The management and clinical outcome of paracetamol poisoning in South African adults: A single-centre retrospective review

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Background. Paracetamol is a commonly prescribed drug, and often implicated in pharmaceutical overdoses. Paracetamol-induced hepatotoxicity is a common cause of acute liver failure in many high-income countries, but little is known about the factors associated with severity of liver injury and poor clinical outcomes among those treated in sub-Saharan African settings.

Objective. To describe the characteristics of patients presenting with paracetamol poisoning, and to identify factors associated with severity of liver injury and poor outcomes in adults with biochemical evidence of paracetamol-induced liver damage treated at a South African (SA) tertiary hospital.

Methods. A retrospective medical record review was conducted of all adult patients (≥18 years old) admitted between August 2013 and August 2018 to a tertiary referral centre in Cape Town, SA, with paracetamol poisoning and biochemical evidence of liver impairment. Demographics, clinical and laboratory data were obtained. Management practices and clinical outcomes were assessed.

Results. The records of 91 patients were included in the analysis. The median (interquartile range (IQR)) age was 29 (23 - 39) years, and 63% were female. The majority of paracetamol poisonings followed an intentional overdose (91%). Acute single ingestions were the most common (81%) type of toxic ingestion, compared with staggered overdose and repeated supratherapeutic ingestion, and the median (IQR) number of tablets ingested was 22 (20 - 39). Two-thirds of patients developed mild liver injury and 12% developed acute kidney injury. The overall mortality rate was 12%. Mortality was lower in those who received intravenous N-acetylcysteine (NAC) before serum paracetamol concentrations were known compared with those who only received NAC after concentrations were known (8.8% v. 36%, p=0.03). A significant proportion of deaths occurred in those with accidental overdose compared with those with intentional overdosing (57% v. 7.2%; p=0.004). People living with HIV (p=0.04), a history of chronic alcoholism (p=0.04), chronic liver disease (p=0.01) and severity of acute kidney stage (p<0.001) were all associated with increased mortality.

Conclusion. A high case fatality rate was observed in the studied population. Early identification of at-risk individuals and prompt initiation of NAC can reduce poor outcomes. Larger multicentre studies are needed to identify independent predictors of paracetamol-induced hepatoxicity and mortality in Africa.

Keywords: paracetamol poisoning, acute toxicity, acetylcysteine, hepatotoxicity

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Paracetamol is a commonly prescribed and easily accessible over-the-counter medication used for the relief of mild to moderate pain and fever.[1] It is also a commonly ingested drug in pharmaceutical overdoses, and accounts for most non-prescription medicine overdoses in the USA, Australia, New Zealand and the UK.[2-5] Furthermore, data from sub-Saharan Africa suggest that paracetamol is also one of the most common non-prescription medications used for deliberate self-harm in Botswana and South Africa (SA).[6-9]

Hepatotoxicity and acute liver failure (ALF) are the most severe adverse events associated with paracetamol overdose. Almost half (42%) of all ALF cases in the USA are attributed to paracetamol-induced hepatotoxicity.[10,11] Similarly, in the UK and Europe, paracetamol has been associated with a significant proportion (57%) of ALF cases.[12] In these high-income countries, the risk factors associated with the development of paracetamol-induced hepatotoxicity, and clinical outcomes of hospitalised patients, are well described.[13] In contrast, outcomes associated with paracetamol overdose in sub-Saharan African countries remain unclear.[14] Sub-Saharan countries often face significant healthcare resource constraints and limited access to healthcare, which often leads to delayed presentation after paracetamol overdose, with worse outcomes.[15] An improved understanding of the circumstances of toxic ingestion and management practices can assist in identifying areas where in-hospital patient care and treatment outcomes can be improved.

The aim of this study was to describe the characteristics of paracetamol overdose, and to identify the factors associated with higher grades of liver injury and poorer outcomes among adults treated for paracetamol poisoning with biochemical evidence of liver injury in a SA tertiary hospital setting.

Methods

Study design and setting

The study was conducted at Tygerberg Hospital, a 1 200-bed teaching hospital located in Cape Town, SA. We performed a retrospective review of electronic hospital records for all adults (aged ≥18 years) admitted to Tygerberg Hospital over 5 years, between 1 August 2013 and 31 July 2018, with oral paracetamol poisoning and laboratory evidence of liver injury.

Patient selection

A stepwise approach was utilised to identify the patients included in the final study sample. First, the National Health Laboratory Service (NHLS) database was reviewed to identify adult patients who had at least one serum paracetamol concentration measured at the hospital over the 5-year study period. This was followed by a review of all alanine aminotransferase (ALT) and international normalised ratio (INR) testing results linked to the admission episode when paracetamol concentration was measured. ALT values that exceeded the upper limit of normal (>40 IU/L in males and >35 IU/L in females), and INR values of >1.1, were considered abnormal. This sensitive screening step served to identify all patients with possible liver impairment.

The medical records of those with both detectable serum paracetamol concentrations and either an abnormal ALT or INR test value were then reviewed to determine if a diagnosis of paracetamol poisoning was made by the treating clinician. Patients were included in the analysis if a diagnosis of paracetamol poisoning was made at any point during the admission episode or if paracetamol poisoning was considered to be the lead differential diagnosis (based on collateral history, clinical and biochemical findings) in those whose clinical condition precluded history-taking. Those found to have elevated baseline hepatic enzymes secondary to pre-existing medical conditions were also included if, after thorough assessment, the treating clinician documented that the paracetamol poisoning episode defined the severity of the patient's condition. The Tygerberg Hospital pharmacy dispensary database was also reviewed to identify the medical records of inpatients who received N-acetylcysteine (NAC) during the study period. This necessary cross-checking step assisted in confirming whether a patient did indeed receive treatment for paracetamol poisoning, and aided in identifying additional patients with paracetamol poisoning who were referred to Tygerberg Hospital for further inpatient care after initial paracetamol concentrations and liver function tests were done at a referring hospital.

Patients were excluded if no diagnosis of paracetamol poisoning was made at admission or during in-hospital care by the treating clinicians. Those who did not receive NAC during the admission episode were also excluded. The records of patients treated for intravenous paracetamol poisoning were reviewed, but excluded from the analysis.

Data collection

The following data points were collected from patient medical records: demographic information (age, sex and comorbidities), risk factors for hepatotoxicity (chronic alcoholism, chronic liver disease, history of taking liver enzyme-inducing medication, presumed glutathione depletion), intentionality of overdose, quantity and timing of paracetamol ingestion, co-ingested medications, laboratory results (liver and renal function tests, coagulation profile), treatment details (type of treatment given, time to NAC administration, dosage of NAC and indication for stopping NAC) and clinical outcomes. We used ALT, INR and serum paracetamol concentrations to determine whether a correct indication for stopping NAC was used, depending on the circumstances of ingestion (Table 1). Paracetamol poisoning presentations were categorised as acute single ingestion, multiple or staggered overdose, repeated supratherapeutic ingestion (RSTI) or unknown dose or time of ingestion, using definitions from established guidelines.[5] Acute single ingestion was defined as the ingestion of >200 mg/kg, or 10 g of paracetamol (whichever was less), over a period of <8 hours, or the ingestion of a single dose capable of causing hepatotoxicity based on available clinical evidence at the time of admission. Multiple or staggered overdose was defined as multiple or staggered paracetamol ingestions over >2 hours with the intention for deliberate self-harm. RSTI was defined as the daily ingestion of a dose of paracetamol of more than or equal to therapeutic doses (4 g/day), for 48 hours, in patients who subsequently developed abdominal pain, nausea or vomiting, or who had any predisposing risk factors for hepatoxicity.

The Drug-Induced Liver Injury Network (DILIN) grading system was used to determine the maximum grade of liver injury (severity) for each patient.[16] Clinical history, in combination with the highest ALT and INR values recorded during the admission episode, were used to determine the DILIN grade. Results of additional tests performed in hospital, such as total serum bilirubin and alkaline phosphatase (if available), were also reviewed prior to assigning a grade. To determine the presence of kidney injury, we reviewed past and present serum creatinine values and utilised the Kidney Disease: Improving Global Outcomes (KDIGO)[17] clinical practice guideline for acute kidney injury to assign an acute kidney injury (AKI) stage if injury was present.

Statistical analysis

All analyses were conducted using STATA version 17 (STATACorp, USA). Categorical variables were expressed as percentages, and continuous variables were expressed as mean, standard deviation (SD) or median with interquartile range (IQR). Categorical variables were analysed using the χ^2 test or Fisher's exact test. Continuous variables were analysed using an unpaired *t*-test or Mann-Whitney *U*-test, according to statistical distribution. The Kruskal-Wallis test was used to compare more than two groups. The overall case fatality rate for those with paracetamol poisoning was calculated, and estimated risk differences were used to present the absolute effect of a risk factor on mortality. $P<0.05$ was considered to be statistically significant.

Ethical considerations

Ethics approval for the study was obtained from the Stellenbosch University Health Research Ethics Committee prior to commencement of study procedures (ref. no. U18/07/028).

Table 1. Recommended indications for stopping N-acetylcysteine[18-21]

After completion of first NAC treatment cycle
If the ALT is <2 × the upper limit of normal and INR <1.3, NAC can be stopped
After 12-hourly ALT and INR measurements
If the ALT is <2 × the upper limit of normal or has not doubled since admission and INR <1.3, NAC can be stopped
If RSTI
NAC may be stopped once serum paracetamol concentration <66 μmol/L (<10 mg/L) and ALT is normal, static or declining

NAC = N-acetylcysteine; ALT = alanine aminotransferase; INR = international normalised ratio; RSTI = repeated supratherapeutic ingestion.

Results

Participants

Over the 5-year period, 1 802 patients (aged ≥18 years) treated at Tygerberg Hospital underwent serum paracetamol concentration measurements. Of these, 109 (6.1%, 95% CI: 5.1 - 7.3) had accompanying biochemical evidence of liver impairment (abnormal ALT and/or INR values), with a confirmed history of paracetamol ingestion or paracetamol ingestion strongly suspected based on initial clinical assessment. Eighteen patients with paracetamol poisoning were excluded from the analysis due to missing medication records (*n*=15) or missing clinical records (*n*=3). One patient with intravenous paracetamol poisoning was also excluded from the analysis (Fig. 1).

Demographics and clinical characteristics

Over the 5-year study period, the mean (SD) number of paracetamol toxicity cases with biochemical evidence of liver impairment requiring intravenous NAC was 18.2 (2.3) cases per year (Fig. 2). The mean age of patients with intentional overdosing was 10 years younger than the mean age of those with accidental overdosing (31 years v. 41 years; *p*=0.04). Fourteen percent (*n*=13) co-ingested hepatotoxic medications, of which anti-epileptic medications were the most common (*n*=8), and 30% (*n*=27) co-ingested potentially nephrotoxic medications, of which non-steroidal anti-inflammatory drugs were the most common (*n*=24).

More than 80% of paracetamol poisonings were categorised as acute single ingestions (*n*=74) (Table 2). Fifty percent of patients with acute single ingestions (*n*=37) presented to the hospital within 8 hours following a toxic ingestion. Forty-four percent (*n*=40) of all patients were able to provide an estimation of how many paracetamol tablets were ingested to the admitting clinician.

Factors associated with worsening grade of liver injury

Eighteen percent (*n*=16) were categorised as high risk for liver injury. Chronic alcoholism was the most common high-risk factor (*n*=14). There was a statistically significant association between DILIN severity grades and having chronic alcoholism (*p*=0.01). Fifty-seven percent of those with chronic alcoholism had DILIN grade 3 - 5 liver injury, compared with 19% of those without chronic alcoholism (*p*=0.004). There was also a significant association between chronic alcoholism and requiring higher levels of care (*p*=0.03).

Factors associated with acute kidney injury stage

Chronic alcoholism was the only factor associated with a higher AKI stage (*p*=0.02) in the studied population.

Paracetamol poisoning management

Activated charcoal was instituted for 18% of patients (13/74) who presented with acute single ingestions. Two patients received activated charcoal >2 hours after the recorded time of toxic ingestion. In those with acute single ingestions who had paracetamol concentrations measured in the first 24 hours after ingestion, the paracetamol treatment nomogram was correctly interpreted in 98% (57/58) of cases. The single error was due to an ingestion time that was incorrectly recorded in the patient notes.

The median (IQR) number of NAC infusions administered during in-hospital care (including the three infusions given as part of the three-bag NAC protocol and further doses) was 3 (3 - 5). In 88% (80/91) of patients, NAC was administered before the serum paracetamol concentration was known. Thirty-eight patients (42%, 38/91) had more than one paracetamol concentration measured during their admission. NAC was well tolerated, and only one patient developed a non-allergic anaphylactic reaction, presenting as urticaria, to NAC administration. Among those with complete prescription data, the initial NAC infusion dosage, for a three-bag infusion protocol, was calculated correctly in 94% of patients (83/88). The majority of those with incorrectly calculated dosages were overdosed (3/5). Subsequent NAC dosages were calculated correctly in 89% of patients (78/88), and the majority of those with incorrect dosages (6/10) were also overdosed. Among those who recovered, an incorrect indication for stopping NAC infusions was found in 6.1% (5/82), and no indication for stopping

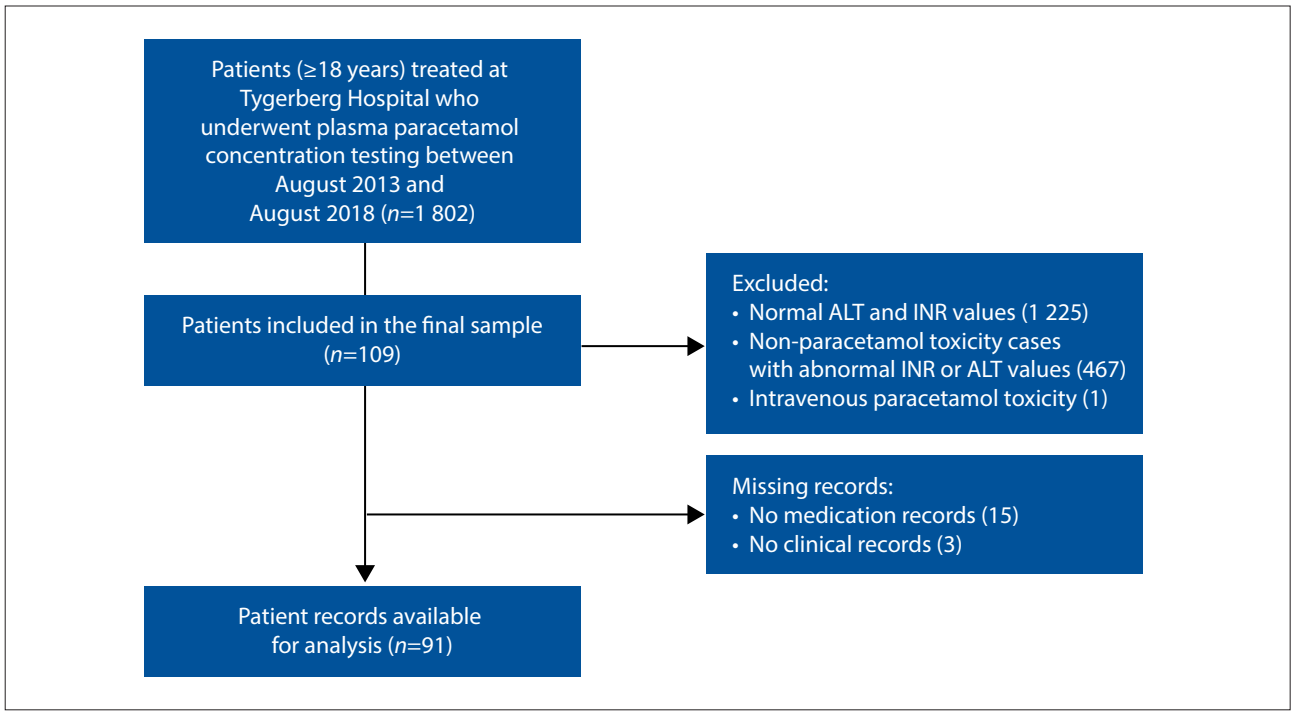

Fig. 1. Flow diagram of patients included in the study. (ALT = alanine aminotransferase; INR = international normalised ratio.)

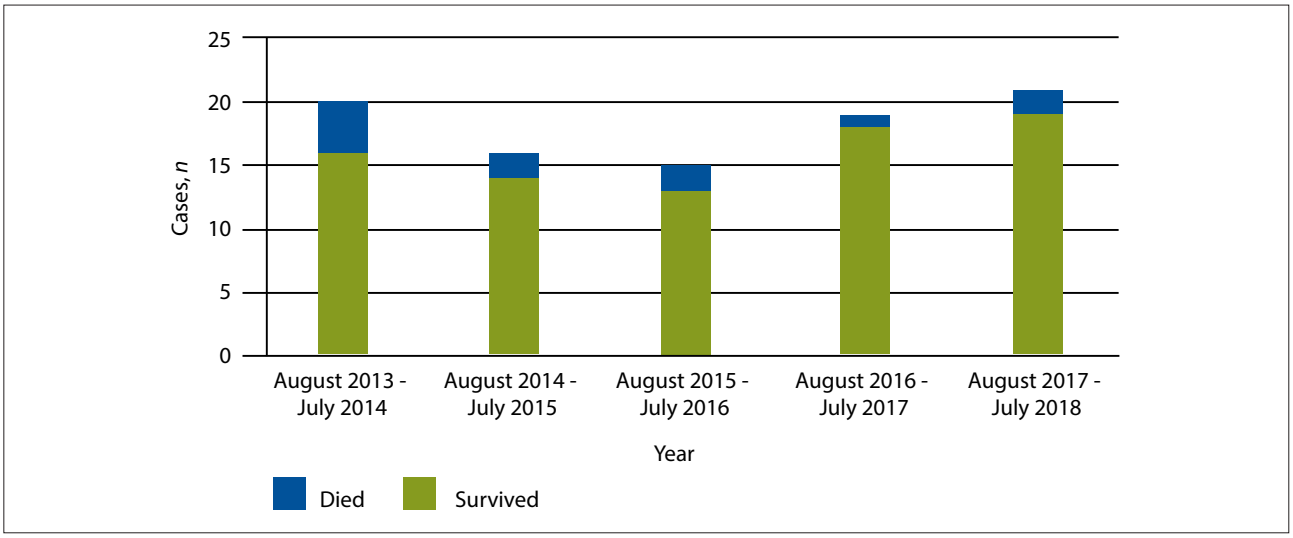

Fig. 2. Paracetamol toxicity cases between August 2013 and August 2018.

NAC could be found in 7.3% (6/82). No patients received a two-bag NAC regimen.

Mortality

Overall, the case fatality rate was 12% (n=11). Fifty-seven percent (n=4) of patients who presented with an accidental overdose died, compared with 7.2% (n=6) of those who presented with an intentional overdose (p=0.004). Among those who died, 6 were acute single ingestions, 2 were RSTIs and 3 had unknown patterns of ingestion (Table 3). There was a significant difference in mortality between those who received NAC before paracetamol concentrations were known and those who received NAC after paracetamol concentrations were known (8.8% v. 36%, p=0.03). Among 82 patients in whom the timing of paracetamol ingestion was known, there was a significant difference in mortality between those who received NAC within 8 hours of ingestion and those who did not (0% v. 18.8%, p=0.01), favouring early NAC use. Other factors that were associated with mortality were HIV positivity (p=0.04), chronic alcoholism (p=0.04), chronic liver disease (p=0.01) and worse AKI stage (p<0.001). Among the 3 patients with HIV who died, all were accidental toxic ingestions, and 2 had at least one pre-existing risk factor for liver impairment (chronic alcoholism or chronic liver disease). The estimated risk difference of death for those who were HIV positive was 0.33 (95% CI –0.04 - 0.71; p=0.08).

Discussion

We described the patient characteristics and risk factors associated with severe hepatotoxicity among adults treated for paracetamol poisoning in a SA tertiary level healthcare setting.

Patients admitted with paracetamol poisoning were predominantly female and young, with a median age of 29 years. Most (91%) were admitted with intentional, acute, single ingestions, and the mean age of those with intentional overdosing was 10 years younger than those admitted for accidental overdosing. These features are in keeping with those of paracetamol poisoning cases from studies conducted in high-income countries.[11,22-26] Increased age has been found to be associated with more severe liver injury and higher mortality rates following paracetamol poisoning; however, in our study, the absence of an association between age and poorer outcomes may be explained by the relatively young study population and residual confounding factors.[23,27-29]

Seven patients (7.7%) presented with accidental paracetamol poisoning, of which the majority were RSTIs. More concerning is that, among those with accidental toxic ingestion, four patients died, which represents 57% of all patients with accidental poisoning and 36% of all those who died. In the UK, unintentional overdose has been found to be independently associated with increased mortality compared with intentional overdose.[26] Possible explanations may include the nonspecific nature of initial symptoms that accompany accidental poisonings, and the diagnosis being missed by clinicians due to a low index of suspicion, resulting in delayed initiation of treatment.

Overall, a high mortality rate (12%) was observed in this study. This finding may be explained, in part, by the fact that we only evaluated patients admitted to a single tertiary referral centre, which provides medical care to those requiring a higher level of care.[26,30] Moreover, the lack of liver transplant services at the centre may have contributed to the observed higher mortality.

There exist limited data on at-risk populations for acute liver injury following paracetamol poisoning.[13] Concomitant use of cytochrome P450-inducing medications, pre-existing liver disease, chronic alcohol abuse and conditions associated with glutathione depletion, such as HIV and malnutrition, have all been proposed to increase risk.[28,29,31,32] Among patients categorised as high risk for liver injury based on these factors, a history of chronic alcoholism was the most common factor in the studied population. Multiple mechanisms for increased hepatotoxicity in patients with chronic alcoholism, such as CYP2E1 induction, delayed presentation and malnutrition, have been suggested. However, evidence for an association between chronic alcoholism and paracetamol-induced hepatotoxicity remains controversial.[13,25,28,33-36] In our study, the DILIN grades and KDIGO AKI stages of those with chronic alcoholism were significantly higher than in those without, and these patients subsequently required higher levels of care and longer admission stays, and had a higher risk of mortality. Our findings suggest that those with chronic alcohol abuse are at increased risk for poor outcomes following paracetamol poisoning.

A unique aspect of this study was that we evaluated whether people living with HIV (PLWH) were at higher risk of worse liver injury and poorer treatment outcomes following paracetamol poisoning. HIV has been found to be associated with a systemic reduction of available glutathione; therefore, it is speculated that PLWH have an increased risk of paracetamol-induced liver injury.[37-39] To date, only two case reports have described hepatoxicity following paracetamol use in PLWH; however, multiple confounding factors make it difficult to

Table 2. Demographic and clinical characteristics of the study sample (*N*=91)

Characteristic	*n* (%)*
Age, years, median (IQR)	29 (23 - 39)
Sex (female)	57 (62.6)
Risk factors for liver injury	16 (17.6)
Chronic alcoholism	14 (15.4)
Chronic liver disease	2 (2.2)
Hepatic enzyme-inducing chronic medication†	9 (9.9)
Glutathione deficiency‡	1 (1.1)
Pre-existing health conditions	
Hypertension	11 (12.1)
Illicit drug use	12 (13.2)
Major depressive disorder	6 (6.6)
HIV	7 (7.7)
Circumstances of ingestion	
Intentional	83 (91.2)
Accidental	7 (7.7)
Unknown§	1 (1.1)
Pattern of toxic ingestion	
Acute single ingestion	74 (81.3)
Multiple or staggered ingestion	2 (2.2)
RSTI	4 (4.4)
Unknown	11 (12.1)
Quantity of tablets ingested known	
Yes	40 (44.0)
No	51 (56.0)
Reported quantity of tablets ingested, median (IQR)	22 (20 - 39)
Co-ingested substances¶	59 (65.0)
NSAIDs	24 (26.4)
Antihypertensives	11 (12.1)
Anti-epileptics	8 (8.8)
Opioid analgesic	7 (7.7)
Tricyclic antidepressants	4 (4.4)
NNRTIs	3 (3.3)
NtRTIs	3 (3.3)
Alcohol	3(3.3)
Antituberculosis drugs	2 (2.2)
Antidiabetics	1 (1.1)
Length of hospitalisation, days, median (IQR)‖	3 (2 - 7)
Length of hospitalisation until death, days, median (IQR)	2 (1 - 5)
Highest level of care	
Medical ward/emergency centre	81 (89.0)
High care ward	5 (5.5)
ICU	5 (5.5)
DILIN grade	
1	61 (67.0)
2	7 (7.7)
3	9 (9.9)
4	3 (3.3)
5	11 (12.1)
AKI stage	
1	1 (1.1)
2	2 (2.2)
3	8 (8.8)
Mortality	11 (12.1)

IQR = interquartile range; RSTI = repeated supratherapeutic ingestion; NSAID = non-steroidal anti-inflammatory drug; NNRTI = non-nucleoside reverse transcriptase inhibitor; NtRTI = nucleotide reverse transcriptase inhibitor; ICU = intensive care unit; DILIN = Drug-induced Liver Injury Network; AKI = acute kidney injury.
*Unless otherwise indicated.
†Chronic cytochrome P450 enzyme-inducing medications such as nevirapine, efavirenz and carbamazepine.
‡Defined as having features of wasting during initial clinical evaluation.
§Clinical condition on admission precluded history-taking.
¶Refers to reported co-ingestions. Plasma drug levels only used for verification when available.
‖Data from mortality cases excluded.

prove that paracetamol is the causal factor.[40,41] We found that PLWH did not have worse DILIN grades, but were associated with higher levels of care and increased mortality. Interestingly, among PLWH who died, all presented with accidental toxic ingestions, and 67% had chronic alcoholism as a risk factor. Our small sample size limited further multivariable analyses, and there are likely many confounding factors contributing to increased mortality in those with HIV.

The management of paracetamol poisoning is informed by the correct interpretation of the paracetamol treatment nomogram, which has been validated as a reliable predictor of risk in the setting of acute single ingestions when the timing of ingestion is known.[5] Importantly, the nomogram is not validated for use before 4 hours or after 16 hours following acute single ingestion. However, serum paracetamol concentrations are extrapolated to 24 hours. We found that the nomogram was correctly interpreted in 98% of acute ingestion cases where paracetamol concentrations were taken within 24 hours of ingestion. All patients received at least one dose from a three-bag NAC infusion regimen, which was calculated correctly in 94% of cases. Worryingly, we observed a decrease in the proportion of correct dosage calculations for subsequent NAC infusions (89%). Among those who received incorrect NAC dosages, overdosing was more common than underdosing. Similar medication errors when using the traditional three-bag regimen have been reported elsewhere.[42,43] Additionally, early adverse reactions to the loading infusion of the three-bag regimen have previously been reported in a high proportion of patients.[44,45] Despite all patients in our study receiving the initial 200 mg/kg loading dose, we observed only one non-immunological anaphylactic reaction, presenting as an urticarial rash, and no serious adverse reactions. Considering our reported rate of incorrect NAC dosing, adoption of the non-inferior two-bag NAC infusion regimen has the potential to reduce the risk of prescription errors, limit costs and reduce the nursing time spent on intravenous bag changes.[4] The two-bag NAC regimen has since been implemented at Tygerberg Hospital.

Study limitations

This study was a retrospective review of electronic hospital records and laboratory data, and has limitations. Our findings were reliant on the quality of medical documentation at the time of clinical review, and an accurate patient history. The information regarding the dose of paracetamol, co-ingested drugs and indications for stopping NAC was particularly limited. Although we tested for significant associations, the sample size was too small to perform multivariate logistic regression and adjust for important confounders. Therefore, we were unable to provide adjusted effect estimates for important associations, and the risk of residual confounding remains high. This study focused only on cases of paracetamol poisoning admitted to a single tertiary-level health facility; therefore, our results may not be generalisable to patients with less severe poisoning or those who received medical care at non-specialised facilities.

Conclusion

We found a high case fatality rate among adults admitted with paracetamol poisoning and evidence of liver impairment over the 5-year period. Accidental overdose, receiving NAC >8 hours after toxic ingestion, HIV positivity, chronic alcoholism, chronic liver disease and higher AKI stage were all associated with increased mortality. Prompt identification of those at risk of poorer outcomes may help to reduce the mortality associated with paracetamol poisoning in a southern African setting. Additionally, the two-bag NAC regimen has the potential to decrease prescription errors and reduce costs. Larger multicentre studies aiming to identify risk factors

Table 3. Comparison of characteristics between patients who died and those who recovered following paracetamol poisoning (*N*=91)

Characteristics	Recovered (*n*=80), *n* (%)*	Died (*n*=11), *n* (%)*	*p*-value
Age, years, median (IQR)	28 (22 - 37)	35 (27 - 44)	0.12
Sex (female)	50 (62.5)	7 (63.6)	0.94
Risk factors for liver injury present	12 (15.0)	4 (36.4)	0.10
Chronic alcoholism	10 (12.5)	4 (36.4)	0.04
Chronic liver disease	0 (0.0)	2 (18.2)	0.01
Hepatic enzyme-inducing medication	6 (7.5)	3 (27.3)	0.07
Glutathione deficiency†	0 (0.0)	1 (9.1)	0.12
Pre-existing health condition			
Hypertension	9 (11.3)	2 (18.2)	0.62
Illicit drug use	9 (11.3)	3 (27.3)	0.16
Major depressive disorder	6 (7.5)	0 (0.0)	1.00
HIV	4 (5.0)	3 (27.3)	0.04
Circumstances of ingestion			
Accidental	3 (3.8)	4 (36.4)	0.004
Intentional	77 (96.3)	6 (54.5)	<0.001
Unknown	0	1 (9.1)	-
Pattern of toxic ingestion			
Acute single ingestion (<8 h)	37 (46.3)	0 (0.0)	0.002
Acute single ingestion (8 - 24 h)	20 (25.0)	2 (18.2)	1.00
Acute single ingestion (>24 h)	11 (13.8)	4 (36.4)	0.08
Multiple or staggered ingestion	2 (2.5)	0 (0.0)	1.00
RSTI	2 (2.5)	2 (18.2)	0.07
Unknown	8 (10.0)	3 (27.3)	0.13
Quantity of tablets ingested known	38 (47.5)	2 (18.2)	0.10
Co-ingested ≥1 hepatotoxic drug	11 (13.8)	2 (18.2)	0.65
Co-ingested ≥1 nephrotoxic drug	23 (28.8)	4 (36.4)	0.73

IQR = interquartile range; RSTI = repeated supratherapeutic ingestions.
*Unless otherwise indicated.
†Defined as having features of wasting during initial clinical evaluation.

for hepatoxicity and mortality in paracetamol poisoning in Africa are needed.

Data availability. The data used and analysed during the current study are available from the corresponding author on reasonable request.

Declaration. None.

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Author contributions. ED and JS conceptualised the study and developed the methodology. CK, JS and ECK collected and curated the data. CK and JS assisted with the statistical analyses. CK, JS and ED contributed to manuscript writing. All authors contributed to data interpretation, provided edits and critiqued the manuscript.

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