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Original Article

Outcome of paraquat poisoning patients admitted in a tertiary hospital in Bangladesh

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Abstract

Background: Paraquat Poisoning is not unknown in clinical practice. However, the data from our country is scanty. Therefore, to find the outcome of paraquat poisoning in a tertiary level hospital was the objective of this study.

Methods: The study was a longitudinal descriptive study and conducted at department of Medicine, Rajshahi Medical College Hospital. Patients of paraquat poisoning were approached for inclusion. Informed written consent was taken from the patients and/or attendants. Data were collected by face-to-face interview by the researcher with an aid of a semi-structured questionnaire. All available investigation reports, follow up notes, discharge papers and death certificates were scrutinized. A total 30 patients were included in this study.

Results: Total 30 subjects were interviewed. Mean age was 25.33±8.86 (SD) years with female to male ratio-2:1.Majority were from rural area (90%). About 94% consumed with an intention of suicide. Most of the patients had renal impairment (53.3%) and hepatic impairment (50%) as complication. 63.3% patients reached to hospital >12 hours after ingestion of poison and 36.7% reached within 12 hours. Of all, 33.3% (n=10) patients survived. Possible cause of death were Multi organ failure (MOF) (40.0%), Acute renal failure (25.0%), ARDS (15.0%) and Hepatic failure (20.0%). However, overall outcome is not dependent with to time reaching hospital after poisoning but with amount of poison ingested (p<0.05).

Conclusion: About 67% patients died following ingestion of the paraquat poisoning and it is not dependant with the time required to reach the hospital rather to the amount of poison ingested.

Key words: Paraquat, outcome, RMCH.

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Introduction

Paraquat (1, r-dimethyl-4, 4'-bipyridium dichloride), a member of the bipyridyl group of herbicides, used widely in our country and is a highly toxic compound. It was first described in 1882.Its herbicidal properties were discovered in 1950s and first marketed in 1962[1,2]. Presently, it is the second highest-selling weed killer globally. It is available in a 20% solution form and that needs to be diluted before agricultural use. The LD50 in humans is approximately 35 mg/kg, which translates into as little as 10-15 ml of a 20% solution[3,4]. The veryhigh case fatality (>50%) of paraquat means that it is theleading single agent causing death from pesticide poisoningin many countries[5,6].In

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cellular level paraquat generates free radicals and activates NFkB. Paraquat-induced toxicity is a manifestation of its ability toundergo redox-cycling and subsequent generation ofreactive oxygen species (ROS)[7,8] causing lipid peroxidation[9], mitochondrial toxicity, Na DPH related injury and apoptosis of the cell.After ingestion, the commonest early manifestation is nausea and vomiting followed byburning oral pain, odynophagia and abdominal pain. The multi-organ involvement with fatality is observed in acute setting. The commonest involvement is features of toxicity including fever, hepatotoxicity and renal toxicity.Diffuse alveolitis followed by extensive pulmonary fibrosis and acute respiratory distress syndrome (ARDS) and ventricular arrhythmias; hypotension and cardio-respiratory arrest are leading cause of death[10].

Recently in Bangladesh, there is tendency to use the paraquat as a deliberate self-harm due to its severe toxicity and fatality. Here is a case series of paraquat poisoning admitted in the Rajshahi Medical College Hospital, Bangladesh with very high mortality that need to be addressed.

Materials and Methods

It was a cross sectional descriptive study. The study was carried out among paraquat poisoning patients admitted into Medicine department of Rajshahi Medical College Hospital from April 2019 to September 2019. Its duration was 06 months. Sampling methos was purposive. Each study participant was selected on the basis of predetermined inclusion criteria. Total 30 patients were enrolled in this study. Data was collected in a pre-structured case record form and was analyzed by SPSS version-16.

Pic: patient's typical tongue

Pic -: patients' tongue, hemetemesis

Results

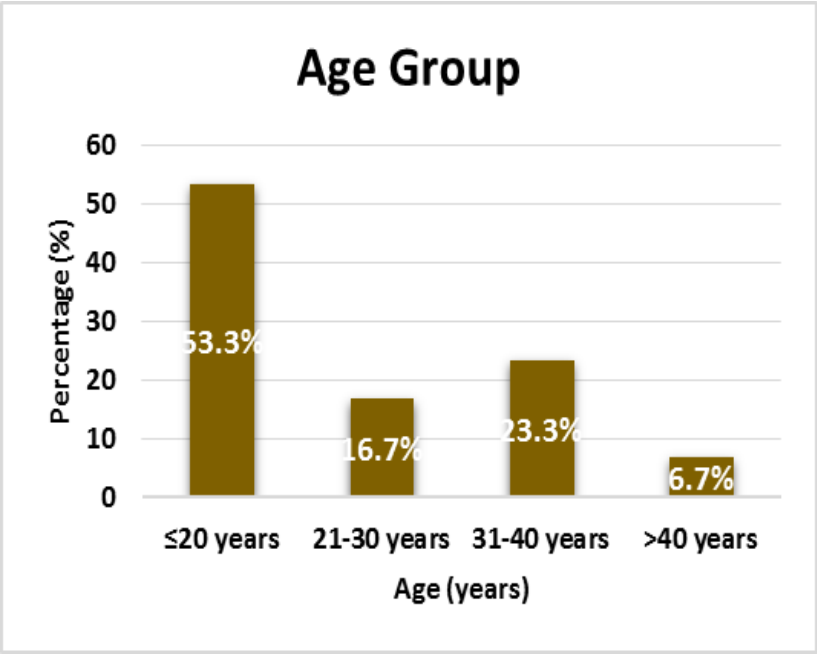

Figure 1: Age distribution of paraquat poisoning patients (n=30)

Majority (53.3%) were below and equal to 20 years of age. The age range was 15 to 45 years. Mean age was found 25.33±8.86 years.

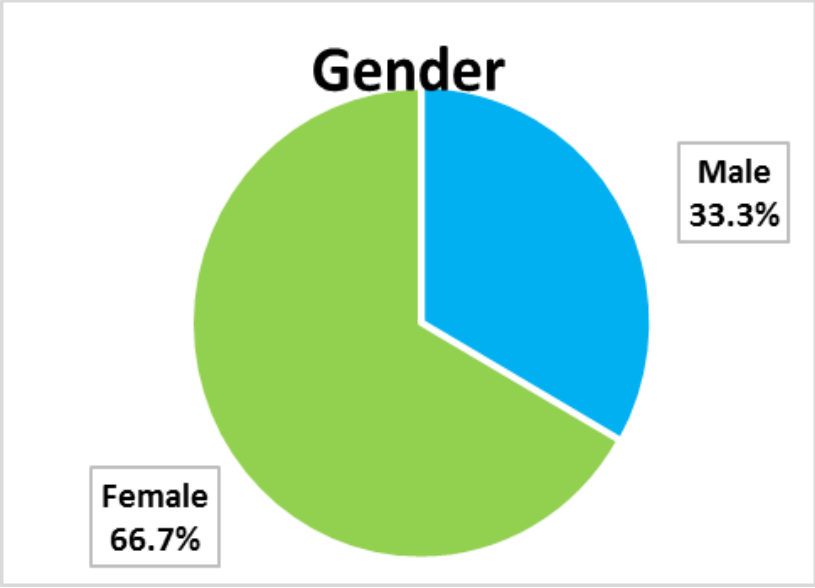

Figure 2: Distribution of paraquat poisoning patients according to gender (n=30)

Gender wise distribution showed that, majority of them were females which constitute 66.7% of the study population. There were 20 female and 10 male patients and female to male ratio was 2:1.

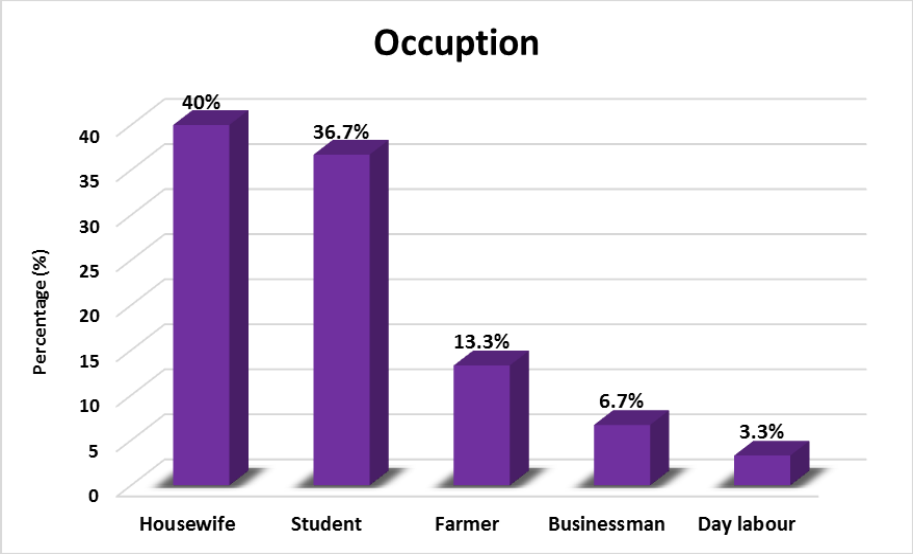

Figure 3: Distribution of study population according to occupation (n=30)

Among the study population, majority of them were housewife (*n*=12 (40.0%)) and students (*n*=11 (36.7%)) followed by farmers (*n*=4 (13.3%).

Majority study population were from rural area (90%) compared to urban (10%).

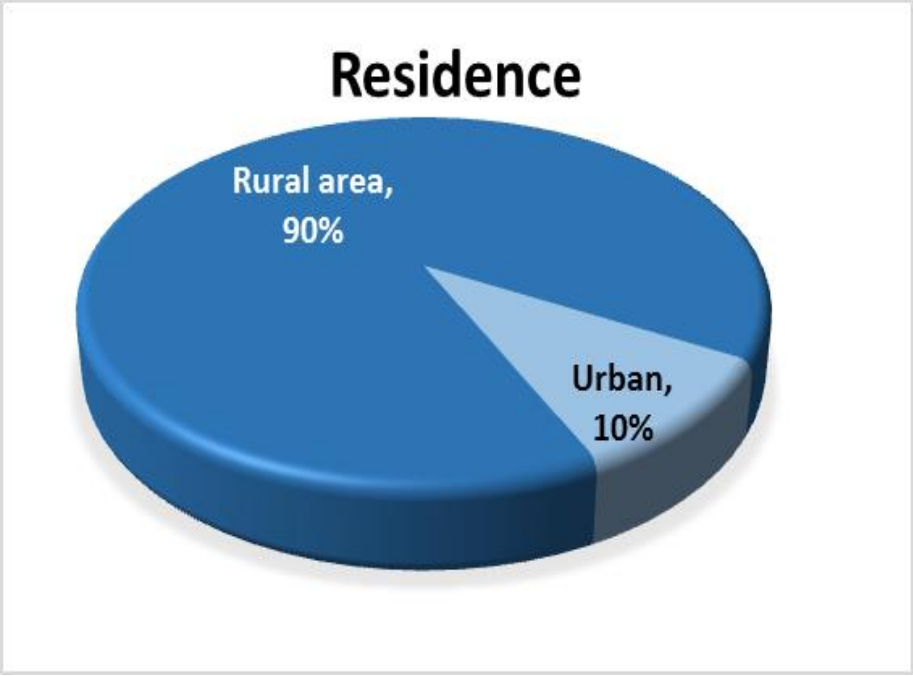

Figure 4: Distribution of study population according to occupation (n=30)

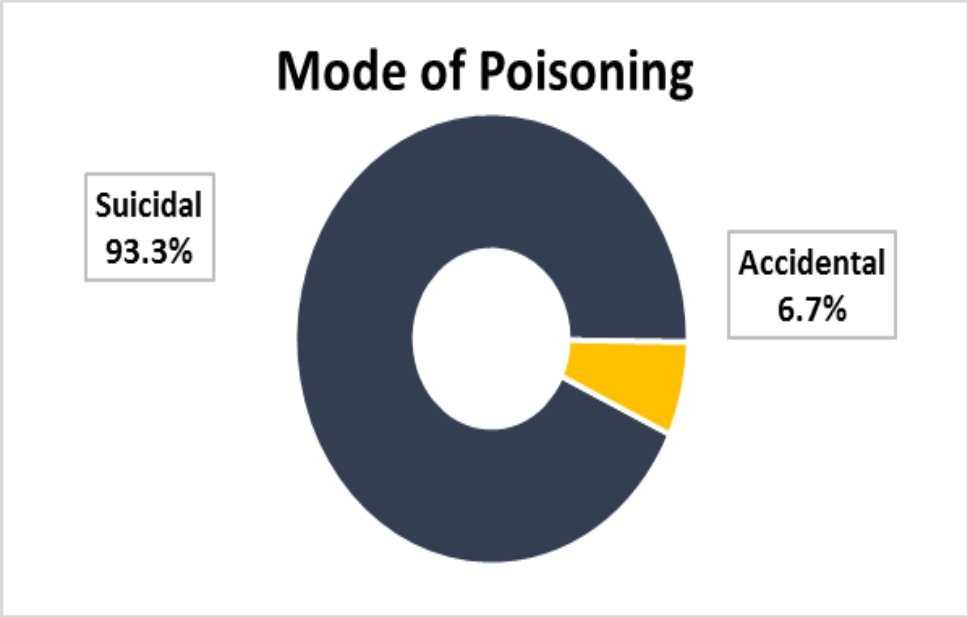

Figure 5: Distribution of study population according to mode of poisoning (n=30)

Majority of poisoning were found to be suicidal (93.3%).

Table 1: Clinical presentations of study populations (n=30)

Symptoms	n (%)	Signs	n (%)
Vomiting	20 (66.7%)	**Oral mucosa change**	30 (100%)
Abdominal pain	20 (66.7%)	Congested	3 (10.0%)
Throat pain	9 (30.0%)	Excoriated	22 (73.3%)
Breathlessness	7 (23.3%)	Ulcerated	5 (16.7%)
Fever	3 (10.0%)	**Icterus**	11 (36.7%)
Drowsy	3 (10.0%)	**Greenish tongue**	6 (20.0%)
Unconsciousness	3 (10.0%)	**Hematemesis**	6 (20.0%)
Convulsion	1 (3.3%)	**Oliguria**	4 (13.3%)
Dysphagia	1 (3.3%)	**Hematuria**	2 (6.7%)

Most common symptom was vomiting and abdominal pain observed in 66.7% patients followed by throat pain (30.0%). Most common sign was oral mucosal excoriation (73.3%) followed by jaundice (36.7%).

Table 2: Blood investigation parameters of study population (n=30)

Variables		n (%)
Mean Hb% (gm/dL)		**10.82±1.06**
Mean ESR (1st hr.)		**32.13±13.38**
WBC	**Normal**	21 (70.0%)
	Leukocytosis	9 (30.0%)
Serum Creatinine	**Normal**	9 (30.0%)
	Increased	21 (70.0%)
Mean Serum Creatinine (mg/dL)		**3.51±3.68**
Mean Serum Bilirubin		**2.59±2.88**
SGPT		**69.30±136.23**

Table 3: Other investigation results of study population (n=30)

Variables		n (%)
Urine Albumin	**Nil**	10 (33.33%)
	+	4 (13.33%)
	++	16 (53.34%)
Urine RBC	**Nil**	17 (56.7%)
	0-1 /HPF	3 (10.0%)
	5-10 /HPF	5 (16.7%)
	Plenty	5(16.7%)
ECG	**Normal**	27 (90.0%)
	Sinus tachycardia	3 (10.0%)
Chest X-ray	**Normal**	30 (100%)

Table 4: Complications of study population (n=30)

Complications	Frequency	Percentage (%)
Multi-organ system failure	8	26.7%
Hepatic impairment	15	50%
Renal impairment	16	53.3%
Respiratory failure	13	43.3%

***Multiple response**

Majority patients had renal impairment (53.3%) and hepatic impairment (50%) as complication.

Following figure shows that, majority patients (46.7%) had ingested >15 mL of paraquat. Mean volume of all population was 30.33±48.19 mL. Other amounts with frequency are given below.

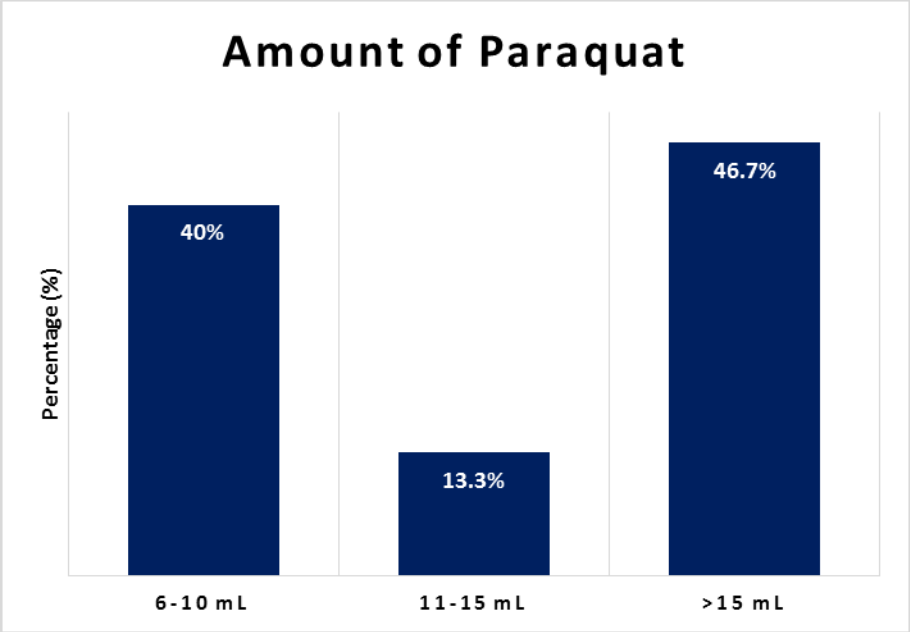

Figure 6: Amount of ingested paraquat by study population (n=30)

Table 5: Distribution of time between Paraquat ingestion and reaching the hospital (n=30)

Time interval	Frequency	Percentage (%)
≤12 hours	11	36.7%
>12 hours	19	63.3%
Total	30	100

Majority of the patients (63.3%) reached to hospital >12 hours after ingestion of poison followed by 36.7% reached within 12 hours.

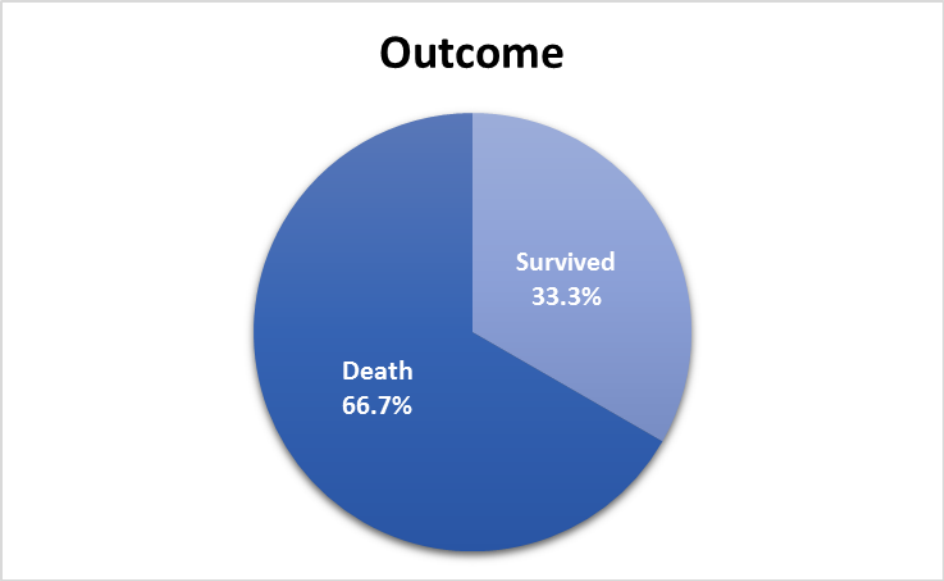

Figure 7: Outcome of Paraquat poisoning in study population (n=30)

Of all, 33.3% (n=10) patients survived.

Table 6: Outcome of the patients according to time reaching hospital after poisoning (n=30)

Time interval	Survived n (%)	Death n (%)	P-value
≤ 12 hrs	4 (36.4%)	7 (63.6%)	**0.548***
>12 hrs	6 (31.6%)	13 (68.4%)	
Total	**10 (100%)**	**20 (100%)**	
Mean duration (hrs)	23.50±23.64	37.05±38.89	**0.322****

***P-value determined by chi-square test**

****one-way ANOVA done to extract p-value**

The study was statistically non-significant (p>0.05)

Table 7: Outcome of the patients according to amount of paraquat ingestion (n=30)

Amount ingested	Survived n (%)	Death n (%)	P-value
6-10 mL	10 (100%)	2 (10%)	
11-15 mL	0	4 (20%)	**<0.001**
>15 mL	0	14 (70%)	
Total	**10 (100%)**	**20 (100%)**	
Mean (mL)	5.0±0	43.0±55.12	**0.039****

***P-value determined by chi-square test**

****one-way ANOVA done to extract p-value**

Possibility of death increased significantly with increasing amount of paraquat in our study samples (p value <0.001).

Table 8: Cause of death in paraquat poisoning patients in our study (n=20)

Cause of death	Frequency	Percentage (%)
Multi organ failure	8	40.0%
Acute renal failure	5	25.0%
ARDS	3	15.0%
Hepatic failure	4	20.0%
Total	**20**	**100%**

In the present study, the major underlying cause of death in paraquat poisoning was found multi-organ failure (40.0%) which was followed by acute renal failure (25%).

Table 9: Survival and death outcome with different treatment modality (n=30)

Outcome	Treatment method	
	Conventional	**With Immunosuppressants and Antioxidants**
Survived	3 (15.8%)	7 (63.6%)
Death	16 (84.2%)	4 (36.4%)
Total	**19 (100%)**	**11 (100%)**

63.6% patients treated with immunosuppressants and antioxidant therapies were survived while mortality was 84.2% conventionally treated patients.

Discussion

In this study, 30 patients with paraquat poisoning were enrolled among whom 53.3% aged ≤20 years with mean age of 25.33±8.86 years. Minimum and maximum age was found 15 and 45 years. Similar study conducted in Soonchunhyang Hospital (SCH) in Cheonan, Korea by Kim et al., 2009 showed similar results with male to female ratio of 1.3:1 with mean age 26.58 ± 9.473 years in males and mean age of 23.58 ± 8.480 years in females[12]. Overall prevalence of paraquat poisoning in our study under 30 years of age was 70%. Dewan found the prevalence of poisoning under 30 years of age was 71.9% which was comparable to us [13]

Gender wise distribution of study population showed that females (66.7%) predominated over males (33.3%). The female to male ratio was 2:1. It is very much similar to Halesha et al. in India but different from other studies [14-16].

93.3% poisoning were suicidal in nature. Cherukuri et al. also reported majority of the herbicide

poisonings were due to deliberate self-harm in their study[15]. Majority study population was housewife (40%) and student (36.7%). 90% patients were from rural area. The study by Shah et al in Bangladesh revealed that, suicide was more common in rural areas and in Bangladesh females are more prone to suicide[17]. It proves the female predominance and rural percentage of paraquat poisoning in this study.

Common clinical symptoms in our study were vomiting (66.7%), abdominal pain (66.7%), throat pain (30%) and breathlessness (23.3%). Common signs were oral mucosal excoriation (73.3%), icterus (36.7%), greenish tongue and hematemesis in 20% cases. As per study conducted by Sandhu *et al*., 2003 the common symptoms for paraquat poisoning were vomiting (100%) followed by oral ulceration (59%), dysphagia (53%) and dyspnea (41%)[18]. Halesha et al. also reported nausea, throat pain, oral ulcers as the common presentations of paraquat poisoning[14].

Leukocytosis was observed in 30% patients in blood study. Elevated serum creatinine was found in 70% cases while mean serum bilirubin was 2.59±2.88 mg/dL and serum creatinine were 3.51±3.68 mg/dL. Urine albumin was found in 66.67% patients and RBC in urine was found in 43.3% patients. Chest X-ray and ECG were normal in 100 and 90% cases respectively. Major complication was found in our study was renal and hepatic impairment (53.3% and 50%). Halesha et al. found similar results about complications[14].

Among 30 patients, the outcome of the poisoning showed that, overall mortality was 66.7% (20 patients) and 33.3% (10 patients) recovered fully. 46.7% patients admitted to hospital with a history of ingestion of >15 mL paraquat. Outcome according to ingested amount shows significance. Possibility of survival increased with decreasing amount of paraquat ingestion. 100% survival rate observed in our study subjects who ingested 6-10 mL of paraquat while 70% died who ingested >15 mL. Wong et al. in their case series review showed that, among their cases, who ingested large amount of paraquat concentrate died eventually in spite of taking immunosuppressant and anti-oxidants[19]. Manoj et al in India also stated in their study that, who have taken less quantity of paraquat survived for longer period in comparison to the patients with large amount of paraquat intake[20].

63.3% patients reached to the hospital >12 hours after ingestion. The outcome according to their reaching in hospital shows insignificant result. Survival rate among patients came within 12 hours was 36.36% and after 12 hours were 30% in our study. As paraquat is highly toxic and by intuition, preventing absorption remains the only method to reduce toxicity and improving outcome[11]. Hence measures to prevent absorption from gut and removal from blood by extracorporeal elimination remain the methods for reducing toxicity, unlikely benefiting those with high amount of ingestion due to early extensive tissue damage[21]. And again, ingestion of more than 40 mg of paraquat ion/kg body weight can lead to multiorgan failure with

acute renal failure, hepatic necrosis, myocardial necrosis, acute pneumonitis, internal haemorrhages, pulmonary fibrosis and finally death[22]. So along with duration of ingestion and treatment, amount of ingested paraquat had also an importance which reveals in our study.

Multiorgan failure was the major underlying cause of death in our study followed by acute renal failure (25%), hepatic failure (20%) and ARDS in 15% cases. Jagadeesan et al. also reported similar result[16]. Other study also reported that multiple organ dysfunction is the main etiology of death from paraquat intoxication[23].

11 patients with paraquat ingestion of our study were treated with immunosuppressants and antioxidants. Among them, survival rate was 63.6% compared to other conventional method (15.8%). A group from Taiwan carried out a series of clinical studies using immunosuppression[1,24,25]. In these three studies, they had found 25% vs 70%, 68% vs 82% and 31% vs 86% mortality between immunosuppressant and conventional treatment method for paraquat poisoning. These studies support us. In animal studies, an immunosuppressant named dexamethasone in particular has been shown to increase the expression of P-glycoprotein in rats (and may well increase expression of other transporters)[26]. There was a significant reduction of paraquat accumulation in the lung tissue and an increase of fecal excretion of paraquat in rats treated with lethal doses of paraquat. Dexamethasone has also been shown to possess the ability to ameliorate the histological and biochemical changes induced by paraquat and to reduce lipid peroxidation and survival rates in Wistar rats[27].

Conclusion

In this study, average of the poisoned patients was twenty-fiveyears with female predominance. Majority patient came from rural areas. Following management of the patients, it was seen that about 67% died. And cause of death was due to multi organ failure, acute renal failure, ARDS and hepatic failure. Moreover, the outcome of paraquat poisoning is not dependant with the time required to reach the hospital rather to the amount of poison ingested.However, this is an important finding should be explored further with appropriate study design.

Limitation of the study: This was a single center study and sample size was small.

Recommendation:
Depending upon the study findings, following recommendations are suggested:

1. Community based larger population study is recommended to use this finding.
2. Awareness program should be run in whole country to mitigate the suffering of the patients.

Conflict of interest: None declared

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