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EFFECT OF LEAD EXPOSURE ON SOME SELECTED BIOCHEMICAL AND HAEMATOLOGICAL VARIABLES WITH SPECIAL REFERENCE TO REPRODUCTIVE TOXICITY IN FEMALE RABBITS.

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ABSTRACT

The present study was designed to assess the effect of different levels of lead on ovarian activity and to elucidate some biochemical and haematological variables that can be associated with these levels. Immature female New Zealand rabbits were used, divided into four groups, each of six rabbits. Group I and II received low (5.4 mg/kg b. wt.) and high (10.8 mg / kg b.wt.) doses of lead acetate orally, respectively, daily for 5 days/week over a period of 8 weeks. Groups III and IV were kept as control. All groups (except group IV) were treated with 200 I.U pregnant mare serum gonadotrophin (PMSG) I/m, followed by i.m injection of 200 I.U human chorionic gonadotrophin (HCG), 48hrs after commencement of PMSG treatment. The results indicated that injection of PMSG, followed by HCG had stimulated the ovarian activity of the control virgin does and elevated the total ovarian response, ovulation rate and ovulation percentage. However, administration of low and high doses of lead acetate resulted in a significant decrease in total ovarian response, ovulation rate and ovulation percentage. Lead administration significantly decreased the levels of total proteins and total lipids. However, a significant increase in the levels of triglycerides was obtained with low and high doses of lead. Cholesterol level was significantly increased with the high dose only. Estradiol-17β and progesterone were significantly decreased following oral administration of both doses of lead acetate. However, lead acetate administration resulted in a significant increase in the levels of the cortisol and lead in the blood with a significant decrease in the level of zinc, calcium and phosphorus in plasma of both lead treated groups. Blood picture revealed a significant decrease in the RBCs count and HCT, while WBCs and platelets counts were significantly increased with the low and high doses of lead acetate. However, haemoglobin concentration and MCV were not significantly changed. Thus, lead administration caused adverse effects on the ovarian activity and total ovarian response, with profound changes in the biochemical, haematological and hormonal profiles.

INTRODUCTION

Lead is a well known reproductive hazard capable of affecting female fertitity as well as acting as a teratogen and has gametotoxic or mutagenic effects on the female reproduction [1]. Long term effect of lead was found in exposed female animals to delay the onset of puberty and disrupt the estrous cyclicity in the presence of detectable blood levels of lead prior to the onset of puberty[2,3]

Prolonged lead exposure was found to cause damage of the reproductive system and impairment of fertility and this is supported by the high prevalence of sterility among lead exposed females[4]. It has been shown that the reproductive capacity is markedly reduced in female mice exposed to triethyl lead[5]. They exhibited a significantly lower frequency of implanted ova and lower frequencies of pregnancy than control females. This decrease in the reproductive capacity may be due to changes in the synthesis and / or the break down of steroid hormones, where the implantation of the blastocyst in the uterine endometrium has been shown to be inhibited by 1mg of inorganic lead given i.v to mothers on the 4th day of pregnancy,the day before implantation [6]. This interference of implantation could be overcomed by administration of estradiol-17β and progesterone to the lead- treated mice[7]. In fact ,it is well known that heavy metals including lead may affect the binding of estradiol and progesterone to their receptors in uterine cytosol [8]. Lead may also cause genetic damage in the ovum before conception resulting in failure of implantation, miscarriage, stillbirth defects [9]. The women fertility and ovarian cycle seem to be affected by lead exposure [10]. with high prevalence of menstrual disturbances. Multiple levels of hypothalamopituitary gonadal axis are affected by lead exposure during the period of gestation.Lead-treated pregnant guinea pig had a reduced hypothalamic level of gonadotrophic releasing hormone (GnRH) and somatostatin in a dose dependent manner. Increased myometrial concentrations of the metal would be expected to be increased in pregnancy complicated by preterm labour as it increases the myometrial uterine activity and the reactivity to oxytocin and $PGF_{2\alpha}$ in rats in a reversible manner. Concluding that contamination with lead ions might be one of the etiological factors in spontaneous abortion and preterm labour[11]. Low lead levels may disrupt haeme synthesis and depress the serum erythropoietin concentration at mid pregnancy and at delivery resulting in anaemia which is accentuated by increased demand for Hb during pregnancy. Placenta does not have a restrictive barrier effect to protect against lead transfere from the mother to fetus early in pregnancy[13] . Lead crosses the placenta possibly by both passive diffusion and active transport with increasing amounts of lead in fetal tissues, with advancing gestational age [13]. Therefore, the present experiment was conducted to study the effects of exposure to lead on some biochemical and

haematological variables, ovarian activity and total ovarian response, as well as determination of progesterone and oestradiol concentrations in plasma of female rabbits pretreated with PMSG.

MATERIAL AND METHODS

Animals and Experimental design:

Twenty four immature female New Zealand rabbits, 14-16 weeks of age (virgin does) were used and maintained in individual wire cages, reared in the Animal House, National Research Centre. Animals were given concentrated pellets of food and water ad libidum. They were divided into four groups, each of six. The first and second groups were given low (5.4 mg/kg b.wt.) and high (10.8 mg/kg b.wt.) doses of lead acetate respectively, 5 days/ week for 8 weeks, orally by intubation.

The 3rd and 4 th groups were kept as control. All groups (except group IV) were treated with pregnant mare serum gonadotrophin (Folligon^{R}, PMSG, Intervet, Holland), 200 I.U, i/m followed by injection of human chorionic gonadotrophin (pregnyl^{R} HCG, Organon, Holand), 200 I.U, i.m., 48hrs after initiation of PMSG treatment, 48-72 hrs before decapitation of rabbits.

Ovaries were immediately collected after slaughtering of rabbits in Ham's F-10 medium (Ham's nutrient mixture, F-10, JRH Biosciences Lenexa, KS, USA). The number of follicles, corpora haemorrhagica and corpora lutea (total ovarian response) was counted for determinatian of ovarian activity. Twenty four ovaries (50% of the total ovaries) were randomly selected for this study. Group IV was used as control for group III to determine the effect of PMSG on the ovarian activity.

Blood Samples

Blood Samples were collected during decapitation of rabbits in 2 tubes containing either EDTA (for haematological examination) or heparin (for separation of plasma). Blood plasma was collected in heparinized tubes & kept at - 20°C, until analysed for biochemical and hormonal assays.

Total proteins content was determined according to Petters[14]; cholesterol levels according to Watson [15]; plasma cortisol concentration (Kowalski and Paul, [16]. Total lipids Fringe and Dunn [17]. Whereas, Progesterone and estradiol-17 B were determined by using radioimmumoassay techniques according to the methods of Abraham[18] and Allen and Redshow [19]. Aliquots of blood were also collected freshly on EDTA for haematological parameters (RBCs, WBCs, Hb, platelets, HCT, MCV) using cell counter Serono Diagnostic 190T, in the Central Lab., National Research Centre.

Lead (in blood), Zn, Ca and inorganic phosphorus concentrations (in plasma) were determined by using atomic absorption spectrophotometry [20] after wet digestion by nitric acid.

Statistical analysis :

Data were analysed statistically according to the method of Snedecor and Cochran [21] using Student's "t" test.

RESULTS

Influence of lead toxicity on ovarian activity:

In the present study, all the virgin does (except group IV) were treated with 200 i.u PMSG to augment the follicular growth, followed by injection of HCG, i.m, 2hrs after mating to induce ovulation in virgin does. Injection of PMSG, 4-5 days before slaughtering of female rabbits (does), stimulated the ovarian activity and resulted in increased total ovarian response (Total number of growing follicles + corpora haemorrhagica + corpora lutea),Table (1). Administration of low dose of lead acetate (5.4mg / kg b.wt) to rabbits (group I) resulted in a remarkable decrease in total ovarian response and decrease in ovulation rate and ovulation percentage compared to control group (group III).

Moreover, animals received high dose of lead acetate (10.8mg/kg b.wt, group II were highly affected with the treatment and showed a significant ($p<0.05$) decrease in total ovarian response, and significant ($p<0.01$) decrease in ovulation rate and ovulation percentage compared with the control group.

Biochemical and Hormonal changes :

The effect of lead administration on the biochemical and hormonal levels in the blood plasma of female rabbits was shown in Table (2).

Total proteins were significantly decreased with low and high doses of lead compared with the control group. Total lipids concentration was significantly ($p<0.01$) decreased in groups I and II respectively, compared with the control group. Cholesterol levels, have recorded also a high significant ($p<0.01$) increase in the plasma of rabbits received only high dose of lead. Moreover, exposure of female rabbits to lead resulted in a highly significant ($p<0.001$) increase in the plasma levels of triglycerides in groups I and II.

Estimation of reproductive hormones concentrations in the plasma of treated rabbits are shown in table (2). Estradiol-17β was significantly ($p<0.01$) decreased in group I and group II as compared with that in the

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Table (1) : Effect of PMSG on Ovarian activity of rabbits pretreated with lead. (Mean ± S.E)

n = 6

	Control without PMSG treatment	Control with PMSG treatment	Low dose lead (5.4mg/kg. b.wt.)	High dose lead (10.8mg/kg.b.wt)
Total Ovarian response	No clear follicular growth	25. 75 ± 1.65	19.86 ± 1.88 *	19.13 ± 2.11*
Ovulation rate	—	16.83 ± 1.65	10.86 ± 1.16 *	9.0 ± 1.51 **
Ovulation %	—	65.36 %	54.68 %	47.05%

* P < 0.05 ** P < 0.01

Table (2) : Some biochemical and hormonal variables in the blood plasma of female rabbits received different doses of lead acetate . (Mean ± S.E)

n = 6

Variables	Control with PMSG	Low dose lead (5.4mg/kg. b.wt.)	High dose lead (10.8mg/kg.b.wt)
Total proteins (g / L)	5. 88 ±0.37	4.91 ± 0.13 *	4.53 ± 0.17 **
Total Lipids (mg / dL)	401.002 ±50.18	209.49 ± 13.21 **	190.03 ± 13.05 **
Cholesterol (mg / dL)	111.22 ±6.11	127.49 ± 12.81	140.04 ± 6.35 **
Triglyceride (g / dL)	115.55 ±5.65	290.2 ± 13.47 ***	284.2 ± 18.55 ***
Estradiol (pg / ml)	87.98 ± 15.6	26.59 ± 2.53 **	26.47 ±5.09 **
Progesterone (ng / ml)	13.53 ± 2.83	3.15 ± 1.27 **	2.90 ±0.73 **
Cortisol (ug / dL)	2.12 ± 0.07	4.70 ± 0.36 ***	10.03 ±3.10 ***

* P < 0.05 ** P < 0.01 *** P < 0.001

Table (3) : Concentrations of Some minerals in the blood or plasma of female rabbits received different doses of lead acetate . (Mean ± . S.E)

n = 6

	Control with PMSG	Low dose lead (5.4mg/kg. b.wt.)	High dose lead (10.8mg/kg.b.wt)
Lead (Mg /dL)	3.79 ± 0.36	21.75 ± 0.84***	37.86 ± 1.95***
Zinc (Mg / dL)	214.62 ± 16,.39	197.12 ± 5.11	152.90 ± 5.62**
Calcium (total) (mg / dL)	9.93 ± 0.49	8.39 ± 0.37*	6.12 ± 0.10**
Phosphorus (mg / dL)	7.83 ± 0.37	5.83 ± 0.21***	4.53 ± 0.19***

* P < 0.05 ** P < 0.01 *** P < 0.001 lead (blood). Zn/ca/ p (plasma)

Table (4) : Haematological picture of female rabbits treated with different doses of lead acetate . (Mean ± . S.E)

n = 6

Variables	Control with PMSG	Low dose lead (5.4mg/kg. b.wt.)	High dose lead (10.8mg/kg.b.wt)
R . B . Cs $\times 10^6$	6.18 ± 0.16	5.33 ± 0.32*	4.70 ± 0.15**
Hb gm %	13.90 ± 0.70	13.63 ± 0.18	13.50 ± 0.19
HCT	42.03 ± 0.36	37.15 ± 0.58***	36.50 ± 1.04***
MCV	75.50 ± 13.00	70.40 ± 1.81	69.75 ± 1.93
W . B . Cs $\times 10^3$	10.33 ± 0.76	13.23 ± 0.52*	17.53 ± 2.03**
platelets $\times 10^3$	182.93 ± 12.88	365.75 ± 8.16***	358.25 ± 26.13***

* P < 0.05 ** P < 0.01 *** P < 0.001

control group. Progesterone concentration measured 48hrs after administration of HCG was low, concurrent with the stage of the cycle and the ovaries contained few numbers of growing follicles with scanty number of corpora lutea but contained mainly corpora haemorrhagica. Therefore, progesterone levels were significantly ($p<0.01$) lowered in lead treated groups.

A highly significant ($p<0.001$) increase in cortisol concentration was recorded in plasma of both lead treated groups.

The levels of some elements such as lead, zinc, Ca & phosphorus in the plasma of treated animals were illustrated in Table (3). A highly significant ($p<0.001$) increase in the level of lead was recorded in both lead treated groups. Whereas, a significant decrease in the level of zinc was observed in high dose group (group II). Total ca concentration in the plasma recorded a significant decrease in animals of group I. A highly significant decrease ($p<0.001$) in phosphorus level was also observed in both lead treated groups.

Haematological changes :

As shown in Table (4), a significant decrease in RBCs count was recorded after low & high doses of lead administration. A highly significant ($p< 0.001$) decrease in HCT value was also noted in both lead treated groups. Whereas, a significant increase in WBCs and platelets Counts were recorded in groups I and II respectively. On the other hand, haemoglobin concentration and MCV were not significantly changed.

DISCUSSION

In the control group (gp.III), injection of PMSG followed by HCG had stimulated the ovaries of treated does and increased the number of Graffian follicles (Table 1.) which are subsequently ovulated under the

influence of LH forming corpora haemorrhagica and corpora lutea in the ovary.

In the present study, oral administration of lead acetate (5.4 mg /kg, group I and 10.8 mg /kg, group II) for 8 weeks led to a significant decrease in total ovarian response, ovulation rate and ovulation percentage. These findings coordinated with the results reported before [22].

They indicated that lead administration was accompanied by variable effects on circulating luteinizing hormone (LH) levels , pituitary LH , and pituitary LHB m RNA , suggesting a dual site of lead action : (a) at the level of the hypothalamic pituitary unit , and (b) directly at the level of gonadal steroid biosynthesis .

It has been reported also that divalent cations , including lead , may interfere with pituitary hormone release via interactions with calcium-dependent secondary messenger systems which mediate hormone release from secretory granule storage [23].

Regarding the biochemical changes, the results of the present study showed that administration of lead resulted in a significant decrease in the level of total proteins . These results agrees with that previously reported [24]. They stated that chronic lead toxicity in humans resulted in renal loss of important nutrients such as amino acids , glucose and phosphates.

These changes were in correlation with the inhibition of renal mitochondrial functions as a result of structural damage to mitochondria and morphological changes in the proximal tubules [25] in association with inhibition of several enzymes [26] . Stowe et al. [27] reported that pupies fed on 100 ppm lead acetate from 6 to 8 weeks of age exhibited hypoproteinaemia and decreased serum albumin . Other studies on adult goats [28] and sheep [29] revealed a significant decrease in total proteins . The lowered plasma protein level may be also attributed to the elevated levels of plasma cortisol . This hormone is known to catabolize proteins by degrading them into amino acids and thus lowering of protein levels .

On the other hand, our results were not consistent with those of Clausen et al . [30] who detected that cattle with lead poisoning did not show any change in total proteins content when compared with healthy ones . The discrepancy in the results might be due to the difference in the dose , species of the animal and duration of treatment .

The significant increase in the plasma cholesterol and triglycerides in lead treated groups (I and II) may be due to decreased peripheral uptake and increased release from the liver [31,32] . This elevation indicates also that synthetic activity of ovarian tissues is severely affected and became incapable of converting them into sex steroids. The change in cholesterol level is considered very important as it plays a vital role in follicular develepment, since it is known to be a precursor in steroid hormones produced in the gonads and adrenal cortex and as an integral part of all cells and their component part . In general , cholesterol is used to monitor lipid metabolism . The increase in cholesterol level in lead treaed groups (I and II) may be due to increased uptake of cholesterol-containing lipoprotein by a non receptor mediated pathway or uptake of free cholesterol from cholesterol rich lipoprotein to the cell membrane [32] .

The levels of total lipids were significantly decreased with both lead treated grougs (I and II) , this decrease may possibly be due to or secondary to malabsorption and occasionally with parenchymal liver disease [33] .

The present study showed a significant decrease in the levels of estradiol-17B and progesterone , with a significant increase in the levels of cortisol in both lead treated groups (I and II) . This could be explained by the effect of the metal on the brain organization resulted in decreased frequency and / or amplitude of the pulsatile gonadotrophin secretion . This is also might be due to toxic effect of lead on the ovary and / or combination of both (2) . Aphotupa et al [34] reported that lead decreases the catabolism of sex steroids by decreasing the enzymes essential for their breakdown . If so , the results presented in this study indicated that the synthesis of progesterone and oestradiol-17B was inhibited . The most probable causes of such inhibition is the decreased production of sex steroids in animals exposed to lead , which seems to be : an inhibition of the synthesis and release of gonadotropic releasing hormone (GnRH) in hypothalamus ; an inhibition of the synthesis and release of LH and or FSH in the hypophysis ; a reaction between organic lead and the gonadotropins in the plasma ; and finally a direct effect on the synthesis activity of sex steroids in the gonads and /or adrenals [35] .

Increased cortisol level is considered a valid indicator of stress imposed to the animals . The stressful condition induced by lead may alter the pattern of secretion of some reproductive hormones and consequently affected the reproductive potentials [36]. Stress reduces the reproductive efficiency in several species presumably through activation of the hypothalamic-pituitary -adrenal axis and this involves a suppression of gonadotrophin secretion by glucocorticoids [37]. It has been shown also that high plasma concentration of corticosteroids can cause a decline in plasma LH and

ovarian regression [38]. Stressful circumstances may thus depress LH secretion and delay the growth of the ovary and alter the pattern of secretion of some reproductive hormones and consequently affected the reproductive potentials [36]. In support of this suggestion , Kazan [39] reported that cortisol suppressed estrogen production, reduced the expression of estrous behaviours and suppressed follicular growth and plasma LH secretion .

Concerning blood profile, the present study revealed a significant decrease in the count of RBCs and HCT in both lead treated groups (I and II) . While haemoglobin content and MCV did not altered significantly . On the other hand, a significant increase in total WBCs and platelet count were recorded in lead treated groups . In lead - induced anaemia, the red blood cells are microcytic and hypochromic and usually there are increased numbers of reticulocytes with basophilic stippling [40] . The anaemia that occurs in lead poisoning may result from two basic effects:shortened erythrocyte life span and impairment of haeme synthesis. Shortened life span of the red blood cell is thought to be due to increased mechanical fragility of the cell membrane. The biochemical basis for this effect is not known but is accompanied by inhibition of sodium and potassium dependent ATPase[41,44]. Lead inhibits at least two enzymes essential for the formation of haeme, namely δ - amino - levulenic acid dehydratase (δ -ALAD) and ferrochelatase[45,47]

The decrease in HCT in the present study may be due to ineffective erythropoiesis caused by lead [48].

The non altered Hb content in our study is in consistent with studies of Soliman[49] in goats ; Nasralla et al [50] and Solliway et al [51] in human and Telisman et al[52] in cattle . On the other hand , Falke and Zwennes [53] reported that subcutaneous administration of 1mg / Kg b.wt lead acetate into female rabbits for 7.5 months resulted in a significant decrease in Hb contents and MCV. Hernberg and Nikkanen [54] in human , Lynch et al . [55] in young calves and kolesnikov et al [56] in yearling sheep , reported a significant decrease in Hb content and PCV .

These discrepancies might be propably due to the difference in the dose, route of administration and duration of exposure.

The increase in the total WBCs count in the present study may be due to a left shift , neutrophilic leukocytosis , and basophilic stippling [57,58]. The increase in the platelet concentration due to lead exposure may be due to increased thrombocytopionia or decreased plasma volume . Kolesnikov et al . [56] reported that lead administration to yearling sheep increased the leucocytic counts initially followed by a later fall below the original value with slight eosinophilia, monocytosis and lymphocytopenia . While Gruda et al[28] found that lead administration to goats did not alter the total leucocytic count although they recorded significant neutrophilia and lymphocytopenia.There are several possibilities with regard to mechanism that would account for changes in leucocytes: lead may traumatize receptive tissues then causing release of leucocytosis inducing factors which would initiate elevate the peripheral leucocytic counts [59].

Oral lead administration (groups I and II) resulted in a significant decrease in total Ca^{++} concentration and inorganic phosphorus in blood plasma . The depressed plasma Ca^{++} values found in lead supplemented rabbits in the present investigation may reflect a competitive absorption between Ca^{++} and lead at the level of intestinal epithelium[60].

The lowered calcium levels may be due to the depressive effect of lead acetate on parathyroid gland function[29] or renal function impairment [61]. However , Barton et al [62] demonstrated that both calcium and lead are able to bind to the same binding protein in rat intestine. Shared binding sites on absorptive proteins might explain why dietary calcium decreases lead absorption.

The current study showed that the inorganic phosphorus was significantly decreased by lead administration (groups I and II) inspite of the fact that an inverse proportion is found between calcium and phosphorus [61].

Lead administration in the present study resulted in a significant increase in the level of lead in the blood of both lead treated groups (I and II) , while , a significant decrease in the level of zinc was observed in group II only (high lead dose). These results coincised with those reported by Gupta et al [63], who stated that the level of zinc loss in lead treated animals correlated with endogenous level of lead with a high degree of correlation. Lead appears be an effective divalent physiological and nutritional competitor of zinc in a multiplicity of systems [64]. The reasons for this effective competition are unknown. Several mechanisms have been proposed, including changes in the secondary structure of specific receptor target sites normally occupied by zinc and enhanced binding by lead to these sites so that the normal regulation governed by receptors and/or pores is disrupted [64] . Zinc finger receptors loose their DNA binding ability in the presence of other competing divalent

ental sons as lead [65]. The disruptive effects of elevated lead level on the functioning of adult hypothalamic-pituitary-gonadal (HPG) axis is also well established [66] and previous evidences indicated that lead acts at both gonadal and hypothalamic sites to disrupt reproductive physiology and behaviour [67, 68].

In conclusion, lead administration caused adverse effects on the ovarian activity and total ovarian response, with a profound changes in the biochemical, haematological and hormonal profile. So, the overall pattern of results from this study revealed a marked disruption of reproductive potential and physiology by lead exposure. The neuroendocrine and biochemical mechanisms underlying lead toxicity need further investigation.

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تأثير التعرض للرصاص على بعض المستويات البيوكيميائية والهرمونية وصورة الدم مع التركيز على ما يصاحب ذلك من تأثيرات على الجهاز التناسلي لإناث الأرانب

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أجريت هذه الدراسة على عدد ٢٤ من إناث الأرانب النيوزيلاندية الغير بالغة (العذاري) وقد تم تقسيمهم إلي أربعة مجموعات بواقع ٦ أرانب لكل مجموعة. المجموعتان الأولي والثانية تم تجريعهما بالفم بجرعة منخفضة (٤ر٥مجم / كجم من وزن الجسم) وعالية (٨ر١٠ مجم / كجم من وزن الجسم) من خلات الرصاص علي التوالي يومياً لمدة ٥ أيام في الأسبوع وقد تم التجريع علي مدار ٨ أسابيع متصلة. المجموعتان الثالثة والرابعة أعتبرا كمجموعات ضابطة وقد تم حقن كل المجموعات (ما عدا المجموعة الرابعة) بجرعة مقدارها ٢٠٠ وحدة من هرمون الجونادوتروفين (PMSG) ثم أعقبها بـ ٤٨ ساعة حقن هرمون الجونادوتروفين المشيمي (HCG) بجرعة مقدارها ٢٠٠ وحده وذلك عن طريق الحقن العضلي وقد تم ذبح الحيوانات بعد أخر حقن بـ ٤٨ ساعة.

وقد توصلت النتائج إلي أن حقن هرمون الجونادوتروفين قد أدي إلي زيادة نشاط المبايض في حيوانات المجموعة الثالثة الضابطة وذلك بصورة واضحة عن الحيوانات الغير محقونه (المجموعة الرابعة) بينما أدي التجريع بخلات الرصاص بجرعتيه المنخفضة والعالية إلي تثبيط نشاط المبايض حيث أنخفض معنوياً عدد الحويصلات المتكونه وأنخفضت أيضاً الإستجابة الكلية للمبايض وكذلك معدل التبويض وفيما يتعلق بالمتغيرات البيوكيميائية فقد أدي التجريع بخلات الرصاص إلي انخفاض مستوي البروتين الكلي والدهون الكلية مع زيادة معنوية في مستوي الجليسريدات الثلاثية وقد كان هناك زيادة معنوية في مستوي الكوليستيرول مع الجرعة العالية فقط من خلات الرصاص.

وبتقدير مستوي هرمون الاستراديول والبروجستيرون وجد أن هناك نقص معنوي في مستوياتهما في بلازما المجموعتين الأولي والثانية مع وجود زيادة معنوية في مستوي الكورتيزول في بلازما هاتين المجموعتين.

وبالنسبة لمستوي بعض العناصر وجد أن هناك زيادة معنوية في مستوي عنصر الرصاص في الدم مع إنخفاض معنوي في مستوي نسبة الزنك والكالسيوم والفوسفور في بلازما المجموعتين التي تم تعرضهم للرصاص (الأولي والثانية).

وبفحص صورة الدم وجد أن هناك انخفاض معنوي في عدد خلايا الدم الحمراء وسرعة الترسيب بينما كان هناك زيادة معنوية في عدد خلايا الدم البيضاء والصفائح الدموية ولكن لم يتأثر مستوي الهيموجلوبين والـ MCV في أي من المعاملات السابقة.

- مما سبق نستنتج أن التعرض لمستويات مختلفة من عنصر الرصاص قد أدي إلي إنخفاض الكفاءة التناسلية لإناث الأرانب وذلك بتثبيط نشاط المبايض مع إنخفاض في نسبة التبويض وأدي أيضاً إلي إختلال في التوازن الهرموني في الجسم مع إحداث بعض التغيرات في المستويات البيوكيميائية وأيضاً في صورة الدم.