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The Protective Role of Vitamin E Against Minoxidil on Reproductive Indices and Histological Alteration in Female Rats and Their Embryos

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Abstract
The current study was therefore carried out in order to evaluate the role of vitamin E in protecting against the oxidative and reproductive indices induced by minoxidil The pregnant rats were randomly divided into four experimental groups, with six animals in each group (n = 6), giving a total of 24 animals. Group 1 (Control) received distilled water orally by gavage and served as the control group. Group 2 (Vitamin E) received vitamin E orally at a dose of 100 mg/kg/day. Group 3 (Minoxidil) received topical minoxidil at a dose of 10 mg/kg/day. Group 4 (Vitamin E + Minoxidil) received vitamin E orally at a dose of 100 mg/kg/day followed one hour later by topical minoxidil at a dose of 10 mg/kg/day. All treatments were administered from gestation day 1 to day 19. The findings showed that minoxidil significantly elevated the content of malondialdehyde (MDA) and suppressed catalase (CAT) activity. Also, adverse effects on reproductive performance, including reduced implantation sites , embryonic death, and fetus survival rate. The histopathological findings showed severe kidney damage in the maternal and fetal tissues. On the other hand, Vitamin E improved oxidative status, reproductive performance, and tissue structure. In summary, Vitamin E has an important role in protecting against the toxic effects of minoxidil .
Keywords**: Vitamin E, Minoxidil, Oxidative Stress, Reproductive Performance, Histological Alterations**

الملخص
هدفت الدراسة الحالية إلى تقييم دور فيتامين **E** في الحماية من الإجهاد التأكسدي والتغيرات في المؤشرات التكاثرية الناجمة عن استخدام المينوكسيديل. تم تقسيم الجرذان الحوامل عشوائيًا إلى أربع مجموعات تجريبية، بواقع ستة حيوانات في كل مجموعة**(n = 6)** ، ليكون العدد الكلي 24 حيوانًا. المجموعة الأولى (السيطرة) تلقت ماءً مقطرًا فمويًا بواسطة التغذية الأنبوبية **(gavage)** ومثلت مجموعة السيطرة. المجموعة الثانية) فيتامين **(E** تلقت فيتامين **E** فمويًا بجرعة 100 ملغم/كغم/يوم. المجموعة الثالثة (المينوكسيديل) تلقت المينوكسيديل موضعيًا بجرعة 10 ملغم/كغم/يوم. أما المجموعة الرابعة) فيتامين + **E** المينوكسيديل **(**فقد تلقت فيتامين **E** فمويًا بجرعة 100 ملغم/كغم/يوم، تلاه بعد ساعة واحدة إعطاء المينوكسيديل موضعيًا بجرعة 10 ملغم/كغم/يوم. أُعطيت جميع المعالجات من اليوم الأول إلى اليوم التاسع عشر من الحمل.أظهرت النتائج أن المينوكسيديل أدى إلى ارتفاع معنوي في مستوى المالونداياليديهايد **(MDA)** وانخفاض في نشاط إنزيم الكاتالاز **(CAT).** كما لوحظت تأثيرات سلبية على الأداء التكاثري، شملت مواقع الانغراس، وزيادة معدل موت الأجنة، وانخفاض نسبة بقاء الأجنّة. وأظهرت الفحوصات النسيجية المرضية وجود أضرار شديدة في الكلى لدى الأمهات والأجنة. في المقابل، أظهر فيتامين **E** تأثيرات إيجابية على الحالة التأكسدية، والأداء التكاثري، والبنية النسيجية. خلاصة القول، يلعب فيتامين **E** دوراً مهماً في الحماية من التأثيرات السامة للمينوكسيديل
الكلمات المفتاحية : فيتامين E **، المينوكسيديل، الإجهاد التأكسدي، الأداء التكاثري، التغيرات النسيجية.**

Introduction

Pregnancy causes significant physiological changes to enable the mother to provide the essential nutrients required by the fetus; this involves massive alterations in metabolic pathways, which may lead to an imbalance between antioxidant defenses and oxidative stress [1] . Oxidative stress is recognized as one of the primary sources of cellular and tissue modifications, particularly in terms of cellular and membrane structures since they undergo lipid peroxidation [2]. This results in an excess of free radicals and damage to proteins and nucleic acidsthat affect the transport and exchange of materialsbetween the mother and the fetus, thereby affecting fetal growth and normal development, especially during the initial stages of gestation, which are considered critical because it is the period when organ development occurs [3,4] . Thus, there is a need to boost the antioxidant system within the body [5].

Vitamin E is considered one of the essential lipophilic antioxidants [6] because it can prevent damage to the cell membranes caused by the increase and accumulation of free radicals as a result of donating a hydrogen atom (or electron) ; then the substance is stabilized and the terminating lipid peroxidation chain reactions in membrane phospholipids stop [7] ; mainly tissues with high metabolic activity such as the liver and kidneys [8]. In developing fetal

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tissues, vitamin E has an important effect on cell division and regulation of cell signaling by influencing cell division and the regulation of cell signaling pathways involved in growth and development. [9 ,10] .

Minoxidil is one of the most commonly used drugs for activating ATP-sensitive potassium channels [11], increases blood flow to tissues, hence it is prescribed orally to control hypertension, but it was found that it could be applied topically to improve hair follicles to prevent hair fall and become one of the major drugs to prevent hair fall [12]. Nevertheless, due to concerns about its systemic effects, especially on pregnant women, due to their increased sensitivity and lack of studies that focus on the transfer of the drug across the placentawhich may constitute a latent threat to the growth of the fetus. Many studies indicate that drug induced toxicity is often associated with oxidative damage, which can be assessed by the lipid peroxidation product malondialdehyde (MDA). Glutathione (GSH) is considered a major component of the cellular antioxidant defense against such damage. [13 ,14] .

Reproductive indices are among the most important parameters used to assess female reproductive toxicity and protection. counting the number of corpora lutea in the ovary is proof of the number of ova produced in the process of ovulation; therefore, when calculating, it can give a reflection of how effective the ovulation process is [15]. The number of implantations sites will give a reflection on the number of embryos implanted in the uterus in addition to the loss rate of embryos [16], and Histopathological assessment is considered one of the accurate assessments for estimating tissue damage [17]. In this context, the aim of this study is to assess the histological and embryonic effects of vitamin E and minoxidil.

Materials and Methods

1- Animal preparation and mating

Laboratory rats of either sex weighing 160-210 grams were obtained from the College of Veterinary Medicine of Tikrit University. In order to reduce stress and allow acclimatization to the laboratory conditions, they were allowed to stay for a week prior to any experimentation. After one week of acclimatization, there was in a ratio of 2 females to 1 male per cage of rats in cages to perform mating. The next morning when there was a sign of a vaginal plug indicating pregnancy, the female rats were then isolated for experimentation [18].

2- Use of vitamin E and drug

The vitamin and drug were administered from days 1 to 19 of pregnancyin the following way:

The vitamin was given by oral gavage using a rat gavage needle, and the drug was administered one hour later. For the drug, the preparation of the skin for topical application involved shaving off a section (2 cm) of hair on the dorsal region of the rat; this was done gently without the use of chemicals [19]. Then using a dropper, the drug 2% minoxidil solution was applied [20].

3 .Grouping

The pregnant rats were randomly divided into four experimental groups, with six animals in each group (n = 6). Group 1 (Control) received distilled water orally by gavage and served as the control group. Group 2 (Vitamin E) received vitamin E orally at a dose of 100 mg/kg/day. Group 3 (Minoxidil) received topical minoxidil at a dose of 10 mg/kg/day. Group 4 (Vitamin E + Minoxidil) received vitamin E orally at a dose of 100 mg/kg/day followed one hour later by topical minoxidil at a dose of 10 mg/kg/day. All treatments were administered from gestation day 1 to day 19.

4- Measurement of maternal serum antioxidant indices

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After euthanasia of the pregnant rats, 2 mL of blood were collected by cardiac puncture and allowed to clot at room temperature (22–25°C) for 30 min . The blood samples were then centrifuged at 3000 rpm for 10 minutes, which produced serum samples that were analyzed for MDA, GSH, and other biochemical parameters

5- Reproductive indices measurements

- Pregnant rats were euthanized on gestation day 19, and the ovaries and uterus were harvested with the uteri kept attached to the ovariesfor estimating the total numbers of CLs and implantation sites as per [21]:
- Ovaries: the number of corpora lutea (CL; yellow bodies).
- Uterus: Number of implantation sites, number of viable and non-viable fetuses, and clear zones representing lost embryos at the implantation site in the uterus.

Using the following formulas, the reproductive indices were calculated:

Pre-implantation loss (%) = (CL – implantation sites) / CL x 100

Post-implantation loss (%) = implantation sites – viable fetuses / implantation sites x 100

Survival rate of fetuses (%) = number of viable fetuses number of implantation sites x 100 [21]

6- Histological study

To study the histology of the maternal and foetal kidneys, they were obtained to stain them through the use of regular staining such as hematoxylin and eosin to examine changes in the histology of the kidneys. These kidneys were then washed well to ensure there was no blood or other tissue residue on them before being put into 10 % neutral buffered formalinfor fixation purposes, which take 24 hours. Then the preparations were made for the tissue to be cut into thin sections by immersing the tissues in 70%, 90%, and 99% alcohol solutions, followed by xylene solution before embedding them in paraffin molds at 60°C. [22]

The tissue samples were fixed in a 10% neutral formalin solution for 24–48 hours, then washed with running water. After that, the samples were dehydrated using ascending concentrations of ethanol (70%, 80%, 90%, 95%, and absolute alcohol), then cleared with xylene and embedded in paraffin wax. The paraffin blocks were cut into tissue sections with a thickness of 5 micrometers using a rotary microtome, and then the sections were fixed onto glass slides. The paraffin was removed from the slides using xylene, and then rehydrated thru descending concentrations of ethanol to distilled water. Then, the sections were stained with hematoxylin for 5 minutes, washed with water, and the cytoplasm was stained with eosin for 1–3 minutes. Finally, the sections were dehydrated with ascending concentrations of alcohol, then cleared with xylene and mounted with a mounting medium (DPX) and a coverslip, in preparation for microscopic examination [22].

6.1 Maternal kidney histology

Control group

Histological sections of maternal kidneys proximal and distal convoluted tubules proximal and distal convoluted tubules show normal morphology of renal glomeruli and proximal and distal renal tubules.

2- Vitamin E group

Sections of tissue revealed the normal morphology of glomeruli, tubules, and cells that constitute both structures.

3- Minoxidil group

There is a marked damage to the glomeruli since The renal glomeruli showed a normal structure with intact Bowman's capsule

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and normal urinary spaces and the cells of the glomerulus are necrotic with indistinct nuclei. Additionally, there is degeneration in the renal tubules, which contain necrotic cells, With the narrowing of the tubule lumen due to the swelling of the epithelial cells. containing individual cells which are detached from their basement membrane.

4- Vit E + minoxidil group

It is quite apparent that there has been an The section showed a decrease in glomerular and tubular damage, with clearer glomerular structures and better preservation of tubular lumens and epithelial cells compared to the minoxidil group.

According to the histological specimens from this group, the structure of the glomerulus is vague, and the developmental stages of the glomeruli are poorly defined. Most of the developed tubules also consist of dead and deteriorated cells.

4- Vitamin E + Minoxidil group:

The sections showed developmental stages close to normal, despite the continued observation of focal necrosis in the tubular cells. The mature renal tubules also showed prominent nuclei and lumens similar to those in the control and vitamin E groups.

Statistical Analysis

Data analysis was done using SPSS statistical software and presented as mean ± SD. The one-way ANOVA followed by the Tukey

combined effects of minoxidil and Vitamin E resulted in a significant reduction in MDA and improved antioxidant enzymes, demonstrating that Vitamin E acts as an antioxidant.

6.2- Fetal kidney tissues

1- Control group

Sections of the embryonic kidneys showed renal tubules and glomeruli at different stages of maturity, indicating the natural development of kidney formation.

2- Vitamin E group

Also seen on the sections was the normal formation of the glomeruli and tubules at various stages of development, with no apparent cellular damage, closely resembling the control group.

3- Minoxidil group

post-hoc test was used to compare differences between groups. Statistical significance was taken at $P < 0.05$.

Results

According to the findings presented in Table 1, In the minoxidil-treated group, a significant increase in MDA levels was observed, accompanied by a significant decrease in antioxidant indicators (GSH, CAT, and SOD), indicating an increase in lipid peroxidation and oxidative stress with a weakening of the antioxidant defense system. In contrast, the group treated with vitamin E showed values comparable to the control group, with a slight improvement in antioxidant levels. However, the

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Table 1: Maternal Oxidative Stress and Antioxidant Markers

Group	MDA (nmol/mL)	CAT (U/mL)	GSH (µmol/L)	SOD (U/mL)
Control	2.1 ± 0.3	52 ± 4.2	8.5 ± 0.6	120 ± 8.2
Vitamin E	1.9 ± 0.2	55 ± 5.3	9.2 ± 0.7	128 ± 7.5
Minoxidil	4.8 ± 0.5	30 ± 3.4	5.1 ± 0.5	85 ± 6.1
Vit E + Minoxidil	2.6 ± 0.3	47 ± 4.2	7.8 ± 0.6	110 ± 7.3

Table 1 shows that the administration of minoxidil resulted in a significant decrease maternal body weight , ovaries, and uterus compared with the control group.. In addition, there was a significant reduction in the number of corpora lutea and implantations, reflecting poor ovulation and implantation.

On the other hand, Vitamin E group had almost identical results to the control group, indicating no negative impact on reproduction

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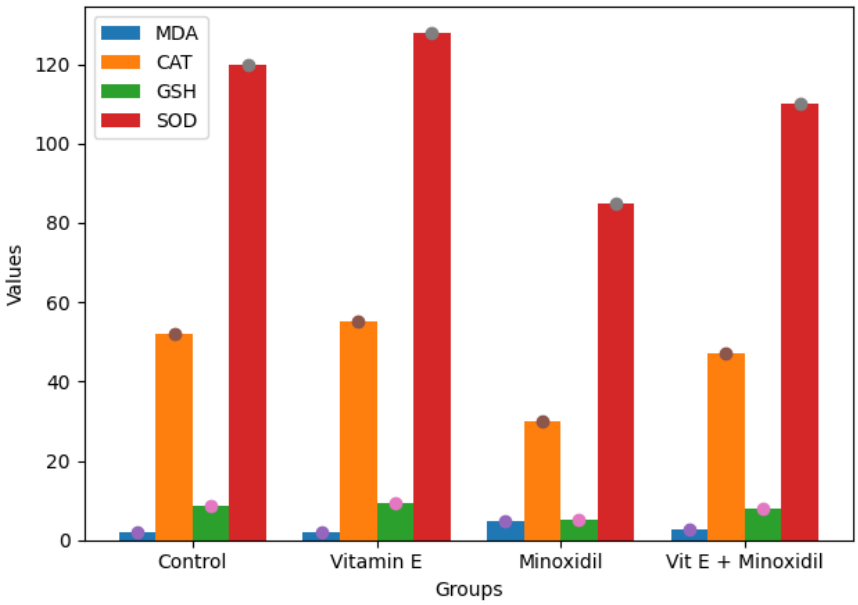

Figure 1: Effect of Vitamin E and Minoxidil on Oxidative Stress Biomarkers

However, in the case of the combination therapy (Vitamin E & Minoxidil), partial recovery was observed for all the parameters, .where a significant increase in the weights of the ovaries and uterus was observed, in addition to a significant increase in the formation of corpora lutea and implantation sites compared to the minoxidil group.

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Table 2: Maternal Reproductive Indices

Parameter	Control	Vitamin E	Minoxidil	Vit E + Minoxidil
Maternal weight (g)	210 ± 10	215 ± 12	185 ± 9.2	200 ± 10.4
Ovarian weight (g)	0.75 ± 0.05	0.78 ± 0.06	0.60 ± 0.04	0.70 ± 0.05
Uterine weight (g)	3.5 ± 0.3	3.6 ± 0.3	2.6 ± 0.2	3.1 ± 0.3
No. of corpora lutea (CL)	12.5 ± 1.2	13 ± 1.0	10 ± 1.1	11.5 ± 1.0
No. of implantation sites	11.8 ± 1.1	12 ± 1.2	8.2 ± 0.9	10.5 ± 1.1

Table 2. Maternal reproductive endpoints in pregnant rats treated with vitamin E and/or minoxidil. Data are expressed as mean ± SD (Mean ± SD). Reproductive performance during pregnancy was evaluated using maternal weight, ovarian and uterine weight, number of corpora lutea (CL) and implantation sites to assess the effects of minoxidil with or without vitamin E on reproductive parameters.

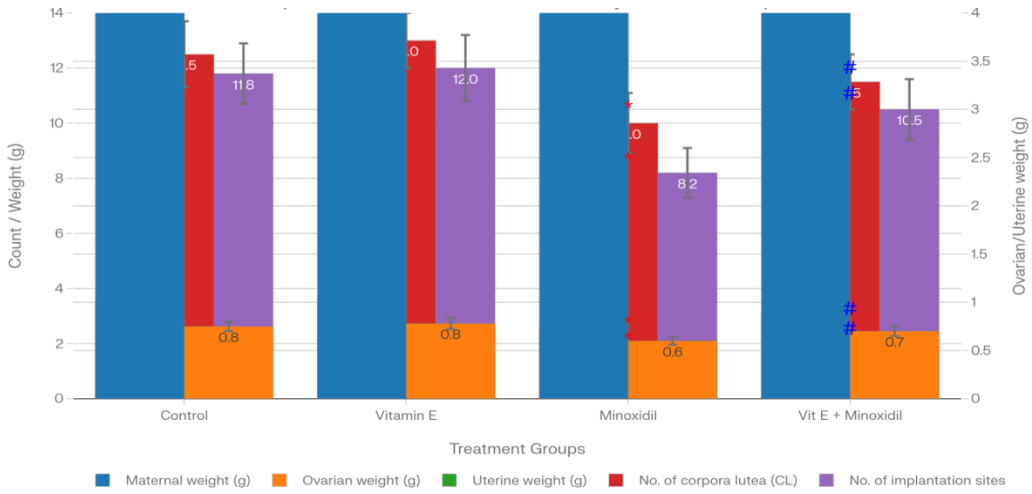

Figure 2: Effects of Vitamin E and Minoxidil on Maternal and Reproductive Parameters in Rats

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It is evident from the data presented in Table 3 that minoxidil treatment caused a marked decrease in embryo weight, embryo length, and placental weight, indicating impaired fetal growth and development . Also, there was a reduction in the number of live fetuses, while the number of dead fetuses was markedly increased.

The results of Vitamin E group were similar to the control group with regard to embryonic development parameters.

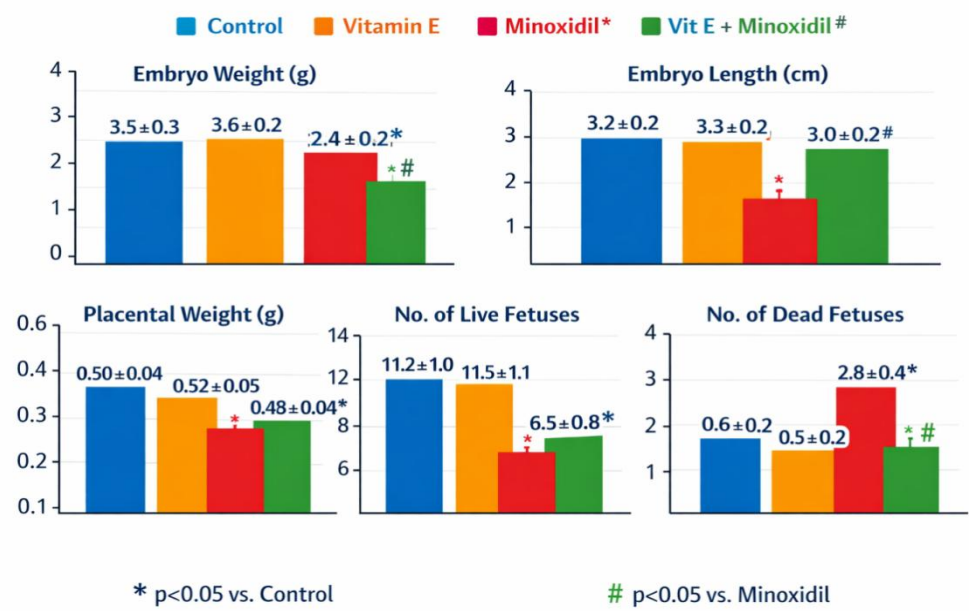
Co-administration with Vitamin E enhanced the embryonic growth parameters along with an increase in the number of viable fetuses.

Table 3: Embryonic Development Parameters

Parameter	Control	Vitamin E	Minoxidil	Vit E + Minoxidil
Embryo weight (g)	3.5 ± 0.3	3.6 ± 0.2	2.4 ± 0.2	3.1 ± 0.3
Embryo length (cm)	3.2 ± 0.2	3.3 ± 0.2	2.6 ± 0.2	3.0 ± 0.2
Placental weight (g)	0.50 ± 0.04	0.52 ± 0.05	0.38 ± 0.03	0.45 ± 0.04
No. of live fetuses	11.2 ± 1.0	11.5 ± 1.1	6.5 ± 0.8	9.8 ± 1.0
No. of dead fetuses	0.6 ± 0.2	0.5 ± 0.2	2.8 ± 0.4	1.2 ± 0.3

Table 3. Embryonic developmental parameters in fetuses of pregnant rats treated with minoxidil and/or vitamin E. Data are presented as mean ± standard deviation (Mean ± SD). Embryonic weight, embryonic length, placental weight, and the numbers of live and dead fetuses were evaluated to determine whether gestational exposure to minoxidil impaired fetal growth and development and to assess the potential protective role of vitamin E against these adverse effects.

Figure 3 : Impact of Vitamin E and Minoxidil on Fetal Development



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As presented in Table 4, the Minoxidil group showed an increase in pre-implantation loss, post-implantation loss, and rate of resorption . These results suggest reproductive toxicity. In addition, the fetal survival rate was significantly reducedin the Minoxidil group. In the Vitamin E group, the results were comparable to the control group, suggesting no adverse effect on reproduction.

reduced pre implantation loss, post implantation loss, and resorption rate in addition to increasing survival rate of fetuses, as compared to minoxidil alone, showing the effectiveness of vitamin E supplementation in protecting reproductive processes.

Table 4: Reproductive Efficiency Indices (%)

Parameter	Control	Vitamin E	Minoxidil	Vit E + Minoxidil
Pre-implantation loss (%)	5.6 ± 1.3	4.8 ± 1.3	18 ± 2.3	9 ± 1.1
Post-implantation loss (%)	4.2 ± 1.7	3.9 ± 1.6	25 ± 3.1	10 ± 2.4
Resorption rate (%)	5 ± 1.4	4 ± 1.4	28 ± 3.2	12 ± 2.6
Fetal survival rate (%)	95 ± 2.3	96 ± 2.3	72 ± 4.1	88 ± 3.4

Histopathological grading in Table 5 shows that there were normal renal tissues without any renal damage. In contrast, in the minoxidil group, severe damage to the glomeruli, tubular degeneration and necrosis, together with infiltration of inflammatory cells , indicated that there was severe renal damage.

However, in the group administered Vitamin E along with minoxidil, marked improvement, with only mild residual changes , implying that Vitamin E could ameliorate minoxidil induced renal damage.
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Table 5: Histopathological Scoring (Semi-Quantitative)

Parameter	Control	Vitamin E	Minoxidil	Vitamin E + Minoxidil
Glomerular damage score	0	0	3	1
Tubular degeneration	0	0	3	1
Necrosis	0	0	3	1
Inflammatory infiltration	0	0	2	1

Table 5. Semi-quantitative histopathological scoring of renal tissue in pregnant rats treated with vitamin E and/or minoxidil. Data represent the severity of histopathological alterations, including glomerular damage, tubular degeneration, necrosis, and inflammatory cell

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infiltration. Histopathological lesions were scored semi-quantitatively according to the degree of tissue damage observed microscopically.

Histopathological Study

1. Maternal Kidney Tissues

Control Group

The histological examinations of the maternal kidneys revealed normal renal architecture with normal glomeruli(G), proximal tubules(PT), and distal renal tubule (DT).

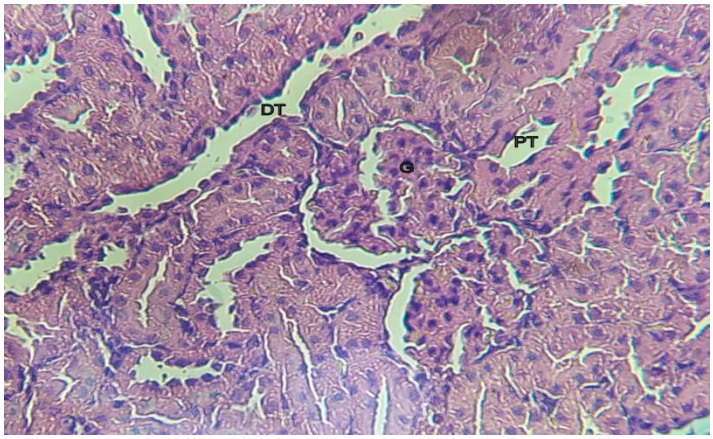

Figure1: maternal kidney section from control groups, (H&E), 400X.

Vitamin E Group

Histological sections of the maternal kidneys in the vitamin E group revealed normal structure of glomeruli(G) and renal tubules (PT,DT), with their constituent cells comparable to those of the control group.

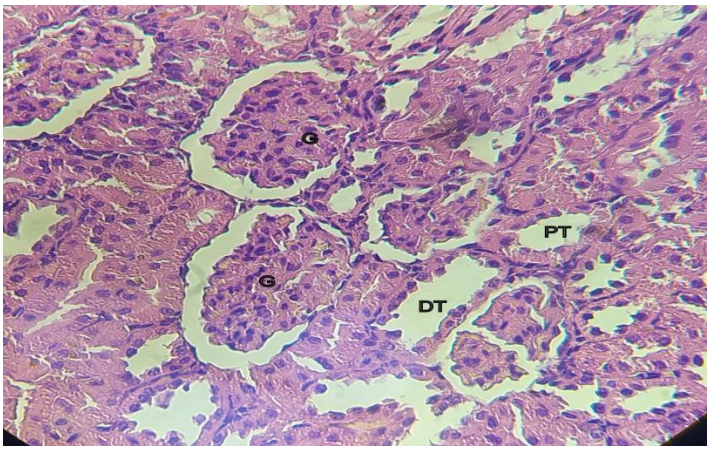

Figure2: maternal kidney section from vit E groups, (H&E), 400X.

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Minoxidil Group

Histological sections showed clear evidence of glomerular injury, with some glomeruli appearing fragmented. There was evidence of necrosis(N) with pyknotic nuclei (P) within the cells lining the glomeruli(G). The cells lining the renal tubules(PT,DT) had undergone necrosis and degeneration, and most of the tubular lumens contained sloughed cell(S) .

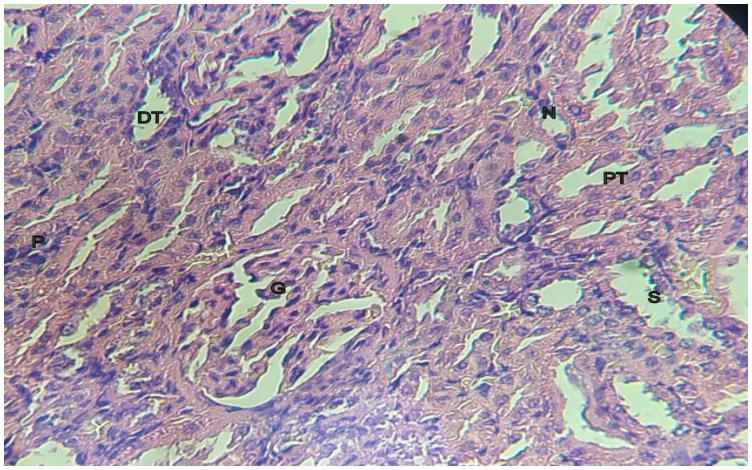

Figure3: maternal kidney section from minoxidil groups, (H&E), 400X.

Vitamin E + Minoxidil Group

sections stained with H&E showed an improvement in the condition of the affected cells of the glomerulus(G), with the glomeruli showing well-defined structures. There was improvement in the renal tubules(PT,DT)and tubular lumens.

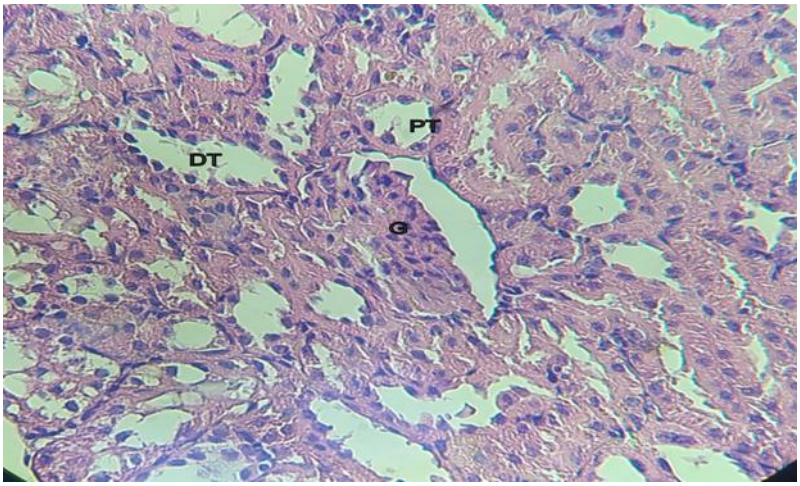

Figure4: maternal kidney section from vit E+ minoxidil groups, (H&E), 400X.

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2. Fetal Kidney Tissues

Control Group

There were normal histological sections of fetal kidneys with normal structure such as well-developed glomeruli(G)and renal tubules(PT,DT).

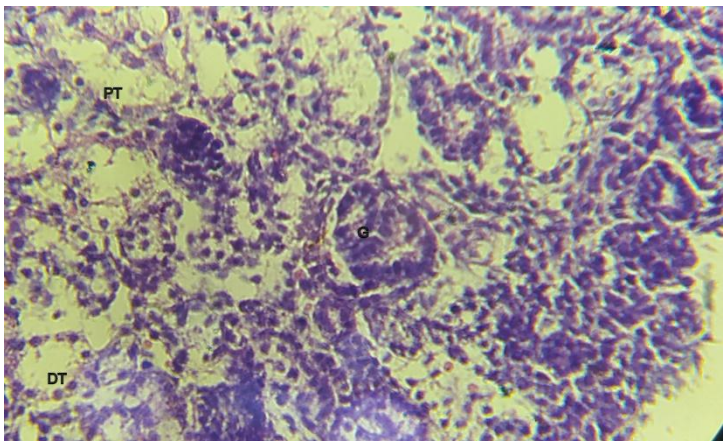

Figure5: embryo kidney section from control groups, (H&E), 400X.

Vitamin E Group

Histological sections (H&E) showed normal glomeruli(G) and tubules (PT,DT)at different developmental stages, without any visible cellular injury, similar to the control group.

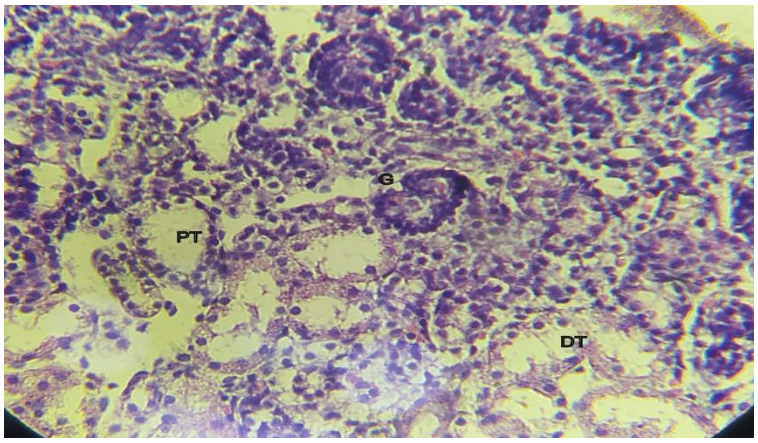

Figure6:embryo kidney section from vit E groups, (H&E), 400X.

Minoxidil Group

Poorly defined glomeruli with undetermined developmental stages were in histological sectionsof glomerulus (G) .

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Degenerative and necrotic changes characterized most of the renal tubules(PT,DT) and affected their structural organization

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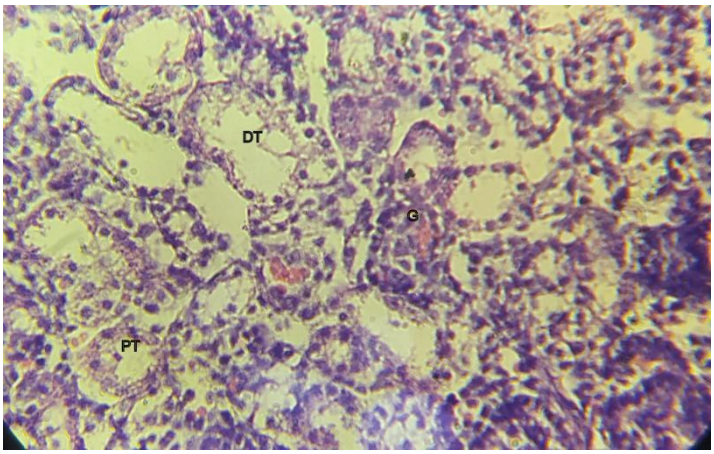

Figure7:embryo kidney section from minoxidil groups, (H&E), 400X.

Vitamin E + Minoxidil Group

Although necrotic cells were still noted , the tissue showed marked improvement toward normal structural regeneration of glomerulus (G). The renal tubules(PT,DT) had better-defined nuclei, while their lumen was seen to be similar to those of the control group and the Vitamin E group.

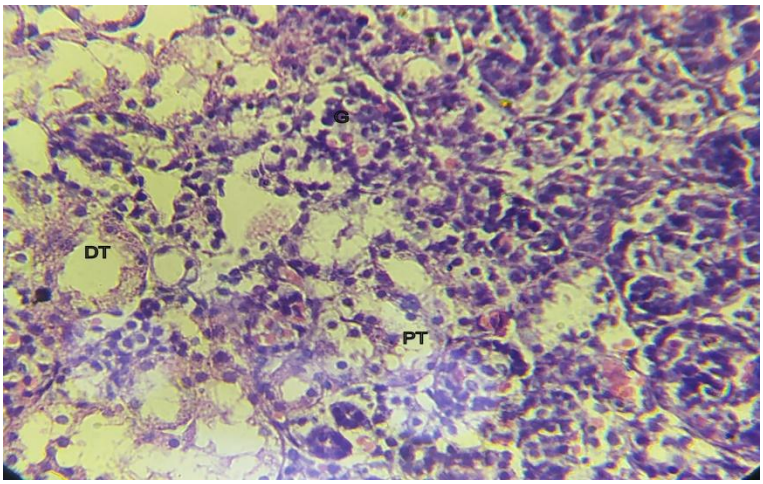

Figure 8: embryo kidney section from vit E+ minoxidil groups, (H&E), 400X.

Discussion

In the current study, exposure to vitamin E maintained the oxidative balance in pregnant rats. The levels of the observed biomarkers, including MDA (1.9 ± 0.2 nmol/ml), CAT (55 ± 5 units/ml), GSH (9.2 ± 0.7 µmol/l), and SOD (128 ± 7 units/ml), were comparable to those recorded in the control group, indicating the maintenance of the normal oxidative state and supporting the protective effects indicated . [23] This is due to Vitamin E plays an effective antioxidant role, as it helps in inhibiting lipid peroxidation and the formation of free radicals while decreasing the level of MDA. The findings with regard to reproductive biomarkers and weights of both the mother and fetus in the experiment did not show any significant difference from those of the control group, and this is because Vitamin E has a protective effect on reproductive parameters. This is what

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was proved by the current experiment, and this is also in accordance with the mother and fetal kidney tissues since the antioxidants increased helped in protecting cell membranes during fetal tissue proliferation , which resulted in the proper development of the cells [24] .

In contrast , the results for the minoxidil group revealed a rise in the MDA index along with a drop in GSH. This can be attributed to the fact that the drug causes an elevation in potassium efflux , causing an elevation in Reactive Oxygen Species(ROS) generation in the body tissues. These reactants combine with unsaturated fatty acids, leading to a phenomenon known as lipid peroxidation. The latter contributes to an elevation in the oxidative stress markers while reducing the antioxidant capacity [25]. An imbalance in hormonal levels that influences the generation of reproductive hormones like estrogen and progesterone reduces the process of embryo implantation and the number of embryos produced. Additionally, this could be caused by the drug's influence on the reproductive organs' cellular level, affecting their ability to produce or implant the embryos and reduce the total number of live births. Lastly, the reduction in the weight of the mother and fetus is caused by impaired metabolism and nutrient delivery from the mother to the fetus. All of the aforementioned factors lead to the disruption of the formation and tissue structures, leading to the manifestation of symptoms associated with the influence of the drug on kidney tissues in both the mother and fetus [26].

Conversely , the group receiving the vitamin as a protector had a significant improvement in terms of oxidative system parameters when compared to the group that received only minoxidil, proving the direct protection provided by it. When it is provided before taking the drug, it boosts antioxidant defenses , thereby stopping the interaction between ROS and lipids, and hence lowering the MDA concentration right from the start [27] . Furthermore, the presence of high concentrations protects reproductive systems against any form of damage, hence ova and implantation mechanisms remain unaffected. Similarly, the protection of other important body organs such as the liver and kidney before being damaged due to minoxidil ensures that metabolic processes remain almost normal, and hence maintaining the weight of the mother and fetus [27].

From this study, it is evident that Vitamin E plays a protective function against the adverse effects that may be caused by minoxidil on the mother and the embryo, where MDA decreased while GSH increased , [28] there was an increase in the corpora lutea and implantation sites, resulting in the overall birth rate of live offspring and a reduction in the resorption rate of embryos both before and after implantation, and an increase in the body mass of the mother and the fetus [29]. Additionally, there was an improvement in kidney tissues in the mother and fetus, supporting the hypothesis that antioxidants like Vitamin E may mitigate the side effects of minoxidil, especially during pregnancy and normal fetal development [30].

Conclusion

Minoxidil showed harmful negative effects on oxidative stress indicators and reproductive parameters in female rats and their fetuses, as evidenced by damage observed in the kidney tissues of the mother and fetus. In contrast, vitamin E administration proved to be protective, enhancing antioxidant activity and reproductive performance while alleviating kidney tissue damage.

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