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Original Research Article

A Study of Acute Inflammation in Paraquat Poisoning and it's Correlation Within-Hospital Outcome

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ABSTRACT

Background
Paraquat poisoning remains a significant health concern with high mortality rates due to its severe multi-organ toxicity.[1] Paraquat (1, 1-dimethyl-4, 4-bipyridium dichloride) ingestion is a major cause of fatal poisoning in South East Asia.[2] Its mortality rate is as high as 50- 90 %.[3] This study aimed to evaluate acute inflammation in Paraquat poisoning and correlate it with in-hospital outcomes, seeking to enhance understanding of the condition's pathophysiology and potential prognostic indicators

Objectives
A. To evaluate acute inflammation in Paraquat poisoning.
B. To correlate acute inflammation in Paraquat poisoning with in-hospital outcome.

Method
This observational study included 50 inpatients with Paraquat poisoning. Clinical manifestations including oral ulcers, renal failure, liver failure, and lung injury were assessed. Inflammatory markers (ESR, CRP, LDH, and ferritin) were measured. Statistical analyses were performed to evaluate the association between these parameters and in-hospital mortality.

Results
The study population was predominantly male (86%) with a mean age of 29.7 years. Oral ulcers, renal failure, and liver failure were present in 98% of patients, while lung injury affected 88%. The overall mortality rate was 88%. Lung injury showed a perfect correlation with mortality ($p<0.001$). Non-survivors had significantly higher levels of inflammatory markers compared to survivors: ESR (51.1 vs 24.7 mm/hr, $p=0.01$), CRP (36.8 vs 7.0 mg/L, $p=0.04$), LDH (461.1 vs 261.2 U/L, $p=0.001$), and ferritin (449.6 vs 233.2 ng/mL, $p=0.001$).

Conclusion
This study proves that, there is a significant and high degree of acute inflammation will be there in acute paraquat poisoning patients. Once again, this study reiterates that acute inflammation could be a major risk factor for the morbidity and mortality of paraquat poisoned patients.

Keywords: Paraquat, Inflammation, Mortality.

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INTRODUCTION

Agrochemicals and pesticides are most commonly implicated in acute poisonings in India.[4] There is more than 90% mortality is found in paraquat poisoning. Even with a variety of therapeutic approaches, it is challenging to improve the prognosis for individuals with severe poisoning.[5] Currently, a number of prognostic indicators, including plasma paraquat levels, have been identified to have prognostic value in the evaluation of individuals with paraquat poisoning.[6,7] However, these prognostic markers cannot be applied widely in numerous hospitals in the developing countries, due to the higher requirement of assay or complicated calculation.

This study was undertaken to know the clinical features, inflammatory biomarkers and their significance in outcome following PQ poisoning. The exact reason are not known. So this study is undertaken to know that, is there any association between acute inflammation with that of morbidity and mortality of acute paraquat poisoning.

OBJECTIVES

- To evaluate acute inflammation in Paraquat poisoning.
- To correlate acute inflammation in Paraquat poisoning with in-hospital outcome.

MATERIALS & METHODS

The present Cross sectional –observational study was conducted on 50 Patient admitted in department of general medicine at Krishna Rajendra hospital, Mysore Medical College and Research Institute, Mysuru from July 2022 – December 2023

Sample Size Estimation

Based on previous study conducted by Mittal C, Singh S, Kumar-M P, Varthya SB. Toxic epidemiology of poisoning exhibited in Indian population from 2010 to 2020: a systematic review and meta-analysis.[8]

Sample size is calculated using the formula.[9]
$N = Z^2PQ/D^2$
Z = Standard table value for 95% confidence interval
PQ = variance of population. Q = 1-P
D = absolute precision

$$N= \frac{1.96*1.96*0.033*0.96}{0.05*0.05} = 48.66$$

Total Sample Size: ~50 subjects

Inclusion Criteria

1. All patients with history of paraquat poisoning aged above 18 years.
2. Patient willing to give informed consent.

Exclusion Criteria

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1. Other pesticide poisoning
2. Chronic liver disease,
3. Malignancy,
4. Chronic kidney disease.
5. Previous history of pulmonary disorders
6. History of drugs like steroid, antimetabolite use.
7. Connective tissue disease.
8. Anemia

Study Procedure

Patient with history of paraquat consumption and passing selection criteria was taken into study, complete clinical examination was done in all of the study subjects. On day one and second, a blood sample was taken from each individual who had swallowed poison.

Following investigations were done : complete blood count(CBC),Renal Function test(RFT) ,Liver function test(LFT), Erythrocyte Sedimentation Rate(ESR), serum Lactate Dehydrogenase(LDH), C-Reactive Protein(CRP), serum Ferritin. Throughout their hospital stay, the individuals were monitored, and the results were documented using the predesigned proforma.

The information was entered in excel sheet and analyzed using the relevant statistical approach.

Reference range: a. LDH= 150 -250U/L, b. ESR =0-9 mm/hr in males, 0-20mm/hr in females. **c.** In adults; 100-250ng/ml. d. <0.3mg/dl = normal value of CRP.

Statistical Analysis

Data obtained from the study will be entered in excel sheets and it will be double checked. Data analysed using SPSS software version 29.0.2.0 By IBM Corp, New York, United States Of America and will be presented as descriptive statistics in the form of frequency tables, figures and graphs. Association between variables will be done using chi-square test and unpaired t test for qualitative and quantitative variables. Results will be expressed as mean ± SD. A p value of <0.05 is considered statistically significant.

RESULTS

The study was conducted on 50 subjects. The majority of patients (52%) were between 21-30 years old, with a mean age of 29.7 years (SD 7.8). In our study gender distribution was heavily skewed towards males, with 86% of participants being men. 49 (98%) subjects had oral ulcers, liver dysfunction, acute kidney injury. 44(88%) had lung injury. Out of 50 subjects who have consumed paraquat, 44(88.0%) subjects succumbed to death [table 1]. Most of the subjects had elevated inflammatory markers as depicted in Table 2

Demographic Parameters		**N (%)**
Age (in years)	18-20	6(12.0)
	21-30	26(52.0)
	31-40	15(30.0)
	41-50	2(4.0)
	51-60	1(2.0)
Gender	Male	43(86.0)

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	Female	7(14.0)
Clinical Features	PRESENT [N (%)]	ABSENT [N (%)]
Oral ulcers	49(98.0)	1(2.0)
Acute kidney Injury	49(98.0)	1(2.0)
Liver Dysfunction	49(98.0)	1(2.0)
Lung Injury	44(88.0)	6(12.0)
Outcome	Death	44 (88.0)
	Survived	6(12.0)

Table 1: Showing distribution of study subjects based on demographic, clinical presentation and outcome

Variables	Mean	SD	Minimum	Maximum
Age (years)	29.7	7.8	18	55
ESR (mm/hr)	47.9	25.7	10	110
CRP (mg/L)	33.2	41.4	3	269
LDH (U/L)	437.1	268.9	126	1723
Ferritin (ng/mL)	423.6	285.8	30.4	1063

Table 2: Clinical characteristics of the study markers (N=50)

Clinical characteristics of the study markers is depicted in Table 2. The mean (SD) age of the study participants was 29.7 (7.8) years. The mean (SD) ESR was 47.9 (25.7) mm/hr. The mean (SD) CRP, LDH and ferritin were 33.2 (41.4) mg/L, 437.1 (268.9) U/L and 423.6 (285.8) ng/mL respectively.

Oral Ulcers	**Outcome**		**P value**
	Survived	Death	
Present	5 (83.3)	44 (100)	**<0.001**
Absent	1 (16.7)	0 (0.0)	
Total	**6 (100)**	**44 (100)**	

Table 3: Association of oral ulcers with outcome among the study participants (N=50)

**Chi-squared test*

Among patients who survived 83.3% (n=5) had oral ulcers and among patients who died 100% (n=44) had oral ulcers. This difference was statistically significant (p <0.001).

Renal failure	**Outcome**		**P value**
	Survived	Death	
Present	5 (83.3)	44 (100)	**<0.001**
Absent	1 (16.7)	0 (0.0)	
Total	**6 (100)**	**44 (100)**	

Table 4. Association of renal failure with outcome among the study participants (N=50)

**Chi-squared test*

Among patients who survived 83.3% (n=5) had renal failure and among patients who died 100% (n=44) had renal failure. This difference was statistically significant (p <0.001).

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Liver failure	Outcome		P value
	Survived	Death	
Present	5 (83.3)	44 (100)	**<0.001**
Absent	1 (16.7)	0 (0.0)	
Total	**6 (100)**	**44 (100)**	

Table 5: Association of liver failure with outcome among the study participants (N=50)

**Chi-squared test*

Among patients who survived 83.3% (n=5) had liver failure and among patients who died 100% (n=44) had liver failure. This difference was statistically significant (p <0.001).

Lung Injury	Outcome		P value
	Survived	Death	
Present	0 (0.0)	44 (100)	**<0.001**
Absent	6 (100)	0 (0.0)	
Total	**6 (100)**	**44 (100)**	

Table 6: Association of lung injury with outcome among the study participants (N=50)

**Chi-squared test*

Among patients who survived, 0% (n=5) had lung injury and among patients who died 100% (n=44) had lung injury. This shows lung injury has poor prognosis .This difference was statistically significant (p <0.001).

Variables	Mean (SD)		P value
	Survived	**Death**	
ESR (mm/hr)	24.7 (9.5)	51.1 (25.6)	**0.01**
CRP (mg/L)	7 (4.5)	36.8 (42.9)	**0.04**
LDH (U/L)	261.2 (86.1)	461.1 (276.8)	**0.001**
Ferritin (ng/mL)	233.2 (108.4)	449.6 (293.2)	**0.001**

Table 7: Association of clinical characteristics of study markers with the outcome among the study participants (N=50)

**Independent t test*

Association of clinical characteristics with the outcome among the study participants is depicted in Table 13. The mean (SD) age of patients who survived was 29.3 (7.3) years and among patients who died was29.8 (7.9) years. The mean (SD) ESR of patients who survived was 24.7 (9.5) mm/hr and among patients who died was 51.1 (25.6) mm/hr. This difference was statistically significant (p=0.01). The mean (SD) CRP of patients who survived was 7 (4.5) mg/L and among patients who died was 36.8 (42.9) mg/L. This difference was statistically significant (p=0.04). The mean (SD) LDH of patients who survived was 261.2 (86.1) U/L and among patients who died was 461.1 (276.8) U/L. This difference was statistically significant (p=0.001). The mean (SD) ferritin of patients who survived was 233.2 (108.4) ng/mL and among patients who died was 449.6 (293.2) ng/mL. This difference was statistically significant (p=0.001).

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DISCUSSION

This study was conducted to look for the acute inflammation in paraquat poisoning and their correlation with the in-hospital outcome. In this study, we found that, there was significant correlation between the level of acute inflammation with that of poor in-hospital outcome in paraquat poisoning. Paraquat poisoning remains a significant health concern, particularly in agricultural regions where this herbicide is widely used. Despite its effectiveness in weed control, Paraquat's extreme toxicity to humans has led to numerous cases of accidental and intentional poisoning, often with devastating consequences.[10] The lack of a specific antidote and the rapid onset of multi-organ failure in Paraquat poisoning cases present substantial challenges to healthcare providers and have contributed to persistently high mortality rates.[11] The acute inflammatory response triggered by Paraquat ingestion plays a crucial role in the pathophysiology of poisoning and subsequent organ damage. This inflammatory cascade, involving both local and systemic reactions, is believed to be a key factor in determining patient outcomes.[12]

The findings of this investigation not only contribute to the existing body of knowledge on Paraquat toxicity but also highlight the urgent need for improved management protocols and preventive measures.

In this study, we found that majority of patients (52%) were between 21-30yrs of age with mean age of 29.7 yrs. it was correlated with study conducted by Delirrad et al found out that that a significant number of patients poisoned by paraquat were aged between 21 and 30 years (46.3%), with a median age of 25 years.[13] Another study conducted by Ravichandran R et al. also had majority of study sample was falling into age group between 20-40 (69%).[14] This suggests that Paraquat poisoning primarily affects young adults in their most productive years

This study's overwhelming patient population (86%, n=43) was male, in line with a study by M Jagadeesan et al that found 80% of participants were male.[15] Also in study by Wilson W et al had 69% participants were male.[16] In our study gender distribution was heavily skewed towards males, with 86% of participants being men. This significant gender disparity may indicate occupational exposure or other gender-specific risk factors that warrant further investigation.

The majority of patients in this study (98%, n=49) had mouth ulcers, which was consistent with research done at a tertiary care facility in south India by Vadlani VB et al which revealed that 86% of subjects had oral ulcers.[17]

In our study, we found majority of patient (98%, n=49) had acute renal dysfunction and hepatic dysfunction was correlated with study conducted by Jose N et al, where 100% of subjects had acute kidney injury.[18] A study conducted by K Venugopal et al. showed liver dysfunction 76% of the subjects.[19] This finding underscores the importance of early and aggressive renal support in managing these patients.

In our study, we found 88 % of study subjects had lung injury (n=44) was correlated with study conducted by ramamoorthi et al in tertiary care center in south india, which showed 55% of subjects had respiratory failure.[20] Study conducted by Kwon-Hyun Lee et al had 62 % of subjects had respiratory failure.[21] Lung injury showed a perfect correlation with mortality. All patients who died (100%) had lung injury, while none of the survivors did. This suggests that lung injury may be a critical determinant of survival in Paraquat poisoning.

In present study, we compared the acute inflammatory marker i.e CRP among survived and death subjects in paraquat poisoning and it was found that CRP was significantly elevated and had higher values [mean (SD) =36.8(42.9) mg/L] among death individuals than survived with

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statistically significant data (p value <0.04). This observation was correlated with a study by Wang et al.[22] mean CRP for dead patients was 25.4 ± 26.4 and same for alive patients was 19.7 ± 24.8. The acute inflammatory marker, or ESR, was compared in this study between subjects who survived and those who died from paraquat poisoning. The results showed that ESR was significantly higher in the latter group, with a mean (SD) of 51.1(25.6) mm/hr, and that the difference was statistically significant (p value <0.01). This observation was correlated with the mean ESR of 30.14 mm/hr reported in a case report by Yung et al.[23] and a case series report by Ng Tiang seng et al.[24]

In this study, we compared the acute inflammatory marker i.e., LDH among survived and death subjects in paraquat poisoning and it was found that LDH was significantly elevated and had higher values [mean (SD) =461(276.8) U/L] among death individuals than survived with statistically significant data(p value <0.001). This observation was correlated with a study conducted by Y H Tang et al. 2023 which showed elevated LDH was an independent risk factor for the prognosis paraquat poisoning.[25]

In the Present study, we compared the acute inflammatory marker i.e Ferritin among survived and death subjects in paraquat poisoning and it was found that ferritin was significantly elevated and had higher values [mean (SD) =449.6(25.6)ng/ml] among death individuals than survived with statistically significant data(p value <0.001). Literature authored by Saito M et al, says that PQ damaged mitochondria, released free iron from ferritin, and elevated production of reactive oxygen species, resulting in damage to multiple organs.[26]

The study revealed a strikingly high mortality rate of 88% among the participants. This underscores the extreme toxicity of Paraquat and the challenges in managing poisoning cases.

CONCLUSION

This study proves that, there is a significant and high degree of acute inflammation will be there in acute paraquat poisoning patients. Once again, this study reiterates that acute inflammation could be a major risk factor for the morbidity and mortality of paraquat poisoned patients

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