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# Effect of buspirone hydrochloride on kidneys of the pregnant and their fetuses an experimental study

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## ABSTRACT

A member of the anxiolytics pharmacological class, buspirone is an anti-anxiety medication. Buspirone is a sedative medication that is frequently used to relieve tension. The goal of this study was to see how buspirone hydrochloride affected the kidneys of pregnant rats and their offspring. Thirty-three pregnant female rats were divided into three groups. Pregnant rats in the first group received distilled water orally as a control. The second category of pregnant rats received an oral dose of buspirone hydrochloride at a daily dose of 0.27 mg/100 g for fifteen days. From the sixth to the twentieth day of pregnancy, pregnant rats of last group were given buspirone hydrochloride at a dose of 0.41 mg/100 gm for fifteen days. For the histological and histochemical examinations, kidney tissues were collected from pregnant rats and selected from their fetuses of all groups killed on the 20th day of gestation. Both treated groups' maternal and foetal kidney tissues showed various alterations after treatment with buspirone, which were particularly noticeable at the high concentration dose. The current investigation discovered that using the drug Buspirone caused many histological and histochemical changes in the kidney tissues.

**Keywords:** Buspirone Hydrochloride, Pregnant, Fetuses, Kidney

## 1. INTRODUCTION

For either pregnancy problems or maternal disorders that existed previous to the pregnancy, a range of medications are recommended. Increased incidences of intrauterine growth retardation and adverse renal effects have been reported. There have been reports of an increase in intrauterine growth retardation and severe kidney damage. Renal failure can occur in both the

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fetus and the infant, and ranges from temporary oligohydramnios to severe neonatal renal failure resulting in death (Boubred et al., 2006).

Anxiety is an uncomfortable condition of interior feelings that is frequently accompanied by nervous behavior (Zaki & Abouel-Magd, 2018). Generalized anxiety disorder, panic disorder, and panic attacks, agoraphobia, social anxiety disorder, and particular phobias are among the mental conditions associated with intense fear or worry (Eskow et al., 2007). Anxiety can now be treated with a variety of psychoactive substances. Anxiety or tension caused by everyday stress normally does not necessitate the use of an anti-anxiety medication. Buspirone hydrochloride (BuSpar) is a new antianxiety medication that is not connected to benzodiazepines, barbiturates, or other sedative/anxiolytic medications chemically or pharmacologically.

Anxiety disorders are treated with BuSpar. It is also relieving the symptoms of anxiety in the short term. It can also help with depression, obsessive-compulsive disorder, and attention deficit hyperactivity disorder (ADHD) (El-Gawwad & Hanaa, 2020). The goal of this work was to see how buspirone affected the kidneys of pregnant female rats and their offspring.

## 2. MATERIALS AND METHODS

PSA University's Ethical Committee accepted our research, which followed the Animal Research Guideline for the Use and Care of Animals in Research (PSAU-2021 ANT 90/43PI). Between May 2021 and May 2022, an experimental study was performed. Bristol Mayers Squibb provided buspirone hydrochloride in the form of tablets. A gastric tube was used to provide the drug orally after it had been dissolved in distilled water. The single oral doses were 0.27 and 0.41 mg per 100 g of body weight each day, accordingly. According to the procedure, the dose for rats was estimated. On the basis of the human dose, Paget and Barnes developed a formula (Paget & Barnes, 1964). Adult Albino rats weighing between 190 and 210 g were used in this study. They were taken from the Collage of Pharmacy's animal house, AlKharj.

Animals were housed separately, with males in one cage and females in another, and provided a standard meal. Overnight, adult females and males were mated at a ratio of two females to one male. A vaginal smear was obtained every morning to check for the presence of a vaginal plug. The day sperms or plugs were discovered in the vaginal canal was considered the first day of pregnancy. Thirty-three pregnant female rats were divided into three categories. Control rats were given pure water and were pregnant and healthy. From the $7^{th}$to the $19^{th}$ gestational day, the second pregnant rats were given an oral dose of buspirone hydrochloride corresponding to 0.27 mg/100gm body weight/day for 14 days. From the 7th to the 19th gestational day, the last group of pregnant female rats received an oral dose of buspirone hydrochloride corresponding to 0.41 mg/100g body weight/day for 14 days. After four hours from the latest dose delivery, all pregnant rats were slaughtered on the 19th gestational day.

For the histological and histochemical analyses, small samples of kidney tissue from mothers and their fetuses were chosen. Sections of mother's and foetus' kidney tissues were put in a 10% neutral buffer formol and Bouin's solution. The slides were then stained with haematoxylin and eosin using the Bancroft and Gamble procedure (Bancroft & Gamble, 2008; Drury & Willington, 1980). Mallory trichrome stain was used to detect collagen fibers.The PAS method was used to detect polysaccharides, while the Congo red technique was used to detect amyloid protein (Valle, 1986). The statistical package (SPSS) application was used to examine the data. The student T-test was used to evaluate whether there were significant differences between the treatments.

## 3. RESULTS

Kidney of pregnant rats: The histopathological observations: In the first group, the renal cortex of a pregnant rat was found to be normal. The majority of glomeruli were normal, and both the parietal and visceral epithelium had typical distal and proximal convoluted tubules (Fig. 1). The second group of pregnant rats had distension of the glomerular capsular space, glomerular tuft degeneration, and some congested, lobulated, or atrophied glomeruli with pyknotic nuclei. The control group's Mallory's trichrome stained slices of pregnant female kidney cortex revealed a well-distributed collagen fiber distribution (Fig. 2).

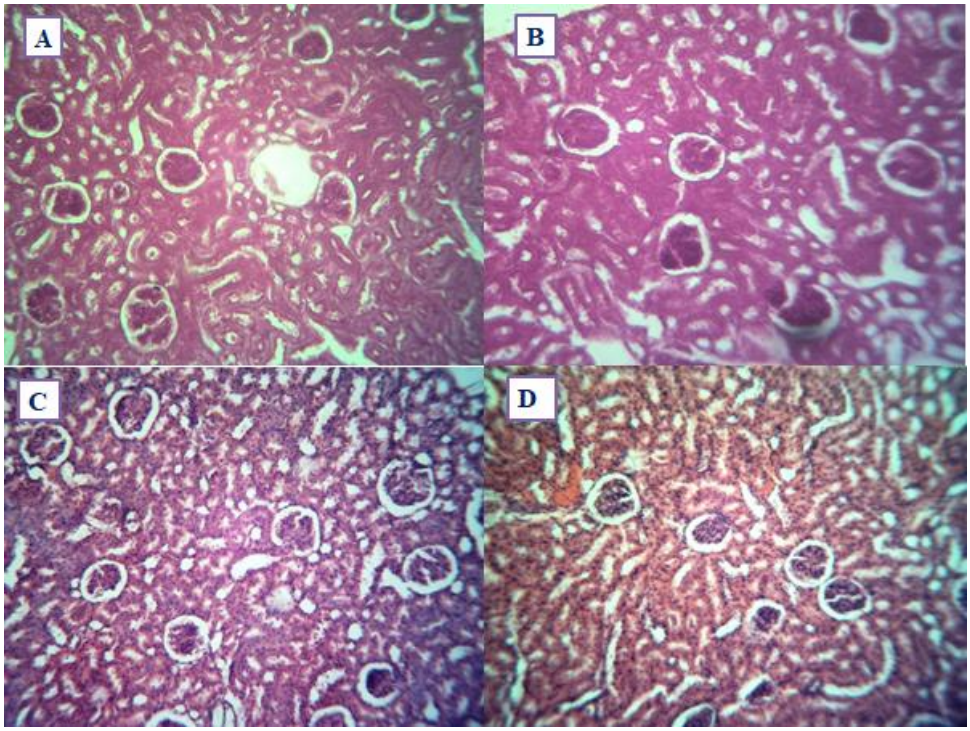


**Figure 1** From A to D sections of the kidneycortex of pregnant healthy control group (H&E X200).

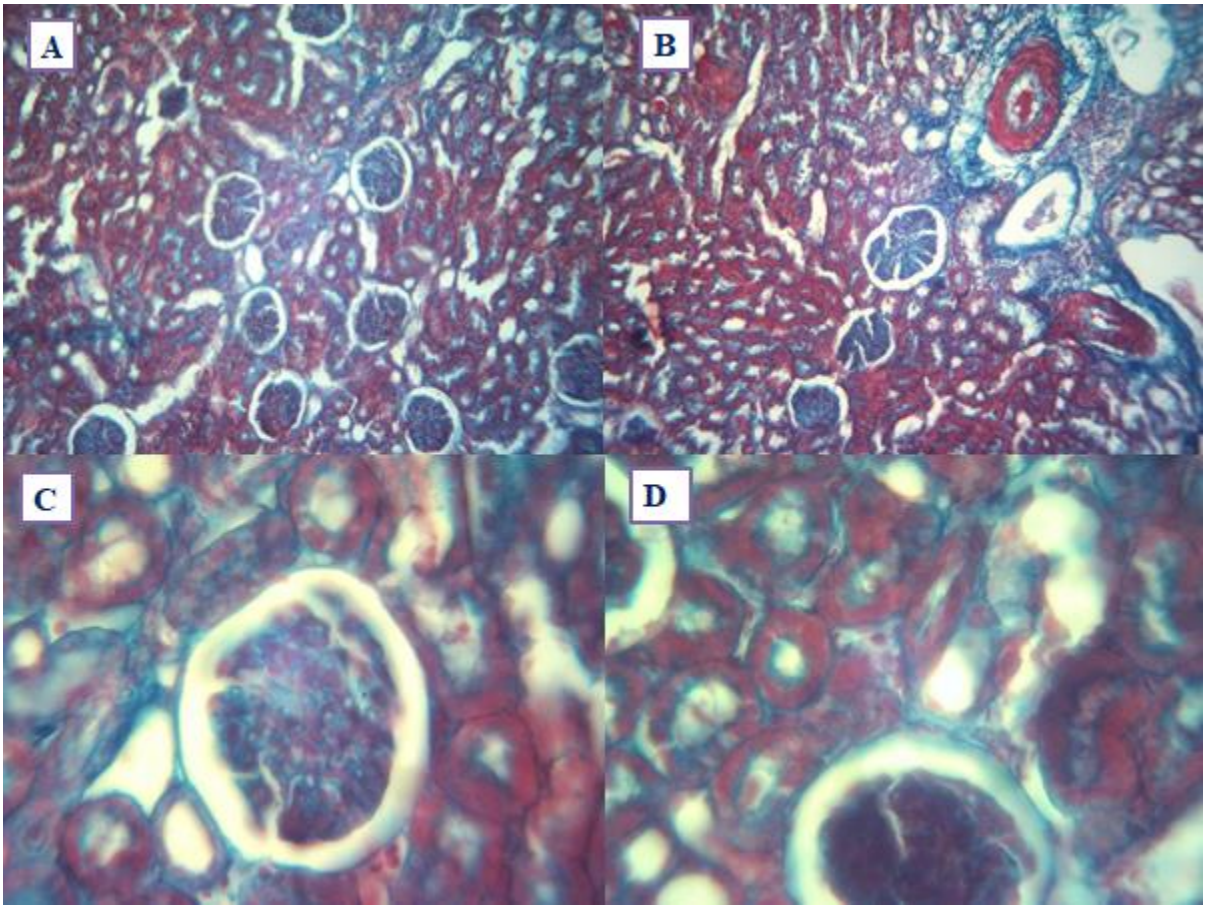


**Figure 2** A and B show sections of the cortex of the kidney of pregnant healthy control groupstain Mallory's trichrome. (X200). C and D demonstrate increased collagen when stained with Mallory's in the second and third group (X400)

Collagen fibres increased in the brush margins of the proximal convoluted tubules and basement membranes of the distal convoluted tubules were seen after treatment with the second and third groups of buspirone hydrochloride, along with congested blood vessels and arterial wall fibrosis. Cubic cells of epithelium of the proximal tubules revealed positive PAS stain reactivity in pregnant rats in the control group. In the second and third groups, however, there was a modest drop in polysaccharides (Table 1). The kidney cortex of the second group of foetal rats revealed degeneration of distal convoluted tubules, a decrease in the number of proximal convoluted tubules, necrotic region, and glomeruli atrophy. The foetal kidney of the third group, on the other hand, had congested blood vessels, hemorrhagic areas, glomeruli degeneration and atrophy, necrotic areas, and degeneration of distal convoluted tubules. The control group's Mallory's trichrome stained slices of foetal rat kidney cortex exhibited normal collagen fiber distribution. The second group received a smaller amount of buspirone, whereas the third group received a high dose of buspirone, resulting in increased collagen fibres in the cortex. The control group's foetal kidney tissue stained with PAS revealed polysaccharides with a normal magenta color. However, evaluation of the foetal renal cortex of the second and third groups revealed a small reduction in polysaccharides. The total protein concentration of glomeruli, distal and proximal convoluted tubules was moderately distributed in the kidney of rats in the control group. On the other hand, total protein density was shown to be lower in the foetal kidney cortex of the second and third groups. The control group's foetal kidney cortex had a modest accumulation of protein. The amyloid beta protein levels in the second and third groups were higher.

**Table 1** Kidney cortex pregnant rat Optical density of PSA and proteins in different groups

| Different Groups | Protein (total) | Protein (Amyloid β) | Polysaccharides |
|---|---|---|---|
| Healthy control | 0.2815±0.0134 | 0.2301 ±0.01451 | 0.4036 ±0.01624 |
| Second with low dose group | 0.2973 ±0.01338 | 0.4112 ±0.0212 | 0.1108 ±0.0126 |
| Third with high dose group | 0.2522 ±0.01312 | 0.405 ±0.0216 | 0.0883 ±0.022 |

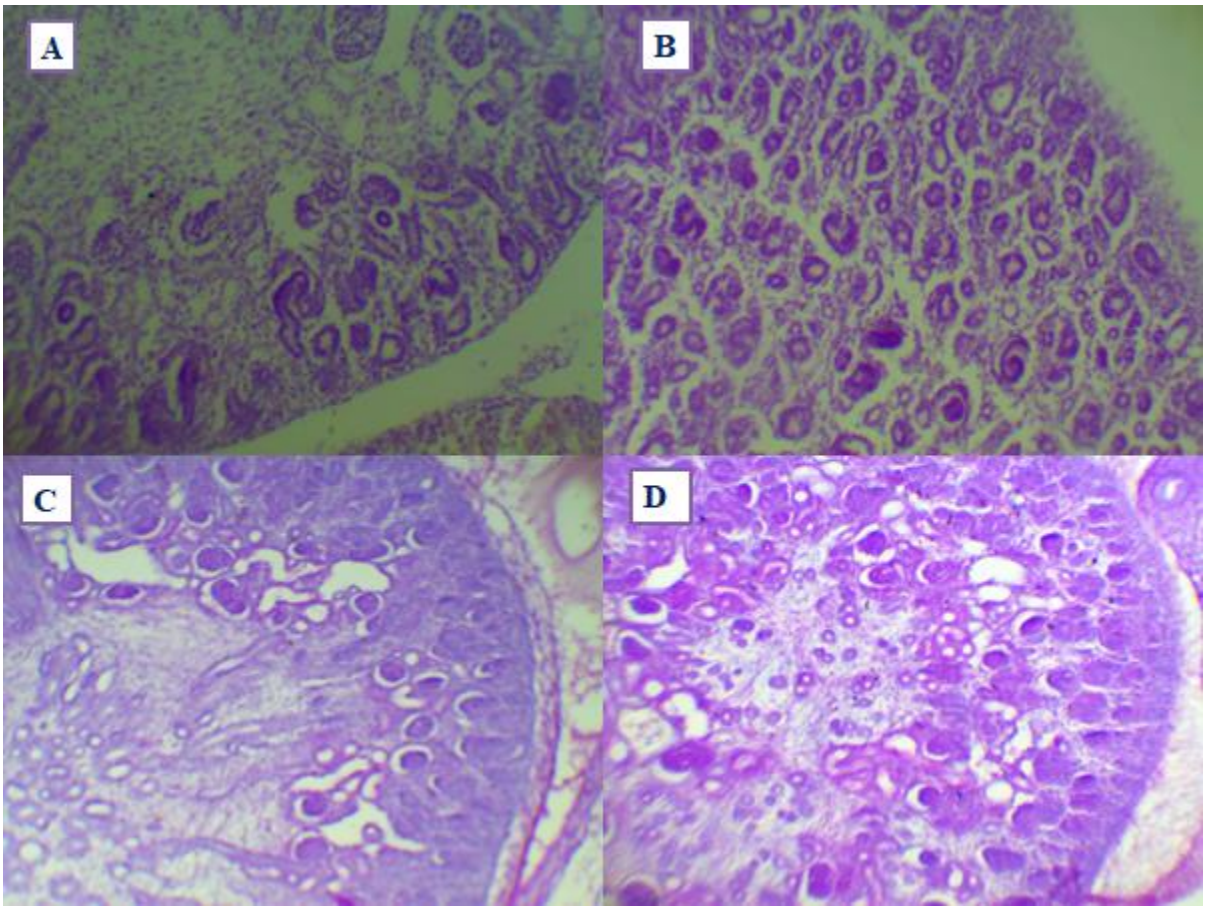


**Figure 3** A and B show sections of the cortex of the fetal kidney of healthy control group stain PAS shows normal distribution of polysaccharides. (X200). C and D demonstrate decreased polysaccharides in the second and third group of fetal kidneys. (X200)

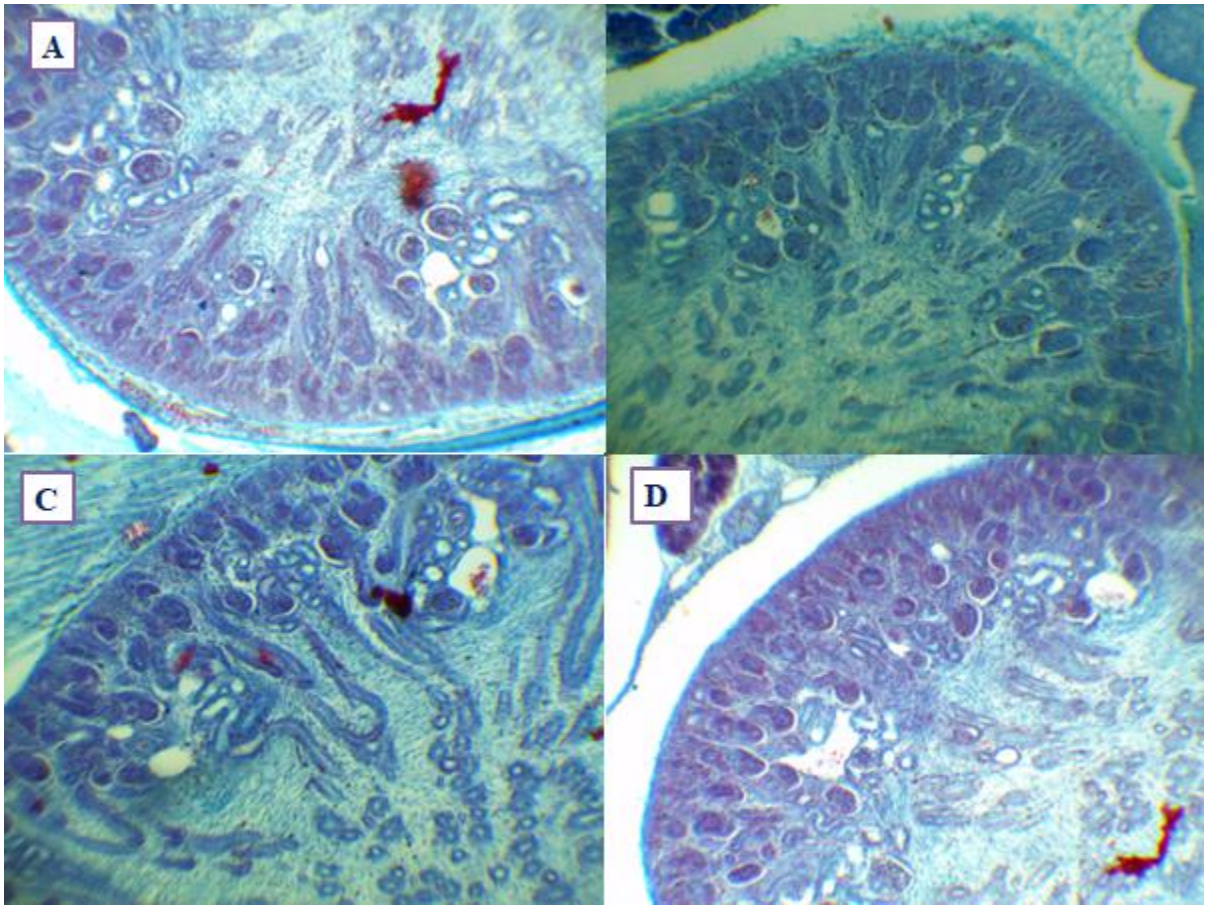


**Figure 4** A and B show sections of the cortex of the kidney of fetues healthy control group stain Mallory's trichrome. (X200). C and D demonstrate increased collagen when stained with Mallory's in the second and third group (X200)

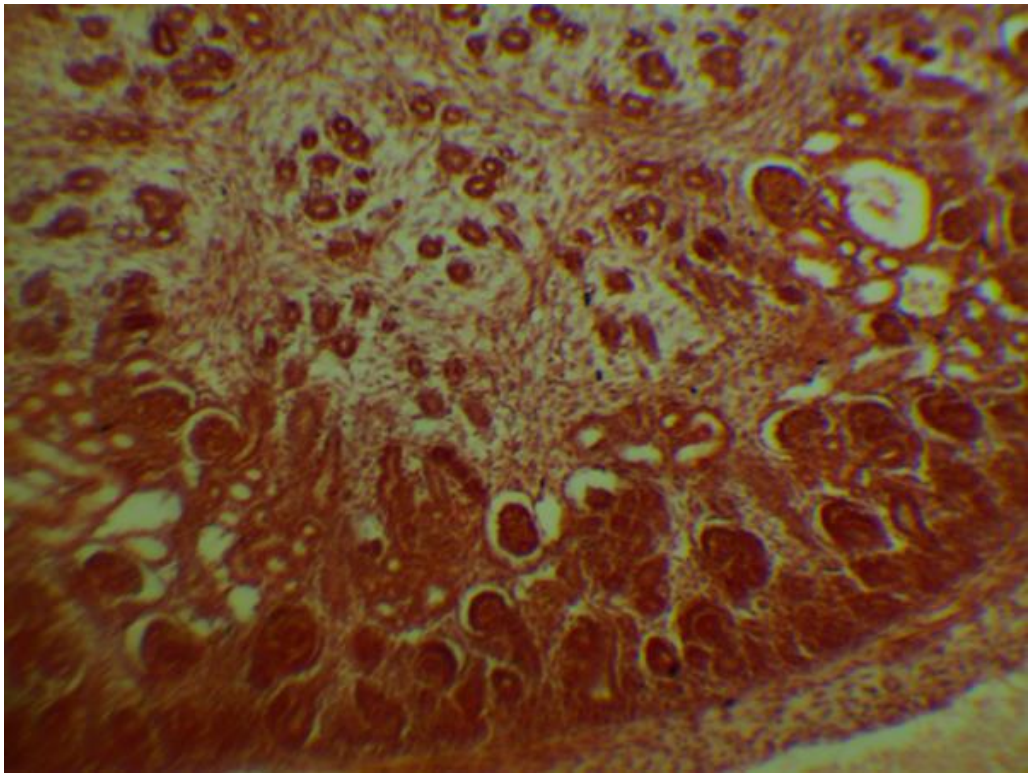

**Figure 5** Congo-stained section of the third group showing increased deposits of protein (amyloid β)in the region of the cortex of fetal kidney. (X200)

Kidney of foetuses: the typical glomeruli, distaland proximalconvoluted tubules, distalandproximal convoluted tubules of a control foetus's foetal kidney cortex. The kidney cortex of the second group of foetal rats revealed degeneration of distal convoluted tubules, a decrease in the number of proximal convoluted tubules, necrotic region, and glomeruli atrophy. The foetal kidney of the third group, on the other hand, had congested blood vessels, hemorrhagic areas, glomeruli degeneration and atrophy, necrotic areas, and degeneration of distal convoluted tubules. The control group's Mallory's trichrome stained slices of foetal rat kidney cortex exhibited normal collagen fiber distribution. While the second group had a lower dose of buspirone and the third group received a high dose, the cortical region of the third group revealed more collagen fibres. The control group's foetal kidney tissue stained with PAS revealed polysaccharides with a normal magenta color. Polysaccharides were found to be slightly lower in the second and third groups' foetal kidney cortex (Fig. 3 and 4). The total protein concentration in glomeruli, distal and proximal convoluted tubules was moderately distributed in the kidney tissue of rats in the control group, but total protein density was decreased in the other groups. The control group's foetal kidney cortex had a modest accumulation of amyloid beta protein and increased in the other groups (Fig. 5 & Table 2).

**Table 2** Feotal Kidney cortex pregnant rat Optical density of PSA and proteins in different groups

| Different Groups | Protein (total) | Protein (Amyloid β) | Polysaccharides |
|---|---|---|---|
| Healthy control | 0.7136 ±0.02155 | 0.372 ±0.0113 | 0.29421 ±0.01326 |
| Second with low dose group | 0.6455 ±0.01338 | 0.576 ±0.1246 | 0.1340 ±0.01327 |
| Third with high dose group | 0.4154 ±0.1153 | 0.714 ±0.0221 | 0.117 ±0.01153 |

## 4. DISCUSSION

Anxiety and worry are common emotions that have been selected for along the evolutionary process because of their high adaptive value. In addition, fear happens in reaction to particular risks. Due to variations in blood levels of progesterone and oestrogen, these anxiety-related disorders are most commonly more prevalent in pregnant women (Sestakova et al., 2013). In the current investigation, buspirone hydrochloride medication during pregnancy caused certain histological abnormalities in the cortical region in both the mothers and their offspring. These alterations were manifested by enlarged urinary gaps, clogged blood vessels, glomerular lobulation in some cases, necrotic areas, and glomerular degeneration in others. The current investigation, which revealed a modest decline in the PAS+ve materials compared with control ones, supports these findings. The drop in total protein and rise in amyloid protein deposition indicated that buspirone was having serious side effects (Kumar et al., 2016).

Mello et al., (2013) and Bari et al., (2015) also observed the lowered total protein and elevated amyloid protein. The histological abnormalities found in the various cortical regions of the maternal and fetal kidney cortex may be to blame for this decline. Buspirone hydrochloride exposure during pregnancy caused certain dystrophic alterations in the Purkinje cells layer, as demonstrated by Zaki and Abouel-Magd (2018). The cerebellum's oedematous regions and decreased number of granular layer cells that had deteriorated and aggregated were its hallmarks.

According to another study, the accumulation of collagen fibers and the scattered histochemical pattern of polysaccharides may have been caused by the damaged cells' lower production of collagen lytic enzymes (Khana et al., 2009). After administering a low and high dose of buspirone to pregnant female rats, earlier research revealed partial failure of development of some pancreatic acini along with degenerative and necrotic alterations in specific cells (EL-Shaer & Abd EL-Aziz, 2019).

## 5. CONCLUSION

Buspirone hydrochloride administration for a prolonged period of time caused histological and histochemical changes that were demonstrated by abnormalities in the mother's kidney and her fetuses as well as noticeably higher levels of amyloid protein.

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**Authors' Contributions**

All authors contributed to the research and/or preparation of the manuscript. Ali Hassan A. Ali, Turky NI Alhuwail and Mohammad Saleh Alhamdan participated in the study design and wrote the first draft of the manuscript, Ibrahim Mohammed

Alobaidi, Salman S Bin Ofisan, Abdullah Taher Uahua Marer and Bader Manaja Alotaibi collected and processed the samples. Nasser Salman ALSaloom, Abdulrahman Abdullah Aldaghfag and Faisal Abdulaziz O. Alghamdi participated in the study design and performed the statistical analyses. All of the authors read and approved the final manuscript.

**Ethics Approval**

All series of steps that were implemented in this study that included animal models were in compliance with Ethics Committee of Prince Sattam bin Abdulaziz University Institutional Review Board (PSAU-2021 ANT 90/43PI).

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**Conflicts of interest**

The authors declare that there are no conflicts of interests.

**Data and materials availability**

All data associated with this study are present in the paper.

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