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MEASUREMENT OF CADMIUM CONCENTRATION IN BLOOD AND FOLLICULAR FLUID TO ASSESS ITS RELATION WITH OOCYTE AND EMBRYO QUALITY IN WOMEN UNDERGOING INTRA CYTOPLASMIC SPERM INJECTION

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ABSTRACT

Background: Cadmium, is known to cause opposing reproductive effects, and classified as an endocrine disrupting chemical. **Objectives:** General population has relatively higher exposure to environmental pollution, the goal in this study is to assess the effect of Cadmium concentration level in blood and follicular fluid on oocyte, embryo quality and pregnancy success in women undergoing ICSI. **Patient, Materials and Methods:** This study included 70 infertile couples joined in assisted reproductive technology (ART) programs to enter ICSI cycle in high Institute for Infertility Diagnosis and Assisted Reproductive Technologies and Kamal AL-Samarai Hospital, center of fertility and IVF(Baghdad/Iraq) during the period from October 2016 to February 2017. The level of Cadmium concentration will be measured and assess their effect on oocyte and embryo quality. **Results:** highly significant difference was observed in follicular fluid cadmium (p- value 0.0429, $P < 0.05$) also there was No-significant difference was observed in blood cadmium($P < 0.05$). Blood Cadmium in pregnant there was negatively correlated with (M1, M2, GV, rapture and abnormal) type of oocyte, fertilization rate and number of embryo transfer but in no- pregnant group there was positive correlated with (M1,M2,GV,rapture and abnormal) type of oocyte, fertilization rate and number of embryo transfer. Follicular fluid cadmium in pregnant group shows positive correlation with M2 and abnormal type of oocyte, fertilization rate and number of embryo transfer and negative correlation with GV, rapture and M1 type of oocyte. Follicular fluid cadmium in no-pregnant

there was positive correlation with GV, rapture and M1 type of oocyte and negative correlation with M2 and abnormal type of oocyte, fertilization rate and number of embryo transfer. **Conclusions:** There was a Significant difference in follicular fluid cadmium between pregnant and no–pregnant. The Increasing number of oocyte lead to increase the fertilization rate, high number of embryo transfer(grade1) this lead to increase chance of pregnancy outcome.

KEYWORDS: Cadmium, oocyte, embryo, ICSI.

INTRODUCTION

Cadmium (Cd) is a silvery-white, soft, ductile chemical metal with atomic number 48 an atomic mass of 112 and belonging to the group 12 element in d block and period 5.[1] Cd administration profoundly alters ovarian steroidogenesis associated with a reduction in progesterone secretion. Similarly, exposure of cultured human and rat ovarian granulosa cells to Cd causes a reduction in progesterone production. Cd has also been shown to increase the rate of oocyte degeneration in sheep and impair oocyte maturation in sheep and pigs. Studies have demonstrated increased accumulation of Cd in the ovary with an increase in age thus leading to failure of progression of oocyte development and ovulation.[2] Presence of Cd has been identified in follicular fluid and have been associated with adverse reproductive outcomes in epidemiologic studies.[3]

Assisted reproductive techniques (ART) as defined by International Society of Monitoring Assisted Reproduction (ICMART) and World Health Organization (WHO) is" all treatments or procedures that include in the vitro handling of both human oocytes and sperm or of embryos for the purpose of establishing a pregnancy. This includes, but is not limited to, in vitro fertilization and embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocytes and embryo donation, and gestational surrogacy. ART does not include assisted insemination (artificial insemination) using sperm from either a woman’s partner or a sperm donor. On the other hand, the term medically assisted reproduction (MAR) is given to the wider scope involving reproduction brought about through ovulation induction, controlled ovarian stimulation, ovulation triggering, ART techniques mentioned above and artificial insemination.[4]

PATIENT, MATERIAL AND METHODS

This study included 70 infertile couples enrolled in assisted reproductive technology (ART) programs to enter ICSI cycle in high Institute for Infertility Diagnosis and Assisted Reproductive Technologies and Kamal AL-Samarai Hospital, center of fertility and IVF (Baghdad/Iraq) during the period from October 2016 to February 2017. The average age of included women ranged between 18 and 42 years had primary and secondary infertility with duration between2-8year.

Collection of Blood and Follicular Fluid Sample

2.5milliliters of blood sample were collected by venipuncture, from each infertile woman on day of oocyte retrieval, put in EDTA tube and use to evaluate blood cadmium**.**

Measurement of Blood Cadmium

1- shaking of blood sample for one hour to broken the red blood cell (RBC) to away from hemoglobin because this effect on the result.

2- put the blood sample in plane tube and addition 2,5ml of Tri-chloral acetic acid (TCA) this work on hemoglobin deposition in the base of the tube.

3- use wooden stick to mixing sample (blood + TCA) and left for ten minutes.

4- centrifuged for 10 minutes at 3000 rpm and then taken filtrate and read the result directly by using flameless AAS. (graphite furnace) at the wave length 228.8nm the sample inject to graphite furnace with the same principle of flame AAS with high sensitivity and specificity method than the flame AAS.[5] Normal value 0-0,3 microgram\DL.[6]

Measurement of follicular fluid Cadmium

The result directly read by using flameless AAS without any dilution at the wave length 228.8nm. Normal value 0-0,19 microgram\L.[6]

Statistical Analysis

The Statistical Analysis System- SAS (2012) program was used to effect of difference factors in study parameters. Least significant difference –LSD test (ANOVA) or T-test was used to significant compare between means. Chi-square test was used to significant compare between percentage. Estimate of correlation coefficient between parameters in this study. A P value < 0.05 was considered to be statistically significant.[7]

RESULTS

Table (1) show Compare between pregnant and non-pregnant in Cd in blood, The Cd level in blood expressed as (microgram/dl) of the total patients, pregnant, and non-pregnant group (0.325 ± 0.009 and 0.314 ± 0.008, respectively). There was no significant difference was observed in Cd in blood between the pregnant and non-pregnant group. also Table (1) show Compare between pregnant and non-pregnant in Cd in Follicular Fluid. The Cd level in FF expressed as (microgram/L) of the total patients pregnant and non-pregnant group(0.235 ± 0.008 and0.210 ± 0.007, respectively).

Table. 1: Compare between pregnant and non-pregnant in Cadmium in blood and follicular fluid.

The group	Mean ± SE of Cd in blood (microgram/dl)	Mean ± SE of Cd in FF (microgram/L)
Pregnant	0.325 ± 0.009	0.235 ± 0.008
Non-pregnant	0.314 ± 0.008	0.210 ± 0.007
T-Test	0.026 NS	0.024 *
P-value	0.426	0.0429
Mean(M) ± Standard Error(S.E.)		

In this study, there was found that is No significant negative correlation was observed between the Cd in blood and M1($r = 0.02, P < 0.05$). Asignificant negative correlation was observed between the Cd in blood and M2($r = 0.31, P < 0.05$), Fertilization rate (%) ($r = 0.35, P < 0.05$) and number of embryo transfer ($r = 0.31, P < 0.05$). No significant positive correlation was observed between the Cd in blood and GV ($r = 0.11, P < 0.05$), Abnormal ($r = 0.17, P < 0.05$) and Rapture ($r = 0.02, P < 0.05$) all of theis in pregnant pateints. A significant positive correlation was observed between the Cd in blood and M1($r = 0.30, P < 0.05$), Abnormal($r = 0.38, P < 0.05$) and Rapture($r = 0.30, P < 0.05$), No significant positive correlation was observed between the Cd in blood and M2($r = 0.04, P < 0.05$), Fertilization rate (%)($r = 0.02, P < 0.05$) and No. of embryo transfer($r = 0.06, P < 0.05$). A highly significant positive correlation was observed between the Cd in blood and GV($r = 0.45, P < 0.05$) all of theis in non pregnant pateints. in pregnant group observed the correlation between Cd in Follicular Fluid with Type of oocyte in pregnant. No significant negative correlation was observed between the Cd in FF and M1($r = 0.07, P < 0.05$), and rapture ($r = 0.08, P < 0.05$). A significant positive correlation was observed between the Cd in FF and M2($r = 0.29$, $P < 0.05$), and Number of embryo transfer ($r = 0.31$, $P < 0.05$), significant negative correlation was observed between the Cd in FF and GV ($r = 0.31, P < 0.05$). No significant

positive correlation was observed between the Cd in FF and abnormal (r = 0.14,P < 0.05) type of oocyte and Fertilization rate (%) (r = 0.17,P < 0.05). In non- pregnant group no significant negative correlation was observed between the Cd in FF and GV (r = 0.12,P < 0.05), rapture (r = 0.14,P < 0.05), abnormal(r = 0.09,P < 0.05) and Fertilization rate (%) (r = 0.14,P < 0.05). A significant positive correlation was observed between the Cd in FF and M1(r = 0.29,P < 0.05), No significant positive correlation was observed between the Cd in FF and M2(r = 0.13,P < 0.05) and Number of embryo transfer (r = 0.04,P < 0.05) as show in table (2).

Table. 2: Correlation between Cd in Follicular Fluid and blood with Type of oocyte Fertilization rate and number of embryo transfer in pregnant and non-pregnant.

Type of oocyte	Cd (microgram/L)in pregnant in FF	Cd (microgram/L)in non- pregnant in FF	Cd (microgram/dl)in blood of pregnant	Cd (microgram/dl) in blood of non-pregnant
M1	-0.07 NS	0.29 *	-0.02 NS	0.30 *
M2	0.29 *	0.13 NS	-0.31 *	0.04 NS
Gv	-0.31 *	-0.12 NS	0.11 NS	0.45 **
Abnormal	0.14 NS	-0.09 NS	0.17 NS	0.38 *
Rapture	-0.08 NS	-0.14 NS	0.02 NS	0.30 *
Fertilization rate (%)	0.17 NS	-0.14 NS	-0.35 *	0.02 NS
No. of embryo transfer	0.31 *	0.04 NS	-0.31 *	0.06 NS
Significant * (P<0.05), NS : Non-significant, highly significant ** (P<0.01) Correlation coefficient-r				

DISCUSSION

Environmental factors differ between areas with higher amounts of pollutants closer to sources of industrialization. Environmental factors, such as exposure to heavy metals, can cause reproductive dysfunction in women.[8] The mean concentration of cadmium in pregnant group was (0.325) microgram/dl among those with average. blood Cd concentration in non-pregnant group (0.314) microgram/dl It is approximate to the normal value (0.3) microgram/dl.[9] So, it not seen highly effect on pregnancy rate in the result of this study, also because there was small sample size duo to the limitation with duration of sample collected this lead to this result. Follicular fluid provides a very important microenvironment for the development of oocytes. FF is a product of both the transfer of blood plasma constituents that cross the blood follicular barrier and of the secretory activity of granulosa and thecal cells.[10] It is reasonable to think that some biochemical characteristics of the FF surrounding the oocyte may play a critical role in determining oocyte quality and the subsequent potential to

achieve fertilization and embryo development. The analysis of FF components may also provide information on metabolic changes in blood serum, as the circulating biochemical milieu may be reflected in the composition of FF.[11] In the present study, the results showed that being FF Cd concentration lower than those in serum correlated significantly between pregnant and non-pregnant group(p<0,0429).[12] Also In the present study, the results showed that Cd in pregnant group was statistically negative correlation with M1 and M2 type of oocyte, positive correlation with abnormal, GV and rapture type of oocyte This agreement with Studies have demonstrated increased accumulation of Cd thus leading to failure of progression of oocyte development and ovulation[13], Also the result of this study show Negative correlation with Fertilization rate (%) and No. of embryo transfer, This agreement with Studies have demonstrated increased accumulation of Cd thus leading to degeneration, apoptosis and breakdown in cell adhesion thus inhibiting its progression to the blastocyst stage.[13] on the other hand in this study Cd in non-pregnant group was statistically positive correlation with, M1, M2 GV, abnormal and rapture type of oocyte, Fertilization rate (%) and No. of embryo transfer These results confirm the findings of published reports in an article by Gaku Shimoi et al[14], who have found Cd exposure during the maturation period disturbed fertilization of oocytes, and Cd exposure during the fertilization period disrupted the normal development of embryos after fertilization. This suggested that the manifestation of Cd toxicity in oocytes clearly differed with the exposure period. In addition, it was shown that Cd exposure during the maturation or fertilization period influenced the early development (including the fertilization) at a lower concentration than exposure after the 2-cell stage. Also this study was observed that follicular fluid Cd in pregnant group was statistically negative correlation with M1, rapture, GV type of oocyte, positive correlation with M2, abnormal type of oocyte, Fertilization rate and number of embryo transfer. on the other hand, Cd in non-pregnant group was statistically positive correlation with M1, M2 type of oocyte, and number of embryo transfer. Negative correlation with GV, abnormal, rapture type of oocyte, and Fertilization rate (%). this result is agreement with result in the same study show increasing heavy metals in follicular fluid were suggested to negatively affect the quality of oocytes, Fertilization rate (%) and number of embryo transfer.[15]

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