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ORIGINAL ARTICLE

The effects of acrylamide and vitamin E on kidneys in pregnancy: an experimental study

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ABSTRACT

Objectives: The objective of this study is to investigate possible damages to kidney tissues of pregnant rats and their fetuses exposed to acrylamide during pregnancy and possible protective effects of vitamin E against these damages.

Material and methods: Rats were randomly assigned to five groups of control, corn oil, vitamin E, acrylamide, vitamin E + acrylamide, six pregnant rats in each. Mother and fetal kidney tissues were examined for malondialdehyde (MDA), reductase glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), total antioxidant status (TAS), total oxidant status (TOS), urea, creatine, trace elements such as Zn and Cu in the serum and histopathological analyses were conducted.

Results: It was determined that acrylamide, administered during pregnancy, statistically significantly increased MDA and TOS levels, maternal serum urea, creatinine, and Zn levels, while it decreased GSH, TAS, SOD, and CAT levels ($p \leq .05$) when compared with all other groups in the kidney tissues of pregnant rats and their fetuses and caused tubular degeneration, hemorrhage, narrowing, and closure in Bowman's space, and, in the E vitamin group, it statistically significantly increased GSH, TAS, SOD, CAT, urea, creatinine, and Zn levels when compared with other groups and lowered TOS and MDA levels to those of the control group ($p < .05$) and there were no differences between the groups histologically.

Conclusion: It was observed that acrylamide administered during pregnancy caused oxidative stress in kidney tissues of mother rats and their fetuses, resulting in tissue damage, and vitamin E application, which is considered to be a powerful antioxidant, inhibited oxidative stress.

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Acrylamide; fetus; kidneys; mother; oxidative stress; pregnancy; vitamin E

Introduction

Synthetically produced acrylamide (AA) is not found in nature; it is a water-soluble substance that is widely used in research laboratories as polyacrylamide gel, especially in biochemistry and genetics, in the textile, printing, and cosmetic industries [1].

The real danger for humans is the formation of AA spontaneously via the Maillard reaction between asparagine amino acid and monosaccharides during frying and baking food at temperatures of 120 °C and above [2,3]. Based on this fact, studies on food-borne AA toxicity have increased. It was determined that acrylamide is highly toxic for humans and animals, with especially neurotoxic and carcinogenic effects and in reproductive systems [4–6]. In previous studies, it was found that in mothers consuming food that contain acrylamide (fried potatoes, potato chips, crackers, breakfast cereals, etc.), AA penetrates through the placenta reaching the fetus due to its high solubility in water [7–9]. Under normal physiological conditions, there is a balance between oxidant and antioxidant systems in the body, and when the balance is disturbed in favor of oxidants by AA, this could lead to oxidative stress, causing oxidative stress-induced cell and tissue damage [10].

Vitamin E, the active form of which is α (alpha) tocopherol, is a potent antioxidant soluble in lipids and could easily penetrate the placenta to reach the fetus [11,12]. Vitamin E, due to its strong antioxidant properties, detoxifies free radicals and prevents lipid peroxidation and oxidative stress-induced tissue damage by preventing free radicals from attacking the lipid layer of the cell [13,14]. The prospects of exposure to AA

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toxicity are due to the fact that body size in intrauterine and infancy period is much smaller when compared with adults [15], which in turn could cause permanent life-long damage to the fetus.

Although daily AA dose was reported as 0.5 μg/kg/d [16,17], unconscious exposure to AA toxicity increased both in daily life and in pregnancy due to the increasing fast food consumption. Changes in maternal and fetus kidney tissues that occur during pregnancy were investigated in the present study for the first time by administration of 10 mg/kg/bw acrylamide and 100 mg/kg/bw vitamin E.

Materials and methods

Animals

İnönü University, Faculty of Medicine, Experimental Animals Ethics Committee approval was obtained (2016/A-83). 30 young female Sprague–Dawley rats weighing 250 ± 25 g each were procured from Inonu University Faculty of Medicine Experimental Animal Breeding and Research Center (İNÜTF-DEHÜM). Two female and one male rat were taken into special cages at 17:00 hours to spend the night and kept in these cages until 8:00 hours the next morning. At that time, the males were separated from the females. Vaginal smears were taken from the female rats and examined under a microscope and the females whose smear tests exhibited sperm were considered half-day pregnant. Females whose pregnancies were not identified as positive with the smear test were excluded from the study. Pregnant rats were kept in cages at 21 ± 2 °C at İNÜTF-DEHÜM for 20 d (gestation period) under 12 h of light, 12 h of dark, and the cage was constantly ventilated. The rats were fed ad-libitum during the experiment.

Study design

Before starting the experiment, 30 pregnant Sprague–Dawley rats, which were identified as pregnant with vaginal smear test, were randomly selected from the mated rats separated as six rats per group to conduct the experiments and the applications were conducted between the 0th and 20th days of pregnancy.

Control group: fed ad-libitum during pregnancy.

Corn oil group: 1 mL corn oil was administered during pregnancy.

Acrylamide group: 10 mg/kg/d acrylamide (Sigma A8887, St Louis, MO) was applied during pregnancy [18].

Vitamin E group: 100 mg/kg/d α-Tocopherol (SigmaT3251, St Louis, MO) was applied during pregnancy [19].

Acrylamide + vitamin E group: 10 mg/kg/d acrylamide +100-mg/kg/d vitamin E was applied during pregnancy.

Applications were conducted as 1 mL oral gavage for 20 d at the same hour of the day. On the 20th day of pregnancy, kidney tissues were taken from the mothers and fetuses removed with cesarean section and used for biochemical and histological analyses.

Preparation of the tissues for biochemical analyses

Kidney tissues that were kept in deep freezing in cryotube (−80 °C) were taken out and weighed on the day of the experiment. Phosphate buffer was added to obtain a 10% homogenate and this was homogenized at 12,000 rpm for 1–2 min in ice (IKA, Staufen, Germany). Tissue homogenates were centrifuged at 5000 rpm at +4° for 30 min to obtain the supernatant.

Measurement of malondialdehyde (MDA) level

MDA analysis was conducted with the method developed by Uchiyama et al. [20]. The MDA concentration was determined by measuring the supernatant that was extracted from the n-butanol phase of the pink colored product formed by the reaction between the MDA in supernatant and thiobarbituric acid at 95 °C at 535 and 520 nm by spectrophotometry.

Measurement of reduced glutathione (GSH) level

GSH analysis was conducted according to the method described by Ellman [21]. It was conducted by determining the GSH by reading the light intensity of the greenish color produced by the reaction between the GSH in the analysis tube and 5,5′-dithiobis 2-nitrobenzoic acid at 410-nm wavelength.

Measurement of the superoxide dismutase (SOD) level

Total reduction of nitroblue tetrazolium by the superoxide anion produced by xanthine and xanthine oxidase was used to measure SOD activity [22]. SOD activity unit was accepted as the quantity of protein inhibiting the rate of NBT reduction by 50% and the results were given as units per milligram protein. Kidney tissue homogenate sample total protein

content was determined with the method developed by Lowry et al. [23].

Measurement of the catalase (CAT) level

CAT activity was determined with the method developed by Aebi [24]. The constant rate k for H2O2 (initial concentration 10 mM) was determined as indicated by absorbance at 240 nm.

Measurement of total oxidant status (TOS) level

For TOS measurements, the absorbance at 530 nm was measured by mixing 500-μL reagent 1 (measurement buffer) and 75-μL serum, adjusting the ELISA to 25 °C as indicated in the kit procedure. Mixing 25-μL reagent 2 (prochromogenic solution) was added and incubated for 10 min. After incubation, TOS levels were determined by measuring the absorbance at 530 nm again [25].

Measurement of total antioxidant status (TAS) level

For TAS measurement, as described in the kit procedure, the ELISA was set at 25 °C, and 500-μL reagent 1 (measurement buffer) and 30-μL serum were mixed and the absorbance was measured at 660 nm. Seventy-five microliter reagent 2 (colored ABTS solution) was added to the mixture and it was incubated for 10 min. TAS levels were determined by measuring the absorbance at 660 nm again after incubation [26].

Measurement of urea and creatine level

Blood samples were drawn into tubes that contain ethylene-diamine-tetra-acetic acid and immediately transferred onto ice for the measurement of plasma urea and creatine levels. The tubes were centrifuged within a few minutes after collection and stored at −80 °C until the experiment. Plasma urea and creatine levels were measured with commercial Architect c 1600 automatic analyzer kits (Abbott, Abbott Park, IL).

Measurement of serum zinc (Zn) and copper (Cu) levels

Zinc and copper content in the serum was measured with an air/acetylene flame atomic absorption spectrometer (AAS). The tubes containing blood were washed in a 10% (v/v) hydrochloric acid (HCl) solution and after 12 h, they were immersed in 10% (v/v) nitric acid solution (HNO3). Then the tubes were rinsed twice with distilled water and dried. Protein precipitation was conducted by diluting 1-mL serum in 4 mL hydrochloric acid solution (2 M). The product was homogenized using the technique proposed by Banjoko et al. [15] and allowed to settle. The resulting clear supernatant was fed directly into flame atomic absorption spectrophotometer at the wavelength of 324.8 and 213.9 nm for copper and zinc, respectively. The calibration range was prepared with a multi element 1000-ppm standard solution (Merck, Kenilworth, NJ), which was diluted to 1/500 with nitric acid-deionized water (0.03 M). The concentrations were measured three times and adjusted for white (HCl solution 2 M).

Histological analysis

For histological analysis, maternal and fetal kidney tissue specimens were fixed under ambient temperature for 48 h with 10% neutral phosphate buffered formaldehyde. After fixation, kidney tissue specimens were passed through the ethanol and xylene series and then buried in paraffin blocks. Six micrometers sections were excised from the paraffin blocks and stained with hematoxylin–eosin (HE). All sections were examined by a histologist (blind) using a light microscope (Eclipse Ni-U) and camera (DS-Fi2) and the sections were analyzed with Image Analysis System (NIS-Elements Documentation 4.50) (Nikon Corporation, Tokyo, Japan).

Histological damage total score analysis

Kidney damage in mother and rat fetuses was measured by grading glomerular, tubular, and interstitial variations. Glomerular damage (collapse and sclerotic changes, narrowing or disappearance of the Bowman's space, capillary collapse) was scored as follows: 0, absent; 1, $<25\%$ of glomeruli affected; 2, 25–50% of glomeruli affected; 3, $>50\%$ of glomeruli affected. Tabular injury was scored as follows: 0, absent; 1, $<25\%$ of tubules injured; 2, 25–50% of tubules injured; 3, $>50\%$ of tubules injured. The presence of inflammation and interstitial edema and vascular congestion were assessed as follows: 0, absent; 1, mild; 2, moderate; and 3, severe (maximum total score $=15$).

Statistical analysis

Statistical analyses were conducted using the SPSS 21.0 software (SPSS, Chicago, IL). Whether the data demonstrated normal distribution was assessed by the Shapiro–Wilk test. The data were summarized with

median (min–max), since data did not exhibit normal distribution. Kruskal–Wallis test was used for comparison among the groups. After the Kruskal–Wallis test, paired comparisons were conducted with the Conover method. The significance level was accepted as .05 in all tests ($p \leq .05$).

Results

Examination of kidney tissues of mother rats and fetuses demonstrated that the MDA and TOS levels increased significantly in the AA group when compared with all other groups, while the GSH, TAS, SOD, and CAT levels exhibited a statistically significant decrease. In the vitamin E group, statistically significance increases were observed in GSH, SOD, CAT, and TAS levels when compared with the control group. We found that increased MDA and TOS levels decreased and decreased SOD, CAT, GSH, and TAS levels increased when AA applied group was treated with vitamin E when compared with the control group. The application of corn oil did not cause a significant difference when compared with the control group in oxidative stress parameters (Tables 1 and 2).

The kidney sections of the maternal rats in control, corn oil, and vitamin E groups generally displayed normal histological structure. However, in the corn oil and vitamin E groups, minimal tubular damage and inflammation were detected rarely. Different degrees of glomerular collapse, narrowing and local occlusion in Bowman's spaces were observed in the kidney sections of the acrylamide group. Proximal and distal tubular epithelial cells were damaged and tubular degeneration was observed locally. Inflammatory cell infiltration, vascular congestion and in certain areas, minimal interstitial edema were noted in the parenchymal structures of the kidney. Damage findings observed in the acrylamide group significantly decreased in the acrylamide + vitamin E group in both prevalence and degree (Figure 1 and Table 3).

The kidney sections of control, corn oil, and vitamin E group maternal rats generally exhibited in normal histological structure. However, a minimal level of tubular epithelial damage was detected in corn oil and vitamin E groups. It was noted that the interstitial connective tissue between the parenchymal structures in the fetal kidney sections in the acrylamide group was wider. Glomerular damage and local degenerate glomeruli were observed. Interstitial edema was noted around the tubular damage and degenerated regions. In certain sections, minimal vascular congestion and inflammatory cell infiltration were observed. It was observed that all damage parameters in the acrylamide + vitamin E group decreased significantly in prevalence and severity (Figure 2 and Table 4).

Urea and creatinine levels in the maternal serum statistically significantly increased with AA administration when compared with other groups, while urea and creatine levels decreased significantly to control group levels when AA + vitamin E were administered together (Table 5). In the maternal serum, we observed that Zn content decreased with AA application, it increased to control group levels with AA + vitamin E administration, while there were no difference between the groups based on Cu levels (Table 6).

Discussion

Since acrylamide dissolves well in water, contrary to other xenobiotics, it diffuses rapidly through all

Table 1. Maternal kidney tissue oxidant–antioxidant parameters of all groups.

Groups	MDA (nmol/gwt)	GSH (nmol/gwt)	SOD (U/g protein)	CAT (K/g protein)	TAS (mmol/L)	TOS (μmol/L)
C	805 (760–870)^{a}	620 (602–641)^{a}	71 (63–78)^{a}	29 (22–38)^{a}	0.82 (0.74–0.96)^{a}	10.3 (8.5–12.1)^{a}
Co	760 (609–951)^{a,b}	615 (602–698)^{a}	73 (68–82)^{a}	29 (21–32)^{a}	0.99 (0.81–1.04)^{b}	13.6 (9.9–18.3)^{b}
Vit E	737 (556–793)^{b}	981 (896–1096)^{b}	120 (64–148)^{b}	44 (40–49)^{b}	1.22 (1.12–1.36)^{c}	11.1 (9.7–11.5)^{a}
AA	1038 (987–1094)^{c}	542 (518–628)^{c}	50 (40–59)^{c}	17 (14–20)^{c}	0.66 (0.38–1.03)^{d}	20.3 (18.1–21.8)^{c}
Vit E + AA	768 (710–864)^{a,b}	722 (679–961)^{d}	86 (80–94)^{b}	26 (22–28)^{a}	0.96 (0.88–1.03)^{b}	13.2 (11.3–16.8)^{b}

C: control; CO: corn oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. MDA: malondialdehyde; GSH: reduced glutathione; SOD: superoxide dismutase; CAT: catalase; TAS: Total Antioxidant status; TOS: Total Oxidant Status. Data are expressed Median (min–max) of six animals. gwt: gram wet tissue. The groups with different superscripts represent the statistical significance ($p < .05$)

Table 2. Fetal kidney tissue oxidant–antioxidant parameters of all groups.

Groups	MDA (nmol/gwt)	GSH (nmol/gwt)	SOD (U/g protein)	CAT (K/g protein)	TAS (mmol/L)	TOS (μmol/L)
C	525 (515–546)^{a}	946 (925–976)^{a}	43 (41–49)^{a}	3.3 (3.2–3.9)^{a}	1.3 (1.2–1.4)^{a}	9.6 (9.2–11.2)^{a}
Co	527 (498–569)^{a}	937 (921–1057)^{a}	49 (44–53)^{a}	3.6 (3.3–3.8)^{a}	1.3 (1.2–1.9)^{a,d}	13 (12.1–14.2)^{b}
Vit E	348 (335–351)^{b}	1249 (1217–1282)^{b}	69 (67–79)^{b}	5.1 (4.8–5.1)^{b}	2.1 (1.9–2.3)^{b}	8.2 (7.5–10.4)^{a}
AA	782 (649–894)^{c}	846 (818–872)^{c}	33 (25–36)^{c}	2.5 (2.3–2.8)^{c}	0.9 (0.75–0.97)^{c}	22.4 (19.3–27.2)^{c}
Vit E + AA	415 (351–482)^{d}	1020 (998–1101)^{d}	57 (52–62)^{d}	3.9 (3.2–4.7)^{a}	1.62 (1.34–1.85)^{d}	16.1 (14.5–18.5)^{d}

C: control; CO: corn oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. MDA: malondialdehyde; GSH: reduced glutathione; SOD: superoxide dismutase; CAT: catalase; TAS: Total Antioxidant status; TOS: Total Oxidant Status. Data are expressed Median (min–max) of six animals. gwt; gram wet tissue. The groups with different superscripts represent the statistical significance ($p < .05$).

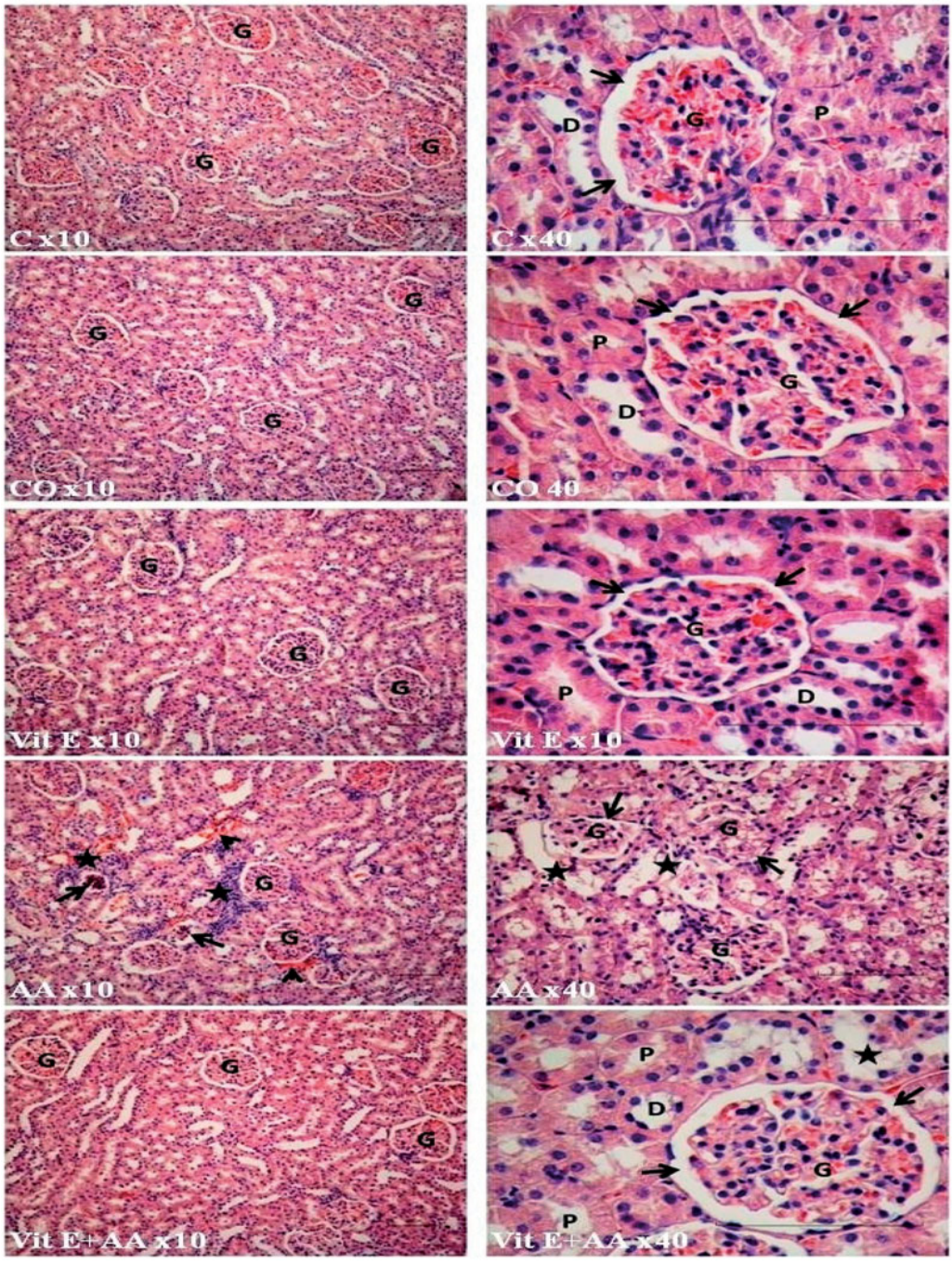

Figure 1. Maternal kidney tissue histological images of all groups C: Control Group: Glomerule (G) × 10, distal tubule (D), proximal tubule (P), Bowman's space (arrow) × 40. Co: corn oil group: Glomerule (G) × 10, distal tubule (D), proximal tubule (P), Bowman's space (arrow) × 40. Vit E: Vitamin E group: Glomerule (G) × 10, distal tubule (D), proximal tubule (P), Bowman's space (arrow) × 40. AA: Acrylamide group: Glomerule (G), Glomerular collapse (arrow), congestion (arrowhead), inflammatory infiltration (asterisk). × 10. Glomerule (G), narrowing and occlusion in Bowman's space (arrow) tubular degeneration (asterisk) × 40. Vit E + AA: Vitamin E + Acrylamide group: Glomerule (G) × 10, Bowman's space (arrow), distal tubule (D), proximal tubule (P), tubular epithelial damage (asterisk) × 40. ×10, ×40 (10× magnification and 40× magnification).

maternal tissues and those of the fetus through placenta quickly after ingestion and could lead to permanent lifelong damage depending on the dose. Increase in biochemical, histological, morphological, and genetic studies on AA toxicity during pregnancy [27,28] was due to the fact that AA moves the oxidant/antioxidant balance to favor oxidants, causing oxidative stress [10,28,29].

Due to its role as an organ of excretion, reabsorption, and general homeostasis, kidney has an extensive blood flow. However, the reabsorption and secretion processes, especially those of the organic acids and

Table 3. Maternal kidney tissue histological damage total score of all groups.

Groups	HDTS
C	0 (0–0)[a]
Co	0 (0–1)[a]
Vit E	0 (0–1)[a]
AA	5 (5–7)[b]
Vit E + AA	3 (2–3)[c]

C: Control; CO: Corn Oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. Data are expressed Median (min–max) of six animals. HDTS: histological damage total score. The groups with different superscripts represent the statistical significance ($p < .05$).

bases, could result in the accumulation of toxins within the tubules, causing kidneys to become more susceptible to toxicity when compared to other organs [30]. This phenomenon is due to poor antioxidant defense enzyme system in kidneys compared to other organs [31].

During the intrauterine period, the vitamin E permeates the placenta easily and largely absorbed by the kidney and other tissues of the fetus [12]. Especially kidney is highly susceptible to oxidative stress due to its low antioxidant capacity and is inevitably needs the protective action of strong antioxidants such as vitamin E [32,33]. Previous studies reported that 100 mg/kg/bw vitamin E administration as a protective agent in Gossypol-induced reproductive toxicity model reduced mating rate, vitamin E administration increased mating rate, as well as GSH levels in testicular tissues, decreased MDA levels, emphasizing that vitamin E reduced oxidative stress by increasing antioxidant capacity [34]. In studies conducted with 50-mg/L arsenic and 500 mg/LE as a preservative addition in drinking water daily during pregnancy and lactation period, it was determined that arsenic administration statistically significantly increased MDA levels in fetus kidney tissues and decreased CAT and TAS levels, while vitamin E administration increased GSH and TAS levels and decreased MDA levels when compared with the arsenic group [35].

In another study where a pregnancy model was constructed, 20 mg/kg/bw AA and 50 mg/kg/bw aluminum were administered between the 14th day of pregnancy and postnatal 14th day and the effects of AA and aluminum were examined. It was found that both aluminum and AA increased MDA levels and decreased SOD, CAT, and GSH levels in the cerebellum of both maternal and fetal rats [36]. In our previous study on pregnancy, when the effects of AA on antioxidant capacity in fetal brains, where the antioxidant capacity is low such as kidney tissues, were examined during pregnancy, we found that AA administered to pregnant rats increased the MDA and TOS levels, seriously decreased GSH, TAS and BDNF levels in the fetal brain, passing through the placenta, it caused a decrease in the numerical density of neurons, the formation of degeneration and edematous neurons, increased the GSH, TAS, and BDNF levels reduced by the application of vitamin E, and the histological appearance was almost the same as the control group [37]. In another previous study by the current authors, when we examined the effects of 5 mg/kg/bW AA and 100 mg/kg/bW vitamin E administration to rats during pregnancy on maternal and fetal liver tissues, we demonstrated that AA increased TOS, MDA, and XO levels in maternal liver tissues, causing oxidative stress, and tissue damage; however, vitamin E administration inhibited oxidative stress. But we could not observe any structural change in fetal liver tissues. We have stated that this was due to the detoxification of a large part of the acrylamide administered to pregnant rats orally by the maternal liver, in other words, the prefilter function of the maternal liver for acrylamide detoxification, and as a result, the amount of acrylamide that could reach the fetus liver remained very low and also the antioxidant defense capacity system in the fetus liver could have been developed [38]. In a study conducted by creating an electromagnetic field (EMF) model with 2.45-GHz wavelength, its effects on the kidney tissues during the 18 prenatal days, pregnancy, and 12 postnatal weeks were investigated biochemically and histologically. The researchers reported that EMF increased TOS levels in both prenatal and postnatal periods when compared with the control group, SOD and TAS levels were statistically significantly reduced, and tubular casts and tubular degeneration in kidney tissues were observed [39]. When the trace element levels were examined in the serum of the rats that were administered 2 mg/kg/bw and 5 mg/kg/bw doses of AA in drinking water for 90 d, it was reported that serum zinc levels decreased when compared with the control group at 5 mg/kg/bw dose; however, Cu levels did not differ among the groups [40].

The findings of the present study demonstrated that elevated levels of MDA and TOS and decreased TAS, SOD, CAT, and GSH levels due to AA administration increased urea and creatine and decreased Zn levels in maternal and fetal kidney tissues and maternal serum resulted in AA induced oxidative stress, and increased GSH, TAS, SOD, CAT levels, decreased MDA, and TOS levels, increase in Zn levels, and decrease in urea and creatinine levels in maternal serum demonstrated that vitamin E had a powerful antioxidant

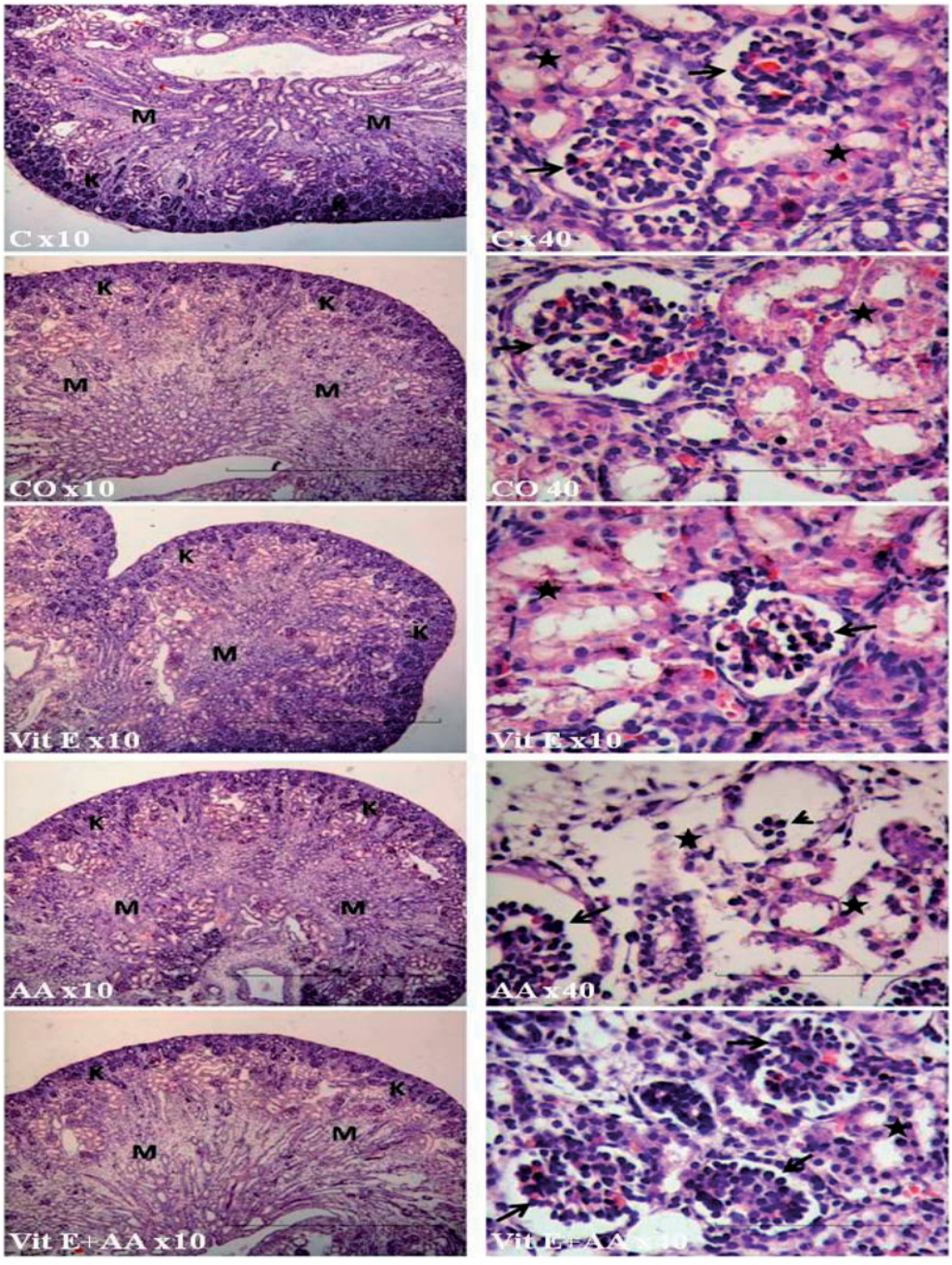

Figure 2. Fetus kidney tissue histological images of all groups C: Control group: Glomerule (arrow), × 10 Glomerule (arrow), renal tubules (asterisk) × 40. CO: Corn oil group: Glomerule (arrow). X10 Glomerule (arrow), renal tubules (asterisk) × 40. Vit E: Vitamin E group: Glomerule (arrow). ×10 Glomerule (arrow), renal tubules (asterisk) × 40. AA: Acrylamide group: glomerule (arrow), interstitial connective tissue (asterisk) × 10 Degenerate glomeruli (arrow), tubular epithelial damage (arrowhead), hemorrhage (asterisk) × 40. Vit E + AA: Vitamin E + Acrylamide group: Glomerule (ok). × 10 Acrylamide + Vitamin E group: Glomerule (ok), renal tubules (asterisk) × 40. ×10, ×40 (10× magnification and 40× magnification).

effect and the applied dose was sufficient to inhibit the oxidative stress, parallel to the findings of previous studies.

In another pregnancy model study on zearalenone (ZEN) toxicity, kidney tissues of pregnant mothers and newborns that were administered 0.3, 48.5, 97.6, or 146 mg/kg ZEN on days 0–6 of gestation in the feed, and then fed with normal diet between the 7th and 20th days of gestation. A dose-dependent increase in MDA levels and a decrease in SOD levels when compared with control group were determined biochemically and renal interstitial fibrosis, tubular degeneration, and shrunken glomeruli were observed histologically [41]. Researchers administered

Table 4. Fetal kidney tissue histological damage total score of all groups.

Groups	HDTS
C	0 (0–0)[a]
Co	0 (0–1)[a]
Vit E	0 (0–1)[a]
AA	4 (2–4)[b]
Vit E + AA	2 (0–2)[c]

C: Control; CO: Corn Oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. Data are expressed Median (min–max) of six animals. HDTS: histological damage total score. The groups with different superscripts represent the statistical significance ($p < .05$).

Table 5. Maternal serum levels of urea and creatine levels of all groups.

Groups	UREA (mg/dL)	CREATINE (mg/dL)
C	18 (17–20)[a]	0.44 (0.39–0.46)[a]
Co	15 (12–17)[b]	0.43 (0.42–0.46)[a]
Vit E	16 (14–18)[b]	0.38 (0.36–0.44)[a]
AA	21 (19–22)[c]	0.54 (0.48–0.56)[b]
Vit E + AA	18 (16–20)[a]	0.42 (0.41–0.48)[a]

C: Control; CO: Corn Oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. Data are expressed Median (min–max) of six animals. The groups with different superscripts represent the statistical significance ($p < .05$).

Table 6. Maternal serum some trace elements levels of all groups.

Groups	Zn (μg/dL)	Cu (μg/dL)
C	128 (123–155)[a]	187 (179–209)[a]
Co	144 (125–161)[a]	161 (143–178)[a]
Vit E	177 (159–189)[b]	189 (138–202)[a]
AA	99 (96–106)[c]	157 (146–202)[a]
Vit E + AA	137 (122–156)[a]	170 (164–208)[a]

C: Control; CO: Corn Oil; Vit E: vitamin E; acrylamide: AA; Vit E + AA: acrylamide + vitamin E. Data are expressed Median (min–max) of six animals. The groups with different superscripts represent the statistical significance ($p < .05$).

150 mg/kg/bw $AlCl_3$ during pregnancy in a nephrotoxicity study and administered 150-mg/kg/d vitamin E as a protective via oral gavage, and examined maternal kidney tissues in postnatal period on the 20th day histologically. They reported renal corpuscle, dilated Bowman's capsule, congestion of glomerular capillaries, and multiple areas of hemorrhage between the proximal convoluted tubules in aluminum chloride group and stated that they observed a decrease in hemorrhage regions with concurrent AlCl3 + vitamin E administration [42]. In a study where 25 μg/kg/bw AA was administered with oral gavage starting the 6th Day of pregnancy and during lactation, the researchers examined the kidney tissues histologically and observed degeneration and massive tubular necrosis in the renal tubules when compared to the control group [27].

In the present study, glomerular collapse at different degrees, narrowing and occlusion of the Bowman's were observed in the maternal kidney tissue sections in the acrylamide group. Damage in proximal and distal tubular epithelial cells and local tubular degeneration were observed. Extensive inflammatory cell infiltration, vascular congestion and local minimal interstitial edema in the parenchymal kidney structures were noted. Findings of damage detected in the acrylamide group significantly decreased in the acrylamide + vitamin E group in both prevalence and intensity. Maternal rat kidney sections in vitamin E groups displayed general histologic appearance. It was noted that the interstitial connective tissue between the parenchymal structures in the fetal kidney sections in the acrylamide group was wider. Glomerular damage and locally degenerate glomeruli were observed. Interstitial edema was noted around the tubular damage and degeneration regions. In certain sections, minimal vascular congestion and inflammatory cell infiltration were observed. All damage parameters in the acrylamide + vitamin E group significantly decreased in prevalence and severity, and these results were similar to those of other studies.

Conclusion

Administration of 5 mg/kg/bw/day AA in our previous pregnancy studies had not affected fetal liver tissues due to the proliferation effect of maternal liver tissues, however when the impact of 10 mg/kg/bw/day AA dose was investigated to simulate humans, we have demonstrated in the present study for the first time that AA caused oxidative stress in maternal rats and in fetuses by permeating through placenta, resulting in kidney damage. It is very likely that this would cause permanent damage in maternal and fetal rats. Vitamin E, which was considered as a protective agent, increased the antioxidant capacity and demonstrated serious improvement in the abovementioned damages. If it is considered that it is impossible to prevent exposure to AA toxicity in maternal and infant health, we recommend consuming sufficient amounts of fresh vegetables and fruits with high antioxidant properties, especially vitamin E, on a daily basis.

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Disclosure Statement

No potential conflict of interest was reported by the authors.

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