MJMR, Vol. 35, No. 2, 2024, pages (72-79)

Open Access
ISSN: 2682-4558

Research Article

Evaluation of the impact of an acute single paracetamol overdose on renal functions and serum electrolytes

Aya Mohamed Roshdi Abd-ELAzeem[1]; Osama Abdel Aziz Hassan[1]; Mohamed Bakr Ahmed[1] and Asmaa Salah Taghian[1]

[1]Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Minia University, Minia, Egypt

DOI: 10.21608/mjmr.2024.259956.1597

Abstract

Background: Paracetamol overdose is a common cause of drug-induced acute liver injury worldwide. The easy availability of the drug makes it a common method of suicide especially among young adults. Aim of the work: The study aims to assess the impact of an overdose ingestion of paracetamol over renal functions and electrolytes in patients without a pre-existing renal disease who were admitted in the Poison Control Center of Minia University Hospital after an acute single paracetamol overdose. **Methods:** The study included patients hospitalized at the Poison Control Center from the start of February 2022 to the end of January 2023. Patients were classified into mild, moderate and severe groups depending on paracetamol plasma level 4-hrs post ingestion. Sociodemographic data were collected from all the patients including age, gender, residence and body weight. Blood samples were drawn from each patient for laboratory investigations on admission and follow up. **Results:** The patient's age ranged from 18-47 years, mostly came from cities with a female predominance. Statistically significant differences were recorded among groups as regarding the ingested dose of the drug, paracetamol plasma levels and liver transaminases (ALT and AST) especially from 2nd and 3rd days of admission. Renal function tests and serum electrolytes recorded statistically insignificant changes within groups either on admission or during the follow up. All patients improved and discharged after treatment**. Conclusion:** Despite toxic dose ingestion of paracetamol renal affection or electrolyte imbalance may not occur.

Keywords: Paracetamol, hepatotoxicity, Alanine aminotransferase (ALT), Aspartate aminotransferase (AST)

Introduction

Paracetamol (acetaminophen, N- acetyl- para-aminophenol or Tylenol) is known to be one of the commonest over-the-counter (OTC) drugs that is used worldwide. It can be used safely in all age groups and during pregnancy as an analgesic and antipyretic.(1) It is commonly used in treatment of headache, migraine, osteoarthritic, dental or menstrual pain. If conjugated with a strong analgesic as an opioid, it can be used in the management of severe pain.(2)

Therapeutic doses of paracetamol are safe and well tolerated although, it is a dose-related toxin and its overdose is considered to be the main cause of emergency department visits in the United States (US) after intentional or unintentional ingestions. Paracetamol-induced acute liver injury is the commonest among drug-induced liver injury (DILI).(3)

The toxic dose of paracetamol is calculated to be 140 mg/kg body weight in adults and children above 12 years old. However, for young adults and children, the toxic dose appears to be between 150-200 mg/kg. The calculation of the toxic dose may vary depending on the patient's general condition and the predisposing risk factors.(4)

The main cause of paracetamol-induced hepatotoxicity is the accumulation of the toxic and highly reactive metabolite N-acetyl-para-benzoquinone imine (NAPQI) after a large dose. Most people after acetaminophen toxicity develop non-specific gastrointestinal symptoms during the first 24 hrs like nausea, vomiting, abdominal and epigastric pain with a normal liver enzyme level.(5)

During the period from 24-72 hrs, patients mostly appear symptomatically free while laboratory investigations show significant changes especially liver transaminases. From 72 to 96 hrs symptoms reappear and even worsen accompanied by jaundice and manifestations of central nervous system affection. Liver enzymes reach their peak values as well, deterioration and death commonly occur during this phase. The last phase is called the recovery phase and ranges from 4 to 14 days during which complete hepatic resolution occurs after proper treatment with N-acetyl cysteine either orally over 72 hrs, or intravenously over 21 or 48 hrs.(6)

Acute kidney impairment induced by a paracetamol overdose typically presents with delayed symptoms and may be missed if the patient is discharged from the hospital within 48 hours of the overdose. As a result, continuous monitoring of blood urea and creatinine levels is critical to closely monitor the possibility of nephrotoxicity following paracetamol overdose even without evident hepatotoxicity.(7)

Recurrent vomiting episodes which occur secondary to paracetamol poisoning may explain the dose-related electrolyte disturbance. Dehydration, hyponatremia and hypokalemia can be the end results of untreated gastrointestinal symptoms associated with acetaminophen overdose. Recent studies explain another cause for electrolyte imbalance that may be renal tubular affection with subsequent sodium and potassium loss.(8)

Aim of the work

The present study aims to assess the impact of toxic dose ingestion of paracetamol on renal functions and serum electrolytes in patients without a pre-existing renal disease who admitted in Poison Control Center (PCC) of Minia University Hospital after an acute single paracetamol overdose.

Patients and Methods

This cross sectional study included forty patients of both sexes who were admitted to the Minia University Hospital-Poison Control Center (PCC), after an acute single paracetamol overdose from the start of February 2022 to the end of January 2023.

Ethical permission was acquired by The Ethical Committee, Faculty of Medicine, Minia University, Number: 273: 2/2022. After obtaining comprehensive information about the study, all patients or their legal guardians were asked to submit informed written consent for participation. The patient's data were kept private by using the coding numbers.

All male and female patients over the age of eighteen who had a recent history of acute single paracetamol overdose and a delay of four up to twenty-four hours were included in the study.

All individuals who fulfill the following criteria, male or female patient under the age of eighteen, patients who had received treatment prior to arriving at the hospital, patients with a history of hepatic or renal disease, co-ingestions of other hepatotoxic or nephrotoxic agents, chronic alcohol intake, or any drug abuse that would affect liver or kidney functions were excluded from the study.

Based on the calculated paracetamol plasma levels 4-hours post ingestion as described by the Rumack Mathew nomogram, the patients were subdivided into 3 groups, mild group which included eighteen patients, moderate group which included fourteen patients, and the severe group with eight patients only. Paracetamol plasma concentration 4-hours post ingestion $(PRC)_{4h}$ was calculated in patients presented after 4 hours delay by the use of the plasma level of paracetamol at the time of admission $(PRC)_{pl}$ as explained by the following formula $(PRC)_{4h} = (PRC)_{pl} /2e-(0.693/4)t$ described by Waring et al., 2008.(9)

The mild group included 18 patients with calculated paracetamol plasma level 4 hrs post

ingestion less than 150 µg /ml, moderate group included 14patients with calculated paracetamol plasma level 4 hrs post ingestion ranging from 150-200 µg/ml, and severe group included 8 patients with calculated paracetamol plasma level 4 hrs post ingestion more than 200 µg /ml.

Each patient in the study was in accordance with the following: full personal history with detailed intoxication data regarding the drug taken, calculation of the ingested dose based on the patient's body weight (140 mg/kg), mode and time of drug consumption. Laboratory investigations included paracetamol plasma levels at the time of admission, serum liver enzymes (ALT and AST), international normalized ratio (INR), prothrombin time (PT) serum urea, serum creatinine, and serum electrolytes (Na+ & K+). All patients received treatment with intravenous NAC over 21hrs, and discharged after complete improvement.

The colorimetric technique described by Frankel and Gradwohl (1970) was used to measure serum transaminases: aspartate aminotransaminase (AST) and alanine aminotransaminase (ALT).[10]

Blood samples were collected from venous blood for testing PT & INR and then directly collected into a tube with a light blue top. The tube contained an anticoagulant material which was sodium citrate 3.2%.

Only a random blood sample was required for renal function testing. The serum urea level was determined by the use of enzymatic kinetic method according to Lawrence et al., (1993). Normal value is 15-45 mg/dl.[11]

Serum creatinine level It was determined by the colorimetric method according to Houot et al., (1985). Normal value is 0.5-1.5 mg/dl.[12]

Standard samples were injected in blood gas analyzer (Model 288 Ciba Corning Co.) and they were 140 mEq/L for Na^+ and 5.0 mEq/L for K^+. Serum samples were injected in the set to determine the serum sodium and potassium levels. Na^+ normal value is 135-145 mEq/L and K^+ normal range is 3.5-5.5 mEq/L.

Statistical analysis:

Statistical analysis, coding and tabulation of the gathered data were performed by the use of statistical package for social sciences (SPSS) program software version 25. Descriptive statistics were computed for parametric (normally distributed) quantitative data using the mean, standard deviation (SD), minimum and maximum of range. For non-parametric quantitative data were done using the median and interquartile range (IQR).

Analyses were performed to compare the three studied groups using a one-way ANOVA test for parametric quantitative data, followed by post hoc analysis between each two groups. For parametric quantitive data among two times within the same group Paired samples T-test was done. The significance level was determined at (P value $\leq$ 0.05).

Results

The selected patients in the study were classified into three groups (mild, moderate and severe) based on the paracetamol plasma level 4-hrs post ingestion with statistically significant differences among the studied groups (P-value <0.001). Median values of paracetamol plasma levels were 94.5 µg/ml, 169.5 µg/ml, 292.5 µg/ml, in mild, moderate and severe groups, respectively.

Regarding the sociodemographic statistics, patients' ages ranged from 18 to 47 years old with the majority of them came from cities. The female number of cases exceeded the male number throughout all the three groups studied with a statistically insignificant difference between them. Acetaminophen ingested doses ranged from 5.5 to 16 grams with statistically significant differences between the 3 groups.

Liver transaminases, including Alanine aminotransferase (ALT) (normal value 7-55 u/l) and Aspartate aminotransferase (AST) (normal value 5-40 u/l) showed significant variations among the examined groups with a P-value of <0.001. Patients of the moderate and severe groups showed significant elevations of the liver enzymes during the second and third days of admission with peak levels during the third

day, while the values of the mild group patients were within the normal range either on admission or during the follow up. Mean values for liver transaminases during the 3rd day were 32 u/l, 236.8 u/l, 507.5 u/l for ALT, and 28.8 u/l, 261.1 u/l, 488.8 u/l for AST in mild, moderate, and severe groups, respectively.

Measurement of the coagulation parameters including the international normalized ratio (INR) (normal value 0.5-1.5) and prothrombin time (PT) (normal value 10-13 sec) revealed significant changes in their values recorded from the second day of admission, and reached the peak values during the 3rd day among patients of the moderate and severe groups in comparison to the mild group. Mean values during the 3rd day were 1.04, 1.4, 1.7 for INR and 11.9 sec, 15.9 sec, 22.8 sec for PT in mild, moderate and severe groups, respectively.

Elevated liver transaminases and coagulopathy were both obvious indicators for liver affection from the ingested doses. However, statistically insignificant changes were recorded as regarding serum urea (Table 1 & Fig. 1) serum creatinine (Table 2 & Fig. 2) and serum electrolytes Na^+ and K^+ (Table 3) either on admission or during the follow up regardless to hepatotoxicity.

Significant differences among groups were recorded as regarding the duration of hospital stay especially in comparison of mild group with moderate and severe groups. Mean duration of hospital stay was 3.3 days, 4.7 days, and 5 days in mild, moderate and severe groups, respectively. No need for mechanical ventilation and no mortality was recorded in all examined groups. All studied patients improved and discharged without complications after proper treatment by intravenous N-acetylcysteine over 21 hrs.

Table I: Comparison between the three examined groups intoxicated with paracetamol regarding the serum urea level on admission and during the follow up.

Urea (mg/dl)		Mild (I)	Moderate (II)	Severe (III)	P value			
		N=18	**N=14**	**N=8**	**3 groups**	**I vs II**	**I vs III**	**II vs III**
On admission	Range Mean ± SD	(18-37) 25.2±5.3	(15-35) 25.7±6.6	(17-29) 23±4.3	0.545	0.787	0.373	0.285
At day 2	Range Mean ± SD	(15-31) 23.2±5.1	(12-31) 22.2±4.9	(22-30) 25.2±2.8	0.364	0.548	0.327	0.158
At day 3	Range Mean ± SD	(17-35) 21.3±4.7	(15-29) 20.5±4.6	(16-29) 21.9±4.4	0.776	0.613	0.783	0.503

- **One Way ANOVA test for parametric quantitative data between the three groups followed by post hoc analysis between each two groups.**
- ***: Significant level at P value < 0.05**

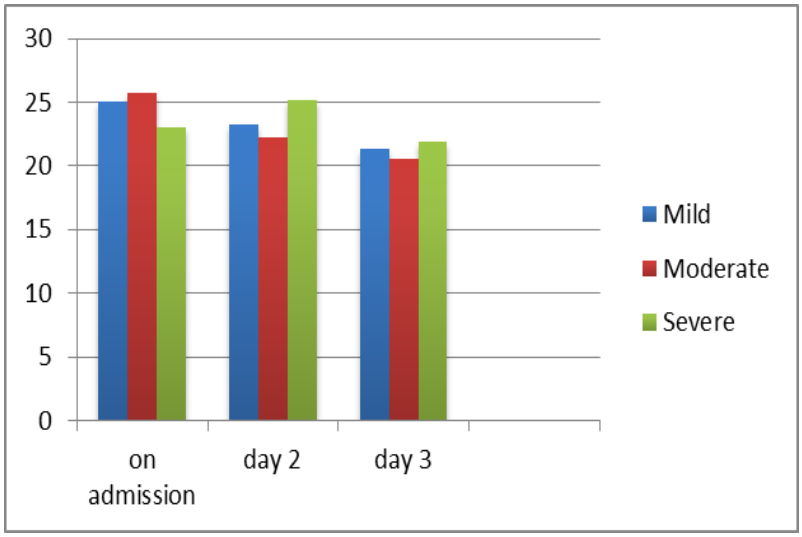

Figure (1): Normal serum urea levels (15-45) mg/dl among the 3 examined groups intoxicated with paracetamol on admission and during the follow up

Table II: Comparison between the three examined groups intoxicated with paracetamol regarding the serum creatinine level on admission and during follow up.

Creatinine level (mg/dl)		Mild (I)	Moderate (II)	Severe (III)	3 groups	I vs II	I vs III	II vs III
		N=18	N=14	N=8		P value		
On admission	Range Mean ± SD	(0.5-1.1) 0.8±0.2	(0.5-1.7) 0.9±0.3	(0.5-1.5) 1±0.3	0.305	0.349	0.140	0.500
At day 2	Range Mean ± SD	(0.4-1.2) 0.8±0.2	(0.5-1.5) 0.8±0.3	(0.6-1.2) 0.9±0.2	0.360	0.629	0.156	0.325
At day 3	Range Mean ± SD	(0.3-1.3) 0.9±0.3	(0.5-1.3) 0.9±0.3	(0.4-1.2) 0.9±0.3	0.985	0.997	0.872	0.880

- **One Way ANOVA test for parametric quantitative data between the three groups followed by post hoc analysis between each two groups.**
- ***: Significant level at P value < 0.05**

Table III: Comparison between the three examined groups intoxicated with paracetamol regarding serum K^+ and Na^+ levels on admission and during the follow up.

K^+ (3.5-5.5) mEq/L		Mild (I)	Moderate (II)	Severe (III)	P value			
		N=18	N=14	N=8	3 groups	I vs II	I vs III	II vs III
On admission	Range Mean ± SD	(3.3-4.5) 3.9±0.3	(3.2-4.8) 4±0.5	(3.2-4.5) 3.8±0.4	0.466	0.422	0.563	0.233
At day 2	Range Mean ± SD	(3.4-4.8) 3.9±0.4	(3.4-5) 4±0.4	(3.6-4.7) 3.9±0.4	0.683	0.523	0.752	0.415
At day 3	Range Mean ± SD	(3.2-4.8) 3.7±0.7	(3-5.3) 4±0.5	(3.4-4.2) 3.8±0.3	0.453	0.220	0.822	0.437
Na+ (135-145)mmol/L		Mild	Moderate	Severe	3 groups	I vs II	I vs III	II vs III
On admission	Range Mean ± SD	(131-143) 137.4±3	(132-145) 139.1±3.4	(132-141) 136.8±3.2	0.181	0.141	0.609	0.097
At day 2	Range Mean ± SD	(135-142) 138.3±2.3	(130-143) 137.6±3.5	(132-142) 138.5±3.5	0.732	0.501	0.897	0.505
At day 3	Range Mean ± SD	(132-143) 137.6±3	(133-140) 136.7±1.9	(130-144) 137±4.1	0.699	0.408	0.656	0.809

Discussion

One of the prevalent causes of drug-induced liver injury (DILI) and acute liver failure is paracetamol-induced hepatotoxicity, either after intentional or unintentional ingestions in different age groups.[13]

Paracetamol-induced hepatotoxicity is known to be a result of the build-up of the harmful metabolite N-acetyl-p-benzoquinone imine (NAPQI) after an overdose. After paracetamol overdose, saturation of the sulfation and glucuronidation pathways occurs, with subsequent depletion of endogenous glutathione stores.[14]

The accumulated amount of non-detoxified toxic metabolite (NAPQI), binds to the cellular biological macromolecules such as proteins, lipids and nucleic acids, resulting in mitochondrial dysfunction which considered an important step in hepatotoxicity. Endoplasmic reticulum stress and oxidative reactants also cause necrotic cell death and damage of hepatocytes.[15]

In terms of the sociodemographic variables in the current study, the age varied from 18-47 years with the upper hand to the female gender. Female to male ratio was 2.5:1. Shekunov et al., (2021) found similar results, observing that female patients were more than male patients.[16]

A statistically significant difference was detected between groups regarding to the consumed doses of paracetamol, with high ingested doses had observed in the moderate and severe groups compared with the mild group, ranging from 5.5-16 gm. Mean ingested doses were 6.4±0.7 gm, 8.6±0.3 gm, and 11.5±1.7 gm in mild, moderate, and severe groups, respectively. In the same way, Zyoud et al., (2012) observed that if the ingested dose exceeded eight grams, the associated paracetamol plasma level would be more than 50 mg/l and the risk of toxicity would be higher.[17]

Elevation of the liver transaminases ALT and AST in the present study among patients of the moderate and severe groups was in agreement with the study done by Popiolek et al., (2021), who studied the risk factors for hepatotoxicity after acetaminophen overdose among the 3 studied groups mild, moderate and severe, and revealed that liver enzymes were considerably higher in the severe and moderate groups than in the mild group.[18]

The significant changes in the coagulation profile INR and PT among the moderate and severe groups in this study were in accordance with the findings of Mehrpour et al., (2021). Their study of the prognostic factors after paracetamol exposure in the United States revealed that the patients with acute or acute-on-top of chronic acetaminophen overdoses were more likely to develop coagulopathy as evidenced by prolonged PT and elevated INR values.[19]

Contrarily, Ghannoum et al., (2016) who performed a case study on an eighteen-year-old girl who was admitted to the emergency room after consuming hundred grams of acetaminophen. Clinically she was agitated with disturbed conscious level and miserable general state of health but, her laboratory data was normal as regarding liver functions and coagulation profile.[20]

The measurement of renal function tests in the present study revealed nonsignificant changes in their values within the 3 examined groups. Nearly similar results were reported by Zyoud et al., (2012) with normal ranges in serum urea and creatinine concentrations in all patients despite paracetamol toxicity.[17]

According to Khan et al., (2021), the paracetamol-induced nephrotoxicity is a rare condition, and if it occurs, the patient is usually asymptomatic, and only elevated renal functions may be detected after 48 hrs. Hemodialysis is rarely necessary, as renal functions usually return to normal values after supportive treatment only.[21]

These findings conflict with those of Waring et al., (2010), who reported that paracetamol-induced acute renal failure occurs after ingestion of a large toxic dose of 12 gm of paracetamol. This study also revealed a significant elevation in serum creatinine $\geq$ 50% from the baseline serum creatinine concentrations.[22]

Similarly, O'Riordan et al., (2011) assessed the incidence of acute renal affection in patients hospitalized to the hepatic intensive care unit following hepatotoxicity caused by paracetamol, and found that most of the patients developed acute kidney injury and about 8% developed stage 1, 6% of cases developed stage 2, and 65% developed stage 3 which need renal replacement therapy (RRT). Only small number of the studied cases (21%) preserved their normal renal functions.[23]

Assessment of serum electrolytes (Na^+ and K^+) levels in this study revealed insignificant changes in their values among all examined patients either on admission or during follow up. These findings were in the same line with a case study done by Ranasinghe et al., (2021), who recorded an 18-year-old girl with severe paracetamol poisoning, metabolic acidosis, fulminant hepatic failure, elevated renal functions, and disturbed conscious level (GCS 10/15) but serum electrolytes were normal despite case severity.[24]

On the other hand, Zyoud et al., (2011) assessed changes in serum K^+ among patients with acetaminophen overdose, and found that patients with paracetamol concentrations above the possible toxicity line of Romack Matthew nomogram were more likely to have a significant reduction in serum K^+ levels in comparison to patients with acetaminophen concentrations below the line, and the study revealed that about 63.3% of the patients had serum K^+ concentrations less than the normal ranges.[25]

Statistically non-significant differences in serum Na^+ levels in the present study were in disagreement with the case report conducted by Chiu et al., (2021) about a 20-year-old girl after a suicidal attempt with 120 gm acetaminophen, and her serum electrolytes on admission showed both hyponatremia and hypokalemia. [26]

Conclusion

Unlike paracetamol-induced hepatotoxicity, paracetamol-associated nephrotoxicity with subsequent electrolyte disturbance is not a dose-related syndrome, since the majority of patients with a toxic dose ingestion and obvious hepatotoxicity have normal renal function and electrolyte profiles.

References

1- Schilling A., Corey R., Leonard M., et al., Acetaminophen: old drug, new warnings. Cleveland Clinic Journal of Medicine, 2010, 77(1): 19-27.
2- Daifallah A., Jabr R., Al-Tawil F., et al., An assessment of parents' knowledge and awareness regarding paracetamol use in children: a cross-sectional study from Palestine. BMC Public Health, 2021, 21(1): 1-10.
3- Thusius N. J., Romanowicz M. & Bostwick J. M. Intentional or inadvertent acetaminophen overdose-how lethal it really is?. Psycho Somatics, 2019, 60(6): 574-581.
4- Blackford M.G.; Felter T.; Gothard M.D., et al., Assessment of the clinical use of intravenous and oral N-acetylcysteine in the treatment of acute acetaminophen poisoning in children: a retrospective review. Clinical Therapeutics, 2011, 33(9): 1322- 1330.
5- Piotrowska N., Klukowska-Rötzler J., Lehmann B., et al., Presentations related to acute paracetamol intoxication in an urban emergency department in Switzerland. Emergency Medicine International, 2019, 1-7.
6- Larson A. M. Acetaminophen hepatotoxicity. Clinical Liver Diseases, 2007, (11): PP. 525–548.
7- Chun L. J., Tong M. J., Busuttil R. W., et al., Acetaminophen hepatotoxicity and acute liver failure. Journal of Clinical Gastroenterology, 2009, 43(4): 342-349.
8- Zyoud S. H.; Awang R.; Sulaiman S. A., et al., Impact of serum acetaminophen concentration on changes in serum potassium, creatinine and urea concentrations among patients with acetaminophen overdose. Pharmaco-epidemiology. Drug Safety, 2011, 20(2): 203-208.
9- Waring W. S.; Robinson O. D. G.; Stephen A. F. L., et al., Does the patient history predict hepatotoxicity after acute paracetamol overdose?. An International Journal of Medicine,2008,101(2):121-125
10- Frankel S. and Gradwohl E. C. Colorimetric method for determination of

serum transaminases. American Journal of Clinical Pathology, 1970, 28(1): 26-34.
11- Lawrence R. Z., Slaughter M. J., Hall R. E., et al., International trade and American wages in the 1980s: giant sucking sound or small hiccup? Brookings papers on economic activity. Microeconomics, 1993, 24(2): 161-226.
12- Houot O., Zhiri A., Wellman-Bednawska M., et al., Simultaneous determination of uric acid and creatinine in plasma by reversed-phase liquid chromate-graphy. Clinical Chemistry, 1985, 31(1): 109-112.
13- Roh T., De U., Lim S. K., et al., Detoxifying effect of pyridoxine on acetaminophen-induced hepatotoxicity via suppressing oxidative stress injury. Food and Chemical Toxicology, 2018, 11(4): 11-22.
14- Shan S., Shen Z. & Song F. Autophagy and acetaminophen-induced hepatotoxicity. Archives of Toxicology, 2018, 92(7): 2153-2161.
15- Foufelle F. & Fromenty B. Role of endoplasmic reticulum stress in drug-induced toxicity. Pharmacology Research & Perspectives, 2016, 4(1): 2-11.
16- Shekunov J.; Lewis C. P.; VandeVoort J. L., et al., Clinical Characteristics, Outcomes, Disposition, and Acute Care of Children and Adolescents Treated for Acetaminophen Toxicity. Psychiatric Services, 2021, 72(7): 758-765.
17- Zyoud S. E. H., Awang R. & Sulaiman S. A. S. Reliability of the reported ingested dose of acetaminophen for predicting the risk of toxicity in acetaminophen overdose patients. Pharmaco-epidemiology and Drug Safety, 2012, 21(2): 207-213.
18- Popiolek I.; Hydzik P.; Jagielski P., et al., Risk factors for hepatotoxicity due to paracetamol overdose in adults. Medicine, 2021, 57(8): 752-761.
19- Mehrpour O.; Saeedi F.; Hadianfar A., et al., Prognostic factors of acetaminophen exposure in the United States: an analysis of 39,000 patients. Human & Experimental Toxicology, 2021, 40(12): 814-825.
20- Ghannoum M.; Kazim S.; Grunbaum A. M., et al., Massive acetaminophen overdose: effect of hemodialysis on acetaminophen and acetylcysteine kinetics. Clinical Toxicology, 2016, 54(6): 519-522.
21- Khan Z.; Abumedian M.; Ibekwe M., et al., Acute renal impairment in patients due to paracetamol overdose in the absence of hepatic impairment. Cureus, 2021, 13(12): 20-27.
22- Waring W. S., Jamie H. and Leggett G. E. Delayed onset of acute renal failure after significant paracetamol overdose: a case series. Human & Experimental Toxicology, 2010, 29(1): 63-68.
23- O'Riordan A., Brummell Z., Sizer E., et al., Acute kidney injury in patients admitted to a liver intensive therapy unit with paracetamol-induced hepatotoxicity. Nephrology Dialysis Transplantation, 2011, 26(11): 3501-3508.
24- Ranasinghe R.; Azher S.; Karunathilake P., et al., Acetaminophen Intoxication with Fulminant Hepatic Failure Salvaged by Plasmapheresis. International Journal of Clinical Case Reports and Reviews, 2021, 9(1): 1-3.
25- Zyoud S. H.; Awang R.; Sulaiman S. A., et al., Impact of serum acetaminophen concentration on changes in serum potassium, creatinine and urea concentrations among patients with acetaminophen overdose. Pharmaco-epidemiology. Drug Safety, 2011, 20(2): 203-208.
26- Chiu M. H., Jaworska N., Li N. L., et al., Massive acetaminophen overdose treated successfully with N-acetylcysteine, fomepizole, and hemodialysis. Case Reports in Critical Care, 2021, 1(1): 1-5.