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Gene expression of estrogen receptor during different stages of pregnancy in rat model

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Abstract

One essential organ that steroid hormones target is the uterus and ovaries. Many receptors mediate the effects of these hormones such as estrogen receptors ER. The objective of this research is to evaluate the gene expression of estrogen receptors ERα and ERβ in the uterus and ovary on different days of pregnancy, as well as in female rats that are not pregnant. The estrogen receptor's gene expression in the ovary along with the uterine of rats' females was analyzed using the real-time PCR technique and immunohistochemical expression (IHC) of ER alpha in ovary and uterus. Thirty adult female rats were allocated into five groups at random, each group has six animals. non-pregnant groups and groups of pregnant at one, seven, fourteen and twenty days of pregnancy. The ovaries and uterus were extracted from each animal, and Real-Time polymerase chain reaction (RT-PCR) analysis was applied to evaluate the estrogen receptors (ER) expression. The expression of the ERα gene increased significantly within seven and twenty days of pregnancy where as ERβ expression of this gene did not differ between the different days of pregnancy and the ovary of non-pregnant rats. In uterus ERα and ERβ expression significantly increased in twenty days of pregnancy. In conclusion, in both pregnant and non-pregnant rats, this study demonstrates that the ovary and uterine express the gene for the estrogen receptor Erα and ERβ, the gene for the ERβ is strongly expressed during twenty days of pregnancy in the uterus, ERβ in the ovary is highest expressed during the first and second half days of pregnancy.

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Introduction

The production of estrogens by the placenta during pregnancy in several mammalian species suggests that placental estrogens play a function as paracrine mediators in the control of placental differentiation and growth (1). Estrogen is not produced by the rat placenta, and only secretes trace levels of progesterone. In fact, between days 14 and 18 of pregnancy, the main source of testosterone in the peripheral circulation is the rat placenta (2). In the corpus luteum, this testosterone acts as the substrate for the synthesis of estradiol Therefore, the rat placenta maintains the ovarian synthesis of estradiol even though it fails to produce it directly (2). Both progesterone and estrogen are necessary for the rat to become pregnant and stay pregnant. In order for estrogens to have a biological effect, they must attach to the estrogen receptor (ER), which alters its shape to interact with chromatin and affect the transcription of the target gene. Two distinct forms, estrogen receptor alpha (ERα) and estrogen receptor beta (ERβ) These proteins bind to estradiol with great affinity and start the transcription of reporter genes that are expressed in mammalian cell lines and sensitive to estrogen, depending on many factors (3). Steroid hormones rise through pregnancy for longer lengths of time than during the estrous cycle. Pregnancy significantly raises both the central and circulation levels of progestins,

including 3α,5α-THP (4). In females, the placenta and ovaries are the main producers of the steroid molecule estrogen (5). Important modulatory functions for estrogens are found in both physiological and pathological processes (6). Estrogen is a lipid-soluble steroid hormone that is one of the most important female sex hormones. It is mostly made by testes, ovaries, adrenal cortex, and supports several essential physiological functions (7). These hormones are essential for they promote the development of the mammary glands, additional sexual characteristics, and reproductive organs. They also set up estrous cycles for mating behavior (8). Female puberty, an early reproductive organ function marked by the occurrence of ovulation and estrous cycles, is significantly influenced by estrogen (9). Based on when they originate, estrogens are divided into two primary groups: exogenous and endogenous. Mammals' endogenous estrogens are released by glands or cells within their bodies. Exogenous estrogens, on the other hand, come from foods, medications, and synthetic estrogens (10). The four estrogens that are now known to exist are estriol (E3), 17β-estradiol (E2), estetrol (E4), and estrone (E1) (11). When it binds to the estrogen receptor (ER), an intranuclear binding protein, it causes a number of cellular alterations. ERα and ERβ are the two primary types of ERs, and they exhibit different patterns of tissue expression (12).

The objective of this study is to measure the expression of the estrogen receptor genes ERα and ERβ in female rats at one, seven, fourteen, and twenty days of pregnancy. as well as IHC expression of ERα in the female rats' uterus and ovary at the same time throughout pregnancy.

Materials and methods

Ethical approve

The Ethical Committee of the University of Mosul, College of Veterinary Medicine was approved the experimental protocol on 18/9/2024, with reference number UM.VET.2024.100.

Animals

This experimental investigation occurred out at Mosul University's veterinary medicine animal house. The animals were kept in an accredited animal care facility. Thirty female rats (4 months of age) weighing between 200 and 250 g were used. The rats were maintained under controlled conditions (temperature 22±2°C, humidity 55±5% and 12h light/dark cycle), diet and water were provided *ad libitum* and cared for in accordance with the principles of the Guide for care and utilizing animals in experiments (13).

Design of experiments

The rats were evaluated for the estrous cycle by taking daily vaginal swabs for eight days before the experiment began. The "Whitten Effect" (14), which causes the synchronization of estrus in females by exposure to male pheromones, was used to create two unique synchronized groups of females according to the various phases of the estrus cycle. They continued to be examined every day to check for pregnancy. Its vaginal examination was performed (15,16). At random, the rats were split up into five groups, each group has six animals, a control which is an animal that is not pregnant and groups at one, seven, fourteen and twenty days of pregnancy.

Tissue collection

At the end of the duration of each group, cervical dislocation of un-anesthetized animals was the physical mode of euthanasia used on the rats under study (17). The ovary and uterus were quickly removed. washed with cold PBS pH 7.2 Samples of each animal kept for later RNA isolation and RT-PCR work at -80ºC (18).

Protocol for cDNA transcription and RNA extraction

Total RNA was isolated using an Addbio total RNA extraction kit from frozen ovarian and uterine tissues kept at -80° C (addbio, Korea code:10119). Samples were homogenized in denaturing solution, add the lysis buffer (β mercaptoethanol and proteinase K solution) to the sample and thoroughly combine with a vortex, Add the binding buffer to the sample, incubation for 10 minutes, centrifuge at 13,000rpm for 1 minutes, and then transfer the supernatant to the spin. Next, add the DNase reaction to the tube and let it remain at room temperature before adding the washing solution, dry the spin and add the elution solution and then elute total RNA by centrifugation. The extracted RNA stored in-80 ºC. To create cDNA from RNA samples, Transcription was done using Addbio reverse transcription Supermix (Addbio, Korea #10119) Following the manufacturer's instructions, 5µl of input RNA (1 µg–1 pg) was used to generate the reverse transcription master mix for ten reactions. A total amount of 180µl per reaction was obtained by mixing 48µl of RT Supermix with 132µl of nuclease-free water. The following procedure was applied: Priming at 25°C for 5 minutes. Reverse transcription for 20 minutes at 46°C. RT inactivation for one minute at 95°C. In the end, cDNA samples were kept at -20°C until they were processed further (18), and analysis of data of the gene expression according to conformation (18).

Reverse transcription polymerase chain reaction (RTPCR)

Gene expression analysis for ERα and ERβ receptors was performed according to the following sequence (Table 1). The following parameters were used when running the PCR. In the holding stage, 95°C for 10 minutes (45 cycles: 95°C x 10 s–60°C x 10 s–72°C x 10 s); in the melting stage, 95°C x 5 s–65°C x 1 min–95°C x 30 s–40°C x 30 s, which is supplied by humanizing genomics macrogen (Ho00347127) (19).

Table :1 Real-time PCR analysis premiers

Name	Nucleotide sequence (5'–3')	length
ERα -F	GCACATTCCTTCCTTCCGTC	20 (mer)
ERα-R	CTCGTTCCCTTGGATCTGGT	20 (mer)
ERβ-F	ACAGTCCTGCTGTGATGAAC	20 (mer)
ERβ-R	ACTAGTAACAGGGCTGGCAC	20 (mer)
β-act-F	ACCCGCCACCAGTTCGCCAT	20 (mer)
β-act-R	CGGCCCACGATGGAGGGGAA	20 (mer)

Processing and dissection of the uterus and ovaries

The uterus and ovaries were dissected and cleared of any adherent tissues. The newly cleansed ovaries were submerged in neutral buffered formalin immediately. 10% through the paraffin embedding. Each uterus and ovaries nonsequential midsections were then manually microtome at a thickness of 5 μm (16).

Immunohistochemistry

Using the previously described ABC technique for immunohistochemical labeling, ER alpha expression inside the ovary and its closely related tissues was examined. In brief, Initially, the deparaffinized sections to incubate were used with 30% volume of 3% hydrogen peroxide and 70% volume of pure alcohol. then rinsed for three minutes under running water. The samples were treated in H_2O_2 to suppress endogenous peroxidase and preheated for 10 minutes at 100 °C to retrieve antigen, following a five minutes autoclave treatment in citrate buffer at 60°C, the slices were placed in blocking solution (10% normal goat serum in PBS) and incubated for 30 minutes. prior to primary antibody incubation. The primary antibody anti ERα was diluted 1:50 and incubated for the entire night at 4°C. Before being treated with the secondary antibody (E-AB-15624, Elabscience, USA), sections were carefully cleaned three times for 15 minutes using phosphate buffered saline (PBS). a chromogen that, when incubated with the enzyme, produces a brown, insoluble precipitate, after being gradually dried out and placed on coverslips, the sections were viewed under a light microscope (20).

Statistical analysis

Duncan's multiple range test was used to analyze the data and a one-way analysis of variance (SPSS version 24, USA). The results' data are shown as mean ± standard error. A value of $P<0.05$ indicates a significant difference (21).

Results

Expression of ERα and ERβ receptors in the ovary of female rats

We investigated ERα levels in the ovaries of pregnant rats. We found that the levels of ERα gene expression are considerably ($P\leq0.05$) higher in seven and fourteen-day pregnant rats than in non-pregnant rats, one day pregnant rats, and twenty-day pregnant rats. However, there is no significant difference between the non-pregnant, one and twenty days of pregnancy (Table 2 and Figure 1). Real-time PCR revealed that the ovary's ERβ gene expression did not differ significantly between rats that were not pregnant and those that were one, seven, fourteen, and twenty days pregnant (Table 2 and Figure 1).

Table 2: Expression of ERα and ERβ receptors gene in the ovary of female rats

Groups	ERα	ERß
Non pregnant	3.170±1.910 b	1.250±0.420 a
One day	0.092±0.050 b	1.220±0.900 a
Seven days	34.350±13.300 a	0.220±0.080 a
Fourteen days	12.170±4.670 a	2.550±0.010 a
Twenty days	10.920±0.600 b	2.056±1.430 a

Different letters in the column represent (mean ±SE), Different letters in the column indicate significant difference at $P\leq0.05$.

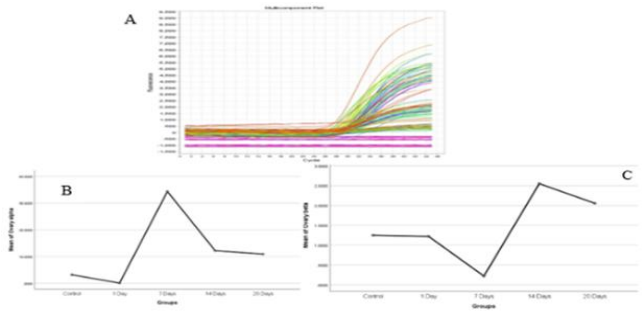

Figure 1: Expression of ER α and ERβ gene in ovary of rats A) Basic analysis of amplification data. B) Mean of ERα gene expression of ovary. C) Mean of ERβ gene expression of ovary.

Expression of ERα and ERβ in the uterus of female rats

In the rats' uterus, there is increased significantly in ERα expression ($P\leq0.05$) in the twenty days of pregnancy in compared with non-pregnant, one seven, fourteen days of pregnancy (Table 3 and Figure 2). The expression of ERβ of non-pregnant rats and twenty days of pregnancy is increased significantly ($P\leq0.05$) in expression of gene in compared with one, seven and fourteen days of pregnancy. The expression of the ERβ is not differed between the one, seven, fourteen days of pregnancy (Table 3 and Figure 2).

Expression of ovary ERα receptor

In non-pregnant female rats ovary the result Showed a positive reaction with ERα, which appeared as a golden brown stain in theca cells (Figure 3), In one day of pregnant the result Showed negative reaction for the IHC expression of ERα in the ovary (Figure 4), In the seven day of pregnant the results showed a positive reaction with ERα, which

appeared as a golden brown stain in germinal epithelial cells and interstitial cells (Figure 5), in rat ovary from fourteen days of pregnancy the result Showed a positive reaction with ERα, which appeared as a golden brown stain in theca cells (Figure 6), In the twenty days of pregnancy results showed a positive reaction with ERα, which appeared as a golden brown stainin theca cells (Figure 7).

Table 3: Expression of ERα and ERβ receptors gene in the uterus of rats

Groups	ERα	ERß
Non pregnant	1.260±0.540 b	2.990±0.530 a
One day	0.110±0.083 b	0.420±0.310 b
Seven days	0.090±0.040 b	0.220±0.160 b
Fourteen days	0.816±0.460 b	0.360±0.090 b
Twenty days	3.921±1.290 a	1.660±1.390 a

Different letters in the column represent (mean ±SE), Different letters in the column indicate significant difference at P≤0.05.

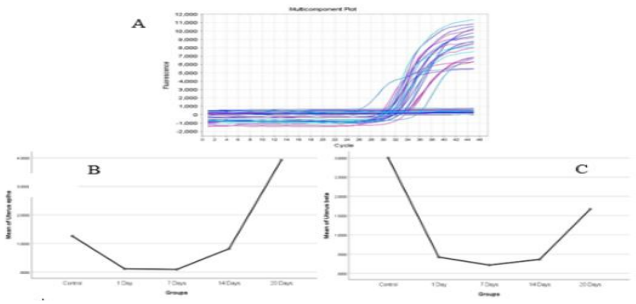

Figure 2: Expression of ER α and ERβ gene in uterus of rats. A) Basic analysis of amplification data. B) Mean of ERα gene expression of uterus. C) Mean of ERβ gene expression of uterus.

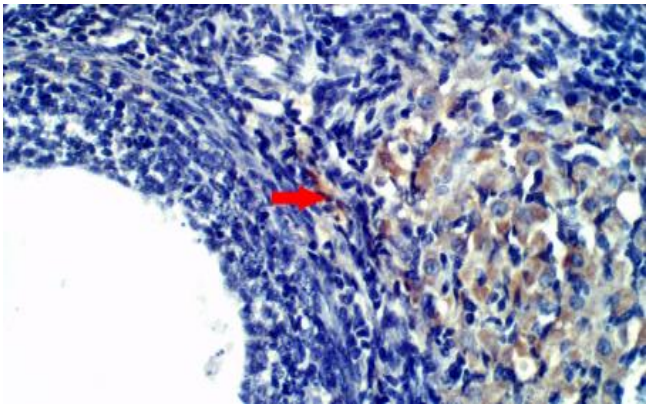

Figure 3: Histological section in rat ovary from the non pregnant group. Showed a positive reaction with ERα, which appeared as a golden brown stain in theca cells (arrow). IHC-ERα, 400x.

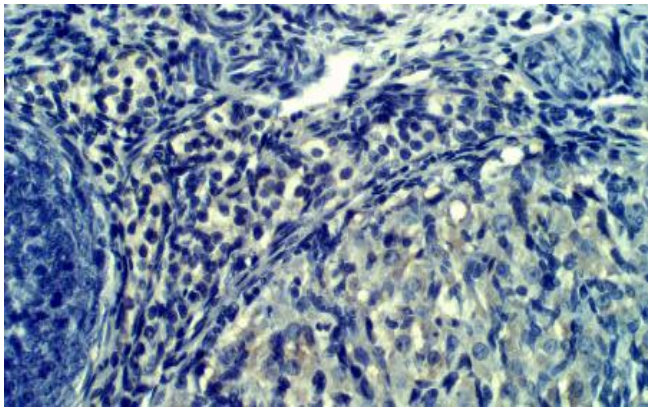

Figure 4: Histological section in rat ovary from one days of pregnancy. Showed negative reaction with ERα. IHC-ERα, 400x.

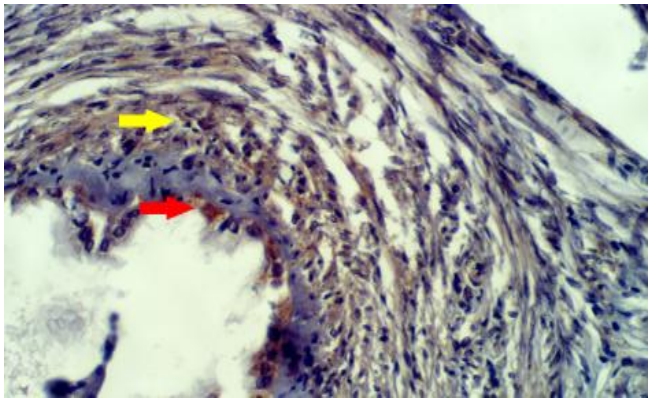

Figure 5: Histological section in rat ovary from seven days of pregnancy. Showed a positive reaction with ERα, which appeared as a golden brown stain in germinal epithelial cells (red arrow) and interstitial cells (yellow arrow). IHC-ERα, 400x.

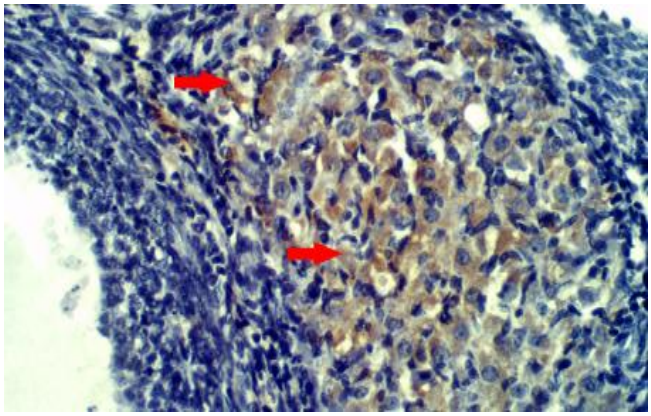

Figure 6: Histological section in rat ovary from fourteen days of pregnancy. Showed a positive reaction with ERα, which appeared as a golden brown stain in theca cells (red arrow). IHC-ERα, 400x.

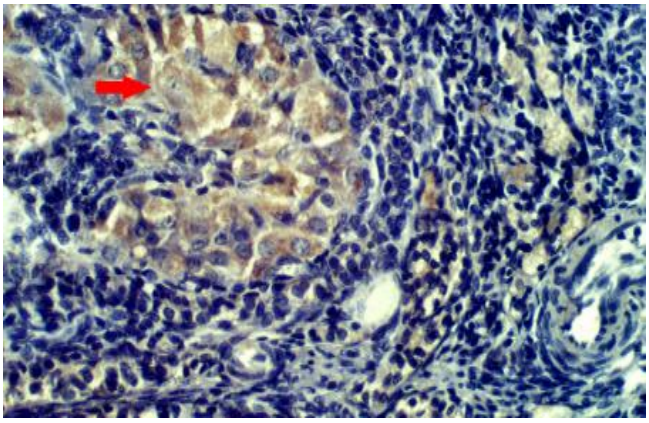

Figure 7: Histological section in rat ovary from twenty days of pregnancy. Showed a positive reaction with ERα, which appeared as a golden brown stain in theca cells (red arrow). IHC-ERα, 400x.

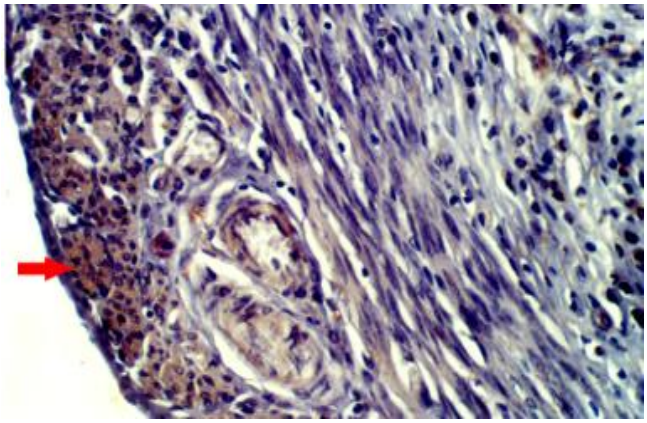

Figure 8: Histological section in rat Uterus from the non pregnant group. Showed a positive reaction with ERα, which appeared as a golden brown stain in endomaterial endotheial cells (arrow). IHC-ERα, 400x.

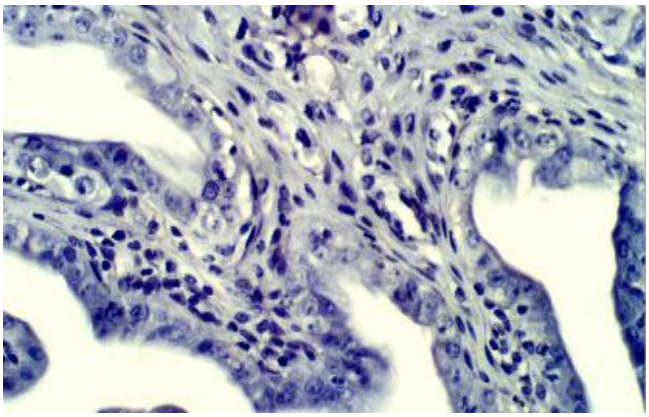

Figure 9: Histological section in rat uterus from one day of pregnancy. Showed negative reaction with Erα in the endotherial cells of endomaterium. IHC-ERα, 400x.

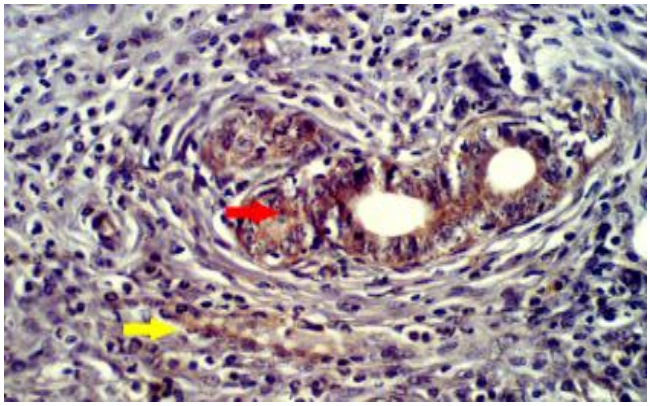

Figure 10: Histological section in rat uterus from seven days of pregnancy. Showed a positive reaction with ERα, which appeared as a golden brown stain in glandular (red arrow) and stromal cells (yellow arrow). IHC-ERα, 400x.

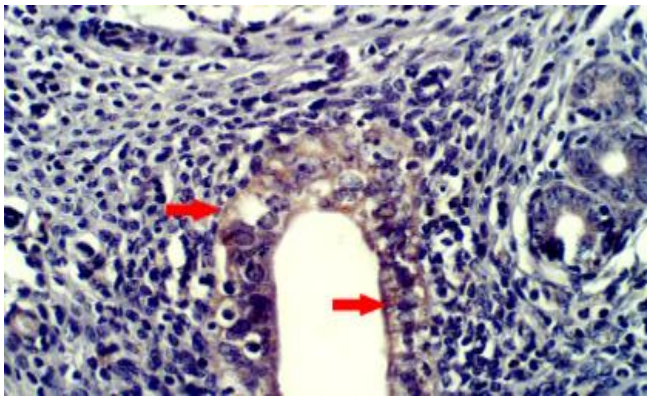

Figure 11: Histological section in rat uterus from fifteen days of pregnancy. Showed a positive reaction with ERα, which appeared as a golden brown stain in endomaterium endotheial cells (red arrow). IHC-ERα, 400x.

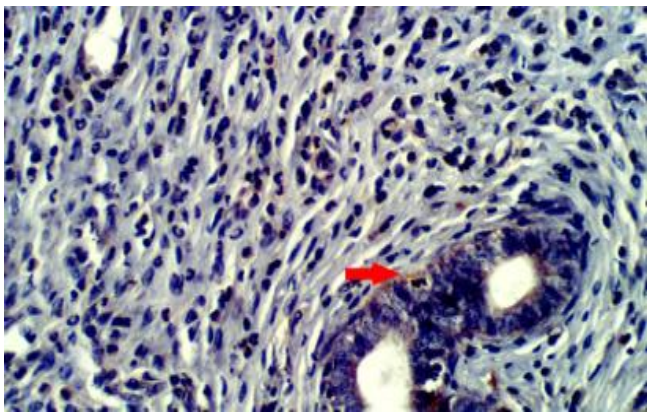

Figure 12: Histological section in rat uterus from twenty days of pregnancy. Showed a weak negative reaction with ERα, which appeared as a golden brown stain in glandular cells (red arrow). IHC-ERα, 400x.

Discussion

It has been demonstrated that pregnancy significantly alters levels of progesterone and estrogen by 30 and 10 times, respectively (22). Additionally, Estrogen's receptors mediate its effects on various tissues (23). Therefore, that was crucial to identify alterations in receptor ER expression throughout pregnancy. In order to produce physiological effects, the nucleus contains the estrogen receptor (ER), which is where estrogen binds, cytoplasm, or cell membrane (24). There are two types based on where they are found: both the membrane-bound estrogen receptor (mER) and the nuclear estrogen receptor (nER). Also, estrogen receptors alpha (ERα) and estrogen receptor beta (ERβ) (25). A number of researchers have shown that during pregnancy, the blood's total estrogen concentrations significantly increase (26). Even though ovarian follicle development depends on estrogen, A marker of the degree of estrogen responsiveness in a given tissue has been the expression level of ER. The decrease in ER protein expression between 16 and 19 days may be due to the down-regulation of the receptors brought on by the high quantity of estradiol in pregnant dams near the end of gestation (27). According to the results, ERα in the ovary increases between days seven and fourteen of pregnancy and returns to its normal levels at day twenty, just like in female rats who are not pregnant. Dopamine and prolactin (PRL) secretion are the main areas where early and late pregnancy differ. The tubero-infundibular dopaminergic neurons produce dopamine, which causes lactotropes' PRL release tonically inhibited by D2 dopamine receptors. Reduced dopamine activity in the first stage of pregnancy (28). with an increase in the middle of pregnanvy (29), dopamine levels in the portal blood dramatically dropped the day before parturition (30). Lactation and the early stages of pregnancy are both physiologically hyperprolactinemic. However, the way PRL secretion is regulated in late pregnancy varies from the early stages of pregnancy. Rats' pituitary PRL secretion is semicircadian and comparatively elevated during the early stages of pregnancy (31). These PRL magnitudes begin to fall on the eighth day of pregnancy and are completely stopped by the tenth day. Conversely, in the latter stages of pregnancy During pregnancy, plasma PRL levels remain low until a notable PRL appears before birth (32). The pituitary gland's ability to positively regulate ER may be significantly altered by changes in dopaminergic activity (33). Progesterone reduces amount of uterine ER by preventing cytoplasmic ER from being replenished, which reduces the tissues sensitivity to estrogen (34). Therefore, the elevated levels of progesterone and estradiol in mother's serum and amniotic fluid would be a contributing factor to the estrogen receptors' down-regulation as pregnancy progressed (35). In research found in Michigan, as early as 16 days, ER α and ERβ mRNA were found in the rat's placenta using RT-PCR (32). However, a team of researchers in France demonstrated that ER mRNA considerably increased in the middle of pregnancy using relative quantitative RT PCR (36). Reduced expression of the estrogen receptor protein during pregnancy means that the placenta can no longer react to estrogens. With respect to the placenta's protective role (36). This confirms the current study's findings that, in addition to non-pregnant rats, the gene expression of ERβ does not alter at any of the many stages of pregnancy, including one, seven, fourteen, and twenty in ovary According to a 2002 study conducted in France, ER gene expression remained constant all through pregnancy, indicating that it was unrelated to levels of estradiol throughout this time of reproduction (36). In the present study, ERα, ERβ is highly expressed in the uterus during the twenty days in contrast to other day of pregnancy, it is proposed that growth factor-stimulated pathways or GnRH activate the ER by phosphorylation. GnRH pulsatile, in gonadotropin cells, ER can be transcriptionally activated without the need for estrogen, and GnRH may be a vital signal in the control of the trans-activation of the pituitary ER (37). These findings correlate with Vaillant *et al*. (38), who observed the middle stage of pregnancy markedly increased ERα the rat pituitary gland 's mRNA during pregnancy and lactation. Since ERβ gene expression remained constant throughout pregnancy, it is likely that estradiol levels during this reproductive stage had no influence on it. A study done in Egypt in 2023elevated ERα expression in the oral tissues and nasal mucosa during late pregnancy in rats (39). In addition, the expression of ERβ in non-pregnant rats is highly expressed in the uterus, as in study (40) that show the reproductive tracts of prenatal mice and rats have no ERβ mRNA. Uterine tissue expresses both ERα and ERβ, and they both have roles in the uterus within the framework of estrogen signaling, which is crucial in regulating the expression of the ERα. The results of the immunohistochemistry indicated that the estrogen hormone had a site-specific effect during pregnancy which reacted negatively to ERα at various times in contrast to the non-pregnant animal, which reacted positively This was demonstrated by the notable rise in ERα expression in ovary. Our immunohistochemistry data revealed a change in ERα expression, which implied a connection between the histological changes of the tissues being studied and the estrogen hormone. The anticholinergic action of the estrogen hormone may account for the glandular and vascular alterations, as well as the mechanism of action of estrogen hyperplasia in the pregnant rat's infected tissues (41). Mata *et al.* (42) discovered that pregnant rats' endothelium and vascular smooth muscle layers have higher levels of ER expression. Also, Shu *et al.* (43) found that estrogen may significantly affect the periodontium by acting through the PDL cells' ERα and ERβ.

Conclusions

In both pregnant and non-pregnant rats, this study demonstrates that the ovary and uterine express the receptor

of estrogen gene (ERα, ERβ). In contrast to other pregnancy days, the estrogen receptor gene (ERβ) is strongly expressed in the uterus during the twenty days of pregnancy. During the first and second half days of pregnancy, the ovary exhibits the highest levels of expression of the estrogen receptor (ERβ) gene. Additionally, throughout pregnancy. The immunohistochemistry of ERα in the uterus and ovaries of female rats showed that on the first day of pregnancy, ERα expression is negative in the ovary, and on days one and twenty of pregnancy, it is negative in the uterus. Additionally, the ovary has positive ERα expression in the seven, fourteen, and twenty days of pregnancy, while the uterus exhibits positive ERα expression in the seven and fourteen days of pregnancy.

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The conflict of interest

The manuscript has no conflicts of interest.

Editorial board note

Muneer S. Al-Badrany and Dhafer M. Aziz, the editors of the Iraqi Journal of Veterinary Sciences, did not participate in any stage of the decision-making process for this article.

Reference

1. Schuler G, Wirth C, Teichmann U, Failing K, Leiser R, Thole H, Hoffmann B. Occurrence of estrogen receptor α in Bovine placentomes throughout mid and late gestation and parturition. Biol Reprod. 2002;66:976-982. DOI: 10.1095/biolreprod66.4.976.
2. ALabiad MA, Elhasadi I, Alnasser SM, Alorini M, Alshaikh AB, Jaber FA, Shalaby AM, Samy W, Heraiz AI, Albakoush KM, Khairy DA. Effect of aromatase inhibitor letrozole on the placenta of adult albino rats: A histopathological, immunohistochemical, and biochemical study. Iran J Med Sci. 2024;49(1):46. DOI: 10.30476/IJMS.2023.96905.2853
3. Lohmiller JJ, Swing SP. Reproduction and breeding. In: Suckow MA, Weisbroth SH, Franklin CL, editors. The Laboratory Rat. 2nd ed. USA: Academic Press; 200z. 147-162 pp.
4. Frye CA, Walf AA. Hippocampal 3α,5α-THP may alter depressive behavior of pregnant and lactating rats. Pharmacol Biochem Behav. 2004;78:531–540. DOI: 10.1016/j.pbb.2004.03.024
5. Fuentes N, Silveyra P. Estrogen receptor signaling mechanisms. Adv Protein Chem Struct Biol. 2019;116:135–70. DOI: 10.1016/bs.apcsb.2019.01.001
6. Faltas CL, LeBron KA, Holz MK. Unconventional estrogen signaling in health and disease. Endocrinol. 2020;161(4):1–7. DOI: 10.1210/endocr/bqaa030
7. Chen P, Li B, Ling OY. Role of estrogen receptors in health and disease. Endocrinol. 2022;13. DOI: 10.3389/fendo.2022.839005
8. Ganong WF. Review of Medical Physiology. USA: Mc Graw Hill Book; 2012.
9. Hafez EE, Hafez B. Reproduction in Farm Animal. USA: Blackwell Publisher; 2013. DOI: 10.1002/9781119265306
10. Flasch M, Bueschl C, Del Favero G, Adam G, Schuhmacher R, Marko D, Warth, B. Elucidation of xenoestrogen metabolism by non-targeted, stable isotope-assisted mass spectrometry in breast cancer cells. Environ Int. 2022;158:106940. DOI: 10.1016/j.envint.2021.106940
11. Kumar RS, Goyal N. Estrogens as regulator of hematopoietic stem cell, immune cells and bone biology. Life Sci. 2021;269:119091. DOI: 10.1016/j.lfs.2021.119091
12. Mueller SO, Korach KS. Estrogen receptors and endocrine diseases: Lessons from estrogen receptor knockout mice. Curr Opin Pharmacol 2001;1(6):613-9. DOI: 10.1016/s1471-4892(01)00105-9
13. Aziz ZW, Altutunji AZ And Husain EO. (2024). Effects of Remdesivir (GS-5734) on Anti-Müllerian Hormone Level and Ovarian Tissues Morphology in Experimental Female Rats. Medical Journal of Babylon, 21(3), 606-613. DOI: 10.4103/MJBL.MJBL_891_23.
14. Whitten WK. Pheromones and mammalian reproduction. In: Mclaren A, editor. Advanced Reproductive Physiology. USA: Academic Press; 1966. 155–177 pp.
15. Marcondes FK, Bianchi FJ, Tanno AP. Determination of the estrous cycle phases of rats: some helpful considerations. Braz J Biol. 2002;62:609-614. DOI: 10.1590/S1519-69842002000400008
16. Husain EO, Albanna AM, Asim RA. The Protective Effects of Acetyl L-Carnitine for The Offspring and Lactating Moms of Rats Received Bromocriptine. Egypt J Vet Sci. 2024;55:1889-1900. DOI: 10.21608/ejvs.2024.264769.1803
17. Shomer NH, Worthington KA, Hickman DL, Jonnalagadda M, Newsome JT, Slate AR. Review of rodent euthanasia methods. J Am Assoc Lab Anim Sci. 2020;59(3):242–53. DOI: 10.30802/aalas-jaalas-19-000084
18. Alchalabi AS. Gene expression of certain heat shock proteins and antioxidant enzymes in microwave exposed rats. Gene Rep. 2019;16:100448. DOI: 10.1016/j.genrep.2019.100448
19. Scudiero R, Verderame M. Gene expression profile of estrogen receptors alpha and beta in rat brain during aging and following high fat diet. C R Biol. 2017;340(8):372-378. DOI: 10.1016/j.crvi.2017.08.001
20. Mohamed HZE, and Mohamed HK. (2021). Histological and immunohistochemical study of the effects of tramadol administration on the ovaries of adult albino rats and the possible recovery after its withdrawal. *Egyptian Journal of Histology*, *44*(1), 256-270. DOI: 10.21608/ejh.2020.24408.1251.
21. Steel RD, Torrie JH, Dickey DA. Principles and procedures of statistics: A biometrical approach. 3rd ed. USA: McGraw-Hill Book Co.; 1997. DOI: 10.4236/blr.2014.5424
22. Amar S, Chung KM. Influence of hormonal variation on the peri odontium in women. Periodontol. 2000;1994(6):79–87. DOI. 10.1111/j.1600-0757.1994.tb00028.x
23. Xu Y, Zhang Z, Wang R, Xue S, Ying Q, Jin L. Roles of estrogen and its receptors in polycystic ovary syndrome. Front Cell Dev Biol. 2024;12. DOI: 10.3389/fcell.2024.1395331
24. Tang ZR, Zhang R, Lian ZX, Deng SL, Yu K. Estrogen-receptor expression and function in female reproductive disease. Cells. 2019;8(10):1123. DOI: 10.3390/cells8101123
25. Paterni I, Granchi C, Katzenellenbogen JA, Minutolo F. Estrogen receptors alpha (ERα) and beta (ERβ): subtype-selective ligands and clinical potential. Steroids. 2014;90:13–29. DOI: 10.1016/j.steroids.2014.06.012
26. Costantine MM. Physiologic and pharmacokinetic changes in pregnancy. Front Pharmacol. 2014;5:65. DOI: 10.3389/fphar.2014.00065
27. De Assis S, Wang M, Jin L, Bouker KB, Hilakivi-Clarke LA. Exposure to excess estradiol or leptin during pregnancy increases mammary cancer risk and prevents parity-induced protective genomic changes in rats. Cancer Prev Res. 2013;6(11):1194-211. DOI: 10.1158/1940-6207.capr-13- 0207
28. Lyons DJ, Hellysaz A, Broberger C. Prolactin regulates tuberoinfundibular dopamine neuron discharge pattern: novel feedback

التعبير الجيني لمستقبلات الأستروجين خلال مراحل مختلفة من الحمل في نموذج الجرذان

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الخلاصة

أحد الأعضاء الأساسية التي تكون هدف الهرمونات الستيرويدية هو الرحم والمبيض. تتوسط العديد من المستقبلات تأثيرات هذه الهرمونات مثل هرمون الأستروجين. الغرض من هذه الدراسة هو تحديد التعبير الجيني لمستقبلات هرمون الأستروجين الفا وبيتا في الرحم والمبيض في أيام الحمل المختلفة، وكذلك في إناث الجرذان غير الحوامل. تم تحليل التعبير الجيني لمستقبلات هرمون الأستروجين في المبيض والرحم لدى إناث الجرذان باستخدام تقنية فاعل البوليمرات المتسلسل للنسخ العكسي والتلوين النسجي المناعي لجين الأستروجين الفا في المبيض. قسم ثلاثون فأرًا ناضجة عشوائيًا إلى خمس مجموعات، ست حيوانات في كل مجموعة، مجموعة غير حوامل ومجموعات حوامل في اليوم الأول، السابع، الرابع عشر والعشرين يومًا من الحمل. استخرج المبيضين والرحم من كل حيوان، واستخدم تقنية تفاعل البوليمرات المتسلسل للنسخ العكسي لقياس التعبير عن مستقبلات هرمون الأستروجين. زاد التعبير الجيني لمستقبلات الأستروجين الفا زيادة معنوية في السبعة والعشرين يوما من الحمل في حين لم يختلف التعبير الجيني لمستقبلات الأستروجين بيتا بين أيام الحمل المختلفة والجرذان غير الحوامل في المبيض. في الرحم زاد التعبير الجيني ل مستقبلات الأستروجين الفا وبيتا زيادة معنوية في العشرين يوما من الحمل. استنتج من الدراسة أن كل من الجرذان الحوامل وغير الحوامل، إن المبيض والرحم يعبران جينيا عن مستقبلات الأستروجين من نوع الفا وبيتا وان التعبير عن جين مستقبلات هرمون الأستروجين بيتا بشكل كبير في الرحم خلال العشرين يوما من الحمل ويتم التعبير عن مستقبل الأستروجين بيتا في المبيض بشكل كبير خلال الأيام الأولى ومنتصف فترة الحمل.

control mechanisms in the lactotrophic axis. J Neurosci. 2012;32(23):8074-83. DOI: 10.1523/JNEUROSCI.0129-12.2012
29. Setyawati I, Wiratmini NI, Narayani I. Estrogen hormone level of prepubertal female rat treated with *Calliandra calothyrsus* ethanolic leaf extract. J Phys Conf Ser. 2018;983(1). DOI: 10.1088/1742-6596/983/1/012197
30. Andrews ZB, Kokay IC, Grattan DR. Dissociation of prolactin secretion from tuberoinfundibular dopamine activity in late pregnant rats. Endocrinol. 2001;142:2719–2724. DOI: 10.1210/endo.142.6.8196
31. Freeman ME, Kanyicska B, Lerant A, Nagy G. Prolactin: Structure, function, and regulation of secretion. Physiol Rev. 2000;80:15231631. DOI: 10.1152/physrev.2000.80.4.1523
32. Rassie K, Giri R, Joham AE, Teede H, Mousa A. Prolactin in pregnancies affected by pre-existing maternal metabolic conditions: A systematic review. Int J Mol Sci. 2023;24(3):2840. DOI: 10.3390/ijms24032840
33. Yoest KE, Quigley JA, Becker JB. Rapid effects of ovarian hormones in dorsal striatum and nucleus Accumbens. Horm Behav. 2018;104:119–129. DOI: 10.1016/j.yhbeh.2018.04.002
34. Da Silva ID, Wuidar V, Zielonka M, Pequeux C. Unraveling the Dynamics of Estrogen and Progesterone Signaling in the Endometrium: An Overview. Cells. 2024;13(15):1236. DOI: 10.3390/cells13151236
35. Al-Bader MD. Estrogen receptors alpha and beta in rat placenta: detection by RT-PCR, real time PCR and Western blotting. Reprod. Biol Endocrinol. 2006;4:1-10. DOI: 10.1186/1477-7827-4-13
36. Vaillant C, Chesnel F, Schausi D, Tiffoche C, Thieulant ML. Expression of estrogen receptor subtypes in rat pituitary gland during pregnancy and lactation. Endocrinol. 2002;143(11):4249-4258. DOI: 10.1210/en.2002-220193
37. Demay F, De Monti M, Tiffoche C, Vaillant C, Thieulant ML. Steroid independent activation of ER by GnRH in gonadotrope pituitary cells. Endocrinol. 2001;142:3340–3347. DOI: 10.1210/endo.142.8.8337
38. Vaillant C, Chesnel F, Schausi D, Tiffoche C, Thieulant M. Expression of estrogen receptor subtypes in rat pituitary gland during pregnancy and lactation. Endocrinol. 2002;143(11):4249-4258. DOI: 10.1210/en.2002-220193
39. Hassan GS, Helal MB, Ibrahim HF. Immunohistochemical expression of estrogen receptor alpha in the maxillary sinus, pulp, and periodontal ligament of adjacent teeth in late pregnancy in rats. Odontol. 2023;111(3):608-617. DOI: 10.1007/s10266-022-00770-0
40. Jefferson WN, Couse JF, Banks EP, Korach KS, Newbold RR. Expression of estrogen receptor is developmentally regulated in reproductive tissues of male and female mice. Biol Reprod. 2000;6:2310–317. DOI: 10.1095/biolreprod62.2.310
41. Philpott CM, Conboy P, Al-Azzawi F, Murty G. Nasal physiological changes during pregnancy. Clin Otolaryngol Allied Sci. 2004;29(4):343-51. DOI: 10.1111/j.1365-2273.2004. 00815.x
42. Mata KM, Li W, Reslan OM, Siddiqui WT, Opsasnick LA, Khalil RA. Adaptive increases in expression and vasodilator activity of estrogen receptor subtypes in a blood vessel-specific pattern during pregnancy. Am J Physiol Heart Circ Physiol. 2015;309:H1679–96. DOI: 10.1152/ajpheart.00532.2015
43. Shu L, Guan S-M, Fu S-M, Guo T, Cao M, Ding Y. Estrogen modulates cytokine expression in human periodontal ligament cells. J Dent Res. 2008;87:142–7. DOI: 10.1177/154405910808700214