

FREQUENCY OF ACUTE RENAL FAILURE IN BLACK STONE POISONING AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the frequency of acute renal failure in patients with black stone poisoning at a tertiary care hospital.

Study Design: Cross-sectional

Place And Duration of The Study: Department of General Medicine, JPMC, Karachi, for six months.

Methodology: The sample of two hundred and eighteen adults (20-60 years of age) who presented more than 6 hours after the ingestion of paraphenylene diamine (PPD) were enrolled by consecutive sampling. The following were documented: comorbidities and serum creatinine at the time of admission. Acute renal failure was defined and staged according to KDIGO criteria, and association was determined with statistical tests of significance with $P \leq 0.05$ by SPSS-27 with crude and adjusted logistic regressions.

Result: The median age was 27 years (IQR 24 to 30), and 176 participants (80.7%) were women. ARF was present in 16 patients (7.3%), of whom 7 (43.8%) had stage III disease. None of the demographic or clinical factors showed a significant association with renal failure, and neither crude nor adjusted regression identified a significant predictor (all $p > 0.05$).

Conclusion: A small but clinically significant percentage of patients with black stone poisoning had ARF, and severe disease was frequent in those who developed it. In this study population, neither demographic nor clinical characteristics were significant enough to predict renal involvement.

KEYWORDS: Acute kidney injury, phenylenediamines, poisoning, suicide attempts, hair dyes, and rhabdomyolysis.

INTRODUCTION

Paraphenylene diamine (PPD), commonly referred to as 'Kala pathar' or 'black stone', is an aromatic amine compound which is valued for its ability to produce a deep, long-lasting colour in henna preparations and in commercial hair dyes [1,2]. Its widespread cellular injury and ability to be readily absorbed make it acutely toxic when ingested, yet it also is a popular cosmetic agent due to its chemical properties. Severe envenomation of the upper airways and soft tissues occurs early, and angioedema, laryngeal oedema, respiratory compromise, and cardiac arrhythmia usually occur within the first four to six hours of exposure [3]. Moderate ingestions usually lead to acute renal failure within the first week, while smaller amounts are more likely to develop hepatitis and clinically important angioneurotic oedema, which are rarely fatal [4]. As PPD has become cheaper and easier to obtain, its toxicological burden has also increased. Many countries have banned its use in hair dyes based on safety concerns, but it is a common ingredient in many hair dyes in Pakistan, India, and other parts of the Far East [5]. Deliberate self-ingestion of PPD-containing compounds has, as a result, become a more common method of self-harm which is

linked to significant morbidity and an alarmingly high case fatality rate [3, 6] in the under-resourced areas of Asia & Africa. The agent has become a specific facilitator of suicide for young women, and in a single year, in the province of Punjab alone, dozens of women committed suicide with black stones owing to financial difficulties, family tensions, and social pressures; the majority of those who took this type of suicide were of a younger age and of a rural background [7].

From a clinical standpoint, the management of PPD poisoning is complicated by the absence of a confirmatory diagnostic assay, so that accurate recognition depends on a high index of suspicion supported by the history of

exposure, the characteristic clinical syndrome and supportive laboratory findings [8, 9]. The sequence of pathophysiological events is now reasonably understood: PPD interferes with cellular oxidation, causing damage to skeletal muscle and leading to rhabdomyolysis and myoglobinuria, which then results in pigment-induced acute tubular necrosis and renal failure, with concurrent cervicofacial oedema posing a threat to the airway [10,11]. Early identification and prompt supportive measures, such as airway protection and timely renal replacement therapy, when necessary, significantly enhance survival, highlighting the importance of recognising renal involvement as early as possible [12].

The renal outcomes associated with PPD ingestion have varied widely among settings and case definitions. In a large regional series, the average age of affected patients was in the middle 20s, there was a definite female predominance, and there was a minority of admissions complicated by acute renal failure, which occurred at all stages of severity [3]. Acute renal failure has been reported in most poisoned patients, with cervicofacial oedema being the most frequent initial finding, and suicide being the most common intention behind the poisoning [6]. Hospital-based studies from Pakistan and neighbouring countries similarly report dialysis-dependent acute kidney injury, dose-dependent severity, and appreciable mortality, confirming that renal failure is the principal determinant of outcomes in this poisoning [15].

Given this growing evidence, the reported incidence of ARF varies significantly based on local referral practices, the amount of toxin ingested, and the speed of presentation, making it unreliable to translate these figures from one population to another. Beneficial local data from the tertiary care centres in this area have yet to be established, and the frequency of renal failure complicating black stone poisoning at the point of definitive care needs to be quantified so that the need for nephrology input and dialysis capacity can be predicted. The current study was therefore designed to find out the epidemiology of ARF in black stone poisoning cases who presented at a tertiary care hospital.

METHODOLOGY

This is a cross-sectional study which was carried out at Department of General Medicine, JPMC, Karachi, for six months. Patients were recruited through non-probability consecutive sampling of adults of both sexes, aged 20 to 60 years, who presented more than 6 hours after PPD ingestion. Those excluded from the study were individuals who died within five hours of ingestion, had a history of renal surgery, any established cardiac disease, cardiac surgery, or poisoning by another agent. Informed consent was obtained from all participants.

PPD poisoning was considered positive when there was a documented or strongly suspected history of exposure to PPD-containing compounds and at least two compatible clinical or laboratory findings within 72 hours (cervicofacial oedema, myoglobinuria, rhabdomyolysis, AKI, hyperkalaemia, metabolic acidosis, or neurological signs) and ARF (the primary measure of interest) was defined as an increase in the level of serum creatinine at least 0.3 mg/dL above the baseline. Severity was categorised as stage 1, 2 or 3 based on the level of serum creatinine (stage 1, 2 or 3). The sample size of 218 patients was derived using an expected prevalence of ARF of (7.5%)³, precision (3.5%) and a C.I of 95%. All eligible patients fulfilling the criteria were enrolled and, following consent, their demographic details together with comorbidities such as diabetes mellitus, hypertension and smoking status were recorded; every patient was managed conservatively on arrival with parenteral steroids, antihistamines and sodium bicarbonate, and a venous sample was obtained at admission for serum creatinine to establish the renal diagnosis, with all observations entered on a predesigned proforma by the principal investigator, a postgraduate trainee in internal medicine, while bias and confounding were minimised by strict adherence to the eligibility criteria and by stratification. Data were analysed in SPSS-27; descriptive statistics in terms of mean, median and percentage were reported. Univariable and multivariable binary logistic regression were performed to estimate crude and adjusted odds ratios with 95% C. I for the association between candidate predictors and ARF; predictors with a univariable p-value below 0.25 were entered into the multivariable model.

RESULTS

A total of 218 patients with black stone poisoning were enrolled. The median age was 27 years (IQR 24 to 30), and women formed the majority of the sample at 176 (80.7%), with 42 men (19.3%). Most participants came from rural areas, 134 (61.5%), while 84 (38.5%) were urban residents. Married patients comprised 114 (52.3%) of the cohort, unmarried 96 (44.0%) and divorced 8 (3.7%). Secondary schooling was the commonest educational level, recorded in 98 (45.0%), and non-smokers predominated at 185 (84.9%), with 22 smokers (10.1%) and 11 ex-smokers (5.0%). Diabetes mellitus (DM) was present in 20 (9.2%) and hypertension (HTN) in 22 (10.1%). Deliberate self-poisoning accounted for 199 (91.3%) of ingestions, accidental exposure for 18 (8.3%) and a single homicidal case (0.5%). The median time to presentation was 12.3 hours (IQR 9.4 to 16.4); the median estimated volume ingested was 26.35 ml (IQR 16.4 to 37.7); and the median admission serum creatinine was 0.88 mg/dl (IQR 0.77 to 1.01). These characteristics are summarised in Table 1.

ARF was identified in 16 patients, giving a frequency of 7.3% within the studied population. Among those who developed renal failure, stage III disease was the most frequent presentation in 7 patients (43.8%), followed by stage I in 5 (31.3%) and stage II in 4 (25.0%). Table 1 also displays the distribution of the primary outcome and its severity.

In stratified analysis, the incidence of ARF did not significantly vary by any demographic or clinical subpopulation. Renal failure occurred in 7 (5.7%) of patients aged 27 years or younger compared with 9 (9.5%) of older patients ($p = 0.288$), and in 13 (7.4%) women against 3 (7.1%) men ($p = 1.000$). No association was

observed with residential status ($p = 0.327$), marital status ($p = 0.674$), educational level ($p = 0.439$), smoking status ($p = 0.854$), DM ($p = 0.827$) or HTN ($p = 1.000$). These comparisons are provided in detail in Table 2. Unadjusted and adjusted logistic regression supported these findings, as none of the candidate predictors reached statistical significance. Older age carried a crude odds ratio of 1.73 for ARF, which reversed direction to 0.60 after adjustment ($p = 0.342$), a pattern consistent with model instability given the small number of outcome events, while DM, HTN, gender, residence, duration of poisoning and estimated volume consumed showed no predictive value.

These estimates should therefore be regarded as exploratory. The regression estimates are presented in Table 3.

Table I: Baseline Characteristics of the Study Population (n=218)

Baseline Characteristics	Median (IQR) / n (%)
Age (years)	27 (24–30)
Duration of Poisoning (hours)	12.3 (9.4–16.4)
Estimated Volume Consumed (ml)	26.35 (16.4–37.7)
Serum Creatinine (mg/dl)	0.88 (0.77–1.01)
Gender, n (%)	
Male	42 (19.3)
Female	176 (80.7)
Residential Status, n (%)	
Urban	84 (38.5)
Rural	134 (61.5)
Marital Status, n (%)	
Married	114 (52.3)
Unmarried	96 (44.0)
Divorced	8 (3.7)
Educational Status, n (%)	
Secondary	98 (45.0)
Intermediate	61 (28.0)
Graduate	48 (22.0)
Postgraduate	11 (5.0)
Smoking Status, n (%)	
Smoker	22 (10.1)
Non-smoker	185 (84.9)
Ex-smoker	11 (5.0)
Reason for PPD Ingestion, n (%)	
Suicide	199 (91.2)
Accidental	18 (8.3)
Homicidal	1 (0.5)
Diabetes Mellitus, n (%)	20 (9.2)
Hypertension, n (%)	22 (10.1)
Acute Renal Failure, n (%)	16 (7.3)
Stage of ARF, n (%)	
Stage I	5 (31.3)
Stage II	4 (25.0)
Stage III	7 (43.8)

Table II: Association of Acute Renal Failure with Demographic and Clinical Factors (n=218)

Demographic and Clinical Factors	Acute Renal Failure Yes (n=16)	Acute Renal Failure No (n=202)	P-Value
Age Groups			
≤27 years	7 (5.7)	116 (94.3)	0.288
>27 years	9 (9.5)	86 (90.5)	
Gender			
Male	3 (7.1)	39 (92.9)	1.000
Female	13 (7.4)	163 (92.6)	
Residential Status			
Urban	8 (9.5)	76 (90.5)	0.327
Rural	8 (6.0)	126 (94.0)	
Marital Status			
Married	8 (7.0)	106 (93.0)	0.674
Unmarried	8 (8.3)	88 (91.7)	
Divorced	0 (0.0)	8 (100.0)	

Educational Status			
Secondary	5 (5.1)	93 (94.9)	0.439
Intermediate	4 (6.6)	57 (93.4)	
Graduate	6 (12.5)	42 (87.5)	
Postgraduate	1 (9.1)	10 (90.9)	
Smoking Status			
Smoker	1 (4.5)	21 (95.5)	0.854
Non-smoker	14 (7.6)	171 (92.4)	
Ex-smoker	1 (9.1)	10 (90.9)	
Diabetes Mellitus			
Yes	2 (10.0)	18 (90.0)	0.827
No	14 (7.1)	184 (92.9)	
Hypertension			
Yes	1 (4.5)	21 (95.5)	1.000
No	15 (7.7)	181 (92.3)	

Table III: Factors Associated with Acute Renal Failure Among Study Participants (n=218)

Predictor	Crude OR (95% CI)	P-Value	Adjusted OR (95% CI)	P-Value
Gender: Male vs Female	0.96 (0.26–3.55)	0.957	—	—
Residence: Rural vs Urban	0.60 (0.22–1.67)	0.332	—	—
Diabetes: Yes vs No	1.46 (0.31–6.94)	0.634	0.74 (0.15–3.61)	0.711
Hypertension: Yes vs No	0.57 (0.07–4.57)	0.601	1.65 (0.20–13.43)	0.639
Age: >27 vs ≤27 years	1.73 (0.62–4.84)	0.293	0.60 (0.21–1.71)	0.342
Duration of poisoning (per hour)	0.99 (0.89–1.09)	0.784	0.99 (0.89–1.10)	0.844
Volume consumed (per ml)	0.98 (0.94–1.02)	0.253	—	—

DISCUSSION

PPD poisoning is now a well-known but challenging emergency in this region due to the lack of a confirmatory assay and reliance on history of exposure and the dynamic clinical picture. The compound's actions involve oxidation of cells, which causes damage to both muscle and liver and kidney, and renal failure has a special significance since it influences the necessity of dialysis and survival [10,11,12]. It is therefore important to quantify the proportion of black stone ingestions complicated by renal failure at definitive care to have a direct impact on resource planning. The aim of the present study was to determine the frequency in adults who presented to a tertiary care hospital.

The cohort was young, with a median age of 27 years, and women made up four fifths of the study sample (80.7%), a trend like regional series where the prototypical patient is a young woman with suicidal intentions [3, 7]. A prospective study in the National Poison Control Centre in Karachi also reported the mean age in the mid-twenties and a clear female preponderance [5], while another cross-sectional study of black rock poisoning in Egypt reported 85% of victims poisoned to be female [14]. A high proportion of rural residents and a high suicidal intent rate of 91.3% in our sample are consistent with the previously reported social factors associated with this form of self-destructive behaviour [7].

Acute renal failure complicated 7.3% of admissions in the current study. This figure sits close to the 7.5% prevalence assumed for sample size estimation and aligns with the lower end of the published range. Kanhar and colleagues, working in a comparable Pakistani setting, recorded renal failure in a minority of poisoned patients [3]. Significantly higher frequencies have been reported at other locations. Arif et al. reported a higher incidence of renal failure in their group

[6], and an Indian clinical and experimental study found that approximately one-third of patients developed acute kidney injury, with many of these patients' requiring dialysis [15]. The recurrence of PPD as a cause of kidney injury due to poisoning was confirmed by a retrospective review at an institute in Karachi [16].

Within the 16 patients who developed renal failure, the most severe stage predominated, accounting for 43.8% of cases. The mechanism is well described, as PPD provokes rhabdomyolysis and myoglobinuria, and the resulting pigment load drives tubular injury and acute tubular necrosis [10,11]. Reported rates of rhabdomyolysis exceed two thirds in several cohorts [14], and acute hepatitis frequently accompanies renal involvement, occurring in around half of intoxicated patients in a Bahawalpur series [20]. The concentration of advanced disease among our affected patients is consistent with the dose-dependent toxicity that other authors have emphasised [13].

There was no statistically significant relationship between renal failure and any of the demographic or clinical variables studied, and no statistically significant predictor of renal failure was found when the variables were analysed by untransformed and transformed regression. Similar studies have also had difficulty finding consistent demographic determinants, and prognosis studies have focused on physiological severity at presentation, such as composite scores like the Rapid Emergency Medicine Score and the Sequential Organ Failure Assessment, as a better predictor of adverse outcome than baseline demographics [17]. The absence of significant associations in our data may reflect the small number of renal failure events relative to the total sample, which limited statistical power.

The study's strengths lie in its defined sample of 218 consecutive patients, standardised case definition and uniform conservative management when patients arrived. There are several caveats to the results. The single-centre cross-sectional design limits generalisability, and the small number of renal failure events limited the exactness of the subgroup and regression estimates, as the large confidence intervals suggest. Although single-admission creatinine was used and no longitudinal follow-up data was obtained, that may have underestimated the development of renal injury, as has been emphasised in reviews, which have requested more regional prospective data [18,19].

The combined results support the hypothesis that renal failure occurs in a clinically important minority of black stone poisoning cases and that the occurrence of advanced-stage disease is frequent. The observed frequency of 7.3% here provides local tertiary care data to a literature of highly variable frequencies when settings and case definitions differ and supports the importance of early renal assessment in patients presenting after ingestion of PPD.

CONCLUSION

A small but clinically significant percentage of patients with black stone poisoning had ARF, and severe disease was frequent in those who developed it. In this study population, neither demographic nor clinical characteristics were significant enough to predict renal involvement.

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