# **ORIGINAL RESEARCH**

# Prognostic Value of Hematological Indices and C-Reactive Protein in Patient with Acute Paraquat Poisoning

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#### Abstract

**Background:** Paraquat poisoning is characterized by acute lung injury, pulmonary fibrosis, respiratory failure, acute kidney injury and multi-organ failure, resulting in a high rate of mortality and morbidity. Several prognostic markers have been found to have prognostic significance in the evaluation of PQ (Paraquat Poisoning) poisoning at present, such as plasma PQ concentration, arterial lactate level, severity scoring system and arterial blood gas analysis and C-reactive protein is an acute phase reactant and its level is positively correlated with the degree of inflammation during the early course of illness. Due to similar inflammatory response in PQ poisoning CBC may also be used as prognostic indicator in patient with PQ poisoning.

**Objective:** To determine the prognostic value of haematological parameters and CRP (C-reactive Protein) in patients with acute paraquat poisoning.

**Method:** It was a prospective observational study done over a period of 1 year (December 2020 to December 2021). The study protocol was approved by the institutional ethics committee at our hospital (IEC Appln. No. 697).

**Observation:** The prognosis of patients with paraquat poisoning based on their SOFA (Sequential Organ Failure Assessment) scores. As many as 40 (80.0%) out of 50 patients were having a SOFA score of less than 6 and only 10 (20.0%) and a score between 7 and 12 at the end of 24 hours. The mean CRP score among patients with multiple organ dysfunction syndrome at 48 hours.

**Conclusion:** NLR, Leukocyte and Neutrophil counts, CRP level may be simple and potentially significant parameters for evaluating prognosis in the patients with PQ poisoning. However, larger prospective studies should be warranted to further confirmation of these findings.

**Key words:** Paraquat Poisoning, Sequential Organ Failure Assessment, C-reactive Protein, Multiple Organ Dysfunction Syndrome.

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# Introduction

Paraquat is the most highly acutely toxic herbicide to be marketed over the last 60 years. Yet it is one of the most widely used herbicides in the world, and in most countries where it is registered it can be used without restriction. Paraquat (PQ is a bipyridilium quaternary ammonium herbicides, is a bright green corrosive liquid with pungent smell. Its herbicidal properties were discovered in 1955 and first marketed in 1962. <sup>[1,2]</sup>In many developing country PQ is widely available and inexpensive, making poisoning prevention difficult and becoming a major source of health hazard. Hence it is important for the clinicians to be familiar with the entire spectrum of symptoms, approach and poor prognostic features of this type of poisoning.

Renal failure, cardiac arrhythmias, coma, convulsions and esophageal perforation leads to death. Highly toxic via ingestion, one teaspoonful of paraquat is fatal under these circumstances; paraquat death from multiple organ failure may follow within hours or days. There is no antidote for paraquat poisoning. In spite of its high toxicity, morality and the lack of an antidote the WHO classified paraquat only as moderately hazardous.<sup>[3]</sup>

The exact mechanism of PQ toxicity is not completely known, however clinical features are mainly due to intracellular toxic effect.<sup>[4]</sup>PQ generates reactive oxygen species which cause cellular damage via lipid peroxidation, activation of NF-kB, mitochondrial damage and adoptosis in many organ. In addition, inflammatory response is the initial and main mechanism of tissue injury after PQ poisoning.<sup>[5]</sup>

The very high case fatality of PQ is due to its inherent toxicity and the lack of any effective treatment. There are no widely accepted guidelines on mortality remain >50% in centers routinely practicing such intensive measures.<sup>[6, 7]</sup> Therefore, a reliable predictor of prognosis may be helpful to guide treatment and future clinical research on antidotes and other therapies.

Several prognostic markers have been found to have prognostic significance in the evaluation of PQ poisoning at present, such as plasma PQ concentration, arterial lactate level, severity scoring system and arterial blood gas analysis. 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. <sup>[8]</sup>C-reactive protein (CRP) is an acute phase reactant and its level is positively correlated with the degree of inflammation during the early course of illness. <sup>[9]</sup>

When the complete blood count (CBC) is evaluated during the acute inflammatory response due to oxidative stress, an increase in leukocyte and neutrophil counts, where as a decline in lymphocyte counts were observed. Due to similar inflammatory response in PQ poisoning CBC may also be used as prognostic indicator in patient with PQ poisoning. <sup>[10-12]</sup> Therefore, the aim of the study is to investigate the potential role of Hematological parameter and CRP as prognostic marker in patients with paraquat poisoning.

# Aim

To determine the prognostic value of haematological parameters and CRP in patients with acute paraquat poisoning.

# Material & methods

This study was conducted in Department of Medicine, Sri Rama Chandra Bhanja Medical College and Hospital, Cuttack. It was a prospective observational study done over a period of 1 year (December 2020 to December 2021). The study protocol was approved by the institutional ethics committee at our hospital (IEC Appln. No. 697). Informed consent was obtained from the patients and / or their family members. Total 50 patients enrolled in this study. All patients were managed under a standard clinical treatment protocol, which involves

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gastric lavage, hemoperfusion or haemodialysis, antioxidants (vitamin-E, vit-C, N-acetyl cystine), high-dose intravenous methyl-prednisolone followed by dexamethasone and other general treatment methods. Patients were followed up until hospital discharge or death. Our study **"Prognostic Value of Hematological Indices and C-Reactive Protein in Patients with Acute Paraquat Poisoning"** surely aim in making or correcting the protocol for treatment of acute paraquat poisoning and also in reducing the morbidity and mortality of the patients admitted of acute paraquat poisoning.

#### **Inclusion Criteria**

#### Case

Any person aged more than 15 years with PQ poisoning admitted to medicine ward, SCB MCH from December 2020 to December 2021 within 48 hours of systemic exposure to PQ as indicated by a positive urine dithionite test and whose caregivers are willing to give written informed consent.

### **Exclusion Criteria**

- 1. Mixed poisoning.
- 2. Other non-paraquat herbicide poisoning.
- 3. Other routes of poisoning (skin, ear, eye)
- 4. Know medical illness like CKD, CLD, ILD, COPD, CAD, Malignancy organ transplantation, Autoimmune disorder.
- 5. Age <15 year
- 6. Pregnancy
- 7. HIV, HBsAG, HCV positive patients.

### Method

Ethical clearance was obtained from institutional ethical committee. Written informed consent was taken from caregiver. Patients admitted to the medicine department with paraquat compound consumption was confirmed by urine dithionate screening test. Detailed history and clinical examination was done and noted as per predesigned proforma. In all study subject sample were collected for CBC, LFT, RFT, viral markers, urine RE/ME and other routine investigations was done. Worsening of symptoms and organ system involvement was noted. Blood sample for CBC was collected very alternate day and CRP was collected on the day of admission, day 7, day 14 of ingestion of poison. Chest X-ray, ECG, and arterial blood gas analysis was done.

### Statistical analysis

The data collected for different heamotological values and the complications were noted and mean values plotted in different times 24 hours, 48 hours and 72 hours and classified. One-way ANOVA was done with post-hoc analysis. The association of different variable with the prognosis were analysis by Pearson's Chi-square test and Independent sample t-test. The significance was noted with p-value <0.005. The analysis was done with the help of SPSS 22.

Table 1: Demography & Clinical Characteristics						
Age Group	Numbers	Percentage (%)				
<20 years	09	18%				
20 to 40 years	31	62%				
40 to 60 years	10	20%				

### Results

Male	32	64%
Female	18	36%
(time arrival at the hospital) <6 Hrs.	11	22.0
6 to 24	34	68.0
>24	05	10.0
Barely distinguishable blue(1+) (urine, serum, dithinoite test)	04	8.0
Light blue (2+)	30	60.0
Dark blue (3+)	16	32.0
Black (4+)	00	00

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Table 1 shows the demography and clinical distribution of study participants. Majority of males were between 20 to 40 years of age i.e. 23 (69.7%) while near about equal proportion of females were less than 20 years and between 20 to 40 years of age i.e. 07 (41.2%) and 08 (47.1%) respectively. Majority of patients were males i.e., 32 (64.0%) while rest were females. Urine dithionite test for patients admitted with paraquat poisoning. Majority of patients i.e. 30 (60.0%) had light blue coloration of urine upon performing this test while none of the patients had a black colour. The time lapse between poisoning and arrival at hospital. More than half of the patients i.e. 34 (68.0%) arrived at the tertiary care centre after 6 to 24 hours of the incident. A small proportion of patients i.e. 05 (10.0%) reached the hospital after 24 hours of the incident.

Table 2: Mean Values of Laboratory Characteristics with Different Times									
Laboratory Values	24 hours	48 hours	72 hours	95% Confident interval	p-value				
Blood pH	7.36	7.27	7.20	(7.310-7.411)	< 0.001				
Partial pressure of									
arterial oxygen	93.97	134.79	124.87	(76.66 – 111.27)	0.004				
$(PaO_2)$									
PaCO <sub>2</sub>	42.83	42.94	42.53	41.80 - 43.87	0.861				
Bicarbonate levels (HCO <sub>3</sub> )	23.05	21.38	20.50	(22.28 – 23.82)	< 0.001				
PaO <sub>2</sub> /FiO <sub>2</sub>	389.30	356.73	336.25	(364.03 - 414.58)	0.018				
Total Leucocyte count (TLC)	13294.96	14694.00	19201.77	(11124.83 - 15465.08)	0.001				
Neutrophil Count	82.42	86.92	89.18	(80.46 - 84.38)	< 0.001				
Lymphocytes	12.24	8.78	8.88	(10.33 - 14.14)	0.019				
Platelets	2.42	2.26	2.36	(2.10 - 2.75)	0.776				
Hb	12.59	11.89	11.00	(12.21 – 12.98)	< 0.001				
NLR	9.37	13.32	16.47	(7.03 – 11.70)	< 0.001				
Urea	70.20	104.38	111.93	(61.43 – 78.96)	< 0.001				
Creatinine	3.27	4.95	5.78	(2.49 - 4.05)	< 0.001				
Bilirubin	2.47	3.36	4.02	(1.76 - 3.17)	0.013				
CRP	33.79	56.21	22.48	(25.72 – 41.87)	< 0.001				
MAP	86.98	85.64	84.84	(84.09 - 89.87)	0.593				
SOFA Score 7 – 12	10	18	20	(10 - 20)	0.029				

Table 2 depicts the mean values of pH of paraquat poisoning patient at times following admission using One-way ANOVA. Following Tukeys post-hoc analysis, it was evident that the mean pH was significantly lower in the patients at 72 hours i.e.  $7.20 \pm 0.26$  as compared

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to the values after 24 hours of admission i.e.  $7.36 \pm 0.08$  at F(2.8.118) and p > 0.001. The mean differences in the partial pressure of oxygen of patients at different times following admission using One-way ANOVA. A significant difference was observed upon post-hoc analysis between the mean PaO<sub>2</sub> at 24 hours and 48 hours at F 2.5.876) and p value of 0.004. The mean difference in the partial pressure of arterial CO<sub>2</sub> of patients at different times following admission using One-way ANOVA. There was no significant difference between the PaCO<sub>2</sub> levels at 24, 48 and 72 hours following admission, however a downward trend was observed with increasing time. The mean difference in the bicarbonate levels (HCO<sub>3</sub>) among patients at different times following admission using One-way ANOVA. There was a significant decrease in the bicarbonate levels between 24 hours and 72 house i.e.  $23.05 \pm 1.73$ mg/dL to  $20.50 \pm 3.42$  mg/dL respectively with F(2, 10.518) and p > 0.001. The mean difference in the PaO<sub>2</sub>/FiO<sub>2</sub> of patients at different times following admission using One-way ANOVA. There was a significant decrease in the PaO<sub>2</sub>/FiO<sub>2</sub> levels from 24 hours to 72 hours i.e.  $389.30 \pm 61.27$  to  $336.25 \pm 10.9.39$  with F (2, 4.150) and p value of 0.018. The mean difference in the levels of leucocytes among PQ poisoning of patients at different times following admission using One-way ANOVA. There was a significant increase in the man leucocyte count from 24 hours and 72 hours i.e. 12394.96  $\pm$  4697.46/cumm and 19201.77  $\pm$ 11560.66/cumm with F (2, 7.282) and p value 0.001. The mean difference in the neutrophil counts of patients at different times following admission using One-way ANOVA. There was a significant increase in neutrophil count from  $82.42 \pm 8.16$ /cumm to  $89.18 \pm 5.72$ /cumm between 24 hours and 72 hours respectively with f (2, 11.481) and p<0.001. The mean difference in the Lymphocyte counts of patients at different times following admission using One-way ANOVA. There was a marked decrease of mean lymphocyte counts from 12.24  $\pm$ 6.09/cumm to 8.88  $\pm$ 9.15/cumm from 24 to 72 hours respectively with f(2, 4.093) and p value of 0.019. The mean difference in the platelet counts of patients at different times following admission using One-way ANOVA. Upon Tukeys post-hoc analysis, no significant difference was observed in the total platelet count at times of observation. The mean difference in the Haemoglobin (Hb) of patients at different times following admission using One-way ANOVA. Upon post-hoc analysis using Tukey test, a significant decrease was found between the haemoglobin levels at 24 hours and at 72 hours i.e.  $12.59 \pm 1.26$  gm/dL and 11.00 is  $\pm$  1.44 gm/dL respectively with f(2, 15.438) and p<0.001. The mean difference in the Neutrophile-Lymphocyte ratio i.e. NLR of PQ poisoning of patients at different times following admission using One-way ANOVA. Upon Tukeys post-hoc analysis, it was found that there was a significant increase in the NLR from  $9.37 \pm 6.62$  to  $16.47 \pm 10.67$  between 24 and 72 hours respectively with F (2, 8.543) and p<0.001. The mean difference in the serum urea levels of patients at different times following admission using One-way ANOVA. There was a remarkable increase in the serum urea levels from  $70.20 \pm 31.56$ mg/dLto  $111.93 \pm 32.23$  mg/dL between 24 and 72 hours respectively with F(2, 24.319) and p<0.001. The mean difference in the serum creatinine levels of patients at different times following admission using One-way ANOVA. Upon Tukeys post-hoc analysis, it was observed that there was a significant difference of serum creatinine levels measured at 24 and 72 hours i.e.  $3.27 \pm 2.64$  mg/dL and  $5.78 \pm 3.33$  mg/dL respectively with F(2, 10.137) and p<0.001. The mean difference in the serum bilirubin levels of patients at different times following admission using One-way ANOVA. There was a marked increase in serum bilirubin levels from 2.47  $\pm$  1.54 mg/dL to 4.02  $\pm$ 3.44 mg/dL as observed at 24 and 72 hours respectively with F(2, 4.483) and p value of 0.013. The mean difference in the CRP levels of patients at different times following admission using One-way ANOVA. There was a marked increase in the CRP levels from  $33.79 \pm 26.41 \text{ mg/dL}$  to  $56.21 \pm 38.01 \text{ mg/dL}$  between 24 and 72 hours followed by a drop in CRP levels to  $22.48 \pm 17.11$  at the end of one week. This finding was statistically significant at F(16.823) and p<0.001. The mean difference in the

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Mean Arterial Pressure among patients at different times following admission using Oneway ANOVA. There was a decrease in the mean arterial pressure with increase in hospital stay but the results were not statistically significant. The prognosis of patients with paraquat poisoning based on their SOFA scores. As many as 40 (80.0%) out of 50 patients were having a SOFA score of less than 6 and only 10 (20.0%) and a score between 7 and 12 at the end of 24 hours. But the proportion of patients with SOFA scores between 7 to 12 increased to 20 (45.5%) at the end of 72 hours. These findings were statistically significant with p value 0.029.

Table 3: Requirement of Mechanical Ventilation								
Mechanical ventilation	Ν	Mean SOFA Score	SD	SE mean	t-value	p-value		
Yes	34	5.11	2.02	0.34	5 150	0.029		
No	16	2.31	1.13	0.28	5.150	0.028		

Table 3 shows the mean SOFA scores of patients based on their status of mechanical ventilation. Those patients, who were on mechanical ventilation, had a higher mean SOFA score i.e.  $5.11 \pm 2.02$  in contrast to a mean SOFA score of  $2.31 \pm 1.13$  of their counterparts. This finding was statistically significant with p value of 0.028.

Table 4: Requirement Of Haemodialysis								
Haemodialysis	Ν	Mean SOFA Score	SD	SE mean	t-value	p-value		
Yes	48	4.31	2.21	0.31	1 462	0.029		
No	02	2.00	0.00	0.00	1.405	0.028		

Table 4 shows the mean SOFA scores of patients distinguished on their status of haemodialysis. Those mean SOFA score of patients on haemodialysis was significantly higher i.e.  $4.31 \pm 2.21$  than those were not i.e.  $2.00 \pm 000$  with p-value of 0.028.

Table 5: Clinical parameters of PQ patients with ARDS and NARDS at 48 hours							
		Ν	Mean	SD	SE <sub>mean</sub>	t-value	p-value
SOEA Score	ARDS	16	8.86	1.35	0.33	0.177	0.281
SOFA Scale	NARDS	34	4.44	1.59	1.21	9.177	0.301
Loucoautos	ARDS	16	17703.12	6525.81	1631.45	2 652	0.052
Leucocytes	NARDS	34	13277.94	4970.32	852.40	2.032	0.055
Noutrophile	ARDS	16	91.43	3.94	0.98	2 607	0.033*
Neutrophils	NARDS	34	84.79	6.82	1.17	5.007	
Lymphoaytag	ARDS	16	5.43	2.33	0.58	2.940	0.002*
Lymphocytes	NARDS	34	10.35	4.84	0.83	5.840	0.002*
	ARDS	16	2.34	0.77	0.19	0.651	0.038*
Platelets	NARDS	34	2.22	0.46	0.36	0.031	
Uh	ARDS	16	11.38	1.44	0.36	1 751	0.742
по	NARDS	34	12.13	1.40	0.24	1./31	
NI D	ARDS	16	19.74	8.12	2.03	5.054	0.042*
INLK	NARDS	34	10.29	5.02	0.86	3.034	0.042**
Linco	ARDS	16	128.87	15.79	3.94	1 600	0.010*
Orea	NARDS	34	92.85	28.65	4.91	4.000	0.012**
S.Creatinine	ARDS	16	7.23	1.95	0.48	6 192	0.254
	NARDS	34	3.88	1.57	0.27	0.465	0.234
C Dilimitin	ARDS	16	5.56	2.53	0.63	5 700 0.005	
S.Bilirubin	NARDS	34	2.33	1.46	0.25	3.720	0.003*

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CDD	ARDS	16	97.21	35.56	8.89	2.691	0.015
NAF NAF	NARDS	34	36.92	19.30	3.31		
ΜΑΡ	ARDS	16	83.37	15.35	3.83	1.055	0.007*
MAP	NARDS	34	86.70	7.11	1.21	1.055	0.007*

Table 5 depicts the mean difference of various patients parameters with acute respiratory distress syndrome (ARDS). The mean neutrophil counts, total platelet counts. NLR, serum urea and serum bilirubin levels were significantly higher among patients suffering from ARDS following paraquat poisoning in comparison to their counterparts. In contrast, the mean total lymphocyte counts and the mean arterial pressure were found to be significantly lower among those suffering from ARDS.

Table 6: Complications of PQ Poisoning							
Complications	Ν	%					
Metabolic acidosis	32	72.7					
AKI	43	97.7					
ARDS	15	34.1					
MODS	27	61.4					

Table 6 shows the various complication diagnosed among paraquat poisoning patients at the end of 72 hours of admission. Acute kidney injury was encountered in 43 (97.7%) of patients, followed by metabolic acidosis i.e. 32 (72.7%) and MODS (Multiple Organ Dysfunction Syndrome) i.e. 27 (61.4%)



Table 7: Factors associated with MODS Patients							
Characteristics	MODS (yes)	MODS (No)	p-value				
Means CRP at 48 Hrs.	67.34	42.05	< 0.001				
Means NLR at 48 Hrs.	15.03	11.14	0.138				
Mean Neutrophils at 48 Hrs.	88.21	85.27	0.251				
Mean TLC at 48 Hrs.	15135.71	14131.81	0.165				

Table 7 show the mean CRP score among patients with multiple organ dysfunction syndrome at 48 hours. The mean CRP score was significantly higher among those with MODS as compared to their normal counterparts with p<0.001. The mean NLR among patients with

MODS. The mean NLR among patients with MODS was observed to be higher than those who did not have MODS. However, these findings were not statistically significant. The mean neutrophils levels among patients with MODS. The mean neutrophile level was found to be higher among those with MODS as compared to those who don't but these results were not statistically significant. The mean TLC levels among patients with MODS. The mean TLC level was found to be higher those MODS as compared to those who don't but these results were not statistically significant.

#### Discussion

The present study was carried out in department of medicine of a tertiary care hospital located in Eastern Odisha. A total of 50 study participants who reported to the OPD and casualty following paraquat poisoning were recruited for the study. During the study, out of 50 patients, 2 were lost to follow-up subjecting to LAMA i.e., Leaving Against Medical Advice. Universally, all the patients admitted with PQ poisoning were managed with Inj. Methylprednisolone, Inj. Dexamethasone, Inj. Vitamin-C, Inj. N-Acetyl cysteine along with haemodialysis and mechanical ventilation when needed.

Majority of males were between 20 to 40 years of age i.e. 23 (69.7%) while near about equal proportion of females were less than 20 years and between 20 to 40 years of age i.e. 07 (41.2%) and 08 (47.1%) respectively. These findings were statistically significant with p-value of 0.009. More than half of the patients i.e. 34 (68.0%) arrived at the tertiary care centre after 6 to 24 hours of the incident. In contrast to our findings, in a study conducted by Zhou CD et.al<sup>[10]</sup> for assessing the haematological parameters among paraquat poisoning patients, they observed that 62.38% patients were females and the median time interval between ingestion of poison and hospitalization was 6.50 hours. Majority of patients i.e. 30 (60%) had light blue coloration of urine upon performing this test while none of the patients had a black colour. This is in contrast to the findings of Zhou CD et.al<sup>[10]</sup>, where a significant proportion had grade 3+ and 4+ urine coloration on dithionite test. However, our study findings were consistent with the findings of studies conducted by Gawaramnna I et. al<sup>[6]</sup> and Ayala BT et.al<sup>[13]</sup> upon paraquat poisoning patients.

In the present study the mean pH was significantly lower in the patients at 72 hours i.e. 7.20  $\pm$  0.26 are compared to the values after 24 hours of admission i.e., 7.36  $\pm$  0.08 at F(2, 8118) and p<0.001. Also there was a significant difference between the mean PaO<sub>2</sub> at 24 hours and 48 hours with p-value of 0.004 as well as the bicarbonate levels between 24 hours and 72 hours i.e. 23.05  $\pm$  1.73 mg/dL and 20.50  $\pm$  3.42 mg/dL respectively with p<0.001. There was a significant decrease in the paO<sub>2</sub>/FiO<sub>2</sub> levels from 24 hours to 72 hours. In a study conducted by Huang C et.a;<sup>[14]</sup> over the prognostic significance of arterial blood gas analysis for early evaluation of paraquat poisoning patients, it was observed that arterial pH was significantly lower after 3 days of poisoning similar to our findings. Several studies conducted by Liu X et.al<sup>[15]</sup> and Weng CH et.al<sup>[16]</sup> found results which are at par with our findings.

There was significant increase in the mean leucocyte count, total neutrophil count and Neutrophil-Lymphocyte ratio at 72 hours of admission as compared to day 01, with p-value of <0.001. Also there was a significant increase in serum urea, creatinine as well as bilirubin levels with p<0.001 and 0.013 respectively. But, on the other hand, there was a significant decrease in total lymphocyte count on day 03 as compared to day 01 with p-value of 0.019. The mean neutrophile counts, total platelet counts, NLR, Serum Urea and Serum Bilirubin levels were significantly higher among patients suffering from ARDS following paraquat poisoning in comparison to their counterparts. On the other hand, there was a marked decrease of mean lymphocyte counts with p-value of 0.019 and haemoglobin levels with p<0.001. These findings are at par with other similar studies conducted by Huang NC et.al<sup>[17]</sup>,

Zhou CD et.al<sup>[10]</sup> and Weng CH et.al<sup>[16]</sup> involving assessment of various haematological parameters for assessing the prognosis of paraquat poisoning patients. In another study conducted by Feng MX et.al<sup>[18]</sup> for assessing the predictive value of the maximum serum creatinine value in acute paraquat poisoning patients, a significant elevation of serum creatinine levels was observed. Our findings are corroborative with other studies conducted by Sengler R et.al<sup>[19]</sup> who claimed that rate of change of serum creatinine levels might be beneficial in paraquat poisoning patients. Another study by Mohamed et.al<sup>[20]</sup>, it was stated that other markers of kidney injury like neutrophil gelatinase associated lipocalin (NGAL) might be helpful in assessing AKI. In another study conducted by Cao ZX et.al<sup>[21]</sup>, it was observed that NLR was a reliable early predictor for patients with acute paraquat poisoning. In a study conducted by Pasha SA et.al<sup>[22]</sup>, for assessing the role of Liver Function Tests and Serum Lactate Levels in predicting the Severity of acute Paraquat Poisoning, it was observed that the mean serum bilirubin and cratinine levels were significantly higher among survivors as compared to non-survivors. This highlights the importance of LFTs for assessing the severity of acute paraquat poisoning. Similarly, in a study by Sharma DS et.al<sup>[23]</sup>, they found that a substantial proportion of patients with acute paraquat poisoning have developed hepatic complications.

There was a remarkable increase in the CRP levels from  $33.79 \pm 26.41$  mg/dL to  $56.21 \pm$ 38.01 mg/dL between 24 and 72 hours followed by a drop in CRP levels to  $24.81 \pm 20.49$  at the end of one week. This findings was statistically significant at F(2, 15.309) and p<0.001. There was a decrease in the mean arterial pressure with increase in hospital stay but the results were not statistically significant. These findings were identical to the observations of various other similar studies conducted by Bismuth C et.al<sup>[24]</sup> and Berry DJ et.al<sup>[25]</sup>. Our findings is in contrast to the findings of Zhang Yu et.al<sup>[12]</sup>, where the peak levels of CRP were observed on day 01. They also observed that the CRP levels were significantly higher among non-survivors as compared to survivors. In another study conducted by Ning Z et.al<sup>[8]</sup> for assessing the prognostic value of plasma C-reactive protein in the evaluation of paraquat poisoning patients, it was found that that serum CRP levels were positively correlated with plasma paraquat levels (r = 0.625, p = 0.013). Also, the CRP levels were highly elevated among the non-survivors suggesting greater inflammatory response in comparison to survivors. In a study conducted by Zhang Yu et.al<sup>[12]</sup> for assessing the Prognostic Value of White Blood Cell Count, C-reactive protein, and Pentraxin-3 levels in patients with Acute Paraquat Poisoning, it was observed that there was a significant increase in CRP, Pentrain-3 and WBC levels among non-survivors on day 1 of admission which might be used for predicting survival of patients.

As many as 40 (80.0%) out of 50 patients were having a SOFA score of less than 6 and 10 (20.0%) had a score between 7 and 12 at the end of 24 hours. But the proportion of patients with SOFA scores between 7 and 12 increased to 20 (45.5%) at the end of 72 hours. These findings were statistically significant with p-value 0.029. Another study conducted by Sawada et.al<sup>[26]</sup> claimed SIPP i.e. Severity Index of Paraquat Poisoning might be a good clinical predictor of mortality. Patients on mechanical ventilation and on haemodialysis had a significantly higher mean SOFA score i.e.  $5.11 \pm 2.02 4.31 \pm 2.21$  respectively as compared to their counterparts identical to the findings of a study conducted by Proudfoot AT et.al<sup>[27]</sup>. Similar results were found in studies conducted by Liu XW et.al<sup>[28]</sup> and Weng CH et.al<sup>[16]</sup>. Acute kidney injury was encountered in 43 (97.7%) of patients, followed by metabolic acidosis i.e., 32 (72.7%) and MODS i.e. 27 (61.4%) similar to the findings of Zhou CD et.al10. Equal proportion of patients succumbed to death within 3 to 7 days and 15 to 30 days while 07 patients i.e. 16.0% lost their lives after 30 days of poisoning. In total 88.0% were non-survivors in our study which is much higher than the findings observed in a study by Ning Z et.al<sup>[8]</sup>, where only 46.2% were non-survivors. In the study conducted by Iskander

KN et.al<sup>[29]</sup>, WBC was observed to be associated with higher risk of multi-organ failure as well as mortality. In another study by Zhang Yu et.al<sup>[12]</sup>, it was observed that higher WBC levels were significantly associated with mortality on day 01 of admission. However, no such significant association was found with the survival status of patients on day 03. Thus WBC levels might be used as a reliable prognostic indicator for assessing the survival status of patients upon admission.

### Conclusion

Serum PQ concentration detection is not available in most of the hospitals, and the amount of ingestion is often difficult and unreliable to estimate, particularly in patients presenting with confusion. For this reason, we want to find out potential and simple parameters for estimating prognosis in acute PQ poisoning patients. The complete blood count, Renal and Liver function test are routine haematological parameters done in patients presenting with acute PQ poisoning. It is important to note that these results are quick, inexpensive and available in almost all hospital, including local hospitals.

In present study, we found that PQ could cause leukocytosis, neutrophilia and lymphocytopenia, high NLR in acute poisoning patients. Moreover, we found non-survivors had significantly higher leukocyte, neutrophil counts, high NLR ratio were as there was no significant difference in platelet counts compared to survivor. In the present study, we observed that plasma CRP level was increased in patients with paraquat poisoning, ad the level was significantly higher in non-survival patients compared with those survivals. This study result indicates that SOFA Score at 48 hours are significantly associated with mechanical ventilation, hemodialysis and ARDS; also there is a significant correlation of Leukocytosis, neutrophilia and lymphocytopenia, increased NLR ratio and RP level with non-survivors. Thus we concluded that NLR, Leukocyte and Neutrophil counts, CRP level may be simple and potentially significant parameters for evaluating prognosis in the patients with PQ poisoning. However, larger prospective studies should be warranted to further confirmation of these findings.

# Reference

- 1. Dinis-Oliveria, R.J., Remiao, F., Durate, J. A., Sanchez-Navarro, A., Bastos, M.L., and Carvalho, F. (2006). P-glycoprotein induction : an antidotal pathway for paraquat induced lung toxicity. Free Radic Biol Med 41, 1213 1224.
- 2. Dinis-Oliveria, R.J. (2007) Research into the mechanism of paraquat induced multiple organ failure. Toxicology 227.
- 3. WHO 2009 World Health Organization. Poison information monograph 399. Paraquat. International Programme for Chemical safety, March 26, 2009.
- Rahmani AH, Forouzandeh H, Tandayon Khatibi M. Medical Management and Outcome of Paraquat Poisoning in Ahvas, Ira : A Hospital – Based Study. Asia Pac J Med Toxicol 2015; 4 : 74 – 8.
- 5. Li LR, Sydenham E, Chaudhary B, Beecher D, You C. Glucocorticoid with cyclophophamide for paraquat-induced lung fibrosis Cochrane Databse of Systematic Reviews 2014, Issue 8. Art. No. : CD0080804.
- 6. Gawarammana IB. Buckley NA. Medical Management of paraquat ingestion. Br J Clin Pharmacol 2011; 72 : 745 57.
- Indika Gawarammana, Nicholas A. Buckley. Fahim Mohamed. Kamal Naser. K. Jeganathan, P.L. Ariyananda, Klintean Wunnapuk. Timothy A. Dobbins. John A. Tomenson, Marin F. Wilks. Michael Eddlestone and Andrew H. Dawson (2017) : High does immunosuppression to prevent death after paraquat self-poisoning a rendomised controlled trial, Clinical Toxicology. DOI : 10.1080/15563650. 2017. 1354465.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 02, 2023

- 8. Ning Z. Bai YL. Lu H et.al. Prognostic value of plasma C-reactive protein in the evaluation of paraquat poisoning patient. Asian Pac J Trop Biomed 2015; 5(10) : 841–844.
- 9. Saw iniec J. Gnyp L. Lewandowska-Stanek H. C-reactive protein as a useful prognostic marker in acute poisoning. Pubmed 2004;61(4):356-8
- 10. Zhou CD et.al. Prognostic value of haematological parameters in patients with paraquat poisoning. Sci. Rep. 6, 36235; DOI : 10.1038/srep36235 (2016).
- 11. Xu Q, Want X, Wu Q et.al. Urinary paraquat concentration and white blood cell count as prognostic factors in paraquat poisoning. Trop J PHarm Res, July 2018; 17(7) : 1391-1396.
- 12. Zhang Y, Sun H, Jiang L Prognostic Value of White Blood Cell Count, C-reactive protein, and Pentraxin-3 Levels in Patients with Acute Paraquat Poisoning. J Clinic Lab Med 2017; 2(2) : DOI.
- 13. Blanco-Ayala, T., Anderica-Romero, A.C. & Pedraza-Chaverri J. New insights into antioxidant strategies against paraquat toxicity. Free Radio Res. 2014; 48 : 623 40.
- 14. Hanng C & Zhang X (2011 Prognostic significance of arterial blood gas analysis in the early evaluation of Paraquat Poisoning patients, Clinical Toxicology, 49 : 8, 734-378, DOI : 103109/15563650.2011.6074.
- Liu, X. W., Ma. T., Qu, B., Ji, Y. & Liu Z., Prognostic value of initial arterial lactate level and lactate metabolic clearance rate in patients with acute paraquat poisoning. Am J. Emerg Med. 2012; 31: 1230 – 1235.
- 16. Weng C. Hu C. Lin J. Huang W. Hsu C. Yet T. Sequential Organ failure assessment Score can Predict Mortality in Patients with Paraquat Intoxication 2012 : 21 7.
- Huang NC et.al. Further evidence of the usefulness of Acute Physiology and Chronic Health. Evaluation – II Scoring system in paraquat poisoning Clin Toxicol. 2006;44:99– 102.
- Feng M. Li Y. Ruan W. Lu Y. Predictive value of the maximum serum creatinine value and growth rate in acute paraquat poisoning patients. Sci Rep [Internet]. 2018 : (February): 1 – 7. Available from : http://dx.doi.org/10.1038s41598-018-29800-0.
- 19. Ragoucy-Sengler, C. & Pileire B. A biological index to predict patient outcome in paraquat poisoning. Hum Exp. Toxicol. 1996; 15 : 265-8.
- 20. Mohamed F et.al. Mechanisms Underlying Early Rapid Increases in Cretinine in Paraquat Poisoning. PLoS One. 2015; 10 : 110-6.
- 21. Cao ZX, Song YQ, Bai WJ, Wang WJ, Zhao Y, Zhang SL, et.al. Neutrophil lymphocyte ratio as an early predictor for patients with acute paraquat poisoning. 2018; 1-5.
- 22. Pasha SA, Prabodh S, Rao N, Suhasini T, Sripad DV, Chowdary NVS, Role of Liver Function Tests and serum Lactate Levels in Predicting the Severity of Acute Paraquat Poisoning. Int J Sci Study International J Sci Study. 2015; 3(8) : 498.
- 23. Sharma DAS, Prajapati AM, Shan DM, Review of a case of paraquat poisoning in a tertiary care rural-based ICU. Indian J Crit Care Med. 2019; 23(6) : 284-6.
- 24. Bismuth C., Garnier, R., Dally, S. Fournier, P.E., Scherrmann J. Prognosis and treatment of paraquat poisoning : A review of 28 cases. J Toxicol Clin. Toxicol. 1982; 19 : 461 74.
- 25. Berry, D.J., Grove J. The Determination of paraquat (1.1' dimethy 1 4.4' bipyridyium cation) in urine. Clin Chim Acta. 1971; 34:5-11.
- 26. Sawada Y et.al. Severity index of paraquat poisoning. Lancet. 1988; 1:1333.
- 27. Proudfoot. A.T., Prescott, L.F., Jarvie DR. Haemodialysis for paraquat poisoning. Hum Toxicol.1987; 6: 67 74.

- 28. Liu XWEI, Ma TAO, Li LULU, Qu BO, Liu ZHI. Predictive values of urine paraquat concentration, dose of poison, arterial blood lactate and APACHE II score in the prognosis of patients with acute paraquat poisoning, 2017; 79-86.
- 29. Iskander KN, Osuchowski MF, Stearns Kurosawa DJ, Kurosawa S, Stepien d. Valentine C, et.al. Sepsis : Multiple abnormalities, heterogeneous responses and evolving understanding. Physiol Re. 2013; 93 (3) : 1247-77.