

**CLINICAL PROFILE AND OUTCOMES OF PARAPHENYLENE DIAMINE (KALA PATHAR) POISONING AT A TERTIARY CARE CENTER, PAKISTAN**Dr. Imran Ali<sup>1</sup>, Dr. Aaima Bakhtawar<sup>2</sup> and Dr. Muhammad Sharief<sup>3\*</sup><sup>1</sup>(Pmdc # 91880-p) Nishtar Hospital Multan.<sup>2</sup>(Pmdc # 90639-p) Nishtar Hospital Multan.<sup>3</sup>(Pmdc # 91915-p) Nishtar Hospital Multan.**\*Corresponding Author: Dr. Muhammad Sharief**

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DOI: <https://doi.org/10.17605/OSF.IO/83S7D>

Article Received on 15/05/2018

Article Revised on 05/06/2018

Article Accepted on 26/06/2018

**ABSTRACT**

**Aim of study:** The objective of this study was to explore the clinical course and outcome of patients with this poisoning. **Methodology:** It is a cross-sectional observational study conducted at Nishtar Hospital, Multan for 6 month of duration from March 2017 to August 2017. History, examination, investigation and treatment given all were recorded on a preformed proforma. Patients having age below 15 years or with pre-existing morbid conditions e.g. Cardiac, Renal and hepatic disorders were excluded from the study. **Results:** There were total 120 patients out of which 88 (73.4%) were females and 32 (26.6%) males. Mean age was 24.5±6.2 and mean duration of hospital stay was 13.8±4.5 days. 58 belongs to age group 15-25 years, 34 patients in age group 26-35 years. 99 patients were from rural areas and 21 were from urban areas. We observed that 55.8% cases were from middle class. 68 patients were illiterate, 27 had got primary education, and only 3 patients were graduates. 77 (64.1%) patients were married. Tracheostomy was performed on 112 patients. 13 patients needed mechanical ventilation and 18 patient needed few sessions of hemodialysis. Angioedema was present in 91.6%, muscle pain in 90%, vomiting in 87.5%, dyspnea in 91.6%, oro-facial edema in 95%, dark colored urine in 115%, oliguria in 34% and 8% patient presented with anuria. 84 patients were having raised TLC i.e. above 11 thousand, raised blood urea in 58 patients, raised serum creatinine in 76, raised CPK in 116 patients, raised CK-MB in 89, hyperkalemia was observed in 40 patients, deranged LFT's in 39 patients, 27 patients were having pathological findings in X-ray chest and 73 patients were having changes in ECG. 113 (94.1%) patients survived and mortality rate in this study was 5.8%. **Conclusion:** Paraphenylene diamine (kala pathar) poisoning is emerging now a days due to easy availability and low cheap price. It is more common in poor, illiterate, married females of younger age group living in rural areas in our set-up. Aggressive treatment and tracheostomy can save life of patients.

**KEYWORDS:** Paraphenylene diamine, kala pathar, Pakistan, outcome, complication, tracheostomy.**INTRODUCTION**

Paracelsus said, "All things are poisons, for there is nothing without poisonous qualities. It is only the dose which make thing poison". Poison can also be defined as, any substance that can kill, injure and impair normal physiological function in human or producing general or local damage in our body [Hakim et al., 2014]. Incidence of suicide is increasing every year, making it a public health concern. There are many substances which are used self-harm e.g. Organophosphate poisoning, kala pathar (Paraphenylene Diamine also known as PPD), narcotic drugs, acetaminophen, wheat pills, acids, alkalis etc. The outcome and prognosis depends upon poisoning agent, dose taken, antidote and timely intervention.<sup>[1]</sup> In Pakistan, although pesticide poisoning remains the leading cause, but poisoning with paraphenylene diamine (PPD), locally known as 'Kala Pathar', is emerging as important means of intentional self-harm.<sup>[2,3]</sup> PPD is used

as chemical ingredient in temporary tattoo ink as well as in fabrics, dark makeup, photocopying inks, printing, products of the rubber and gasoline but its use as black henna for hair dye & tattoo ink is very common in India and Pakistan. Kala pathar or PPD is a substance that quickly dissolves in hydrogen peroxide and then in the body, it is metabolized by cytochrome P450 system leading to its oxidation and ending up in a very toxic product that can start different types of reaction and even anaphylaxis.<sup>[4,5]</sup> Being compound of highly toxic nature, Paraphenylene diamine exerts its effects on the muscular, respiratory, hepatic, renal and cardiac systems by inhibiting cellular oxidation. The signs and symptoms include anaphylaxis reaction with swelling over the face and the oral cavity, dysphagia, and also injury to the pharynx, tongue and upper gastrointestinal tract (GIT). It can also causes allergy kerato-conjunctivitis, skin irritation, conjunctival swelling, and eczema of the

eyelids, different types of arrhythmias, electrolyte imbalance, rhabdomyolysis, severe metabolic acidosis, acute hepatitis and acute renal failure as complications seen at latter stages.<sup>[6,7]</sup> It also can cause renal tubular necrosis occurs due to deposits of the toxic metabolites of paraphenylene diamine leading to high mortality rates which have also been reported by some authors as 68.8%<sup>8</sup> and 60%.<sup>[9]</sup> Cardiotoxicity & hepatic necrosis due to Paraphenylene diamine have also been observed.<sup>[10]</sup> The toxicity of Paraphenylene diamine is dose dependent with estimated lethal dose of 7–10 grams.<sup>[11]</sup> There is no specific antidote to PPDA and it is non-dialyzable. It has quite high mortality and aggressive management in collaboration with various specialties especially ENT for the need of early tracheostomy is important.<sup>[12,13,14]</sup> An early diagnosis & supportive treatment could be helpful. Research to better understand and improve the management including effective and timely interventions especially tracheostomy can reduce the number of deaths from this type of self-poisoning in the developing world. The objective of this study was to explore the clinical course and outcome of patients with paraphenylene diamine poisoning at a tertiary care center.

## METHODOLOGY

The study was conducted at medical emergency department and medical ward of Nishtar Hospital Multan for a period of 6 month from March 2017 to August 2017. 120 cases were included in the study after taking informed consent. Ethical approval letter was taken from the ethical review committee of our institute. Statistical analysis was done with the help of SPSS version 18.0.

### Inclusion Criteria

Patient gave consent.

Age above 15 years.

Having history of suspected exposure to kala pathar poisoning.

### Exclusion Criteria

The cases with no clear evidence of exposure to this agent were excluded.

Patients having pre-existing morbid conditions e.g. Cardiac, Renal and hepatic disorders.

Patients that were un-cooperative or not giving written consent were also excluded.

After receiving the patient in emergency, airway, breathing and circulation was assessed. And there is airway obstruction due to swelling immediate tracheostomy usually done. Detailed history including demographic detail, amount and time of ingestion, mode of poisoning etc., complete physical examination, all the necessary investigations like complete blood count, renal and liver function tests, X-ray chest, CPK, CK-MB, TROP-I, complete urine examination, biochemistry of gastric lavage, ECG, Echocardiography and ultrasound was performed in almost all the patients. History, examination, investigation and treatment given all were

recorded on a preformed proforma. Gastric lavage was done in almost all the patients except those patients in which nasogastric tube could not passed due to excessive swelling.

Steroids, anti-histamine, antibiotics, forced diuresis and excessive fluid replacement was done in all the patients.

## RESULTS

Total 120 cases of PPD/kala pathar poisoning were included in the study. There were 88 (73.4%) females and 32 (26.6%) males, with male to female ratio of 1: 2.7 Out of 120 patients. Mean age was 24.5±6.2 and mean duration of hospital stay was 13.8±4.5 days. 58 belongs to age group 15-25 years, 34 patients in age group 26-35 years, 15 patients were in age 46-55 years and only 13 patients were having age above 55 years. 99 patients were from rural areas and 21 were from urban areas. We observed that mostly patients were from middle class family 55.8% and 41.6% patients were from low income family with monthly income below 15 thousand. Among studied patients, 68 were illiterate, 27 had got primary education, and only 3 patients were graduates. We observed that married cases were more as compared to single 77 and 43 respectively. 112 patients undergo tracheostomy upon presentation to hospital or within 12 hours of admission. 13 patients needed mechanical ventilation and hemodialysis was started in 18 patients who developed oliguria/anuria or having rising trend of renal parameters. Among sign and symptoms the most common were: angioedema in 91.6%, muscle pain in 90%, vomiting in 87.5%, dyspnea in 91.6%, oro-facial edema in 95%, dark colored urine in 115%, oliguria in 34% and 8% patient presented with anuria. After resuscitation of patient, all baseline investigation sent. In laboratory investigation report it was observed that 84 patients were having raised TLC i.e. above 11 thousand, raised blood urea in 58 patients, raised serum creatinine in 76, raised CPK in 116 patients, raised CK-MB in 89, hyperkalemia was observed in 40 patients, deranged LFT's in 39 patients, 27 patients were having pathological findings in X-ray chest and 73 patients were having changes in ECG. 113 (94.1%) patients survived and mortality rate in this study was 5.8%.

Table 1: Personal and demographic detail of 120 patients.

<b>Gender distribution.</b>			
<b>Gender</b>	<b>Male</b>	<b>Female</b>	<b>Total</b>
	32 (26.6%)	88 (73.4%)	120 (100%)
<b>Age distribution.</b>			
<b>Age group (years)</b>	<b>No. of cases</b>	<b>Percentage</b>	
15-25	58	48.3%	
26-35	34	28.3%	
36-45	15	12.5%	
46-55	8	6%	
56 and above	5	4.1%	
<b>Educational status of enrolled patients.</b>			
<b>Education level</b>	<b>No. of patients</b>	<b>Percentage</b>	
Illiterate	68	56.6%	
Primary	27	22.5%	
Secondary	18	15%	
Graduate	7	5.8%	
<b>Marital status of patients.</b>			
	<b>No. of patients</b>	<b>Percentage</b>	
Married	77	64.14%	
Single	43	35.83%	
<b>Scio-economic status</b>			
	<b>No. of cases</b>	<b>Percentage</b>	
Low	50	41.6%	
Middle	67	55.8%	
High	3	2.5%	

Table 2: clinical features of PPD poisoning in 120 patients.

<b>Sign/symptoms</b>	<b>No. of cases</b>	<b>percentage</b>
Angioedema	110	91.6%
Pain in oral cavity	112	93.33%
Vomiting	105	87.5%
Dyspnea	110	91.6%
Muscle pain	108	90%
Epigastric pain/tenderness	78	65%
Oro facial edema	114	95%
Fits	12	10%
Hypertension	25	20.8%
Dark colored urine	115	95.8%
Oliguria	41	34.1%
Anuria	10	8.3%

Table 3: laboratory investigation findings observed in first 4 hours of presentation.

<b>Laboratory test</b>	<b>No. of cases</b>	<b>Percentage</b>
TLC > 11000	84	70%
Rise in blood urea	58	48.3%
Rise in Serum creatinine	76	63.3%
Rise in CPK	116	96.6%
Rise in CK-MB	89	74.16%
Hyperkalemia	40	33.33%
Urine cast	26	21.6%
Deranged LFT's	39	32.5%
Pathological finding in X-ray	27	22.5%
Pathological finding in ECG	73	60.8%

**Table 4: lifesaving intervention done in patients.**

Intervention	No. of cases	Percentage
Tracheostomy	112	93.33%
Mechanical ventilation	13	10.8%
Dialysis	18	15%

**Table 5: Outcome of 120 patients with PPD poisoning.**

	Male	Female	Total
Died	2	5	7
Survived	30	83	113

## DISCUSSION

Poisoning with paraphenylene diamine is emerging as an important means of intentional self-harm with high mortality rate in many developing countries.<sup>[15,16]</sup> In our study we observed that female were 73.4% and male 26.6% with male to female ratio was 1:2.75 which is similar to many other studies i.e. by Akber *et al.*<sup>[17]</sup> and Anugrah Chrispal *et al.*<sup>[18]</sup>. Preponderance of females with a male to female ratio of 1:1.84 has been documented by Nirmala and Ganesh *et al.*<sup>[19]</sup> A study from Hyderabad, India by Sakuntala *et al.*<sup>[20]</sup> reported it in females 80.64% as compared to males 18.75%. This may be due to easy availability, its use as a hair dye and females are more exposed to gender inequalities and social pressures in the developing countries. About 60% of patients in our study were between 20-30 years of age and these results also similar with other studies like, Akbar *et al.*<sup>[17]</sup> reported the mean age as 25.5±4.56 years, Chrispal *et al.*<sup>[18]</sup> as 27.75 years, Nirmala and Ganesh.<sup>[19]</sup> 24.7±6.51 years, and Suliman *et al.* as 40 years. This finding is also in accordance with the WHO report that young age group is more vulnerable to have self-harm in the low and middle income countries. The overall incidence of poisoning is higher in rural areas as compared to the urban areas this may be due to lack of awareness and knowledge, poverty, and social problems. In our study 82.5% cases were from rural background which stats are similar with many other studies e.g. in a study by Khuhro *et al.*<sup>[21]</sup> all their patients were from rural background. We observed that at our hospital most of patients belong to low and middle class family with 41% and 55% respectively. We noted that in our study about 64% of cases were married and remaining 35% were unmarried which shows similar results to a study by Khuhro *et al.* 43.8% were single while 56.3% married, but a study by Khan N *et al.* showed that 71.1% patients were unmarried. In rural areas there is a trend of doing marriage in early age, which is the main reason that in our study most of the cases were married.<sup>[22]</sup> The most common clinical feature observed in this study was angioedema and facial swelling followed by vomiting, dyspnea, and muscle pain. Suliman *et al.*<sup>[23]</sup> who reported cervicofacial edema in all their patients with 15.8% requiring tracheostomy. In other study Dysphagia was the most common complication seen as it affected 44 (73.33%) of cases<sup>[24]</sup>. This was also observed by the study done by Khuhro *et al.* that found it in almost 100% of their 16 cases that had

it orally. Most of the patient who presented with decrease urine output and raised urea, creatinine developed acute kidney injury and some of them needed hemodialysis to survive. 96% patient were having raised CPK value which is the indicator of rhabdomyolysis. In ECG we observed change like ventricular arrhythmias, AV block, atrial fibrillation, hyperkalemia, negative T-waves and supra-ventricular tachycardia. Tracheostomy was performed in 93% patients in this study and in previous study conducted at our hospital the tracheostomy rate of 60% has been documented.<sup>[17]</sup> The mortality rate was 5% which is way lower than other studies. Khuhro *et al.*<sup>[22]</sup> documented the mortality of 37.5% among the patients in their study at Nawabshah whereas 22.48% mortality has been reported by Jain PK *et al.*<sup>[22]</sup>

## CONCLUSION

We concluded that PPD poisoning is emerging now days because of easily availability and cheap price. Hence government should made hard and fix rule regarding selling of such products. We should spread awareness regarding its hazard among people through every kind of media. Young and married female are more susceptible. Early aggressive management can result in better outcome and prognosis. Tracheostomy has proven to be the lifesaving intervention. Rhabdomyolysis and AKI are the most common complications that occurs.

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