



Original Research Article

Histopathological Evaluation of Organ Injury and Its Association with Survival Outcomes in Paraquat Poisoning

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Article Info

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How to cite this article : Bedanta Sarma, Shreemanta Kumar Dash, Rachagiri Suneel, Rishikesh G, Histopathological Evaluation of Organ Injury and Its Association with Survival Outcomes in Paraquat Poisoning

J Ind. Soc. Toxicol 2026;22(1):12-18



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Abstract

Paraquat is a widely used herbicide with a high degree of human toxicity and a significant rate of fatality. The lungs are the primary target organ; however, paraquat exposure is also associated with acute tubular necrosis and hepatic injury. The absence of a specific antidote contributes to its high mortality. Owing to its marked pulmonary affinity, paraquat induces rapid alveolar damage, often culminating in respiratory failure. Clinical outcomes are largely influenced by the quantity of paraquat ingested and the timeliness of medical intervention.

In this case series, histopathological changes across multiple organs were evaluated in six victims of paraquat poisoning. The findings were analysed in relation to the ingested dose and survival duration and interpreted in the context of the existing literature.

Keywords: paraquat; herbicide; acute tubular necrosis; hepatic injury; histopathology

Introduction

Paraquat (PQ) is a bipyridinium non-selective herbicide, commercially available as a 20% (w/v) brown solution with a strong, pungent odour. Owing to its low cost and ease of access, it is the second most widely used herbicide globally.[1,2] Initially introduced in 1961 for controlling unwanted crops in marijuana cultivation, its high toxicity has led many countries to ban or strictly regulate its use. In India, however, no nationwide prohibition exists, except for a ban in the state of Odisha. Recently, Andhra Pradesh and Telangana have also imposed an initial 60-day ban on it.

PQ toxicity in humans and animals results from the generation of superoxide radicals and other reactive oxygen species, which disrupt cellular membrane structure and function.[3,4,5] Following ingestion, the compound is rapidly absorbed and distributed throughout various organs. The lungs are particularly vulnerable due to active uptake of PQ by pneumocytes, ultimately predisposing them to fibrosis. The kidneys also sustain direct injury because most of the compound is excreted unchanged via the renal system within 48 hours.[6] Consequently, mortality is largely associated with pulmonary and renal damage, the severity of which depends on both the dose consumed and the physiological status of the individual.

Currently, no specific antidote or standardised treatment protocol exists for PQ poisoning, leading to extremely high mortality rates (60–80%).[7] Although most cases result from intentional ingestion, accidental exposures have also been reported.[8] Fatalities related to PQ

poisoning are frequently documented in southern India, posing a significant challenge to the healthcare system. This case series presents such incidents, emphasising the histopathological findings across different organs in relation to the victims' survival periods. These insights may assist clinicians in designing targeted, organ-specific management strategies for affected patients.

Clinical Details

History:

In this article, we present six deaths resulting from the intentional ingestion of paraquat. All individuals were young and belonged to farming families. A summary of the case details is provided in Table 1. Except for the third case, who did not seek medical attention until the third day after ingestion, all other patients received treatment within 2–3 hours of symptom onset. All the deceased had consumed paraquat mixed with either water, alcohol, or cola. All cases were referred from primary health centres or nearby hospitals, except for the sixth case, who came directly to our institute.

Upon arrival at our emergency department, all patients had stable vital signs and were conscious; however, each exhibited clinical features suggestive of respiratory, hepatic, and renal involvement. Liver and kidney function tests were deranged in all cases at presentation. Patients who survived for more than five days underwent haemodialysis or hemoperfusion, as well as peritoneal dialysis.

Autopsy Findings:

Autopsies were performed in the mortuary of our tertiary care centre on the same day of death. External examination revealed no injuries in any of the cases. Icterus was present in all bodies, with no evidence of external bleeding. A thorough internal examination of all organs was conducted, and the findings are summarised in Table 2. The predominant pathological changes were observed in the lungs and liver, while no significant gross abnormalities were noted in the kidneys.

In all cases, lung weight increased two- to threefold, with the greatest increase in the third case. Tissue samples from the lungs, liver,

kidneys, heart, and brain were obtained in all cases for histopathological examination. Significant histopathological changes were consistently identified in the lungs, liver, and kidneys.

Intra-alveolar oedema and haemorrhage were present in all cases and were detected as early as within 12 hours in the first case (Fig.1). However, the extent of haemorrhage was comparatively less than in cases with survival beyond five days (from the third case onward). Fibrin deposition and hemosiderin-laden macrophages (engulfing the RBCs) were noted in cases surviving more than five days (Fig. 2). Hyaline membrane formation and lymphocytic infiltration were observed in the last two cases, both of whom survived for more than two weeks (Fig.3).

The most frequent hepatic finding was increased RBCs in between spaces of polygonal shaped hepatocytes, diagnostic of sinusoidal congestion; which was present in all cases and was evident within the first 24 hours (in the first case) (Fig.4). Expansion of the portal tracts with periportal inflammation was identified in only one case, corresponding to a survival period of five days (third case) (Fig.5). Renal tubules showed attenuation of epithelium, increased eosinophilic staining, indistinct nuclei and tubular lumen filled with sloughed off debris suggestive of Acute tubular necrosis was observed early, beginning with the first case (Fig.6). In the third case, splaying and degeneration of cardiac muscle fibres were observed. Detailed histopathological findings are presented in Table 3.

Discussion

After PQ ingestion, its high affinity leads to lung involvement within 1-3 days, depending on the dose. There is damage to the alveolar-capillary barrier, leading to increased permeability, causing septal congestion, intra-alveolar oedema, wall thickening, haemorrhage and neutrophil infiltration. This is followed by overexposure of local tissue factor and activation of the coagulation cascade. The oedema fluid, cell debris and fibrin form the hyaline membrane along the alveolar walls.[9,10] Alveolar epithelial injury was reported early (within 24 hours) compared to endothelial damage (48 hours);

however, both have the same peak at 72-96 hours.[11] Pulmonary oedema and diffuse alveolar damage were evident in most of the cases within 24-48 hours, resulting in the development of acute respiratory distress syndrome.[12,13] Fibrin deposition along the septum and intra-alveolar spaces started on the 4th day and was more prominent from the 7th day, and was seen until 14 days.[14]

Intra-alveolar fibroblast growth and collagen deposition with fibrosis is a late finding, leading to death in 2-3 weeks.[15] However, from the first week onwards, fibroblast proliferation and collagen deposition occur in the alveolar space, leading to pulmonary fibrosis. The lung structure is entirely disorganised and replaced by many small (0.5–2.0 mm in diameter) cysts lined by fibrous tissue (honeycomb appearance).[16] However, Lung fibrosis was observed in one of the patients who died during the first 24 hours of PQ ingestion, challenging its established time-bound appearance.[17]

The kidneys play a central role in paraquat excretion, and renal injury can impair further elimination, thereby exacerbating systemic toxicity.[15] Histopathological findings predominantly include proximal tubular necrosis, interstitial haemorrhage, collagen deposition, and involvement of both tubules and glomeruli.[18,19,20] Although the precise timeline of renal changes is not well established, early involvement is likely within the first day of ingestion, with peak injury occurring within 2–3 days.

Paraquat-induced hepatic injury in humans follows a biphasic pattern. The initial phase, occurring within the first 48 hours, is characterised by hepatocellular damage due to the accumulation of the parent compound. The subsequent phase involves cholangiocellular and cholestatic injury, possibly related to biliary excretion of unmetabolized paraquat or its metabolites. Histopathological features include sinusoidal dilatation, congestion, and portal tract widening due to reticulin deposition.[21] Cardiac involvement is also significant, with paraquat concentration in myocardial tissue directly correlating with survival time. The release of proinflammatory cytokines, such as tumour necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β), contributes to myocardial injury.

Additionally, alterations in calcium and potassium ion dynamics in ventricular myocytes may precipitate arrhythmias.[22,23]

In our cases, pulmonary involvement was notably rapid, with the first two patients succumbing within 48 hours and demonstrating early intra-alveolar oedema within 24 hours. These two cases exhibited similar histopathological findings in the lungs. Although the third and fourth patients reportedly ingested comparable quantities of poison, their histopathological features differed, likely reflecting earlier medical intervention in the fourth case. The shorter survival of the third patient may be attributed to both cardiac muscle degeneration observed around the fifth day and more pronounced hepatic involvement. Their relatively longer survival compared to the first two cases may be explained by lower quantities of the poison ingested. Hyaline membrane formation was observed in the fifth and sixth cases after the second week. Interestingly, the sixth case demonstrated prolonged survival into the third week despite an inconsistent correlation between dose and histopathological severity, possibly due to interventions such as hemoperfusion and peritoneal dialysis, which were not administered in earlier cases. Overall, clinical outcomes did not consistently correlate with histopathological findings, as even severely affected cases survived beyond two weeks.

All patients developed acute renal failure, with the earliest onset occurring within 24 hours. Renal histopathological features did not show a clear relationship with dose or survival duration. Although paraquat is known to cause cardiac toxicity, it was evident histologically in only one case. Classical hepatic histopathological findings were observed in only one patient, who showed portal tract expansion and periportal inflammation, whereas sinusoidal congestion was present in all cases, regardless of survival duration. No consistent dose- or treatment-dependent hepatic changes were identified.

Conclusion

Histopathological evaluation in paraquat poisoning plays a crucial role in understanding its effects across multiple organ systems. Improving this aspect could help clinicians categorise

patients based on toxin burden rather than relying solely on clinical presentation. While emphasis is often placed on pulmonary findings, involvement of other vital organs is frequently overlooked. Comprehensive molecular studies examining organ-specific responses following paraquat ingestion are essential for developing effective treatment protocols. The cases presented here demonstrate the early onset of pulmonary oedema and raise important questions regarding the conventional pulmonary and hepatic histopathological features in relation to survival duration. Additionally, they underscore the impact of paraquat on cardiac muscle. Nevertheless, further large-scale studies are required to gain deeper insights and strengthen the existing evidence base.

Conflict of interest: None

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Table 1: Demographic information with a brief history of cases:

Sl. No.	Age/Sex	Amount consumed	Survival Period	History
1-125	M/27	90-100 ml	1 day	Gastric lavage was done outside following 2-3 episodes of vomiting, and the patient was referred the same day to AIIMS with stable vitals and mild abdominal pain.
2-86	M/21	20-25 ml	2 days	Gastric lavage was done outside following vomiting, and the patient was referred the same day to AIIMS with stable vitals and mild abdominal pain.
3-42	M/36	5-10 ml	5 days	No treatment received for 2 days. Brought to AIIMS when he developed difficulty in eating, vomiting and diarrhoea. Peritoneal dialysis was done here.
4-89	M/20	5-10 ml	11 days	After vomiting, gastric lavage was done, followed by 2 cycles of hemoperfusion outside. Then shifted to AIIMS in a conscious state with stable vitals. 2 cycles of peritoneal dialysis were done at AIIMS.
5-17	M/25	5-10 ml	16 days	Gastric lavage was done outside. Came to AIIMS on the 3 rd day with icterus.
6-80	M/16	200-250 ml	21 days	Presented directly to AIIMS with h/o vomiting. He was conscious with stable vitals. 3 cycles of hemoperfusion and 5 cycles of hemodialysis were done.

Table 2: Gross autopsy findings of organ

Sl. No.	Gross autopsy findings (internal)		
	Lungs	Liver	Heart
1	• Weight: 550 gm. (R) /500 gm. (L) • Adh. (R)	• YD • PH	PH (diffuse)
2	• Weight: 900 gm. (R)/820 gm. (L) • HP (B/L) • Adh. (L)	YD	PH (base)
3	• Weight: 1000 gm. (R)/750 gm. (L) • HP (B/L) • Adh. (L)-PH (diffuse)		
4	• Weight: 800 gm. (R)/650 gm. (L) • HP (B/L)	YD	—
5	• Weight: 825 gm. (R)/750 gm. (L) • HP (B/L)	YD	—
6	• Weight: 750 gm. (R)/500 gm. (L) • HP (B/L)	YD	PH (base)

R (right side), L (left side), B/L (bilateral), Adh. (adhesion), HP (hemorrhagic patch), YD (yellowish discolouration), PH (petechial haemorrhage)

Table 3 - Histopathological examination (HPE) findings of organs

Sl. No.	Lungs						Liver				Kidney	Heart
	IAO	DAH	Fib	HLM	HM	LI	SC	EPT	PI	IHBA	ATN	SDMF
1	+	+					+				+	
2	+	-					+				+	
3	+	+	+	+			++	+	+		+	+
4	++	++					+				+	
5	+				+	+				+	+	
6	+	+			+		++				+	

IAO (Intra-alveolar oedema), DAH (Diffuse alveolar haemorrhage), Fib. (Fibrin deposition), HLM (Hemosiderin laden macrophage), HM (Hyalin membrane), LI (Lymphocyte infiltration), SC (Sinusoidal congestion), EPT (Expansion of portal tract), PI (Periportal inflammation), IHBA (Intra hepatocyte bile pigment accumulation), ATN (Acute tubular necrosis), SDMF (Splaying and degeneration of muscle fiber), HN (Hypoxic neurons), PC (Psammomatous calcification)

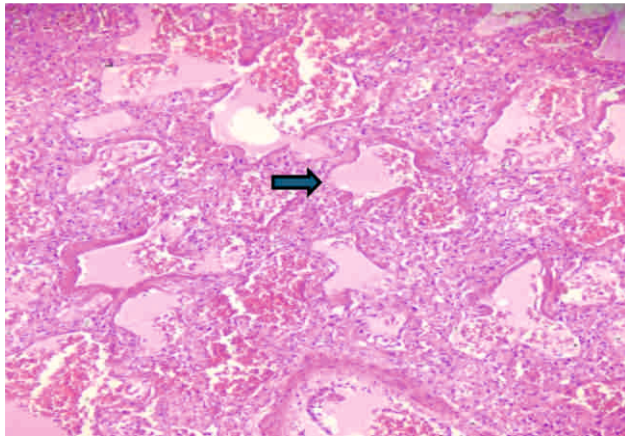


Figure 1: Pulmonary oedema with haemorrhage:
(H&E stain-40X magnification)

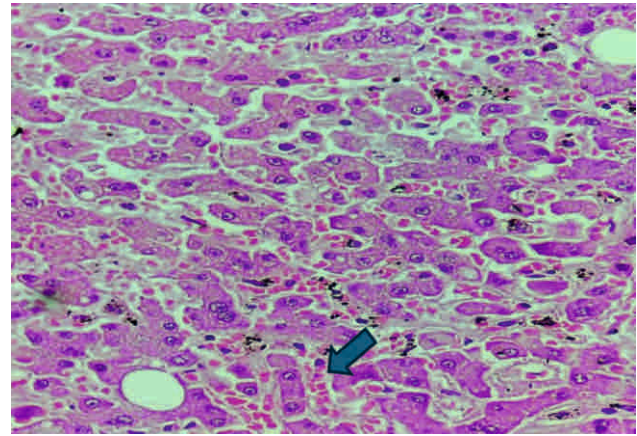


Figure 4: Sinusoidal congestion of the liver:
(H&E stain-40X magnification)

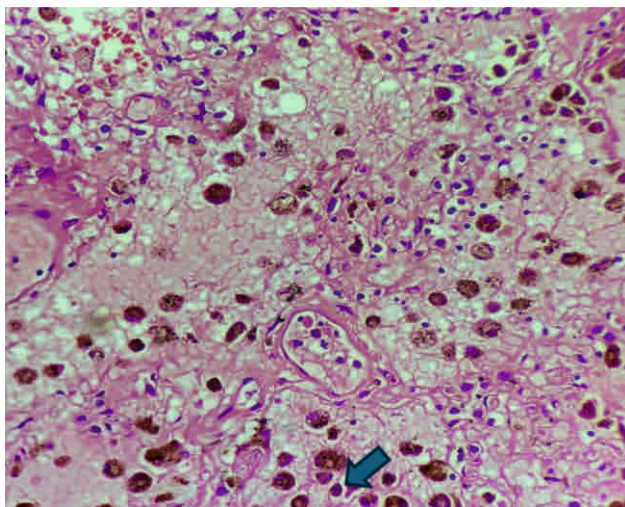


Figure 2: Intra-alveolar haemorrhage leading to deposition of hemosiderin-laden macrophages:
(H&E stain-40X magnification)

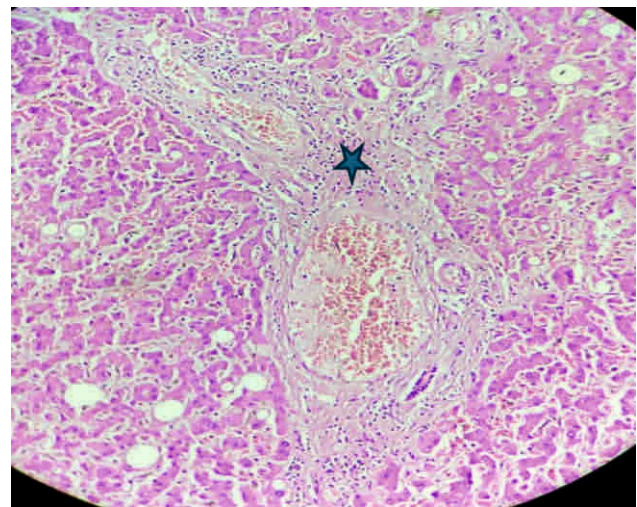


Figure 5: Expansion of portal tract with periportal inflammation:(H&E stain-100X magnification)

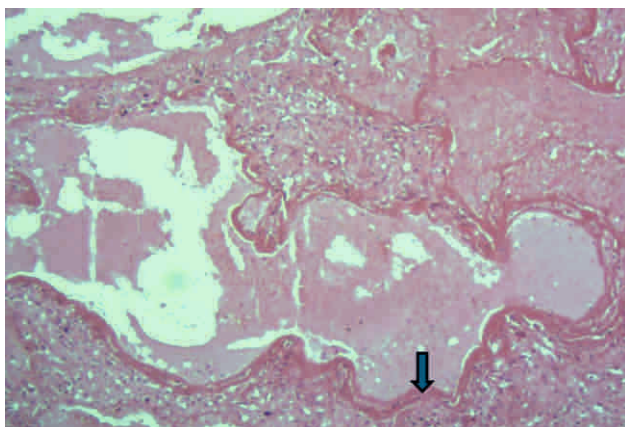


Figure 3: Intra-alveolar oedema with hyaline membrane formation: (H&E stain-100X magnification)

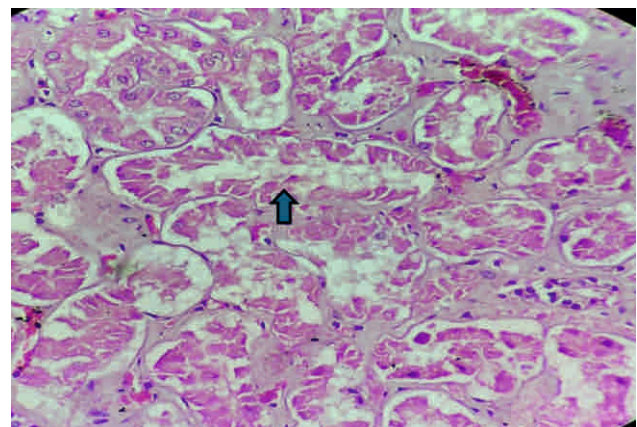


Figure 6: Features of Acute tubular necrosis:
(H&E stain-40X magnification)

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