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The impact of ginger extract on lung maturation, liver, and heart of mouse fetuses maternally treated with dexamethasone

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Abstract

Background Ginger (*Zingiber officinale*), is known for its valuable variety of possible health advantages, including anti-inflammatory, antiemetic, and digestive characteristics. The present study aims to evaluate how ginger extract affects fetal organs. the effect of ginger extract on the fetal organs of mice treated by prenatal dexamethasone exposure. Fifteen pregnant female mice were divided into 3 groups. The first control group, the second group (Dexa) received dexamethasone at a dose of 0.8 mg/kg subcutaneously from 7th day of gestation to 14th day of gestation, while the third group (Dexa & Ging) was injected subcutaneously by 0.8 mg/kg of dexamethasone followed by oral injection of 50 mg/kg ethanolic extract of ginger from day 7 to day 14 of gestation.

Results 18-day-old fetuses maternally received daily treatment of dexamethasone (Dexa) revealed some primary septa walls in the lung tissue became thinner than in the control fetus mice associated with decreased in vascular endothelial growth factor (VEGF) expression in the lung tissues. Numerous vacuolated cardiomyocytes and some degenerated areas in heart tissue and the hepatic strands showed histological alterations. On the other hand, the lung, heart and liver tissue of 18-day-old fetuses maternally received dexamethasone and co administration of alcoholic extract of ginger showed a significant improvement.

Conclusion The present study showed that ethanolic ginger extract markedly attenuates the deleterious effects induced by prenatal dexamethasone exposure.

Keywords Ginger extract, Dexamethasone, VEGF, 18-day old fetus

Introduction

Respiratory distress syndrome is a leading cause of pre-term neonatal mortality and morbidity (Grgić et al., 2003). Therefore, antenatal administration of corticosteroids significantly decreases the incidence of perinatal mortality and pulmonary morbidity (Smrcek et al.,

2005). However, Murphy et al. (2008) found that repeated antenatal administration of dexamethasone significantly delays fetal birth, and changes body length, weight, and head circumference compared to a single administration. Moreover, growth changes, structural malformations and fetal mortality have been observed in animal studies as an adverse effect of corticosteroids, such dexamethasone (Johnson et al., 2023). Synthetic glucocorticoids prenatal exposure for 2 days cause left ventricular hypertrophy and cardiac functional reduction in adult life in sheep (Dodic et al., 2001). Human and animal models report demonstrate that offsprings of mothers receiving

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Antenatal Corticosteroid Therapy (ACT) have aortic stiffness, endothelial dysfunction, elevated heart weight, and hypertension (Garrud and Giussani, 2019, Kelly et al., 2012, Tang et al., 2011, Figueroa et al., 2005, Jellyman et al., 2020). Also, liver steatosis and nonalcoholic fatty liver disease can be observed in offspring exposed antenatally to corticosteroid treatment (Drake et al., 2010, Liu et al., 2021, Tsai et al., 2018).

Ginger (*Zingiber officinale*), is one member of family Zingiberaceae which is valued for its unique flavor and a variety of possible health advantages, including anti-inflammatory, antiemetic, and digestive characteristics (Mao et al., 2019). Research examination reported whether ginger preparations might reduce the adverse effects of toxicities that occur when dangerous drugs are provided with ginger on the fetus and mother during pregnancy and/or development. Mallikarjuna et al. (2008) suggested that ginger act as a guard against hepatotoxicity in rats induced by ethanol as it suppressed oxidative consequences. Also, the results showed no noticeable distinction in liver, kidney, placental, or gestational weight increase when mothers were treated with ginger extract (Wilkinson, 2000). Lower doses of Zingiberaceae extracts (<200 mg/kg/day) were observed to safeguard against gestational and developmental negative effects in animal models throughout most of the examined studies (Williams et al., 2025). Consequently, the goal of current study is evaluating the ginger extract effects on the fetal organs of mice treated maternally with dexamethasone.

Materials and methods

Ethanollic ginger extract

A dried ginger rhizome was purchased from a local market in Cairo, Egypt. It was cut, then ground into a fine powder using an electric blender. The extraction procedure followed the method described by (Abdel-Rasol et al., 2022). One hundred grams of dried powder was immersed in 1000 mL of ethanol (95%). It was then left at ambient temperature for 72 h. Filtration follows the extract is passed through filter sheets. A rotary evaporator was used to concentrate on it (Abdel-Rasol et al., 2022). The extract was stored in airtight amber vials at -20°C to maintain stability.

Animal grouping

According to the Principles of Laboratory Animal Care" (NIH publication no. 85-23, revised in 1985), all the experimental mice were approved by the Faculty of Science Animal Care Committee (ASU-SCI/ZOOL/2025/8/2). Fifteen pregnant female mice were divided into 3 groups. The control group was treated with vehicles only (tap water) and handled with the same frequency and duration as all treated groups to ensure comparable stress exposure. The second group (Dexa)

received dexamethasone at a dose of 0.8 mg/kg subcutaneously from 7th day of gestation to 14th day of gestation (Zhao et al., 2024). Since days 7–14 correspond to the formation of many essential structures, insults during this stage may impact multiple organs simultaneously. The third group (Dexa & Ging) was injected subcutaneously by 0.8 mg/kg of dexamethasone followed by oral injection of 50 mg/kg ethanolic extract of ginger from day 7 to day 14 of gestation (Thomson et al., 2002).

Histological and immunohistochemical examination

At the eighteenth day of gestation, the pregnant mice were sacrificed, and the organs of the 25 fetuses' samples for each group (5 fetuses per dam) were collected and cut into a 5 mm thickness, then immersed in 10% neutral buffered formalin for 12 h. The liver, lung, and heart tissues were then processed in alcoholic series, fixed in paraffin wax, and 5 μm sections were stained with hematoxylin and eosin (H&E) for light microscope examination. Vacuolated areas of heart tissue were expressed as a percentage of the total myocardial area. Measurements were performed on 5 randomly selected fields per section by using the ImageJ software (National Institutes of Health, USA).

Additional sections from the lungs of each experimental group were used to perform immunohistochemistry for the detection of vascular endothelial growth factor (VEGF). Sections to be stained for vascular endothelial growth factor (VEGF) were deparaffinized then dehydrated using xylene and graded alcohols. Antigen retrieval was carried out. Incubating with 3% hydrogen peroxide for 10 min inhibited endogenous peroxidase activity. VEGF (polyclonal VEGF antibody; Abcam, UK) antibodies were diluted at a 1:200 ratio. Negative controls were generated by omitting the main antibody. The procedures were carried out in accordance with the manufacturer's suggestions (Pan et al., 2018). The expression of VEGF was evaluated using the ImageJ software (National Institutes of Health, USA). Five non-overlapping representative fields of fetal lung sections were captured. VEGF expression where the proportion of positive staining was calculated as brown-stained area (%) in comparison with the total tissue area. Photomicrographs were made as requested by a trinocular Leica research microscope (DM1000, LED, Light bright field), with Leica Flexcam C1 (ultrahigh resolution 4 K/full HD, Digital Color Video Camera system).

Statistical analysis

Data was offered as the mean value $\pm$ standard deviation (SD). The one-way ANOVA program followed by post hoc multiple comparisons (Tukey's test) were used to statistically evaluate the data. A statistically significant difference between groups was fixed at a $p\text{-value} \leq 0.05$.

Histological results

The lung

Lung development and maturation in the mouse fetus are classified histologically into four stages: pseudoglandular, canalicular, terminal saccular, and alveolar stages. The fetus on day 18 of gestation is in the terminal saccular stage. Where, the alveolar epithelial cells are differentiated into mature squamous type I alveolar cells and

rounded type II alveolar cells with lamellar bodies that produce surfactants (Fig. 1a, b). A network of capillaries develops gradually in the mesenchyme surrounding the saccules to form a complex network within the primary septae, forming a thick wall of the saccules and lining epithelial cells on the two sides of a connective tissue core. In the control fetal lung, small finger-like or crest-like projections, the secondary septa (Fig. 1b), appear from

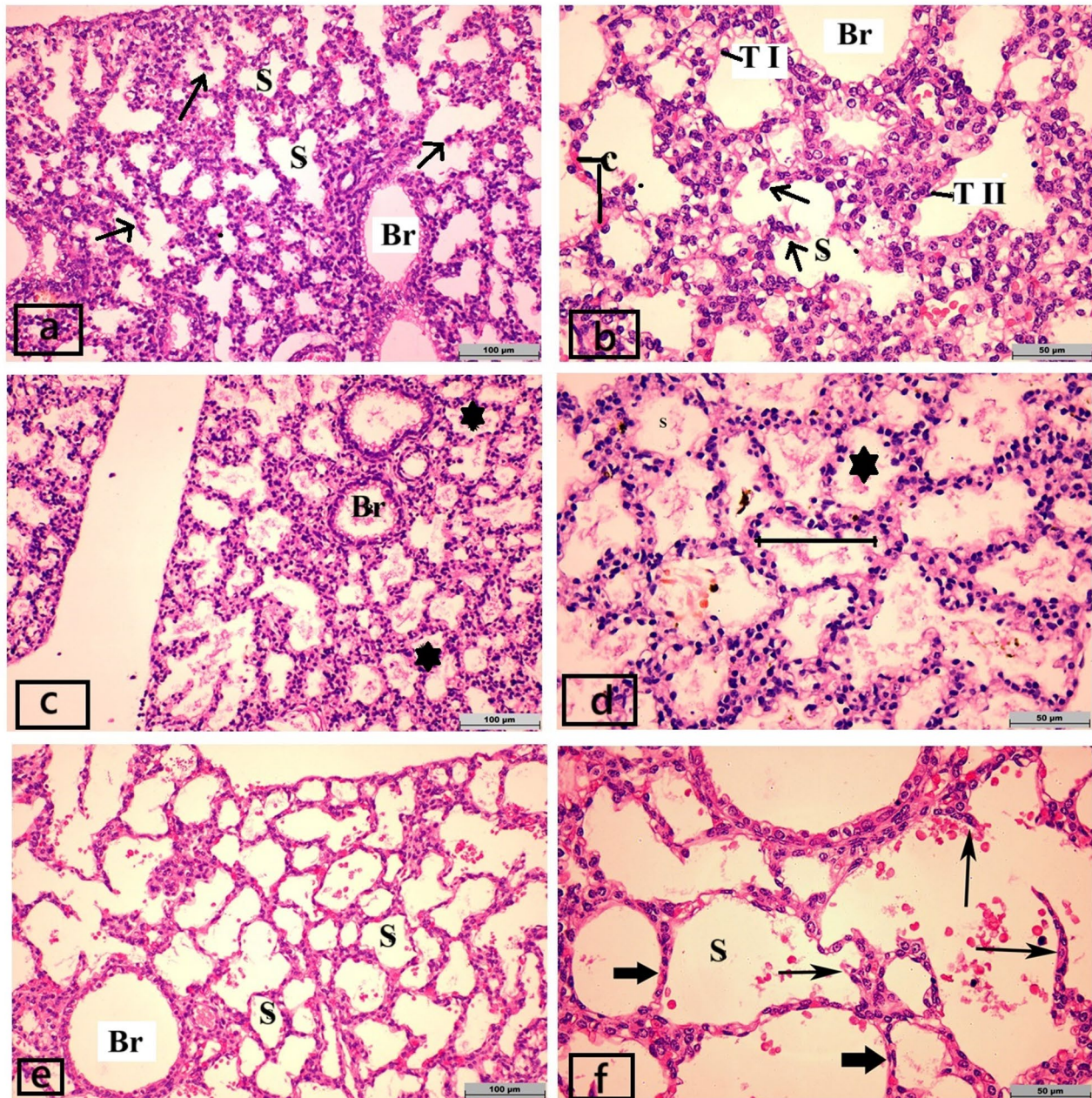


Fig. 1 Photomicrograph of lung tissue of an 18-day-old fetus. **a, b** Normal lung tissue numerous alveolar sacs (S), alveolar septum with type I (T I) and type II (T II) alveolar cells, blood capillaries (C) and secondary septa (arrows). **c, d** of Dexa group showing reduced secondary septa and larger sac space with detached cells or their exudates of epithelial lining and accumulation of red blood cells (asterisk). **e, f** of Dexa & Ging group showing bronchiole (Br) more or less resembles the control group, and the interalveolar septum appeared thinner (thick arrows) with numerous buddings of secondary septa (arrows). H&E stain, scale bar 50 μm & 100 μm

the saccular walls into the lumen to increase the surface area for gas exchange. On the other hand, the lung tissue of 18-day-old fetuses maternally received daily treatment of dexamethasone from day 7 to day 14 of gestation (Dexa) revealed that some primary septa walls became thinner than in the control fetus mice. In addition, the histological section demonstrated there were fewer and less prominent secondary septa budding compared with the control group resulting in larger, less subdivided alveolar spaces (alveolar simplification) (Fig. 1c, d). Additionally, detached cells or their exudates of epithelial lining and accumulation of red blood cells were observed in the alveolar sac space (Fig. 1c, d). Meanwhile, the lung sections showed thinner interalveolar septa in the fetuses maternally treated with ginger extract simultaneously with the dexamethasone injection from day 7 to day 14 of gestation (Dexa & Ging) compared with the control and

dexamethasone groups. More abundant budding secondary septa were observed, along with numerous small saccular spaces. Also, bronchiole more or less resembles the control group (Fig. 1e, f).

The heart

The control (Fig. 2a, b) and Dexa& ging groups (Fig. 2e, f) of heart tissues of 18-day-old fetus revealed the thickest layer of the heart, the myocardium, which is composed of cross-striated muscle cells, cardiomyocytes. The cardiomyocyte possesses one centrally oval nucleus. Intercalated discs connect the muscle cells and permit the conduction of electrical impulses among cells. Numerous capillaries are observed in loose endomysial connective tissue between the cardiac muscle fibers. On the other hand, dexamethasone-maternally treated embryonic cardiac muscle tissue from day 7 to 14 of pregnancy (Dexa)

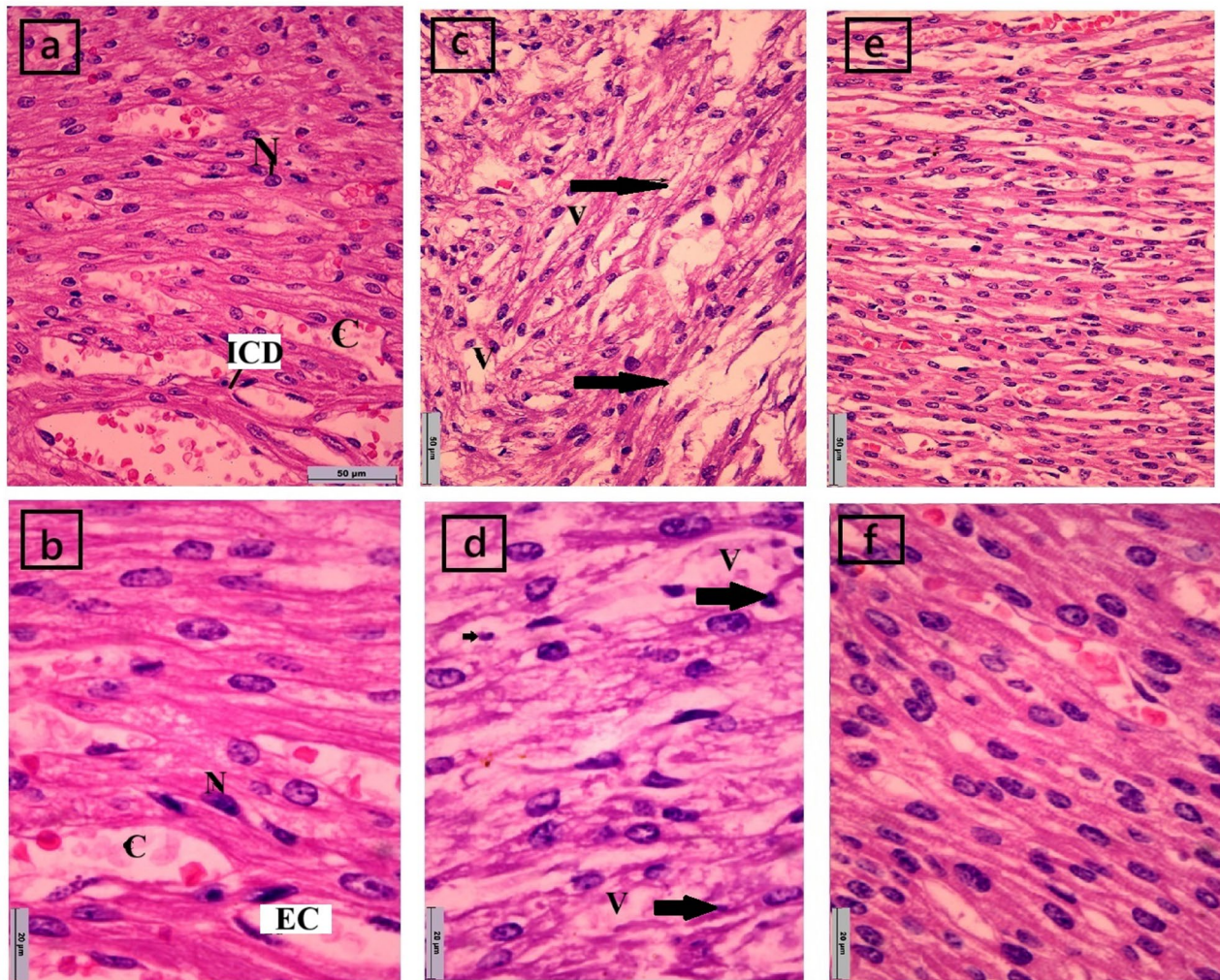


Fig. 2 Photomicrograph of cardiac fetal muscle fibers. The control group (a, b) shows a normal architecture of the myocardium with an oval nucleus (N), intercalated disk (ICD), and capillaries (C). c, d of Dexa showing destruction of myocardial tissue (arrows). Necrotic myocardial cell (thick arrows) and vacuolated myocardial cells (V). e, f Revealed a somewhat normal appearance of myocardial tissue in fetuses of the Dexa & Ging group. H&E stain, scale bar 50 μ m & 20 μ m

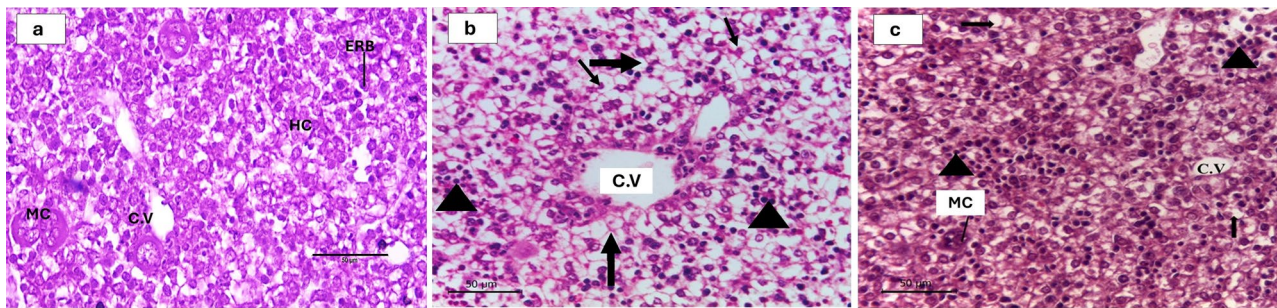


Fig. 3 Photomicrograph (a) a section of the liver of a control 18-day-old fetus showing the hepatic cells (HC) surrounding the central vein (C.V), erythroblasts (ERB), megakaryocytes (MC) with granulated nuclei. **b** The liver of the Dexa group showing inflammatory cells (arrow heads), disorganization of the hepatic strands, vacuolation in hepatocytes (thick arrows), and signs of necrosis in hepatocytes (thin arrows). Vacuolation of a few hepatocytes (thick arrow), inflammatory cells (arrowheads), and a slight disruption of the typical pattern of the hepatic strands were observed in **c** of the Dexa & Ging group. H&E stain. Scale bar 50 μ m

revealed significantly elevated the percentage of vacuolated area of cardiomyocytes ($8.735 \pm 0.8398\%$) compared with the control ($3.3256 \pm 1.358\%$) with degenerated areas and necrotic myocardial cells (Fig. 2c, d). However, the Dexa & Ging group showed a markedly reduced vacuolated areas compared with the Dexa group, although values ($6.7182 \pm 0.51772\%$) remained higher than those of controls.

The liver

The normal liver of 18-day-old fetuses is composed of many parenchyma cells, also known as hepatocytes, grouped in hepatic lobules. The lobules are divided by poorly formed interlobular connective tissue; the spaces between them are indistinct. Each lobule has a central vein with many strands of hepatocytes. (Fig. 3a). The liver tissue of 18-day-old fetuses contains clusters of blood-forming cell types with darkly stained nuclei known as megakaryocytes. The pregnant mice that received daily treatment of dexamethasone (0.8 mg/kg) from day 7 to day 14 of pregnancy (Dexa) showed stages of histological alterations in the liver of their 18-day-old fetuses, including fatty degeneration, pyknotic, and necrosis nuclei. The fatty degeneration was the most significant effect of dexamethasone on the hepatocytes of 18-day-old fetuses (Fig. 3b). Also, the hepatic strands showed histological alterations, revealing disorganization of the typical pattern of hepatic strands (Fig. 3b). On the other hand, 18-day-old fetuses of liver sections of a group of mice maternally treated with dexamethasone followed by ginger treatment from day 7 to day 14 of gestation, displayed some ameliorative signs of liver tissue. Although, there were still some histological changes, including the presence of some vacuolated hepatocytes. Furthermore, central vein and blood sinusoids were surrounded with some infiltrated lymphocytes (Fig. 3c).

Table 1 Scoring of VEGF expression in lung tissue of 18-day-old fetuses of control and treated groups

Groups	Mean $\pm$ SD
Control	21.298 $\pm$ 6.29646
Dexa	12.03425 $\pm$ 1.70593*# ^{ns}
Dexa & Ging	17.98125 $\pm$ 3.48084* ^{ns}

VEGF values are expressed as means $\pm$ SD. Data were analyzed statistically using One-way ANOVA followed by post hoc multiple comparisons (Tukey's test) for comparative analysis between the groups. Control group, Dexa: dexamethasone group and Dexa & Ging: dexamethasone followed by ginger treated group

*Indicates the significant difference of all groups vs. normal group, * $p < 0.05$

#Indicates the significant difference of Dexa group vs. control group, # $p < 0.05$

^{ns}Indicates no significant difference of Dexa group vs. Dexa&Ging group or control group vs. Dexa&Ging group, $p < 0.05$

Immunohistochemical results

VEGF immunostaining was observed in endothelial cells, muscle cells of vascular wall, interstitial cells, and epithelial cells of the distal airway and alveolar cells (pneumocytes) of fetal lung (Table 1; Fig. 4). The bronchial epithelial cells and type II pneumocytes in control lungs had the highest expression levels of vascular endothelial growth factor (VEGF) positivity (Fig. 4a, b). On the other hand, VEGF expression was significantly lower in the airway and alveolar cells of the lungs of 18-day-old fetuses maternally treated with dexamethasone (Dexa group) (12.03425 ± 1.70593) compared to the control group (21.298 ± 6.29646) (Fig. 4c, d). At the same time, the mean value of VEGF expression level in the dexamethasone and ginger group showed no significant difference (17.98125 ± 3.48084) compared with the control group (Fig. 4e, f).

Discussion

Corticosteroids are provided in pregnant women that face a neonatal risk of preterm labor for enhancing fetal lung maturity (Liggins and Howie, 2005). Meanwhile, some adverse effects of antenatal corticosteroids exposure were recorded on fetal weight growth (Farak et al.,

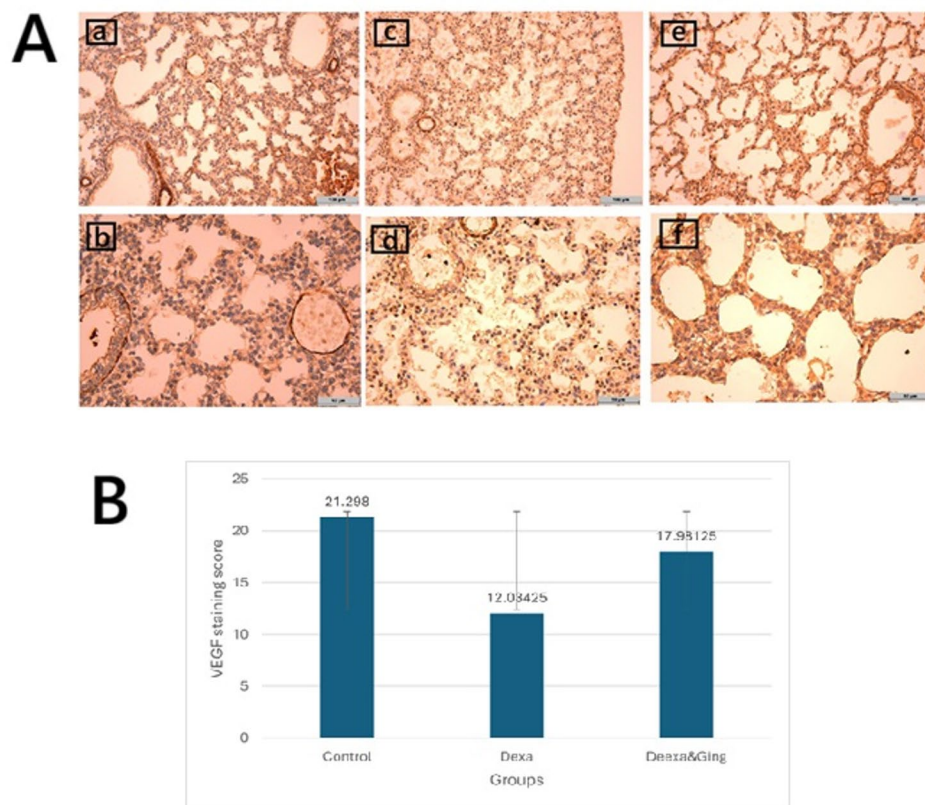


Fig. 4 Immunohistochemical staining for VEGF. **A** Photomicrographs of VEGF expression in the fetal lung of the control group (**a, b**), Dexa group (**c, d**), and Dexa &Ging group (**e, f**). The brownish areas indicate where VEGF is expressed at scale bars 100 μ m and 50 μ m). **B** Scores of VEGF staining expression in the lung tissue. One-way ANOVA followed by post hoc multiple comparisons (Tukey's test) used for comparative analysis between the groups at $p \leq 0.05$. Dexa group vs. the control group revealed a significantly decreased expression of VEGF in lung tissue

2025), lung maturation (Ahmad et al., 2024), and brain maturation (Modi et al. 2001), after repeated treatments. The present investigation revealed some histopathological alternation in the lungs of 18-day-old fetuses maternally received daily treatment of dexamethasone from day 7 to day 14 of gestation (Dexa group) where, some primary septa walls became thinner than in the control fetus mice. In addition, there was a reduction in the budding of secondary septa. Additionally, the saccules appeared larger and less subdivided. The present observations were confirmed by Garber et al. (2006) who observed the increased lung volume and decreased in alveolarization after administration of dexamethasone. Also, agreed with observations of Tschanz et al. (1995) who reported that the administration of dexamethasone led to suppression of alveolarization. The alveolar walls began to deteriorate toward immaturity, a delayed alveolarization burst and precocious microvascular maturation (Tschanz et al., 1995). The thickened alveolar walls and initial peribronchiolar patchy pneumonia, hemorrhage, infiltration of inflammatory cells alveolar space, especially adjacent to the bronchioles, and the formation of severe bronchiolitis were observed after injection with dexamethasone (Xu et

al., 2009). The most important effect of antenatal glucocorticoids was the stimulation of the pulmonary surfactant system where glucocorticoids altered the expression of a large number of genes that are associated with the synthesis of surfactant proteins, fatty acid synthase which affected the maturation of the lung (Grier and Halliday, 2004). Vascular endothelial growth factor (VEGF) is essential for physiological processes, such as embryonic development. Dao et al. (2018) stated that VEGF increased the alveolar units in mice, which sped up lung development. Dexamethasone limits the expression of VEGF, which is vital for the development of alveoli and blood vessels these results were observed in the present work as an immunohistochemistry result for dexamethasone group (Dexa group). The development of the newly formed capillary network within the fetus lung is believed to be significantly influenced by VEGF, which is localized to the basement membrane of the epithelial cell (Acarregui et al., 1999). The absence of VEGF leads to a decrease in blood vessels and alveoli, reduced surfactant production, and a delay in lung maturation (Compennolle et al., 2002). In vitro, studies showed that dexamethasone inhibits the expression of VEGF in different cellular lines

(Nauck et al., 1998, Tanabe et al., 2006, Gille et al., 2001). But, in vivo, the studies showed that dexamethasone decreases VEGF expression (Remesal et al., 2010, Vento et al., 2002, Hewitt et al., 2006).

The current work revealed vacuolated cardiomyocytes and degenerated areas in the fetal cardiac muscle tissue prenatally treated with dexamethasone from gestation day 7 to day 14 (Dexa group). left ventricular hypertrophy and diminished cardiac functional reserve in adulthood as a result of prenatal exposure for two days to synthetic glucocorticoids (e.g., dexamethasone) were observed in sheep (Dodici et al., 2001). Also, DNA content was reduced in the heart after prenatal exposure to glucocorticoids (Slotkin et al., 1991). A noticeable reduction in ventricular weight, increased collagen deposition, and hypertrophy of myocardial cells is observed in newborns that have been exposed to prenatal glucocorticoids (Bal et al., 2009). Currently, prenatal dexamethasone exposure promoted postnatal reactive oxygen species (ROS) levels were elevated (Roghair et al., 2008). In addition, Langdown et al. (2001). demonstrated that prenatal administration of dexamethasone alters postnatal cardiac glucose homeostasis as well as significant activation of the Akt/protein kinase B pathway and upregulation of GLUT1 expression in cardiac tissues. Since Glucose Transporter Type 1 (GLUT1) is the primary transporter mediating basal glucose uptake in the heart, its upregulation suggests a compensatory or maladaptive metabolic response leading to disrupted cardiac glucose metabolism in offspring (Langdown et al., 2001).

In the present work, the liver of 18-day-old fetuses that had received daily treatment of dexamethasone (0.8 mg/kg/day) from day 7 to day 14 of pregnancy showed fatty degeneration. In the previous literature, several mechanisms for fatty degeneration of the fetus's liver suggested that epigenetic regulatory mechanisms have been proposed as mediators of such hepatic effects. Liu et al. (2021) found that prenatal dexamethasone exposure led to fatty liver where lipid accumulation increased, triglyceride synthesis-related gene expression increased, while oxidation-related gene expression decreased in livers of rat offspring (Liu et al., 2021). According to the explanation of Xiao et al. (2024) the exposure to prenatal dexamethasone resulted in reduced blood corticosterone levels which led to downregulate the Histone 3 lysine 27 (H3K27) acetylation level of the Insulin-like growth factor 1 (IGF1) and its expression via glucocorticoid receptor α /special protein 1/p300 (GR α /SP1/p300) signal in the liver during the hepatogenic differentiation of bone marrow mesenchymal stem cells (BMSCs). This ultimately resulting in the inhibition of hepatocyte differentiation, lipid deposition, liver dysplasia, impaired liver function and vacuole-like phenotypes in hepatocytes of the fetal liver (Xiao et al., 2024). Moreover, in the

present study, some of the hepatocytes showed pyknotic nuclei and vacuolated cytoplasm. The hepatic strands revealed histological alterations represented by disorganization of the typical pattern of normal hepatic strands. Also, Mikiewicz et al. (2017) observed that dexamethasone administration was shown to decline the transcriptional and proliferative capacity of hepatocyte, which was observed in gradually hepatocyte glycogen degeneration and finally lipid degeneration, accompanied by sinusoid and central vein dilatation and nuclear chromatin condensation.

Medicinal plants have gained growing recognition as valuable therapeutic options within primary healthcare systems. The use of plants for medicinal purposes dates back thousands of years, reflecting their long-standing role in traditional and natural healing practices (Ruffa et al., 2002). Ginger (*Zingiber officinale*) has numerous potential health benefits including anti-inflammatory, antiemetic, and digestive properties (Mao et al., 2019). Ginger has also been used during pregnancy (Anh et al., 2020). The medicinal efficacy of ginger and its extracts is largely attributed to their phenolic constituents, particularly gingerols, shogaols, paradols, and alpinetin. These bioactive compounds are considered the primary contributors to the plant's therapeutic properties (Marx et al., 2017). In the current work, the lung, heart and liver tissue of 18-day-old fetuses maternally received dexamethasone and alcoholic extract of ginger (mice treated with 0.8 mg/kg/dexamethasone and 50 mg/kg/day ethanolic ginger extract) showed a significant improvement. There were adequate studies that have shown the ginger, and its component have protective effects against gestational and developmental toxicities. Administering gingerol at a dose of 25 mg/kg counteracted methyl ethyl ketone (MEK) effect in offspring (Othman et al., 2022). Moreover, fetal tissues exhibited a marked restoration of antioxidant defense, demonstrated by increased levels of reduced glutathione (GSH) and superoxide dismutase (SOD) (Othman et al., 2022). The genotoxic potential of dexamethasone has been documented in several studies, primarily attributed to its ability to generate reactive oxygen species (ROS). Excessive ROS production can result in DNA damage, chromosomal alterations, and mutagenic changes (Kadhim et al., 2023). On the other hand, multiple studies have demonstrated that ginger extract increases the activity of key antioxidant enzymes, including catalase (CAT) and superoxide dismutase (SOD), both of which play critical roles in the neutralization of reactive oxygen species (ROS) (Si et al., 2018).

Conclusion

Based on the findings of the present study, ethanolic ginger extract markedly attenuates the deleterious effects induced by prenatal dexamethasone exposure. This

protective action is likely associated with ginger's well-established antioxidant and anti-inflammatory properties, which may play a key role in limiting oxidative stress and tissue damage. However, additional research is needed to clarify the mechanisms responsible for this protection fully. In the present study, the ginger extract was administered at a specific time during gestation corresponding to the formation of many essential structures during organogenesis. However, long-term studies are recommended to assess the long-term impact of ginger on fetal development.

Limitation

A limitation of this study is the lack of phytochemical standardization of ginger extract, including quantification of gingerols. Although we followed validated extraction protocols, future studies will include full chemical profiling to improve reproducibility. Also, further studies should explore the optimal dosage and duration of ginger. Investigations into the molecular mechanisms underlying the protective effects of ginger on embryonic development could provide deeper insights into targeted therapies.

Abbreviations

ACT	Antenatal corticosteroid therapy
BMSCs	Bone marrow mesenchymal stem cells
Br	Bronchiole
C	Blood capillaries
CAT	Catalase
C.V	Central vein
DEX	Dexamethasone
ERB	Erythroblasts
GLUT1	Glucose Transporter Type 1
GSH	Glutathione
HC	Hepatic cells
H&E	Hematoxylin and eosin
H3K27	Histone 3 lysine 27
ICD	Intercalated disk
IGF1	Insulin-like growth factor 1
MC	Megakaryocytes
MEK	Methyl ethyl ketone
N	Nucleus
ROS	Reactive oxygen species
S	Alveolar sacs
SOD	Superoxide dismutase
TI	Alveolar septum with type I cell
TII	Alveolar septum with type II cell
V	Vacuolated myocardial cells
VEGF	Vascular endothelial growth factor

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not applicable.

Author contributions

Hend A. Mohammed assisted with work environments, work plan formulation, data analysis, and manuscript writing and revision. Hamza El Shabaka and Iman Z. Abdel Samie assisted in creating the work plan, manuscript writing and revision. Sara Farag completed laboratory tasks and data analysis.

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disclosure.

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Data availability

The data and materials of this study will be available on request.

Declarations

Ethics approval and consent to participate

Institutional and national guidelines for the care and use of animals were followed. The Research Ethics Committee at Faculty of Science Ain Shams University was accepted to conduct and approved of this study. The conduct of this study adhered to the code of ethics and animal rights standards ASU-SCI/ZOOL/2025/8/2.

Competing interests

The authors declare no competing interests.

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