Impact of Angiotensin II Receptor Levels in Serum and Follicular Fluid on ICSI Outcomes in Infertility Cases

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Infertility, Angiotensin Receptor, Intracytoplasmic Sperm Injection (ICSI).

ABSTRACT
Male and female infertility are defined as a medical problems.Childless status syndrome is a condition when a couple has no success in conceiving a child, after 12 months of unprotected sex.In ovary, uterus and placenta, peptide receptors of the renin-angiotensin system are found along with angiotensin.The local function of renin-angiotensin system is observed not only in the ovary, but also in there.IVF experts put Intracytoplasmic Sperm Injection (ICSI) into the use of treating male-factor infertility of a severe degree.One sperm is brought into the mature cell by ICSI which is a way of injecting it directly.This study looks on the levels of the receptors of blood and follicular fluid Angiotensin II and investigates their influence on ICSI, which is one of the infertility treatments options.Designed the cross-sectional research, which involved 90 infertile women who had undergone the intra cytoplasmic sperm injection.The participants were divided by BMI into three groups: the normal range of BMI is 18.5-24.9, overweight falls within the range of 25-29.9, and obesity is defined as BMI of 30-34.9. An ELISA test in the private laboratories was carried out to measure angiotensin receptors in blood and follicular fluid on the day of oocyteBMI of the usually weighted women, the women were overweight and with obesity had significantly diverse mean BMIs.The age, time of infertility, and the type of infertility there was no substantial difference found between groups.The hormone levels were found not to be that different in reproductive-aged and obese-normal weight infertile girls as well as obese women.The study studies demonstrated that higher follicular fluid angiotensin II receptor concentrations were related well with intracytoplasmic sperm injection measures.This study has indeed revealed that all the IVF-ET patients involved in the research did have the angiotensin II receptors 1 in their blood and the follicular fluid.The follicular fluid turns out to have increased levels of receptors rather than the serum.Aetgenin Il receptors 1 blood and follicular fluids levels are in no way connected.The angeliotensin II recept1 (AT1/serum angiotensin II) levels in serum were not correlated to follicles.It is possible that high follicular angiotensin II receptor 1 fluid levels lead to conception, which may explain why the patient is now expecting a baby.There was a definite relationship happening in levels of Angiotensin II Receptor 1 and pregnancy.

1. Introduction

Infertility is defined as the inability of achieving a clinical pregnancy despite having sex without a protection device once or twice every week for 12 months or so.An assumed effect of it is that approximately 8 to 12 % of couples still in the age range capable of reproduction (1) will be impacted.The American Society for Reproductive Medicine (ASRM) has revised its definition of infertility since 2002 and concurs with the inability to attain a successful conception after having unprotected sexual intercourse for twelve consecutive months or more for women aged 20-34 or six months or more for women aged 35 and above, failing to compensate for any form of contraception (One kind of infertility is a health problem that can affect either a man or a woman.The definition for the inability to conceive after you have been into sexual intercourse very often, through a year while you do not use a condom, is called infertility.The latest world health organization statistic gives unbelievable facts- approximately one in six people is infertile worldwide, proving the severity of this problem.Around 8-12% couples in the reproductive age group are estimated to suffer from this disease and this rate is prevalent in the whole world(3) .Infertility may be categorized into two distinct types: primary infertility and secondary infertility which are equally disastrous.Primary infertility is a pathological state of a woman with the main problem being either an incomplete formation of the fetus or premature miscarriage.On the other hand, the secondary infertility is the condition when the person has got a successful pregnancy before and is unsuccessful to get the next pregnancy afterward.The medical definition of infertility is a condition by a woman, who cannot conceive or carry a baby to full term at any time, either in the past or now (4).Sexual infertility can be caused by various factors and the female and male are both at risk.Female infertility accounts for 20%-35% as the cause of the problem, which makes 40% of all cases.Ovulatory disorders that are the

primary cause of the female infertility and manifestation of the irregular or missing menstrual cycles (5) is the main factor. The male, female, and mixed causes ranging from 85% can be traced in the up to 85% of the infertility cases.It is estimated that approximately 30% of the participants with the known cause of male infertility were not diagnosed.While the spermatogenesis impairment is responsible for 2-4% of cases, this is not significantly different from that reported in the literature.It is males who are congenitally responsible for 40 to 50 percent of fertility disorders in particular studies, but female variable may account for additional 30 percent.A set of factors can be assigned to the cause of male infertility: genetic disorders, hypogonadotropic hypogonadism, varicocele, seminal tract infections, undescended testis, testicular torsion or injury, as well as environmental factors.It turns out that genetics can exert significant effect.Obesity already has a risk factor for female infertility, thus should be part of the case.The disorder might be pre-, testicular or post-testicular depending on the site-based (7,6).

Intracytoplasmic sperm injection (ICSI) procedure which was focused on the treating male infertility flaws, including abnormal parameters of sperm was developed.At the moment it is utilized worldwide in managing infertility in couples, .he found this a method through which the gametes parent just beyond the embryo that will be taken to be transferred to the uterus of the mother.This method bypasses any detrimental effect of the acrosome response. Moreover, such oocytes can be used for multiple attempts of fertilization (8).

The renin angiotensin system (RAS) comprises two proteins: remin, a protein produced by the juxtaglomerular apparatus of the kidney due to low blood pressure stimulation, and angiotensinogen, a liver protein that proceeds a series of metabolic processes with subsequently the product of angiotensin II and angiotensin. In this regard, angiotensin II is of vital importance as it regulates body balance and controls the functionality of kidneysIt is also present in the female reproductive organ(the ovary), heart, kidneys, adrenal gland among many others.This is possible by autocrine, paracrine or cellular endocrine pathways and this system may contribute to the organ function in an autonomous manner without considering the local concentration which in some cases exceeds the concentration in plasma (9). The studies have depicted the presence of the local form of the renin-angiotensin system, that is known as the ovarian renin-angiotensin system. Angiotensinogen, angiotensin, and renin were identified by immunohistochemical

The ovary is characterized by the presence of ACE1 and ACE2 receptors, as well as they secrete renin. Therefore, these receptors are duly expressed by follicle and granulosa cells in culture conditions.Non-peptidic antagonists are used to classify angiotensin II (Ang II) receptors into two subtypes: Atrazine resistance can be caused by two mechanisms: type 1 (ATF-R) and type 2 (AT2-R).AT1-R, found in the cardiovascular system, adrenal glands, and kidneys, is the central Classic Ang II receptor that enables Angiotensin II's action which includes vasopressing, cardiotropic activities, and aldosterone production.The highest level of gene AT2-R is expressed in fetal tissues which is much lower after delivery.The impact of the fetus on this receptor is substantially enhanced.However, in an adult brain, AT2-R shows a regional distribution in some nuclei, adrenal glands, uterus, ovary, and the heart (10,11).

Angiotensin II is mostly vegetated in the ovary, uterus, and placental areas within the female reproductive system.In the RAS system exists a great number of active molecules and enzymes, along with hypothalamic-pituitary-adrenal (HPA) axis and the circulating endocrine renin-angiotensin system.Angiotensin II (Ang II) and Angiotensin (1-7) (Ang-(1-7)) are both peptides that act in a localized manner but perform different functions in the RASHence, the altered angiotensin system and its receptors in the reproductive system not only take part in syncytiotrophoblast development but also seem to be associated with the processes of the human reproductive system, including follicle growth and development. In addition, the local factors of RAS which the substances renin and angiotensin II are a part, creates disruption that may give rise to the production of some diseases like cancer and reproductive disorders(12,13).Renin-angiotensin-system in the

ovarian area (in girls) has a strong impact on both the normal working of the ovaries and the deviation from it under some conditions.In both the reproductive tissues as well as the mature ovaries, AT1R is a controllable receptor of AngII that is responsible for the regulation of angiogenesis and follicle development.Angiotensin-II makes eggs get ready by triggering development and releasing process of granulosa cells via AT1R receptors.Thus, it regulates fecundation processes and the formation of the corpus luteum.The hormonal secretion, contraction of blood vessels and creation of new blood vessels, and the formation of oocytes are all responsive to RAS, particularly RAS in the ovaries, which makes these events possible(14) .research conducted by Liu, 2021 underpins angiotensin II and its receptors position in female reproduction.This research found that patients with higher levels of AT1-AA (angiotensin type 1 receptor antibodies) in their blood, as concentration of these antibodies in the serum of patients with endocrine disorders may be the cause of the problem with oocyte maturation and ovulation.The inflammation component that is implicated in A1 is characterized as an AT1-AA.A downstream signal of AT1AA/AT1R in women with infertility may be activated where and when inflammatory responses and ovulation abnormalities occur(14) . The aims is to determine the levels of Angiotensin II Receptors for both blood and follicular fluid, and the effect of their interactions with each other on the success rates of Intracytoplasmic Sperm Injection (ICSI) in infertile cases.

2. Methodology

This study is a prospective clinical cross-sectional one that includes 90 number of infertile females who are receiving ICSI at the infertility center of the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies / Al- Nahrain University / Baghdad / Iraq.The experiment was carried out in a span of seven months, between July 2023 and May 2024.The dissertation got an ethical assessment from the Local Medical Ethic Committee.Patients who experience infertility were to fill out in a standardized manner complete medical, surgical, and obstetric histories according to a previously developed questionnaire.Every woman who couldn’t get pregnant had a comprehensive evaluation with a gynecological examination and a general assessment. Such a workup should follow a multi-disciplinary approach.

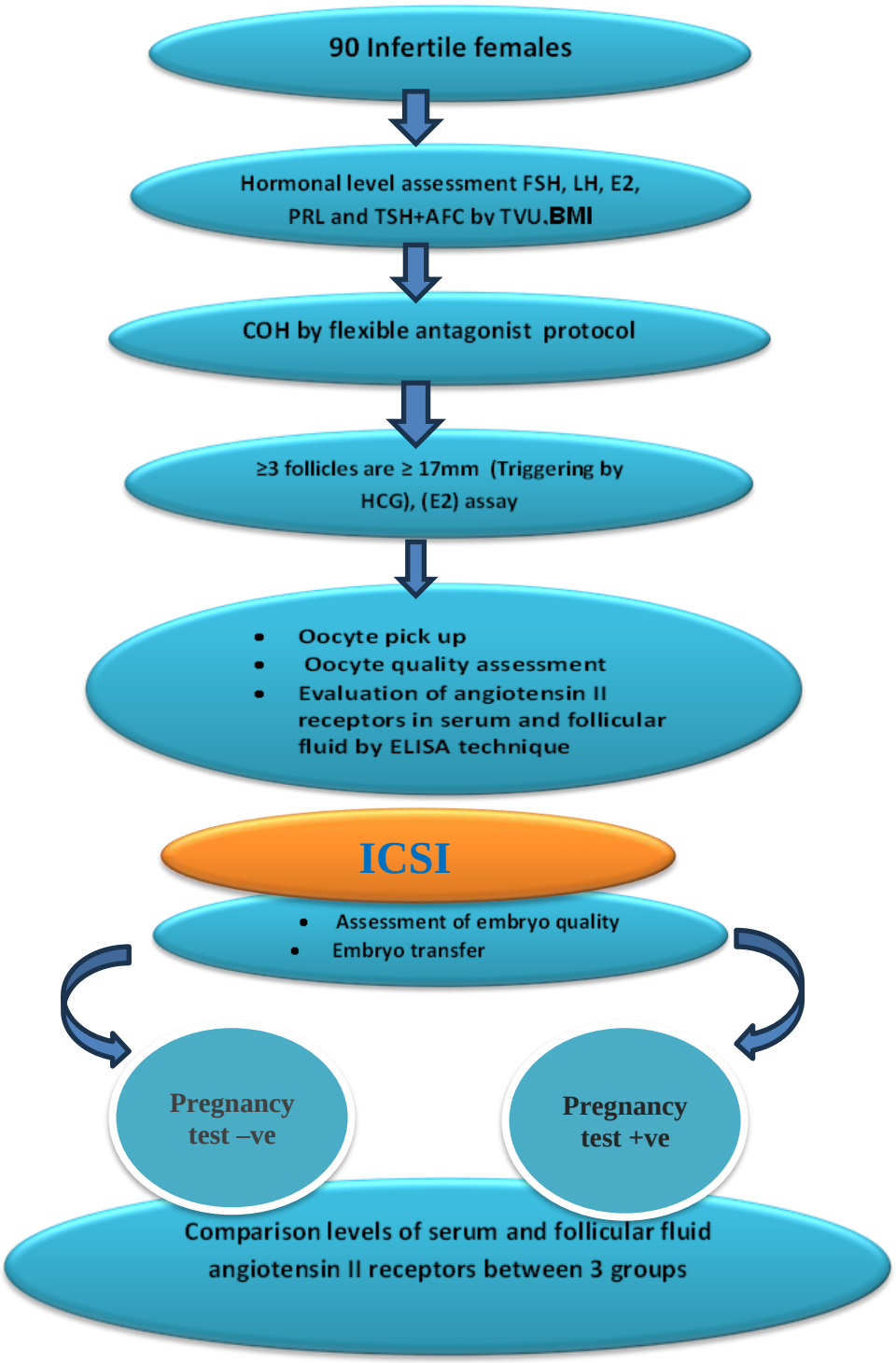
The patients were categorized into three groups based on their BMI: normal, overweight (BMI 25-29.9), and severe obesity (BMI 30-34.9).Where you get the formula of body mass index (BMI) is weight (in kilograms) over height (in meters) squared.On the second day or the third day before the cycle, the female persons had a test of the baseline.

Age range of the subjects included 18-42 years with the limitation criteria being the women's ages.

In the end, all the 90 female patients with the primary as well as the secondary infertility that underwent ICSI cycles were counted.The ongoing project of the ICSI laboratory at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies has resulted in the morphology assessment of oocytes that were extracted from the ovaries of infertile women, and the evaluation of embryos that were resulted from the procedure. The level of the angiotensin receptors in blood and follicular fluid was assessed on the day of oocyte collection, ELISA method was employed in a private laboratory.The induction of ovulation and ovulation were done using different methods.The women were regularly checked both with vaginal ultrasound and estimating blood estradiol levels.The tests served as a basis to perform ovum retrieval (OPU) which was done exactly 35–36 hours after ovulation induction.Receptors on the blood and follicular fluid angiotensin II were measured in each individual donor during the OPU procedure.After the procedure a sample obtained from the patient, maturation rate (MR) and morphological research was made and they normal MII oocytes were intracytoplasmic sperm injected (ICSI) was implanted.The number of embryo grades was documented and an examination of the embryo morphology was also conducted. Alongside that,

the fertilization rates were determined.The thirteenth day of the luteal phase starting from the day of embryo transfer, the luteal phase support, embryo transfer, serum beta-human chorionic gonadotropin amount, and biochemical pregnancy rate were evaluated.

Study Design Scheme



Ice-blasting the IntraCytoplasmic Sperm Injection (ICSI) in-cycles with Gonadotropin-Releasing Hormone (GnRH) Antagonist was used in all cases.Besides, the infertility history, which included the type, the duration and the cause of the infertility as well, was properly recorded. Very thorough general gynecological and physical examinations were done to leave out any possibility of abnormalities. The first session of female patients will include the hormonal assay, for which they need to have a baseline hormonal test done on day two or three of their menstrual cycleFSH, LH,

Demographic features	Normal weight females N. = 27	Over weight females N. = 32	Obese Females N. = 31	*p* value
Age (years)	29.30 ± 1.21	33.03 ± 1.20	31.29 ± 1.03	0.082 ∀

TSH, prolactin, and estrogen levels are determined through blood assessment. On the second and third days of the menstrual cycle, all patients were taken for a baseline transvaginal ultrasound for the assessment of endometrium thickness, antral follicles number, and the presence of ovarian cysts or other abnormalities in the uterus and oIn the previous menstrual cycle one can visualize the condition of the uterus and fallopian tubes with the help of hysterosalpingography, sonohystrosalpingography or with laparoscopy.This is of great importance because the existence of certain anomalies such as endometrial polyps, sub-mucosal myoma, a large septate uterus, and intrauterine adhesions can reduce the chances of a viable implantation.Both of them underwent detailed laboratory tests that incorporated for HIV and hepatitis viruses, blood type, hemoglobin, blood sugar and antibody levels, COVID-19 rapid testing, and seminal fluid analysis to form a screen and fitness test for ICSI, all according to the WHO reference values 2010.

Statistical analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.0 and Microsoft Office 2010.The data was analyzed using descriptive statistics, which included measures of frequency, range, mean, and standard error.The groups were compared using ANOVA, which is a statistical test used to compare more than two distinct groups. Additionally, an independent sample t-test was used to compare between two separate groups, and a chi-square test was used to compare non-continuous variables or percentages. Pearson's correlation coefficient (r) was used to assess the degree of relationship between continuous variables.

3. Results and discussion

A total of ninety infertile females participated in this cross-sectional research. The participants were categorized into three categories according on their body mass indices: 27 females (30.0%) were of normal weight, 32 females (36.0%) were overweight, and 31 females (34.0%) were obese. The patient's data were presented as the mean plus or minus the standard error of the mean (Mean ± SE).

An analysis of demographic characteristics among females categorized as normal weight, overweight, and obese.

There were significant differences in mean body mass indices between females of normal weight, overweight, and obese categories (22.12 ± 0.31 vs 26.92 ± 0.27 vs 31.66 ± 0.30; $p < 0.001$). However, there were no significant differences in age (29.30 ± 1.21 vs 33.03 ± 1.20 vs 31.29 ± 1.03; $p = 0.082$), duration of infertility (6.93 ± 0.69 vs 6.53 ± 0.73 vs 7.94 ± 0.82; $p = 0.388$), types of infertility ($p = 0.074$), and causes of infertility ($p = 0.780$) as shown in Table 1.

Table 1: Comparison of demographic features between normal weight, over weight and obese females

(Mean±SE)					NS
BMI (Kg/m²) (Mean±SE)		22.12 ± 0.31	26.92 ± 0.27	31.66 ± 0.30	< 0.001 ∀ S
Duration of infertility (years) (Mean±SE)		6.93 ± 0.69	6.53 ± 0.73	7.94 ± 0.82	0.388 ∀ NS
Type of infertility N. (%)	Primary	25 (92.6 %)	22 (68.8 %)	25 (80.6 %)	0.074 € NS
	Secondary	2 (7.4 %)	10 (31.3 %)	6 (19.4 %)	
Causes of infertility N. (%)	Female causes	11 (40.7 %)	13 (40.6 %)	10 (32.3 %)	0.780 € NS
	Male causes	6 (22.2 %)	11 (34.4 %)	11 (35.5 %)	
	Unexplained causes	3 (11.1 %)	4 (12.5 %)	5 (16.1 %)	
	Combined causes	7 (25.9 %)	4 (12.5 %)	5 (16.1 %)	

SE: Standard error; NS: Not significant (p> 0.05); ∀: ANOVA (Analysis of variance); €: Chi square

An analysis of hormone levels in females categorized as normal weight, overweight, and obese.

The hormonal levels of normal weight, overweight, and obese infertile females were compared in table 2. According to the results, there were no significant differences in FSH (6.88 ± 0.30 vs. 6.67 ± 0.29 vs. 6.36 ± 0.32; p = 0.490), LH (5.04 ± 0.59 vs. 4.44 ± 0.35 vs. 5.30 ± 0.49; p = 0.407), AMH (3.16 ± 0.59 vs. 1.78 ± 0.33 vs. 2.11 ± 0.45; p = 0.102), basal E2 (37.42 ± 2.19 vs. 37.24 ± 2.30 vs. 37.34 ± 2.97; p = 0.999), E2 at the day of trigger (1408 ± 132 vs. 1459 ± 130 vs. 1310 ± 158; p = 0.297), and prolactin levels (16.35 ± 0.90 vs. 16.59 ± 1.06 vs. 15.77 ± 0.96; p = 0.191).

Table 2: Comparison of hormonal levels between normal weight, over weight and obese females

Hormones (Mean±SE)	**Normal weight females N. = 27**	**Over weight females N. = 32**	**Obese Females N. = 31**	***p* value**
FSH (mIU/ml)	6.88 ± 0.30	6.67 ± 0.29	6.36 ± 0.32	0.490 ∀ NS
LH (mIU/ml)	5.04 ± 0.59	4.44 ± 0.35	5.30 ± 0.49	0.407 ∀ NS
AMH (mIU/ml)	3.16 ± 0.59	1.78 ± 0.33	2.11 ± 0.45	0.102 ∀ NS
Basal E2 (pg/ ml)	37.42 ± 2.19	37.24 ± 2.30	37.34 ± 2.97	0.999 ∀ NS
E2 at time of trigger (pg/ ml)	1408 ± 132	1459 ± 130	1310 ± 158	0.297 ∀ NS
Prolactin (ng/ml)	16.35 ± 0.90	16.59 ± 1.06	15.77 ± 0.96	0.191 ∀ NS

SE: Standard error ; LH: Luteinizing hormone; FSH: Follicle stimulating hormone; AMH; Antimullerian hormone; E2: Estradiol; NS: Not significant (p> 0.05); ∀: ANOVA (Analysis of variance)

An analysis of the features of intracytoplasmic sperm injection (ICSI) in females categorized by body weight: normal weight, overweight, and obese

***Comparative analysis of oocyte features among females of normal weight, overweight, and obese categories*.**

There were no significant differences observed among normal weight, overweight, and obese females in terms of total oocytes (14.22 ± 1.49 vs. 11.34 ± 1.13 vs. 11.16 ± 1.62; p=0.258), MI oocytes (1.19 ± 0.27 vs. 0.53 ± 0.13 vs. 0.77 ± 0.18; p=0.072), MII oocytes (10.11 ± 1.20 vs. 8.41 ± 0.97 vs. 7.45 ± 0.90; p=0.194), germinal vesicles (1.26 ± 0.26 1.47 ± 0.35 1.58 ± 0.50; p=0.847), maturation index (71.26 ± 3.69 vs. 73.84 ± 3.63 vs. 72.55 ± 3.37; p=0.880), and fertilization rate (78.04 ± 3.77 vs.

78.28 ± 3.58 vs. 75.00 ± 3.50; p=0.770) as shown in table 3.

***An analysis of embryonic features is conducted to compare the differences between females of normal weight, overweight, and obese categories*.**

In relation to grade I embryos, there were insignificant differences observed (Table 3) with values of 4.19 ± 0.82, 3.47 ± 0.38, and 3.26 ± 0.48; p=0.495. Similarly, for grade II embryos, there were insignificant differences with values of 2.26 ± 0.34, 1.59 ± 0.23, and 1.61 ± 0.31; p=0.212. Lastly, for grade III embryos, there were insignificant differences with values of 0.41 ± 0.16, 0.22 ± 0.09, and 0.19 ± 0.11; p=0.405.

Table 3: Comparison of ICSI parameters between normal weight, over weight and obese females

ICSI parameters (Mean ± SE)	Normal weight females N. = 27	Over weight females N. = 32	Obese Females N. = 31	*p* value
Total oocytes count	14.22 ± 1.49	11.34 ± 1.13	11.16 ± 1.62	0.258 ∀ NS
Metaphase I oocytes	1.19 ± 0.27	0.53 ± 0.13	0.77 ± 0.18	0.072 ∀ NS
Metaphase II oocytes	10.11 ± 1.20	8.41 ± 0.97	7.45 ± 0.90	0.194 ∀ NS
Germinal vesicles	1.26 ± 0.26	1.47 ± 0.35	1.58 ± 0.50	0.847 ∀ NS
Maturation index	71.26 ± 3.69	73.84 ± 3.63	72.55 ± 3.37	0.880 ∀ NS
Fertilization rates	78.04 ± 3.77	78.28 ± 3.58	75.00 ± 3.50	0.770 ∀ NS
Grade I embryo	4.19 ± 0.82	3.47 ± 0.38	3.26 ± 0.48	0.495 ∀ NS
Grade II embryo	2.26 ± 0.34	1.59 ± 0.23	1.61 ± 0.31	0.212 ∀ NS
Grade III embryo	0.41 ± 0.16	0.22 ± 0.09	0.19 ± 0.11	0.405 ∀ NS

NS: Not significant (p > 0.05); ∀: ANOVA (Analysis of variance)

Comparative analysis of angiotensin II receptors in blood and follicular fluids among females of normal weight, overweight, and obese categories.

There were no significant differences in the levels of angiotensin II receptors in serum and follicular fluids between normal weight, overweight, and obese females. The values for normal weight, overweight, and obese females were 85.96 ± 4.44, 83.15 ± 5.90, and 82.06 ± 2.42, respectively (p=0.838) in serum, and 117.4 ± 12.77, 97.88 ± 5.08, and 90.79 ± 4.31, respectively (p=0.055) in follicular fluids. These results are shown in table 4.

Table 4: Comparison of serum and follicular fluids angiotensin II receptors between normal weight, over weight and obese females

Parameters (Mean ± SE)	Normal weight females N. = 27	Over weight females N. = 32	Obese Females N. = 31	*p* value
Serum angiotensin II receptors (pg/ml)	85.96 ± 4.44	83.15 ± 5.90	82.06 ± 2.42	0.838 ∀ NS
Follicular fluids angiotensin II receptors (pg/ml)	117.4 ± 12.77	97.88 ± 5.08	90.79 ± 4.31	0.055 ∀ NS

S: Significant (p ≤ 0.05); ∀: ANOVA (Analysis of variance)

Correlations between serum and follicular fluids angiotensin II receptors with ICSI parameters

The study found significant positive correlations between the levels of angiotensin II receptors in follicular fluids and certain parameters of intracytoplasmic sperm injection (ICSI). Specifically, there were significant positive correlations between follicular angiotensin II receptors and the total number of oocytes, mature oocytes, and high-quality embryos. These findings are presented in table 5.

Table 5: Correlations between serum and follicular fluids angiotensin II receptors with ICSI parameters

Hormones	Statistics	Serum angiotensin II receptors	Follicular fluids angiotensin II receptors
Total oocytes	r	- 0.096	**0.519**
	p value	0.378 NS	**< 0.001 S**
Metaphase I oocytes MI	r	0.130	0.113
	p value	0.231 NS	0.104 NS
Metaphase I oocytes MII	r	-0.131	**0.511**
	p value	0.227 NS	**< 0.001 S**
Germinal vesicles GV	r	- 0.093	- 0.044
	p value	0.392 NS	0.678 NS
Maturation index	r	- 0.059	-0.020
	p value	0.589 NS	0.851 NS
Fertilization rate	r	0.121	-0.049
	p value	0.263 NS	0.646 NS
Grade I embryos	r	0.067	**0.607**
	p value	0.540 NS	**< 0.001 S**
Grade II embryos	r	- 0.108	0.021
	p value	0.318 NS	0.846 NS
Grade III embryos	r	- 0.035	-0.011
	p value	0.747 NS	0.920 NS

Discussion

This study involved 90 ICSI cycles (ICSI cycles) that were just recently performed in a retrospective cohort fashion.Collected were the laboratory and clinical medical data of female patients and the data were compared through several groups of the women summarized according to their BMI.The localized angiotensin renin system is in the female reproductive system.Studies have demonstrated multiple times that the reproductive system itself is able to synthesize Ang II and Ang-(1–7) in its tissues, Angiotensin II.The main characteristic of polycystic ovary syndrome (PCOS) is the modifications in the hormones production, the monthly changes of the inner uterine lining and the eggs maturation and release.The Renin-Angiotensin System (RAS) is regarded the most significant system which controls the physiological processes in reproduction.While little is known about the specific functions of Ang II and Ang-(1–7) in the physiology and pathology of the female reproductive system, recent studies have revealed that this molecule is deeply implicated in these processes (15,16).

As shown on the Table 1, three groups, which match age, length of infertility, type, and reason of the ferility, are characterized by their Body mass index and denoted by A, B, and C respectively..There were no differences of a significant magnitude noticed among these groups.The body mass index among the three groups is the greatest in Group A indicating a significant difference in weight.Tan and Al-Obaidi noted (2014 and 2023) that in the women undergoing assisted reproduction, the most important and the most matchable factor with age in the women is the factor of age.The reason and consequences of reduced fertility with age could be the inability of the ovaries to get enough follicles needed for their functioning, the number of the oocytes is small, the oocytes quality is poor, and so is the embryos, there are fewer embryos to be fertilized, and the rate of implantation is low as well.Furthermore, even after ongoing assessment, there was no substantial difference in the average age for the three groups(17,18) .Inverhak et al. (2005), the researchers have illustrated that the length of infertility has a substantial influence on the decrease of fertility and there was no significant difference in the duration of infertility of the three group of women participants occurring in this

study (19). Thus, no significant relationship between infertility types and reasons as well as between BMI and type of infertility is evident in the research subjects.However, unlike Benskim et al. (2018) who claimed that most primary infertility cases are due to female variables,... Conversely, Benskim, et al (2018) stated the opposite, that the majority of primary infertility cases are due to female factors.The studies from the source (20,21). (2 lines)Elhussein O. et al. (2019) agreed that the present study stipulated that diabetes ages, the duration of diabetes, and the type of infertility are insignificant after being corrected for confounding due to birth control.The demographic factors for the females with infertility included as a part of this study were measured using the mean and standard deviations (SD).To sum up, there are no striking disparities between the age and duration of infertility in any of the three ICSI groups (22).By the same token, no adequate data was retrieved among primary and secondary infertility of the three IVF patients in each group who had ICSI.

Ovarian reserve tests were meant to serve as a test for patients in laboratories before starting an in vitro fertilization (IVF) cycle.Testing for ovarian reserve can utilize both qualitative and quantitative approaches. For example, ultrasound can be used to determine the number of developing follicles and serum FSH, AMH and E2 can be used to provide serial data for monitoring.The study is facilitated of process of determining a female's ability to conceive and the method of her ovulation in response to controlled stimulation (23).Estradiol within the ovarian follicles is produced by the main cells, which are called Granulosa cells.This process of multiplication and division takes place within a follicle, which in turn produces an increase in the follicle volume. And as this volume increases, so does the E2 level.The total E2 can be used to determine follicular maturation level with high accuracy (24) .The individual's current FSH measurement is often still the baselines for the usual treatments.When female Follicle-stimulating Hormone (FSH) are more than 10–12 IU/L, this commonly indicates that women’s ovarian reserve is too low (17).Aneurotocin-like, pituitary actions of the LH results to steroidogenesis in the ovarian follicles, as LH is associated with folliculogenesis according to the "two-cell, two-gonadotrophin" paradigm.Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) usually function in symphony to achieving these effects: the formation of ovarian follicles and then the production of eggs (25).

However, the present investigation into hormone levels of infertile women did not indicate any statistically significant differences among the three groups regarding basal estradiol (E2), re-estimated estradiol (E2) on the day when hCG was triggering, FSH, LH, and AMH.The connection between our research and the experiment of ICSI was made by considering both the starting hormone levels of the recipients and their E2 levels on the day of triggering with regard to their BMI.Performing an ICSI(26) on a group of overweight and obese individuals, no statistically different results have been found, compared to the normal weight control group.This, however, contradicts the results of Mandakini P, 2010, which documented that the infertile, anovulatory obese women had decreased levels of SHBG and higher levels of insulin, LH, and androgen hormones when compared to a women of normal BMI (body mass index) or obese patient who had regular periods .This do not agree with the observation which Mandakini P, 2003 made that the levels of SHBG are lower whereas levels of insulin, LH, and plasma androgens are higher in infertile obese women with amenorrhoea compared with normal-weight patients and obese women with regular periods (27) .

We still did not find any statistically significant divergence of the three BMI classes regarding the total number of oocytes, MI, MII oocytes, germinal vesicles, maturation index and fertilization index.This study of Orazov M. in 2019 reflected on the quality of oocytes harvested from the obese women. They seemed not to complete maturing completely, and the conception rate was slower than that of normal women.The study done by Kim J. et al. in 2023 proved that obesity might affect the ovarian reserve of women in PCOS in a different manner than the patients that are non-PCOS.But this dose does not change the number of mature oocytes collected after Controlled Ovarian Hyperstimulation (COH) and the presence of female obesity independent of PCOS does not affect the number of mature oocytes obtained (29)The study examines the angiotensin II receptors in the blood

and follicular fluids of females with different body weights: a healthy weight, overweight, and obesity.There were unimportant effect on the levels of angiotensin II receptors in both blood and follicular fluids among females of normal weight, overweight and obese.

Contradictory to the results of melissa W., et al. (2019) who measured significant differences in the expression, activity, and tissue response the RAS by sex, gender and geographical localities.Estrogen leads to decrease in the production of Angiotensin II and increases the production of Ang-(1-7); the latter helps to combat the negative effects of Angiotensin II on the body.Reliable levels of circulating Ang-(1-7) in the animal models of female obesity are found in the same pattern of running.Moreover, they exert an impact on the development of hypertension and metabolic disorders that are induced by angiotensinogen activation, renin, angiotensin-II and AT1R (30).We have observed there were ATR1 protein found in the follicles that associated with total number and the mature oocytes and the quality of grades I of embryos.A study by Kim JY et al. (2017) revealed that the rate of production of mature oocytes in mature follicle culture (MFCC) experimentally treated with angiotensin II receptor agonist - CGP-42112 was markedly higher than the control and angiotensin II receptor antagonist (Saralasin) groups.The group with ATII-Rc agonist in MFCC (Multiple Follicle Culture Condition) experiment showed significant higher ovulation rate per culture droplet than that of the control group.Nevertheless, not birth rate or abnormal oocyte and embryo appearing was identified in the ATII-Rc agonist group as the oocytes developing through reproductive maturation looked like normal (29).

4. Conclusion and future scope

The current study and its results demonstrate that angiotensin II receptors 1 can be identified in both the serum and follicular fluid of all patients undergoing IVF-ET. Furthermore, the concentrations of these receptors are greater in the follicular fluid compared to the serum. The amount of blood angiotensin II receptors 1 is not indicative of the level of follicular fluid angiotensin II receptors 1. There was a negligible association between the levels of angiotensin II receptor 1 in the serum and follicles. Elevated levels of angiotensin II receptors 1 in the follicular fluid may have a beneficial effect on the rate of pregnancy. There is a strong and meaningful correlation between the amount of angiotensin II receptors 1 and the occurrence of pregnancy, which has been shown to be statistically significant.

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