

**CLINICAL PROFILE AND OUTCOMES OF PARAPHENYLENE DIAMINE SHEIKH
ZAYED HOSPITAL RAHIMYARKHAN****Dr. Hafiz Muhammad Adnan Akram¹, Dr. Muhammad Tahir Javed², Dr. Azka Mumtaz^{*3}**¹Jinnah Hospital Lahore.²Jinnah Hospital Lahore.³Sheikh Zayed Hospital Rahimyarkhan.***Corresponding Author: Dr. Azka Mumtaz**

Sheikh Zayed Hospital Rahimyarkhan.

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ABSTRACT

Kala pathar poisoning is an emerging way of poisoning in developing countries. This substance may produce lethal effects like life threatening angioedema, respiratory distress, rhabdomyolysis, acute renal failure and hepatic necrosis. The aim of this study was to elaborate the clinical profile of patients with Paraphenylene Diamine (Kala Pathar). **Methodology:** It is a Prospective study conducted at Sheikh Zayed hospital, Rahimyarkhan for 6 month of duration from January 2018 to June 2018. 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 100 patients out of which 70 (70%) were females and 30 (30%) males. Mean age was 23.5 ± 6.2 and mean duration of hospital stay was 12.5 ± 4.5 days. 52 patients were in 15-25 years age group, 28 patients were in 26-35 years. 81 patients were from rural areas and 19 were from urban areas. Among these 100 patients mostly (55%) were from middle class family. 57 patients were illiterate, 25 had got primary education, and only 2 patients had graduation. Out of 100 patients, 62 (62%) patients were married. 88 patients had to undergo tracheostomy for survival. 12 patients needed mechanical ventilation and 17 patient needed few sessions of hemodialysis. Angioedema was present in 90%, muscle pain in 88%, vomiting in 80%, dyspnea in 90%, oro-facial edema in 90%, dark colored urine in 94%, oliguria in 13% and 7% patient presented with anuria. 72 patients were having raised TLC i.e. above 11 thousand, raised blood urea in 49 patients, raised serum creatinine in 38, raised CPK in 96 patients, raised CK-MB in 77, hyperkalemia was observed in 28 patients, deranged LFT's in 31 patients, 17 patients were having pathological findings in X-ray chest and 69 patients were having changes in ECG. 91 (91%) patients survived and mortality rate in this study was 9%. **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**

According to World Health Organization (WHO) more than 8 lac people die globally from suicide every year. This indicates an annual global age-standardized suicide rate of 11.4 per 100,000 population.^[1] The developing world is thought to be the most affected area and only in Asia their number has doubled in the past half of the century.^[2] 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]. A long list of techniques used to self-harm is found and even longer is the list of the agent used to end the life. Organophosphorus poisoning, kala pathar (Paraphenylene Diamine also known as PPPD), narcotic drugs, acetaminophen, wheat pills, acids, alkalis etc. are

used for this purpose with varying degree of prevalence and success. The factors influencing to these can be availability of the agent, toxicity rate, and the cost of the substance.^[3] 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.^[2,3] 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.^[4,5] Being compound of highly toxic nature, Paraphenylenediamine 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 cause 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.^[6,7] It also can cause renal tubular necrosis occurs due to deposits of the toxic metabolites of paraphenylenediamine leading to high mortality rates which have also been reported by some authors as 68.8%,^[8] and 60%,^[9] Cardiotoxicity & hepatic necrosis due to Paraphenylenediamine have also been observed,^[10] The toxicity of Paraphenylenediamine is dose dependent with estimated lethal dose of 7–10 grams.^[11] 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,^[12,13,14] 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 paraphenylenediamine poisoning at a tertiary care center.

METHODOLOGY

The study was conducted at medical emergency department and medical ward of Sheikh Zayed Hospital Rahimyarkhan 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

There were total 100 patients out of which 70 (70%) were females and 30 (30%) males. Mean age was 23.5±6.2 and mean duration of hospital stay was 12.5±4.5 days. 52 patients were in 15-25 years age group, 28 patients were in 26-35 years. 81 patients were from rural areas and 19 were from urban areas. Among these 100 patients mostly (55%) were from middle class family. 57 patients were illiterate, 25 had got primary education, and only 2 patients had graduation. Out of 100 patients, 62 (62%) patients were married. 88 patients had to undergo tracheostomy for survival. 12 patients needed mechanical ventilation and 17 patient needed few sessions of hemodialysis. Angioedema was present in 90%, muscle pain in 88%, vomiting in 80%, dyspnea in 90%, oro-facial edema in 90%, dark colored urine in 94%, oliguria in 13% and 7% patient presented with anuria. 72 patients were having raised TLC i.e. above 11 thousand, raised blood urea in 49 patients, raised serum creatinine in 38, raised CPK in 96 patients, raised CK-MB in 77, hyperkalemia was observed in 28 patients, deranged LFT's in 31 patients, 17 patients were having pathological findings in X-ray chest and 69 patients were having changes in ECG. 91 (91%) patients survived and mortality rate in this study was 9%.

Table 1: Personal and demographic detail of 120 patients.

Gender distribution.			
Gender	Male	Female	Total
	70 (70%)	30 (30%)	100 (100%)
Age distribution.			
Age group (years)	No. of cases	Percentage	
15-25	52	52 %	
26-35	28	28%	
36-45	10	10 %	
46-55	6	6%	
56 and above	5	5 %	
Educational status of enrolled patients.			
Education level	No. of patients	Percentage	
Illiterate	57	57 %	
Primary	25	25 %	
Secondary	11	11 %	
Graduate	7	7 %	
Marital status of patients.			
	No. of patients	Percentage	
Married	62	62 %	
Single	38	38 %	
Scio-economic status			
	No. of cases	Percentage	
Low	40	40 %	
Middle	55	55 %	
High	5	5 %	

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

Sign/symptoms	No. of cases	percentage
Angioedema	90	90
Pain in oral cavity	92	92
Vomiting	87	87
Dyspnea	90	90
Muscle pain	88	88
Epigastric pain/tenderness	65	65
Oro facial edema	90	90
Fits	10	10
Hypertension	21	21
Dark colored urine	94	94
Oliguria	13	13
Anuria	7	7

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

Laboratory test	No. of cases	Percentage
TLC > 11000	72	72
Rise in blood urea	48	48
Rise in Serum creatinine	38	38
Rise in CPK	96	96
Rise in CK-MB	77	77
Hyperkalemia	28	28
Urine cast	21	21
Deranged LFT's	31	31
Pathological finding in X-ray	17	17
Pathological finding in ECG	69	69

Table 4: lifesaving intervention done in patients.

Intervention	No. of cases	Percentage
Tracheostomy	88	88
Mechanical ventilation	12	12
Dialysis	17	17

Table 5: Outcome of 120 patients with PPD poisoning.

	Male	Female	Total
Died	3	6	9
Survived	18	73	91

DISCUSSION

Poisoning with paraphenylene diamine is emerging as an important means of intentional self-harm with high mortality rate in many developing countries,^[15,16] In our study we observed that female were 70% and male 30% with male to female ratio was 1:2.5 which is similar to many other studies i.e. by Akbar *et al.*,^[17] and Anagram Chrimal *et al.*,^[18] Preponderance of females with a male to female ratio of 1:1.84 has been documented by Normal and Ganesh *ET al.*,^[19] A study from Hyderabad, India by Sakuntala *ET al.*,^[20] 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. We observed that at our hospital most of patients belong to low and middle class family with 40% and 55% respectively. We noted that in our study about 62% of cases were married and remaining 38% were unmarried which shows similar results to a study by Churro *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.^[22] About 60% of patients in our study were between 15-30 years of age and these results also similar with other studies like, Akbar *et al.*^[17] reported the mean age as 25.5±4.56 years, Chrimal *et al.*,^[18] as 27.75 years, Normal and Ganesh,^[19] 24.7±6.51 years, and Suleiman *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 81% cases were from rural background which stats are similar with many other studies e.g. in a study by Churro *ET al.*,^[21] all their patients were from rural background. The most common clinical feature observed in this study was angioedema and facial swelling followed by vomiting, dyspnea, and muscle pain. Suleiman *ET al.*,^[23] who reported cervicofacial edema in all their patients with 15.8% requiring tracheostomy. 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,^[17] The mortality rate was 9% which is way lower than other studies. Churro *et al.*,^[22] 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.*,^[22]

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

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