- nmol/L x 0.288 = ng/mL, μIU/mL (mIU/L) x 0.047 = ng/mL

Determination of Human APLN (Apelin), CHEM (Chemerin), RETN(Resistin) and Visfatin in Blood Serum by ELISA Method

A. Principle of the Assay: principle of determining these adipokines using an ELISA kit from Fin Biotech Co., Ltd., Wuhan, China involves a competitive enzyme immunoassay technique. A monoclonal antibody against apelin hormone is coated on a microplate in this assay, and each of the APLN, CHEM, RETN, and visfatin hormone in the sample competes with a set quantity of each APLN, CHEM, RETN, and visfatin hormone labeled with Streptavidin-HRP for binding to a small number of particular binding sites. TMB substrate solution comprising a chromogenic or fluorogenic substrate for the Streptavidin-HRP is applied to the microplate after a washing step to get rid of any unbound reagents. A reaction between the TMB substrate and streptavidin-HRP is catalyzed, and as a result, a sulphuric acid solution is used to stop the enzyme-substrate reaction, and the color change is detected spectrophotometrically at a wavelength of 450 nm. The O.D of the samples is then compared to the standard curve to determine the Concentration of each of the APLN, CHEM, RETN, and visfatin

present in the samples (Apln & Elisa, n.d.; Chem & Elisa, n.d.; Retn & Elisa, n.d.; Visfatin & Elisa, n.d.).

B. Assay Procedure: APLN (Apelin), CHEM (Chemerin), RETN (Resistin), and Visfatin levels were determined in the serum of the men of participants who men Infertile with reason, men Infertile without reason, and the control group by using Elisa kits supplied by Fine Biotech Co, Ltd. According to the assay procedure in kits . And using ELISA - Microplate Reader supplied by company paramedical, Italy.

C. Calculation of Result: Plot the best-fit curve through the points on the graph by drawing the average OD for each standard on the vertical (Absorption) axis against the concentration on the horizontal (Concentration) axis, as shown in Figure (1), (2),(3),(4).

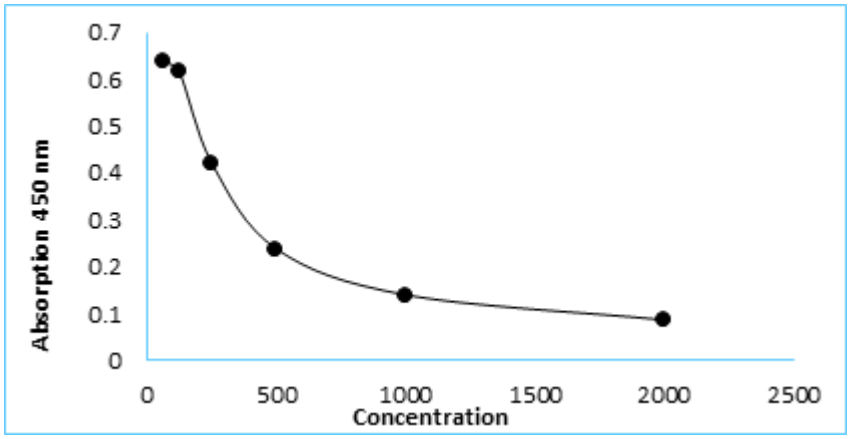

Figure 1 : Standard Curve of APLN

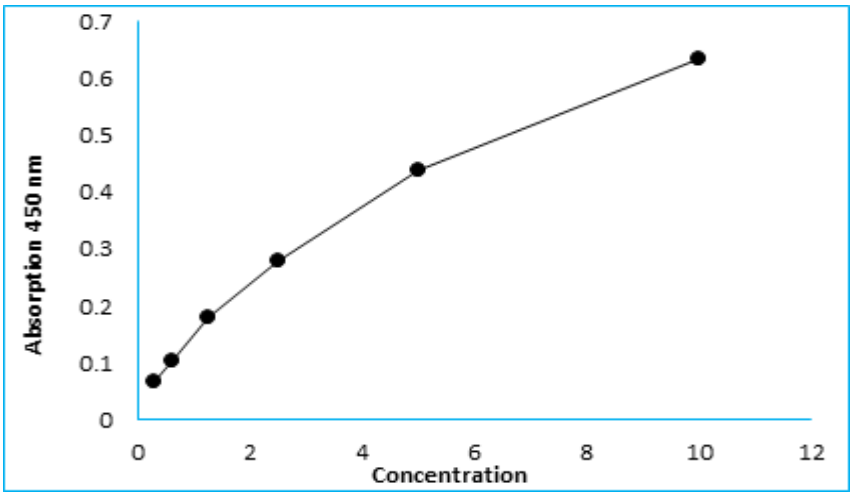

Figure 2. Standard Curve of CHEM

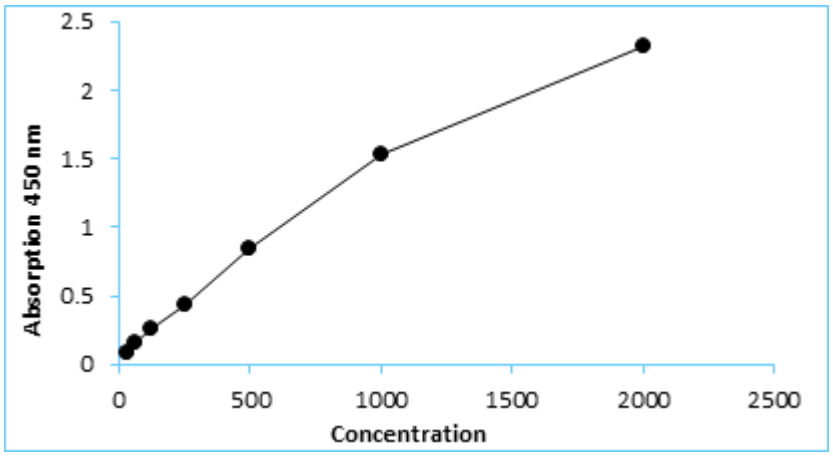

Figure 3. Standard Curve of RETN

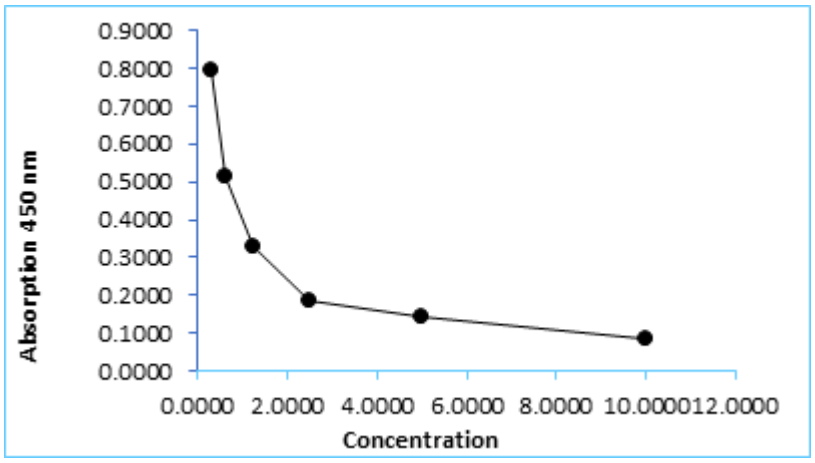

Figure 4. Standard Curve of Visfatin

Statistical Analysis

In order to calculate the mean and standard deviation (SD) and evaluate if there were any significant differences between the research groups, the laboratory test data were analyzed using a one-way Analysis of Variance (ANOVA) and a T-test in the program (SPSS) (version 16 IBM Corp.). When using the $P < 0.01$it means a significant difference at the 1% probability level, P 0.01 - 0.05, it means a significant difference at a 5% probability level, $P > 0.05$, no significant differences between the probabilities.

Results and discussion

This study included the collection of 180 samples from patients with infertility without reason and from males only. The samples were selected from the reviewers at Al-Jamhouri Teaching Hospital in Mosul, to be the study models according to the instructions of the supervisor. A field doctor and specialist in

diseases of the kidneys, urinary tract, prostate, infertility, and sexual dysfunction in the consultation of the Republican Teaching Hospital in the city of Mosul, after obtaining the moral license from the patients and conforming to the controls of the health department in Mosul city.

Comparison of Testosterone, FSH, LH, PRL, and E2 Levels Between the Control Group and Infertility Patients With Reason and Without Reason

Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2) were measured in blood serum of men infertile with reason, men infertile without reason, and men fertile, in blood serum by using sing the ready-made Elecsys measuring kit manufactured by Roche Diagnostics, Germany, and using Cobas®6000 analyzer. Was divided the samples into three groups 50 control , 65 have Infertility with reason , and 65 had Infertility without reason. Revealed testosterone of men infertile with reason with mean of 2.437±0.697ng/mL, FSH with the mean of 18.910±0.349mIU/mL, LH with mean of 13.354±0.125mIU/mL, PRL. with a mean of 19.254 ±0.825ng/mL, E2 with a mean of 70.982±1.385pg/mL . Testosterone of men infertile without reason with a mean of 4.518±0.520ng/mL, FSH with a mean of 6.367±0.662mIU/mL, LH with a mean of 7.688±0.551mIU/mL, PRL. with a mean of 10.168±0.420ng/mL, E2 with a mean of 19.852 ±0.090 pg/mL. Testosterone of the control group with a mean of 4.448±0.949ng/mL, FSH with a mean of 3.022±0.331mIU/mL, LH with a mean of 5.612±0.949mIU/mL, PRL. with a mean of 10.104±0.096 ng/mL, E2 with a mean of 25.066±0.195pg/mL. In men infertile with reason and men infertile without reason a significant decrease in testosterone value compared control group. also, there is a significant increase in FSH, LH, PRL., and E2 values compared control group. The result found significant differences ($P \leq 0.01$) in tests of Testosterone, FSH, LH, PRL, and E2 of men infertile with reason and men infertile without reason compared with a control group, at (1%) probability level. Testosterone results shown in Table (1), and Figure (5) indicate a significant decrease in testosterone value in men infertile with reason compared control group and men infertile without reason. This is consistent with research by Hadeel Abdulelah and Zhian Salah(Ramzi, 2021). The low level of Testosterone in men infertile with reason was due to several reasons: primary Testicular Failure due to the brain's failure to produce sufficient amounts of the hormones LH and FSH, hypogonadotropic hypogonadism, obesity, and Age-related decline mentioned earlier, innately decline with age.

Table 1. Comparison of hormones profile in normal subjects and infertile with reason, and men infertile without reason in blood serum

Biochemical Parameters	Control group		Men infertility with reason		Men infertility without reason		p-value
	M	± SD	Mean	± SD	M	± SD	
Testosterone (ng/mL)	4.448 a	0.940	2.437 b	0.697	4.518 a	0.520	0.000**
FSH (mIU/mL)	3.022 c	0.331	18.910 a	0.349	6.367 b	0.662	0.000 **
LH (mIU/mL)	5.612 c	0.949	13.354 a	0.125	0.688 b	0.551	0.000 **
PRL (ng/mL)	10.104 b	0.096	19.254 a	0.825	10.168 b	0.420	0.000**
E2 (pg/mL)	25.066 b	0.195	70.982 a	1.385	19.852 b	0.090	0.000**

Mean=M

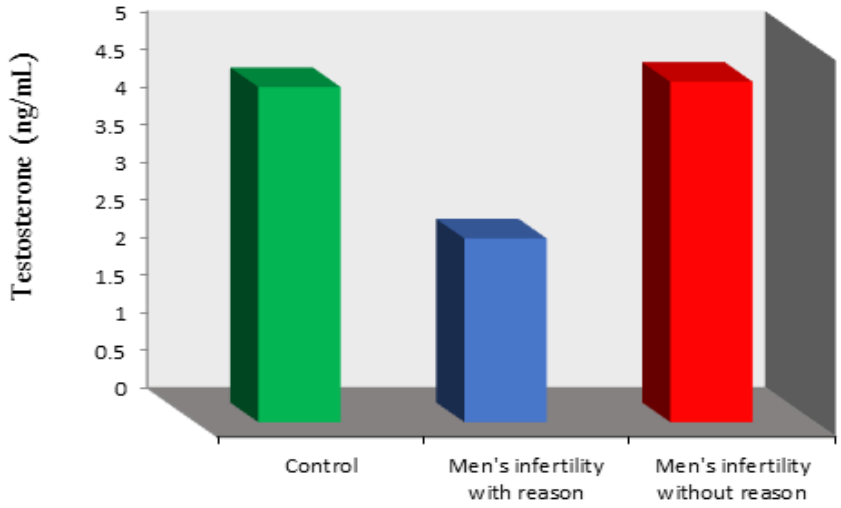

Figure 5. Testosterone levels in study groups

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) hormones results are shown in Table (1), and Figures (6) and (7) indicate a significant increase in FSH and FSH levels in men infertile with reason and without reason compared control group. This is consistent with research by S. Ramesh Babu and his group (Babu et al., 2004). (FSH) and (LH) levels can rise in men who are infertile for a variety of reasons. FSH and LH are important hormones that control sperm production and hormonal equilibrium. This rise in FSH and LH is understood as compensatory or reactive elevation, Increased FSH and LH Levels in men Infertile with reason due to testicular dysfunction result in reduced sperm production that is affected by variable factors such as primary testicular failure or injury, genetic

abnormalities, infections, radiation or chemotherapy exposure, varicocele (enlarged veins in the scrotum), or certain drugs.

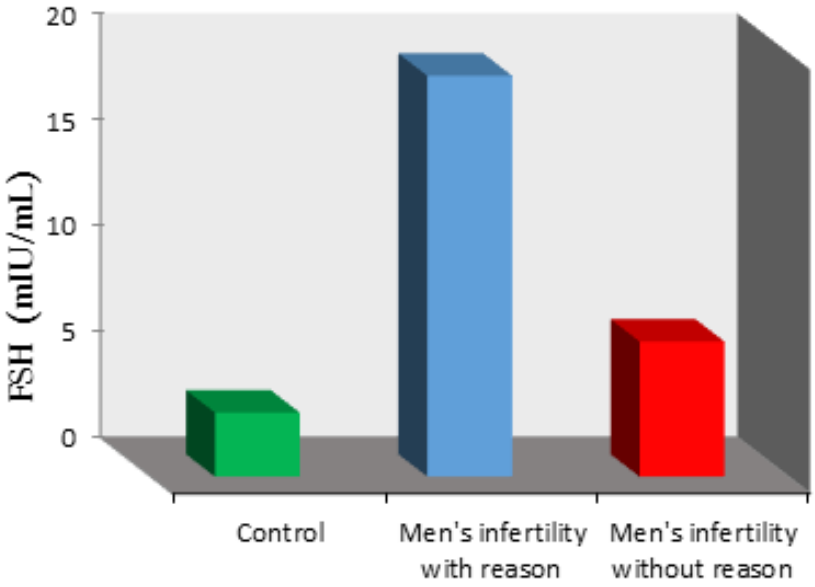

Figure 6: FSH levels in study groups

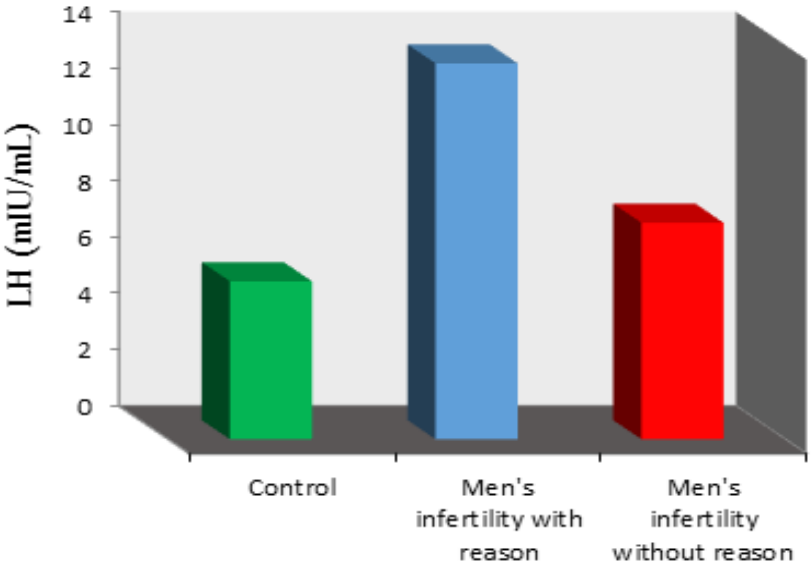

Figure 7: LH level in study groups

Prolactin (PRL) and estradiol (E2) results are shown in Table (1), and Figures (8) and (9) indicate a significant increase in PRL and E2 levels in men infertile without reason compared to control group. This is consistent with research (Turankar et al., 2013). PRL and E2 levels can rise in men who are infertile for a variety of reasons. Although less often than a rise in FSH and LH levels, an increase in

prolactin (PRL) and estradiol (E2) levels can happen. Increased PRL. and E2 Levels in men Infertile with reason. A benign pituitary tumor called a prolactinoma causes an excessive amount of prolactin to be produced. Gonadotropin-releasing hormone (GnRH) can be suppressed by elevated prolactin levels (hyperprolactinemia), which therefore results in less FSH and LH output. The generation of sperm and fertility may suffer as a result of this hormonal imbalance. Also, some drugs can raise prolactin levels in males, including antipsychotics, antidepressants, and drugs that suppress testosterone levels. Prolactin levels can rise due to liver and renal disorders that prevent the hormone from leaving the bloodstream.

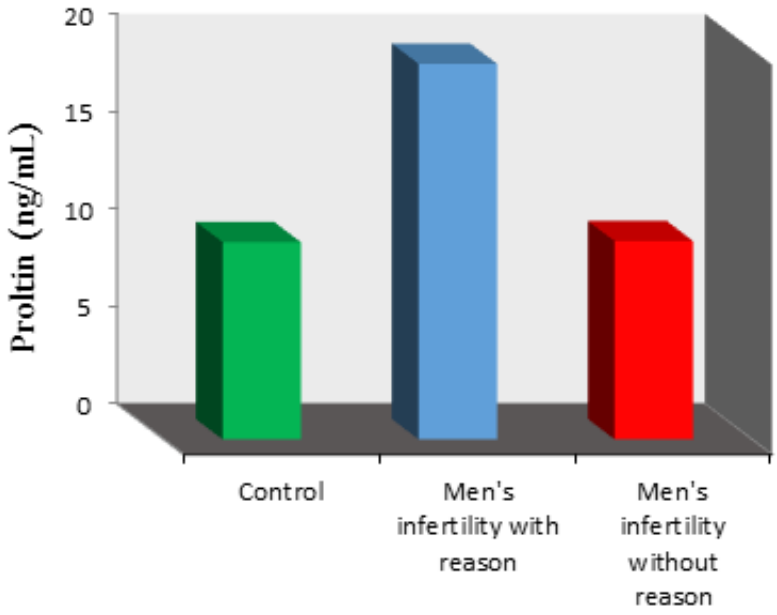

Figure 8. PRL. levels in study groups.

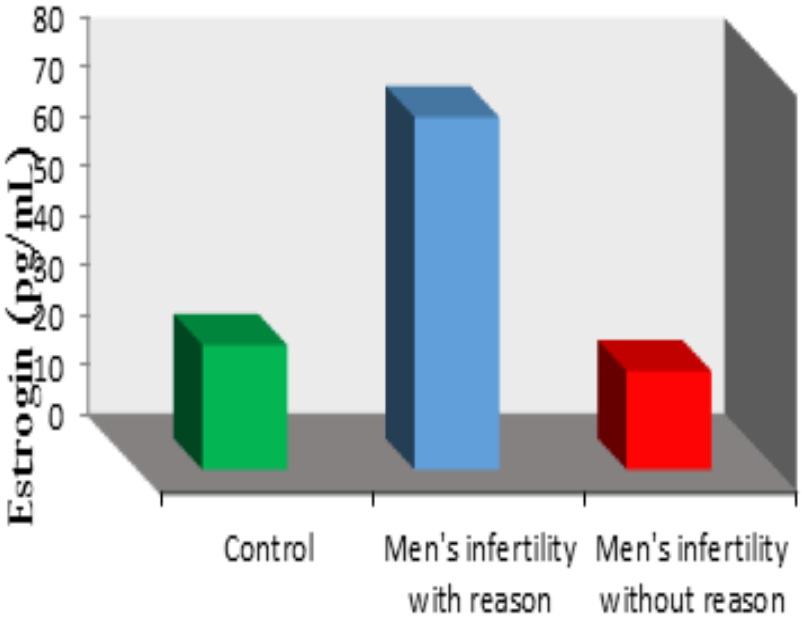

Figure 9: E2 levels in study groups

Comparison of APLN (Apelin), CHEM (Chemerin), RETN (Resistin), and Visfatin levels between the control group and infertility patients with and without reason

APLN (Apelin), CHEM (Chemerin), RETN (Resistin), and Visfatin were measured in blood serum of men infertile with reason, men infertile without reason, and men fertile, in blood serum by using Elisa kits supplied by Fine Biotech Co, Ltd. And using ELISA - Microplate Reader supplied by company paramedical, Italy. Was divided the samples into three groups 50 control, 65 have Infertility with reason, and 65 had Infertility without reason.

Table 2. Comparison of Adipokines profile in normal subjects and infertile with reason, and men infertile without reason in blood serum

Biochemical Parameters	Men infertility with reason		Men infertility without reason		Control group		p-value
	M	± SD	M	± SD	M	± SD	
APLN (pg/mL)	4.291 a	0.449	3.471 a	0.520	5.329 a	0.077	0.111 n.s
CHEM (ng/mL)	32.320 a	0.174	30.985 b	0.313	31.433 ab	0.142	0.035*
RETN (pg/mL)	6.547 a	0.960	8.179 a	0.753	7.670 a	0.960	0.290 n.s
VISFATIN (ng/mL)	1.409 a	0.275	1.582 a	0.472	2.616 a	0.787	0.480 n.s

Divulged APLN of men infertile with reason with mean of 4.291±0.449pg/mL, CHEM with the mean of 32.320±2.174ng/mL, RETN with mean of 6.547±0.960pg/mL, and Visfatin with the mean of 1.409±0.275ng/mL. APLN of mean infertile without reason with a mean of 3.471±0.520pg/mL, CHEM with a mean of 30.985±0.313ng/mL, RETN with a mean of 8.179±0.753pg/mL, and Visfatin with the mean of 1.582±0.472ng/mL . APLN of the control group with reason with a mean of 5.329±0.077 pg/mL, CHEM with mean of 31.433±0.142ng/mL, RETN with a mean of 7.670±0.960pg/mL, and Visfatin with the mean of 2.616±0.787ng/mL . The resultant found, RETN, and Visfatin have not revealed significant differences ($P \geq 0.05$ n.s) among the infertile groups and the control group but CHEM has significant differences with infertile groups except control, not have group significant differences($P \leq 0.05$), at (5%) probability level.

Apelin and Visfatin results are shown in Table (2), Figures (10) and (11) indicating a significant increase in APLN levels in the control group compared to men infertile with reason and without reason. Apelin was also found in infertile with reason and had a significant increase in APLN compared with infertile without reason. This indicates that the low level of APLN is one of the causes of infertility without reason. APLN levels have been discovered to be lower in male infertility. Additionally, Visfatin also found that infertile without reason had a significant increase in APLN compared with infertile with reason. Visfatin levels have been observed to be higher in PCOS-related infertility in several investigations (Rostamtabar et al., 2021).

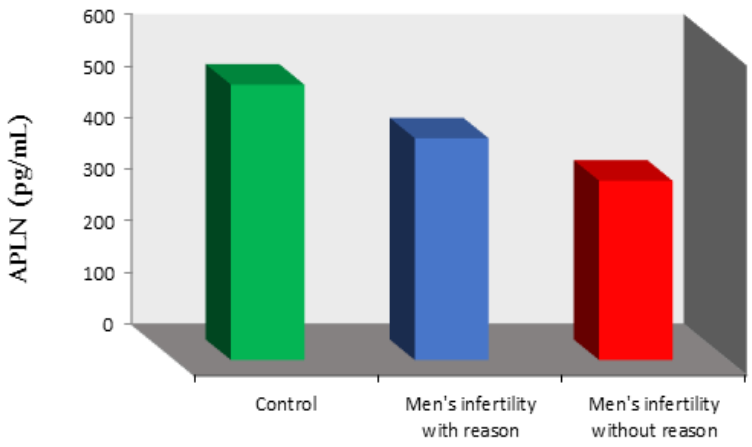

Figure 10: APLN levels in study groups

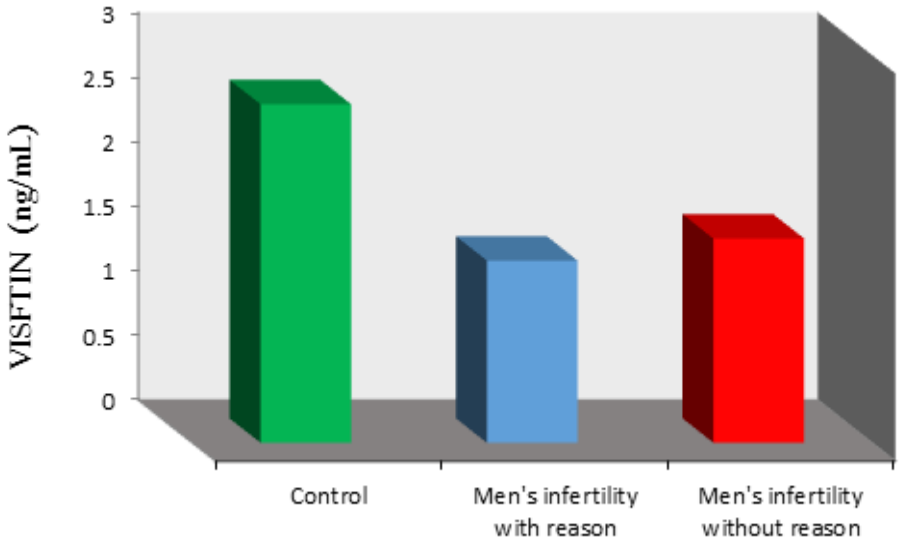

Figure 11. Visftin levels in study groups

Chemerin results are shown in Table (2), and Figure (12) indicate a significant increase in CHEM levels in men infertile with reason compared to the control group and men infertile without reason. Chemerin also found that men infertile without reason had a significant decrease in CHEM compared to the control group. This indicates that the low level of CHEM is one of the causes of infertility without reason. This is consistent with research by Johannes Bobjer and his groups(Bobjer et al., 2018). CHEM levels have been discovered to be lower in male infertility. Additionally, RETN also found both the control group and men infertile without reason had a significant increase in RETN compared with infertile with reason. according to the study Resistin levels have been linked to infertility brought on by endometriosis.

Men infertility

The results were analysed for the statistical values of a period of infertility and their effect on biochemical parameters in infertility patients. The patient group was divided into two groups according to a period of infertility, as shown in Table (3). The results shown in Table (3) indicate that there are no significant differences in APLN, CHEM, RETN, and Visfatin levels according to a period of infertility among patient groups. But found there are significant differences in each level of Testosterone, FSH, LH, PRL, and E2 according to the period of infertility among patient groups. This means that a period of infertility does not affect these adipokines but does affect hormone parameters. This is consistent with research by Atheer Mahde and his group (Mahde et al., 2009). However, the tables do show significant differences in hormone parameters based on the period of infertility among patient groups. This indicates that the duration of infertility does have an influence on hormone levels.

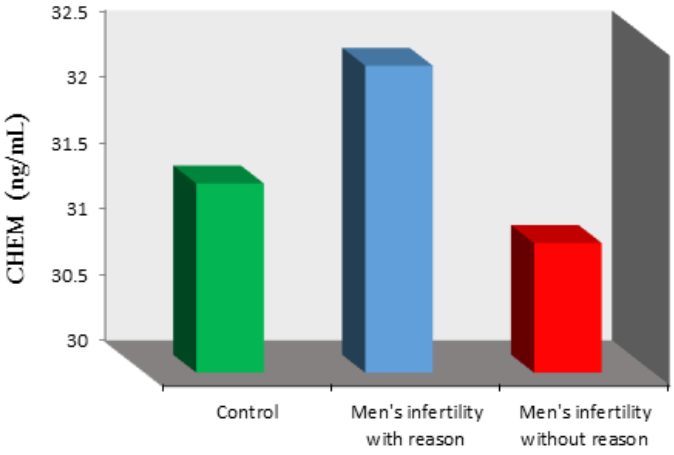

Figure 12. CHEM levels in study groups

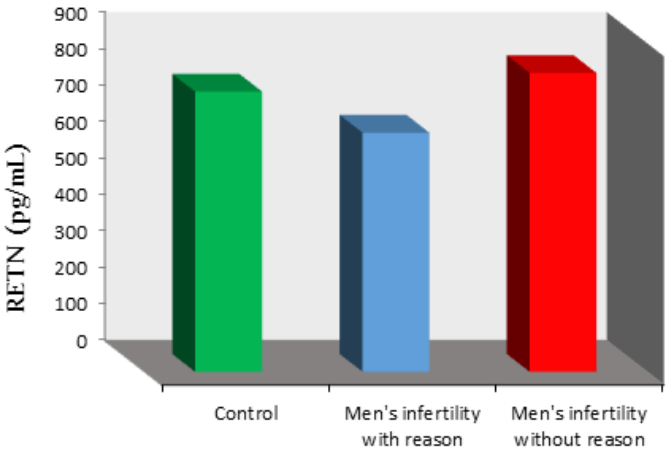

Figure 13. RETN level in study groups

Table 3. The mean and standard deviation of biochemical parameter concentrations in infertility patients based on a period of infertility

Period of Infertility (Year)			Tes. (ng/mL)	FSH (mIU/mL)	LH (mIU/mL)	PRL (ng/mL)	E2 (pg/mL)	APLN (pg/mL)	Visftin (ng/mL)	CHEM (ng/mL)	RETN (pg/mL)
Men infertility with reason	1-5	M	2.452 bc	17.728 a	12.912 a	19.697 a	73.287 a	4.601 a	0.586 a	32.651 a	6.187 a
		S.D	0.650	0.312	0.830	0.468	0.139	0.456	0.215	0.294	0.519
	6-10	M	2.632 bc	21.357 a	14.109 a	19.407 a	64.852 a	4.928 a	2.008 a	31.112 a	0.411 a
		S.D	0.770	0.539	0.506	0.339	1.125	0.556	0.703	0.118	0.433
	> 10	M	2.192 c	18.554 a	13.401 a	18.200 a	73.184 a	2.964 a	2.392 a	32.999 a	6.233 a
		S.D	0.712	0.810	0.465	0.059	1.952	0.135	0.448	0.566	0.268
Men infertility	1-5	M	4.043 ab	5.866 b	7.160 b	10.663 bc	26.223 b	3.566 a	1.934 a	30.861 a	7.437 a
		S.D	0.301	0.699	0.024	0.766	0.421	0.131	0.931	0.107	0.558
	6	M	4.717 a	6.312 b	8.720 b	11.997 b	15.263 b	3.048 a	1.738 a	31.122 a	8.882 a

		S.D	0.868	0.271	0.040	0.789	0.103	0.875	0.472	0.736	0.771
	>10	M	5.054 a	7.344 b	7.022 b	6.443 c	15.666 b	3.959 a	2.270 a	30.993 a	8.406 a
		S.D	0.455	0.333	0.649	0.617	0.093	0.705	0.088	0.533	0.925
p-value			0.001**	0.000**	0.000**	0.000**	0.000**	0.302 n.s	0.611 n.s	0.065 n.s	0.556 n.s

Men infertility according to age

The results were analyzed for the statistical values of age and their effect on biochemical parameters in infertility patients. The patient group was divided into three groups according to age, as shown in Table (4). The results shown in Table (4) indicate that there are no significant differences for APLN (Apelin), RETN (Resistin), CHEM (Chemerin), Visfatin, and Follicle-stimulating hormone (FSH), according to patients' age. However, there are significant differences in the level of Testosterone, Luteinizing hormone (LH), Prolactin (PRL), and Estradiol (E2) according to the infertility patient's age. Individual differences may exist in the rate and degree of decrease, though. Men's testosterone levels were found to decrease but LH, prolactin, and Estradiol levels raised with age. It is thought that this rise is a compensatory response by the body to lower testosterone levels by trying to enhance the synthesis of testosterone, low testosterone, elevated LH, and elevated prolactin levels can impact sperm quality and production, which can lead to infertility. Additionally, estradiol levels may gradually rise as a result of things like fat tissue's enhanced. conversion of testosterone to estradiol. Men with elevated estradiol levels may have hormonal imbalances and reduced fertility. This means that infertile patients' age did not affect these Adipokines and FSH, but does affect each of Testo., LH, PRL., and E2 This is consistent with research by Mary K. Samplask and his group(Samplaski et al., 2013). Men's testosterone levels often decrease with age, and this decrease may have an effect on fertility.

Table 4. The mean and standard deviation of biochemical parameter concentrations in infertility patients based on age

G	Age (Year)		Tes. (ng/mL)	FSH (mIU/mL)	LH (mIU/mL)	PRL (ng/mL)	E2 (pg/mL)	APLN (pg/mL)	Visftin (ng/mL)	CHEM (ng/mL)	RETN (pg/mL)
Control	20-30	M	4.506 ab	2.841 d	5.358 c	11.611 c	23.4256 b	5.176 a	5.958 a	31.914 a	7.994 a
		S.D	0.884	0.066	0.318	0.535	0.295	0.332	0.184	1.346	1.808
	31-40	M	4.206 ab	2.353 d	5.530 c	9.750 cd	25.350 b	6.783 a	4.616 a	29.834 a	8.068 a
		S.D	0.979	0.765	0.862	0.153	0.195	0.569	0.155	1.328	0.117
	> 40	M	3.632 ab	4.150 cd	5.966 c	7.818 cd	27.280 b	3.861 a	3.854 a	32.484 a	5.855 a
		S.D	0.140	1.754	0.662	0.519	0.230	.0389	0.661	1.685	0.548
Men infertility with reason	20-30	M	3.296 c	16.818 b	11.656 ab	22.210 a	31.322 a	2.993 a	3.664 a	32.575 a	6.446 a
		S.D	0.760	0.970	0.278	0.003	1.201	0.899	0.222	0.395	0.3611
	31-40	M	2.405 c	19.026 ab	14.227 a	17.314 ab	32.417 a	5.540 a	1.601 a	31.713 a	6.830 a

		S.D	0.682	0.823	0.878	0.604	1.239	0.744	0.965	0.095	0.379
	> 40	M	1.977 bc	22.512 a	14.990 a	18.480 a	36.006 a	3.672 a	2.321 a	33.318 a	5.336 a
		S.D	0.586	0.746	0.313	0.388	2.040	0.265	0.475	1.685	0.127
Men infertility without reason	20-30	M	4.353 ab	6.868 cd	8.462 bc	12.536 bc	26.006 b	3.146 a	2.051 a	31.020 a	9.338 a
		S.D	0.350	0.201	0.039	0.601	0.454	0.272	0.909	0.277	0.105
	31-40	M	4.028 ab	5.087 cd	9.565 c	9.925 cd	26.777 b	3.527 a	2.284 a	30.867 a	6.899 a
		S.D	0.748	0.417	0.910	0.175	0.964	0.072	0.202	0.487	0.532
	> 40	M	3.393 a	7.767 c	9.971 c	5.887 d	27.312 b	4.013 a	2.433 a	31.144 a	8.263 a
		S.D	0.534	0.434	0.631	0.530	0.242	0.026	0.415	1.243	0.376
p-value			0.000**	0.237 n.s	0.00**	0.00**	0.000**	0.151n.s	0.332 n.s	0.079 n.s	0.598 n.s

Men infertility according to smoking

The results were analysed for the statistical values of smokers and their effect on biochemical parameters in infertility patients. The patient group was divided into three groups according to smokers or non-smokers, as shown in Table (5). The results shown in Table (5) indicate that there are no significant differences in APLN (Apelin), RETN (Resistin), and Visfatin, for the groups of patients smoking. but there are significant differences in other CHEM (Chemerin), Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol (E2) for the groups of patients smoking. This means that for those with patient infertility smoking does not affect these CHEM (Chemerin), Testosterone, Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), Prolactin (PRL), and Estradiol(E2) but does affect each of the APLN (Apelin), RETN (Resistin), and Visfatin. This is consistent with research by Amrita Mitra and his group (Mitra et al., 2012).

Table 5. The mean and standard deviation of biochemical parameter concentrations in infertility patients based on smokers or non-smokers.

Group	Smoking		Tes. (ng/mL)	FSH (mIU/mL)	LH (mIU/mL)	PRL (ng/mL)	E2 (pg/mL)	APLN (pg/mL)	Visftin (ng/mL)	CHEM (ng/mL)	RETN (pg/mL)
Control	Smoker	M	4.098 a	2.080 c	4.265 c	11.416 b	28.133 b	3.050 a	2.515 a	29.403 b	1.046 a
		S.D	0.900	0.495	0.434	2.972	0.234	0.612	0.616	0.695	0.787
	No- Smokers	M	4.597 a	3.425 bc	6.189 bc	9.542 b	23.752 b	6.306 a	2.659 a	32.303 a	6.379 a
		S.D	0.949	0.382	0.070	0.471	0.200	0.766	0.030	0.950	0.287
Men infertility with reason	Smoker	M	2.291 b	19.790 a	14.237 a	18.005 a	69.192 a	4.206 a	1.582 a	32.247 a	6.819 a
		D.D	0.795	0.867	0.414	0.401	0.690	0.282	0.831	0.323	0.663
	No- Smokers	M	2.576 b	18.076 a	12.518 a	20.438 a	72.678 a	4.372 a	1.245 a	32.388 a	6.346 a
		S.D	0.578	0.774	0.756	0.710	0.039	0.343	0.743	1.085	0.216
Men infertility without reason	Smokers	M	4.493 a	6.035 b	7.793 b	12.231 b	18.672 b	3.600 a	1.326 a	31.180 a	8.120 a
		S.D	0.484	0.088	0.069	0.617	0.256	0.137	0.629	0.091	0.226
	No- Smokers	M	4.536 a	6.598 b	7.615 b	8.733 b	20.673 b	3.381 a	1.760 a	30.850 a	8.220 a
		S.D	0.600	0.100	0.237	0.135	0.015	0.020	0.003	0.493	0.181
p-value			0.000 **	0.000 **	0.000 **	0.000 **	0.000 **	0.120	0.895n.s	0.015 *	0.313 n.s

Mean=M

Conclusion

This study defines male hormones and adipokines that affect infertility and shows that the results a significant positive connection between Testosterone, FSH, LH, PRL, and E2 with age, smoking, and period of infertility. Accept Testosterone, E2 has an inverse relationship with periods of infertility, and PRL. has an inverse relationship with aged patients revealing a direct and statistically significant positive connection between both APLN and RETN with age, smoking, and period of infertility. Additionally, Visfatin and CHEM have a significant positive connection between smoking, and periods of infertility

but have an inverse relationship with aged patients. This means Testosterone levels with age gradually decrease, generally starting at about the age of 30, and FSH levels normally remain relatively regular with age this indicates that Hormones and adipokines levels can be influenced by various factors, including genetics, lifestyle, and overall health.

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