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Histo-biochemical Assessment of Paraquat-induced Nephrotoxicity in Pregnant Wistar Rats and their Foetuses

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Abstract

Bacground: The common pesticide paraquat dichloride is well-known for being poisonous and possibly harmful to human health. There is, however, little data regarding paraquat's effects on the kidneys of pregnant women and fetuses. Thus, the effect of paraquat on the kidneys of pregnant Wistar rats and their fetuses was examined in this study.
Materials and Methods: Forty (40) pregnant Wistar rats were used. Following pregnancy confirmation, the rats were divided into three experimental groups (n=10) and a control group. These groups were given different dosages of the herbicide (1 mg/ml/kg.bw, 2.5 mg/ml/kg.bw, and 5 mg/ml/kg.bw). At the end of each trimester, three rats were removed from each group and sacrificed on days 7, 14, and 21, respectively. To look into nephrotoxic consequences, biochemical analysis of blood samples as well as to histologic evaluations were carried out.
Results: Weight gain was higher in the third trimester compared to the scond and first trimesters. In the first trimester, there was no discernible variation in the kidney weight between the groups. The weight of the kidneys changed significantly in those from the second and third trimesters ($p<0.05$). An inflammatory reaction to injury was indicated by the histological data from the pragnant rats' abduction, which showed modest to severe renal parenchymal architectural changes. The most substantial effects (fibrosis) were caused by the highest dose (5 mg/ml/kg.bw), and these alterations were time-dependent. Due to the minimal dosage of paraquat that reached the fetuses, the kidney segment of the fetuses did not exhibit any histological alterations. Hematological tests, urea and creatinine, and electrolytess displayed statistically significant differences across the groups and trimesters compared to the control.
Conclusion: This study showed that pregnant Wistar rats exposed to paraquat experience dose-dependent inflammatory damage to their kidneys. In addition, exposure to PQ was shown to cause histological lesion in the kidney of pregnant wistar rats. and these alterations were time-dependent, even though the kidney segment of the fetuses did not exhibit any histological alterations as a result of the minimal dosage of paraquat that reached them.

Keywords: Paraquat, Kidney, Oxidative Stress, Urea, Creatinine

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Background

A popular quaternary ammonium herbicide, paraquat (PQ) has continuously maintained a sizeable portion of the worldwide herbicide market[1,2]. Fruit orchards, plantation crops like cocoa, coffee, coconut, rubber, oil palm, olives,

bananas, tea, shrubs, vines, and forestry operations are just a few of the agricultural and horticultural systems that use paraquat for efficient weed control. Its efficacy makes it an essential tool for managing ecosystems and sustaining crop output in a variety of farming techniques[3]. According to reports, PQ is extremely harmful when ingested, absorbed through the skin, or inhaled[4]. Moderate PQ use can cause serious side effects such as oesophageal perforation, extensive pulmonary fibrosis, cardiac arrhythmias, and renal failure[1]. Large-scale systemic toxicity from PQ consumption causes numerous organ failure and, if left untreated, death[5]. Significant harm is caused when PQ builds up in vital organs such the kidneys, liver, and lungs. This overwhelms the body's physiological processes and frequently results in irreversible organ malfunction[2,6]. The primary cause of this is PQ's capacity to cause oxidative stress, which has been linked to a variety of illnesses[7-12]. The necessity of early detection and action in preventing tragic results is highlighted by the toxicity's quick progression[13]. PQ buildup in the kidneys and lungs causes progressive organ destruction, and systemic side effects such as arrhythmias and gastrointestinal problems make the patient's already dire situation even worse[8].

One vital organ that is in charge of waste material excretion is the kidney. PQ buildup in the kidneys can result in acute kidney damage[14,15]. The resulting kidney damage may make PQ more hazardous to other organs and decrease its excretion[16,17]. Because of its small size and low molecular weight, paraquat can pass through the placental barrier and reach the fetus. Additionally, through fluid exchange between the mother and fetus, it can be transmitted to the amniotic fluid[18].

Despite being outlawed in the majority of nations, PQ poisoning cases have not substantially declined. The majority of PQ poisoning cases are caused by oral suicide, with a 20% to 78% fatality rate. Rarely documented in the literature, PQ toxicity in pregnant women and their fetuses is difficult to cure and presents moral dilemmas[18]. Fetal blood levels of PQ were found to be 4–6 times greater than maternal levels in cases of attempted suicide during pregnancy, according to research. PQ's bloodstream penetration into organ tissues, which resulted in multiple organ failures, was blamed for fetal mortality. Additionally, long-term PQ exposure during pregnancy has been linked to motor coordination problems in animals, which may have long-term developmental effects[19]. Furthermore, Zhang et al[20] suggested that fetal brain epigenetic changes and oxidative stress could result from maternal exposure to PQ during pregnancy, raising the likelihood of neurodevelopmental problems.

Prior research on PQ exposure in the general population has mostly focused on work environments. In order to save time and effort on physical labor, farmers have been utilizing herbicides to eradicate weeds on their farms in recent years. These tasks are partly carried out by pregnant or unknowingly pregnant women. There is unquestionably a substantial knowledge vacuum regarding PQ's effects on pregnancy and its consequences for the fetuses. There is little information available regarding the effects of PQ on the kidneys of both pregnant adults and fetuses, despite some studies reporting its effects on the liver[21], kidneys[22,23], and lung alveolar cells[24]. Thus, the effect of PQ on serum biochemical parameters and the kidneys of pregnant Wistar rats and their fetuses was examined in this study.

Materials and methods

Apparatus

The following tools were used in this study: a laptop with the Zeiss app compactable with the camera microscope; a Primo Star ZEISS light microscope with camera for taking pictures of the slides; Pasteur pipettes; a water bath; a refrigerator for storing blood samples that were collected; an electronic weighing balance for weighing the tissues and the Wistar rats' litters; glass slides and cover slips on tissues that are placed and passed through staining and covered; a graduated cylinder; a microtome; absorbent paper and serum biochemical parameters auto-analyser

Reagents

The following materials were used in this study: normal saline, ethanol, paraffin wax, xylene, paraquat dichloride (Zenseca AG Products Wilmington), glucose stripe, HGC stripe buffer solution, phosphate-buffered saline (PBS) enzyme conjugates, commercial kits (Beckman), and stabilizer.

Animals

In this investigation, forty (40) pregnant Wistar rats were used (with average weight of 150±3.6 g). For two weeks as they adapted, the animals were kept in standard conditions with a 12-hour light and dark cycle at a temperature between 28 and 31°C. They had unrestricted access to food and water and were fed twice a day. The experiment lasted for three weeks. Grower's mash from Bendel Feeds and Flour Mills Limited in Ewu, Nigeria, was used to feed them. Ad libitum access to drinking water and feed was given.

Experimental Design

The pregnant animals were randomly divided into four (4) groups of ten rats each:
Group A = Control rats (n=10)
Group B = Rats treated with 1mg/ml/Kg.bw of paraquat dichloride for 21 days (n = 10)
Group C = Rats treated with 2.5mg/ml/Kg.bw of paraquat dichloride for 21 days (n = 10)
Group D = Rats treated with 5mg/ml/Kg.bw of paraquat dichloride for 21 days (n = 10)

The first day of gestation from which the treatment of paraquat dichloride would begin was thought to be the presence of a sperm plug in the female rats' vagina. To confirm pregnancy, an HCG test was also performed. At the end of each trimester, three rats were removed from each group and sacrificed on days 7, 14, and 21, respectively.

Paraquat Administration

In this investigation, the animals were given graded dosages of paraquat dichloride at 1 mg/kg, 2.5 mg/kg, and 5 mg/kg body weight, respectively, for 21 days prior to their euthanasia (Nair and Lalithakunjamma 2010). 1 mg/kg body weight, 2.5 mg/kg BW, and 5 mg/kg body weight were determined to be 2%, 5%, and 10% of the LD50 (50 mg/kg) of paraquat dichloride, respectively. Through the use of an orogastric cannula, the various concentrations were given orally.

Weight estimation

Each rats' individual body weights were measured using an electronic weighing balance on the first and twenty-first days of the experiment.

Collection of Samples

Upon the conclusion of the 7, 14, and 21-day study period, the animals were sacrificed via cervical dislocation. Internal organs were exposed after the rats were dissected. Blood samples were obtained via cardiac puncture and used for the assessment of renal biomarkers. An auto-analyzing machine was used for the biochemical analysis. After that, the kidneys and fetuses were removed through dissection. For tissue processing and histopathological study, the excised organ was weighed using a weighing scale, fixed in 10% neutral buffered formalin, and the fetuses were fixed in Boin solution.

Tissue Processing and Histological procedures

After trimming, tissue samples from the removed organs were put in tissue cassettes and manually processed using conventional histology protocols, which include dehydration, blocking, tissue sectioning, and mounting, rehydration and staining. The fetuses had the same procedure. Using a binocular light microscope, the slides were examined. To ascertain the histopathological impact of PQ on the kidneys of the developing embryo/foetuses and pregnant Wistar rats, the results were evaluated.

Photomicrography

The micrograph was read. Photographs of the tissue and slides were obtained using a digital microscope called the "Carl Zeiss (Primo Star)," which has an 8.3 mega pixel camera attached to a computer. To ascertain the impact of paraquat dichloride on the cytology and histology of the kidney, the acquired micrographs were examined.

Statistical Analysis

The results of the blood test analysis were documented for each of the experimental groups. Analysis of Variance was used to check the data for notable variations or departures from the typical average values and the Least Significant Difference (LSD) test was used to locate significant difference within groups and across the trimesters. P-values $\leq$ 0.05 were regarded as statistically significant. Tables and clearly labeled plates for the histology slides were used to display the results.

Results

Effect of Paraquat on the Body Weight of Pregnant Wistar Rats

The effect of PQ on the body weight of pregnant Wistar rats is shown in Table 1. Across the various groups, pregnant Wistar rats in the first trimester had a lesser weight when compared to those in the second trimester and those of the third trimester had even greater weight. In the first trimester, significant difference ($p<0.05$) was observed between the weight of pregnant rats in the control and those administered 1mg/ml/Kg.bw PQ. Similar result was seen in the third trimester.

Table 1: Mean Body Weight of the Wistar Rats (grams)

Groups	Group A (control)	Group B (1MG PQ)	Group C (2.5MG PQ)	Group D (5MG PQ)
First Trimester	152.6±0.82^a	163.5±1.02^b	160.1=1.24^a	156.8±0.98^a
Second Trimester	187.6±1.24^a	186.3±2.01^a	176.3=2.04^b	179.5±2.08^a
Third Trimester	190.3±1.88^a	184.6±1.92^b	189.5=2.86^a	186.8±2.66^b

Key: Values having different superscripts within the same row are significantly different

Effect of Paraquat on the Weight of the Kidney of Pregnant Wistar Rats

The effect of PQ on the weight of the kidneys of pregnant Wistar rats is shown in Table 2. There was no significant difference in the weight of kidney across the groups in the first trimester. Those of the second and third trimesters had statistically significant changes in the weight of the kidneys.

Table 2: Weight of the kidneys of Pregnant Wistar Rats (grams)

Groups	Group A (control)	Group B (1MG PQ)	Group C (2.5MG PQ)	Group D (5MG PQ)
First Trimester	1.15±0.06^a	1.08±0.12^a	1.17=0.42^a	1.20±0.12^a
Second Trimester	1.06±0.04^a	1.09±0.24^b	1.08±0.22^b	1.10±0.24^b
Third Trimester	1.07±0.02^a	1.19±0.12^b	1.20±0.40^b	1.12±0.20^a

Key: Values having different superscripts within the same row are significantly different

Effect of Paraquat on renal function parameters in Pregnant Wistar Rats

The effects of PQ on the blood levels of chloride ion, creatinine, bicarbonate, potassium, sodium and urea are presented in Tables 3-8 respectively.

In the first trimester, it was observed that there was a significant decrease in serum chloride level in pregnant rats administered 1mg PQ compared to the control, while those given 5mg PQ had a significantly higher serum chloride level compared to the control. Similar trend was observed in the second trimester. In the third trimester, there was a significant difference in serum chloride levels in rats administered 1mg PQ, 2.5 mg PQ and 5 mg PQ compared to the control. Whereas there was significant decrease in Groups B and C, there was a significant increase in Group D.

Table 3: Effect of Paraquat on Serum Chloride in Pregnant Wistar Rats (mmol/L)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	104±2.68^a	104±1.82^a	102±2.32^b	107±3.23^c
Second Trimester	104±2.22^a	104±2.42^c	102±1.92^c	106±2.90^d
Third Trimester	106±3.02^a	104±1.88^b	100±0.88^c	109±3.34^d

Key: Values having different superscripts within the same row are significantly different

Table 4: Effect of Paraquat on Serum Creatinine in Pregnant Wistar Rats (mg/dl)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	0.50±0.06^a	0.89±0.08^b	1.21±0.09^c	0.60±0.02^a
Second Trimester	0.50±0.08^a	0.89±0.06^b	1.21±0.08^c	1.00±0.04^c
Third Trimester	0.70±0.10^a	0.90±0.14^b	1.20±0.04^c	0.90±0.06^b

Key: Values having different superscripts within the same row are significantly different

Pregnant rats given 2.5mg PQ (Group C) in first, second and third trimesters had a significant increase in creatinine level compared to the control. Serum creatinine level in the control and that in rats given 5mg PQ was not statistically different in the first trimester but was different in the second and third trimesters. In all the trimesters, serum creatinine levels in rats administered 1mg PQ was significantly different from that in the control.

Table 5: Effect of Paraquat on Serum Bicarbonate in Pregnant Wistar (mmol/L)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	26.00±1.82^a	18.00±1.22^b	21.00±1.00^c	28.00±2.12^d
Second Trimester	26.00±1.80^a	18.00±1.22^b	21.00±1.00^c	19.00±1.82^b
Third Trimester	27.00±1.86^a	18.00±1.22^b	21.00±1.00^c	28.00±2.14^d

Key: Values having different superscripts within the same row are significantly different

The bicarbonate level for all trimesters were the same for Group B (rats given 1mg PQ), hence no statistical significance difference across the trimesters. Similarly, rats given 2.5mg PQ (Group C) had the same level of serum bicarbonate during the trimesters. For Group D, there was a significant increase in the level of serum bicarbonate during the

first trimester but there was a noteworthy decrease in the level of serum bicarbonate during the second trimester compared to the control.

Table 6: Effect of Paraquat on Serum Potassium in Pregnant Wistar Rats (mEq/L)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	3.90±0.98^a	4.80±1.12^b	4.50±1.22^c	4.90±1.28^b
Second Trimester	3.90±0.98^a	4.80±1.12^b	4.50±1.22^c	3.80±1.01^a
Third Trimester	3.10±1.02^a	4.80±1.12^b	4.70±1.26^b	4.90±1.28^b

Key: Values having different superscripts within the same row are significantly different

During the first trimester there was a significant increase in the serum potassium level when comparing rats in the control with those given 1mg PQ (Group B) as well as those in Group C and D. There was no significant difference (across the three trimesters) in serum potassium level for rats given 1mg PQ. In the second trimester, rats in the control had serum potassium level of 3.90, which was not significantly difference from that obtained in rats given 5mg PQ (3.80).

Table 7: Effect of Paraquat on Serum Sodium in Pregnant Wistar Rats (mEq/L)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	134.00±3.12^a	139.00±2.82^b	145.00±3.24^c	139.00±2.22^b
Second Trimester	134.00±3.12^a	139.00±2.82^b	145.00±3.24^c	155.00±3.88^d
Third Trimester	133.00±3.02^a	142.00±3.68^b	148.00±3.02^c	144.00±2.48^b

Key: Values having different superscripts within the same row are significantly different

In Group B, the level of serum sodium was the same for the first and second trimesters, but both were significantly higher than the value recorded in the control group. First trimester in Group C showed a significant increase in the level of serum sodium compared to the control and rats given 1 mg PQ (Group B). Similar result was seen in the second trimester. Pregnant rats administered 5mg PQ (Group D) has significantly higher levels of serum sodium in all the three trimesters compared to the control.

Table 8: Effect of Paraquat on Serum Urea in Pregnant Wistar Rats (mg/dl)

Weeks	Group A (control)	Group B (1mg PQ)	Group C (2.5mg PQ)	Group D (5mg PQ)
First Trimester	35.00±2.10^a	38.00±2.14^b	65.80±3.04c	66.00±2.42^c
Second Trimester	35.00±2.10^a	38.00±2.14^c	65.80±3.04^c	78.60±3.88^d
Third Trimester	48.00±3.26^a	38.00±2.14^b	62.80±2.88^c	54.00±1.98^c

Key: Values having different superscripts within the same row are significantly different

Compared to the control group (Group A), rats given 1mg PQ (Group B) recorded a significant increase in the level of serum urea in the first and second trimesters, whereas a significant decrease was seen in the third trimester, although the same serum urea value was recorded in all the trimesters for Group B. compared to the control, the first trimester in Group C showed an increase in the level of serum sodium and in the second trimester the level of serum sodium was the same. In the first trimester of group D, there was an increase in the level of serum urea and during the second trimester there was a higher increase in the level of serum urea compared to the control and rats given 1mg PQ (Group B).

Histological Effects of PQ on the of the kidney of Pregnant Wistar Rats

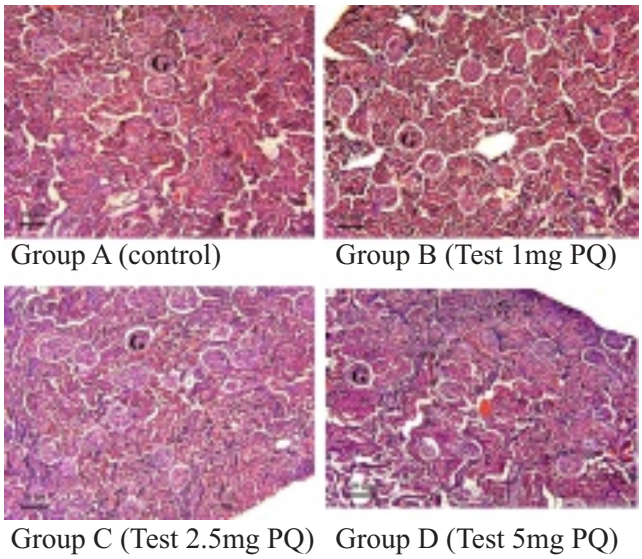
The effect of PQ on the histology of the kidney of pregnant Wistar rats is presented in figure 1 (first trimester), figure 2 (second trimester) and figure 3 (third trimester) of treatment.

For the first trimester, the kidney section in the control (Group A) showed no observable microscopic lesions. Majority of the cortical region with features of the medullary region, presences of glomerulus, encapsulated in the Bowman's capsule separated by a space are visible. In addition, the cells inter-disposed within the glomerulus are simple cuboidal in nature and are composed with a round to oval vesicular nuclei posited in cytoplasm of the cell. Similar features were observed in the section of kidney of rats administered 1mg PQ (Group B). Kidney section of Rats exposed to 2.5mg PQ showed moderate glomerular necrosis, while sections from rats administered 5mg PQ showing severe glomerular necrosis. Seen in the medulla are presence of connective tissue and blood vessels with features of mild hemorrhagic activities.

In the second trimester (figure 2), no observable microscopic lesions were seen in sections obtained from the control animals (Group A). Sections of the kidney showed cortex and medulla. Glomeruli are present in the cortex while tubule extends from the cortex to the medulla. The connective tissue of the glomeruli capillary epithelium and tubular cell all show intact features. Also seen are stroma blood vessels in the cortex. In rats administered 1mg PQ (Group B) severe glomerular necrosis and marked generalized shrunken glomeruli was observed.

Stroma blood vessels were seen in the cortex. Similar result was obtained in rats given 2.5mg PQ (Group C). There was severe glomerular and renal tubular necrosis with vascular congestion. Glomeruli are scantly present in the cortex while tubule extends from the cortex to the medulla, which is obviously seen. Seen also are cuboidal cells lining the Bowman's capsule. Also seen are stroma blood vessels in the cortex, showing features of hemorrhagic activities. Seen also are numbers of collecting ducts disposed in the tissues. In rats given 5mg PQ (Group D), sections of the kidney display obvious region of the cortex composed of glomeruli lined by simple cuboidal cells. The cells are composed of round to oval vesicular nuclei posited in the cytoplasm of the cells. Also seen are stroma blood vessels in the cortex, showing severe hemorrhagic activities. The impression is that of severe vascular congestion, and shrunken glomeruli.

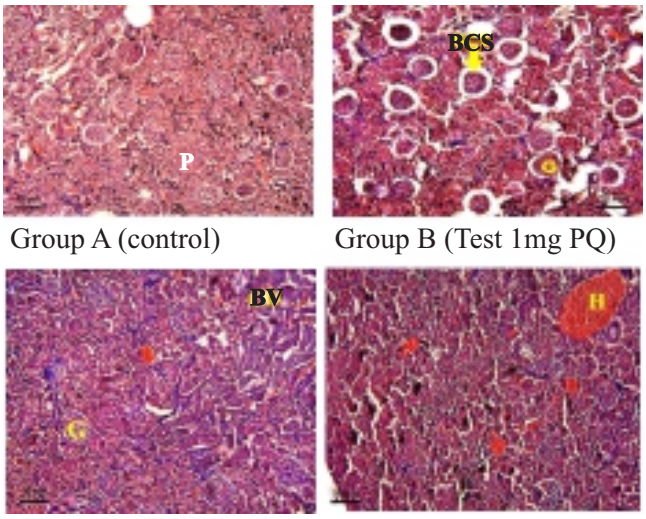
Results obtained in the third trimester for the control animals displayed majority of the cortical region bounded by simple cuboidal epithelial cells. These cells are composed of round to oval vesicular nuclei posited in the middle of the cytoplasm of the cells. Seen in the cortical region are presences of glomerulus, encapsulated in the Bowman's capsule separated by a Bowman's capsule space. Also present are connective tissue and blood vessels. The impression is that there were no observable microscopic lesions. Sections of the kidney in Group B (1mg PQ) showed severe glomerular and renal tubular necrosis with feature of the medulla



Group A (control) Group B (Test 1mg PQ)

Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

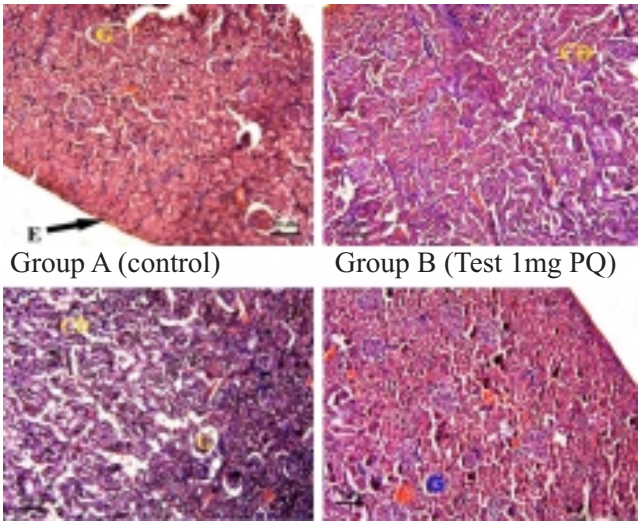
Figure 1: Histology of the kidney of pregnant Wistar rats after one week of a paraquat administration. H & E stain x1000. Key: G-Glomerulus, P- Podocytes, BV-blood vessel, BCS – Bowman's capsule space



Group A (control) Group B (Test 1mg PQ)

Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

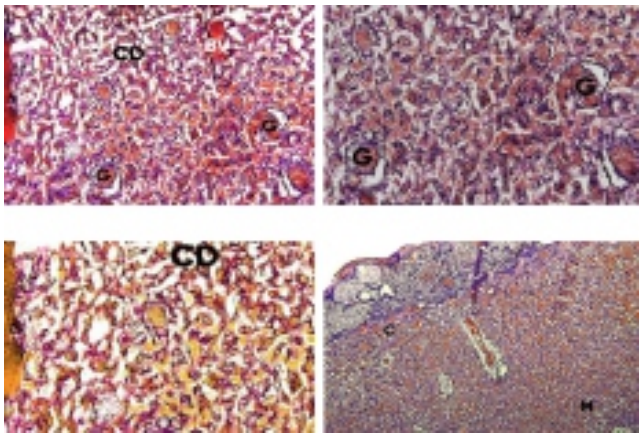
Figure 2: Histology of the kidney of pregnant wistar rats after two weeks of PQ administration. H&E stain x1000. Key: G-Glomerulus, P- Podocytes, BV-blood vessel, BCS – Bowman's capsule space, H – Hemorrhage



Group A (control) Group B (Test 1mg PQ)

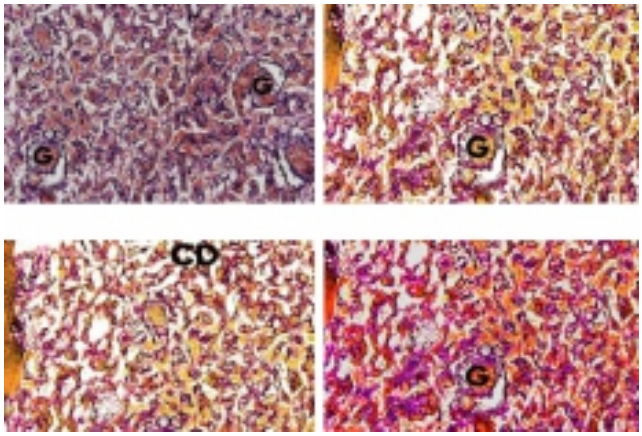
Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

Figure 3: Histology of the kidney of pregnant Wistar rats after three weeks of a Paraquat administration. H&E stain x1000. Key: G-Glomerulus, P- Podocytes, BV-blood vessel, BCS – Bowman's capsule space, H – Hemorrhage



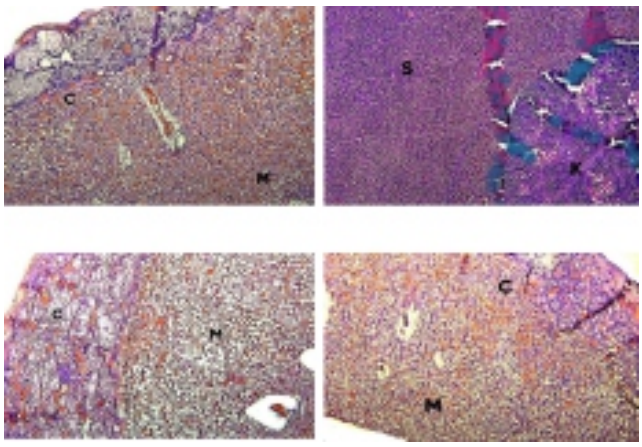
Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

Figure 4: Histology of the kidney of foetus after one weeks of a PQ administration. H&E stain x1000



Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

Figure 5: Histology of the kidney of foetus after two weeks of a PQ. H&E stain x1000



Group C (Test 2.5mg PQ) Group D (Test 5mg PQ)

Figure 5: Histology of the kidney of foetus after two weeks of a PQ. H&E stain x1000

composed of tubule drifting toward the cortical region of the tissue. Similarly, severe glomerular and renal tubular necrosis was observed in sections of the kidney from animals given 2.5mg PQ (Group C). Glomeruli are scantly present in the cortex while tubules extend from the cortex to the medulla, which is obviously seen. Also seen are stroma blood vessels in the cortex, showing feature of hemorrhagic activities. In Section of kidney in rats administered 5mg PQ (Group D), displayed shrunken glomeruli, glomerular necrosis and severe vascular congestion.

Histological Effects of PQ on the of the kidney of Rat Foetus

The effect of PQ administration on the histology of foetus are shown in figure 4 (first trimester), figure 5 (second trimester) and figure 6 (third trimester) of treatment. Generally, no observable microscopic lesions were seen across the groups and across the three trimesters. The cortex and medulla of the kidney were visible in the sections. The cortex contains glomeruli, and tubules connect the cortex to the medulla. The stroma blood artery, capillary epithelium, and tubular cell, as well as the connective tissue of the glomeruli, all have intact characteristics.

Discussion

Despite 125 years of research and use, no particular antidote has been found since the initial synthesis of PQ in 1882[25]. As a result, there isn't a single, efficient remedy for PQ poisoning at the moment[26]. This study looked at the possible effects on the fetus of the renal damage caused by PQ during pregnancy. The effects of PQ on the kidney have been shown in studies, although the kidneys of pregnant Wistar rats were not examined.

Effect of Paraquat on the Body Weight and Kidney Weight of Pregnant Wistar Rats

In order to determine if the injection of PQ to pregnant Wistar rats resulted in weight increase or loss, the body weights of the rats were taken into account at the conclusion of each trimester. Weight gain appears to be dependent on the Wistar rats' ability to eat, the number of fetuses they are carrying, and their sedentary lifestyle. These experimental rats' weight may potentially be

impacted by their sleep or wake patterns. We ensured that every rat was housed in the same setting and condition in order to close these gaps. Weight growth during pregnancy has been validated by literature[27]. Wistar rats in the first week of this study weighed less than those in the second week, and those in the third week weighed even more. The pregnant Wistar rats' increasing gestational age, which indicates an increase in the weight of the growing fetuses, is the primary cause of the weight gain observed in the pregnant Wistar rats. In comparison to the experimental group, the control group was heavier which aligns with the report of Edo[28]. According to the toxic activity of paraquat dichloride in the GIT and the oxidative damage caused by free radicals in a number of critical organs at the subcellular level, weight loss may be ascribed to decreased feed and water intake. This observation aligns with previous research conducted by Pourgholamhossein et al[29]. Perhaps because the control group carried more litters than the experimental group, there was a noticeable weight difference that was greater in the control group. This outcome is consistent with that of Almeida et al[30].

As shown in Table 2, changes seen in the first trimester of the group given 1 mg/ml/kg were not statistically significant, and the weight of both kidneys was taken into account at the conclusion of each trimester. The weight of the kidneys changed statistically significantly in those from the second and third weeks. Based on the results, it can be concluded that the advancement in pregnancy is the cause of this.

Effect of Paraquat on renal function parameters in Pregnant Wistar Rats

Table 3-8 shows the effects of PQ on the blood levels of chloride ion, creatinine, bicarbonate, potassium, sodium and urea in pregnant Wistar rats respectively. Generally, exposure to PQ caused a significant decrease in serum levels of chloride and significant increase in serum creatinine, potassium, and urea compared to the control. The results align with reported nephrotoxic effects of PQ[31]. This study's conclusion is consistent with research on pregnant Wistar rats conducted by Alex et al[32] and Onur et al[33]. Additionally, the results showed that bicarbonate levels rose statistically considerably in groups B and C, with the exception of Group D. The analysis of this study and that of Krishma & Ramachandran[33] are in agreement with the findings of Tizhe et al[31]. Serum potassium levels significantly increased during PQ administration in all trimesters as compared to control. This result is consistent with that of Tizhe et al[31]. The findings supported the findings of Okolonkwo et al[17], Palipoch et al[26] and Tizhe et al[31] by demonstrating that there was a significant increase in creatinine levels among PQ alone treated groups in comparison to control. The notable rise in creatinine levels was a classic evidence of a kidney-harming consequence of PQ treatment. Ijaz et al[12] and Wershana[34] both provided support for this, stating that PQ-treated animals had higher urea and creatinine levels, which are important markers for evaluating renal impairment[36,37].

Histological Effects of PQ on the of the kidney of Pregnant Wistar Rats

The slides in the control group and those given a dose of 1 mg/ml/kg of paraquat dichlorate did not differ at the conclusion of the study. However, when the dose of PQ was raised to 2.5 mg/ml/kg/body weight per dose, alterations in the kidneys of pregnant Wistar rats that suggested mild inflammation to fibrosis began to appear. The pregnant Wistar rats from the group given 5 mg/ml/kg/body weight of paraquat dichlorate showed clear histopathological alterations. Compared to the control and Groups B, it can be said that the larger dose of paraquat that reached the kidney of pregnant Wistar rats is the cause of these histologic alterations. This is consistent with broad findings from research by Hiroshi38, Amin et al[13] and Chen et al[25].

The findings unequivocally show that kidney damage increases with the amount of PQ given[17]. This result is consistent with that of Gawarammana and Buckley[39]. Onur et al[33] also confirmed these findings. Rats exposed to PQ showed dose-dependent kidney damage, according to O Okolonkwo et al[17], with rats subjected to the highest dose showing the most nephrotoxicity and those exposed to the lowest dose showing the least.

Results obtained from the third trimester after giving pregnant Wistar rats 1 mg/ml/kg of PQ revealed effects on the kidney's histologic pattern,

with the tubules appearing to be drifting. This was likely caused by the fact that the pregnant Wistar rats were in their third trimester even though the dosage was low. The effects of giving the pregnant Wistar rats 2.5 mg/ml/kg of PQ were identical to those of giving them 1 mg/kg in the third trimester. The advanced stage of pregnancy (third trimester) is the could be the cause of this impact. This can be a result of pregnancy hormones reaching their peak.

The fetal histology of the kidney of rats given PQ were histological from the control with no lesions detected. This shows that there was not enough PQ that passed through the placenta to significantly alter the fetus's kidney. Thus, it was demonstrated that the effect on the fetus was dose dependent[40]. According to earlier research, there is a greater chance that PQ will breach the placenta barrier if a higher dose is given[18]. According to research by Konthonbut et al[41] and Shi et al[42], PQ can pass through the placenta and reach the fetus in pregnant women because of its small size and low molecular weight. Additionally, their claim is consistent with the report of David et al[43].

Conclusions

The study's findings unequivocally demonstrated that pregnant Wistar rats' renal function is impacted by paraquat dichlorate exposure in a dose-dependent manner. It is clear from the biochemical research that exposure to paraquat causes a considerable rise in electrolyte, urea, and creatinine levels. In addition, exposure to PQ was shown to cause histological lesion in the kidney of pregnant wistar rats. The most substantial effects (fibrosis) were caused by the highest dose (5 mg/ml/kg.bw), and these alterations were time-dependent. The kidney segment of the fetuses did not exhibit any histological alterations as a result of the minimal dosage of paraquat that reached them. Studies with higher doses of PQ and longer time frames are required to clearlu elucidate the histological impact of PQ on the kidney of fetuses.

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List of abbreviations

PQ:	Paraquat
G:	Glomerulus
P:	Podocytes
BV:	Blood Vessel
BCS	Bowman's Capsule Space
H:	Hemorrhage

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Not Applicable

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Animal ethical approval
The Institutional Animal Care and Use Committee (IACUC) established standard standards for the use of laboratory animals, which were followed by all of the animals used in this investigation (Maiken, 2018).

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