**'ACUTE ACETAMINOPHEN TOXICITY: A CASE REPORT ON CLINICAL PRESENTATION, MANAGEMENT, AND OUTCOMES'**

M.Niharika1, Suhana Anjum2

1Department of Pharmacy, Vaageswari College of Pharmacy (Affiliated to JNTUH), beside LMD Police station, Ramakrishna colony, Telangana, India- 505481, 2025

2Department of Pharmacy, Vaageswari College of Pharmacy (Affiliated to JNTUH), beside LMD Police station, Ramakrishna colony, Telangana, India- 505481, 2025

**ABSTRACT**

Acetaminophen poisoning is a major cause of acute liver failure worldwide, often occurring due to accidental or intentional overdose. The harmful effects stem from the overproduction of N-acetyl-p-benzoquinone imine (NAPQI), a reactive compound that depletes glutathione levels and induces oxidative stress and cell death in the liver. Clinical manifestations progress through four stages: initial gastrointestinal symptoms (nausea, vomiting), a period of potential symptom improvement, liver injury with elevated liver enzymes, and, in severe cases, fulminant hepatic failure. Risk factors for developing hepatic encephalopathy include long-term alcohol abuse, poor nutrition, and the use of medications that affect the liver's ability to metabolize certain substances. Early detection of acetaminophen poisoning depends on the patient's medical history and the measurement of plasma acetaminophen levels, typically evaluated using the Rumack-Matthew nomogram for single instances of ingestion. Management involves the timely administration of N-acetylcysteine (NAC), which restores glutathione levels and aids in the detoxification of NAPQI. NAC is most potent when consumed within 8–10 hours, but it still offers advantages even after that time. Patients with severe liver failure require supportive care, which may include liver transplantation, to improve their condition. Measures implemented by public health authorities, such as restricting the number of tablets in a pack and educating the public on safe usage, have led to a decrease in overdose incidents in certain areas. Despite these precautions, acetaminophen poisoning continues to pose a substantial health concern. Ongoing studies are focused on enhancing treatment protocols and investigating additional therapies to enhance treatment outcomes.

**Keywords:** Acetaminophen poisoning, Acute liver failure, N-acetylcysteine, NAPQI, Hepatotoxicity, Overdose management.

**INTRODUCTION**

Acetaminophen (paracetamol) poisoning is a leading cause of drug-related toxicity globally, often arising from unintentional overdoses or intentional ingestion in self-harm. As a widely available over-the-counter analgesic and antipyretic, its accessibility increases the risk of misuse. While generally safe at therapeutic doses, excessive consumption can lead to severe liver damage and even death if not promptly recognized and treated. The toxicity of acetaminophen is primarily due to its metabolism in the liver. Most of the drug undergoes glucuronidation and sulfation, forming non-toxic metabolites that are excreted by the kidneys. However, a minor fraction is metabolized via the cytochrome P450 (CYP2E1) enzyme pathway into a highly reactive intermediate, N-acetyl-p-benzoquinone imine (NAPQI). Normally, NAPQI is detoxified by glutathione. In overdose scenarios, glutathione stores are depleted, leading to NAPQI accumulation, which causes oxidative stress and hepatocyte damage, resulting in acute liver injury. Several factors influence the risk and severity of acetaminophen poisoning. Toxicity typically occurs with single doses exceeding 150-200 mg/kg in children or 7.5-10 g in adults.

Chronic alcohol use, malnutrition, or pre-existing liver disease can lower the toxic threshold by increasing NAPQI production or reducing glutathione reserves. Additionally, repeated high doses over time can result in cumulative toxicity, even at doses close to the therapeutic range. Acetaminophen poisoning progresses through four distinct phases if untreated. In the initial phase (0-24 hours), symptoms are often vague and nonspecific, including nausea, vomiting, and abdominal discomfort. In the second phase (24-72 hours), evidence of liver damage emerges, with elevated liver enzymes and right upper quadrant pain. The third phase (72-96 hours) represents the peak of toxicity, where fulminant hepatic failure may occur, characterized by jaundice, coagulopathy, encephalopathy, and multi-organ failure. In survivors, the fourth phase (4-14 days) is marked by gradual recovery as liver function normalizes. Diagnosis involves a thorough history of ingestion and measurement of serum acetaminophen levels, often assessed using the Rumack-Matthew nomogram within 4-24 hours post-ingestion to predict hepatotoxicity risk. Elevated liver enzymes, particularly alanine aminotransferase (ALT), confirm liver injury. Early intervention is crucial in managing acetaminophen poisoning. Activated charcoal can be administered within 1-2 hours of ingestion to limit drug absorption. The cornerstone of treatment is N-acetylcysteine (NAC), which replenishes glutathione and directly binds to NAPQI. Supportive care, including monitoring for complications like hepatic failure or coagulopathy, is essential in severe cases. Timely recognition and treatment of acetaminophen poisoning, particularly with NAC, significantly improve outcomes, reducing the risk of severe liver damage and mortality.

**CASE** **REPORT**

Name: XXXX

Age: 48 years

Sex: Female

**Chief Complaint:** Consumption of two sheets (assumed 20 tablets of acetaminophen, approximately 10 g total dose). Vomiting: 3 episodes, Giddiness

**History of Present Illness:** The patient presented to the emergency department after ingesting an overdose of acetaminophen tablets. She reported nausea, multiple episodes of vomiting, and giddiness shortly after consumption.

**Past Medical History:** Diagnosed with Rheumatoid Arthritis (RA) for 3 years. Using Ayurvedic medications for symptom management.

**Clinical Examination:**

**Vital** **Signs**: Blood pressure: 110/70 mmHg Heart rate: 92 bpm Respiratory rate: 18 breaths/min Temperature: 37.2°C

**General Examination:** Patient appeared anxious but was alert and oriented. Abdominal Examination: Mild tenderness in the right upper quadrant, no signs of ascites or hepatomegaly.

**Laboratory Investigations:** Serum acetaminophen level (12 hours post-ingestion): 85 mcg/mL Liver function tests: ALT: 320 IU/L (normal: 7-56 IU/L) AST: 280 IU/L (normal: 10-40 IU/L) Total bilirubin: 1.5 mg/dL (normal: patient's history, clinical presentation, and elevated serum acetaminophen level above the treatment threshold, acute acetaminophen poisoning with early hepatotoxicity was diagnosed.

**Management:** Pharmacological Treatment Administered: IV Fluids: Normal Saline (1000 mL/hour). Antiemetics: Inj. Ondansetron: 4 mg IV for vomiting control.

**Gastroprotective Therapy:** Inj. Pantoprazole: 40 mg IV for gastrointestinal protection. Antibiotic: Inj. Ceftriaxone: 1 g IV (prophylactic or secondary bacterial infection prevention).

**Antioxidant Therapy:** Inj. Vitamin C (Ascorbic Acid): 1500 mg IV. Inj. Glutathione: 600 mg IV.

**Acetaminophen Antidote:** Inj. N-Acetyl Cysteine (NAC): Administered based on body weight (loading dose followed by maintenance in dextrose).

**Haematological Support:** Inj. Vitamin K: 10 mg IV for coagulation correction (if needed).

**Electrolyte Correction**: Syrup Potassium Chloride: 60 mL in a glass of water for potassium replenishment.

**Progress and Patient Response:** The patient responded well to the initial treatment. Symptoms of nausea and vomiting were controlled with ondansetron. NAC was administered as the primary antidote to prevent hepatic injury.

Supportive measures, including IV fluids and antioxidants, were effective. Recommendations for Monitoring: Regular monitoring of liver function tests (LFTs), particularly ALT, AST, bilirubin, and INR. Serial acetaminophen plasma levels (if available). Monitoring for signs of hepatic failure (e.g., encephalopathy, coagulopathy).

Renal function tests for nephrotoxicity. Gastrointestinal Decontamination: Activated charcoal (50 g orally) was administered within 1 hour of presentation.

**Antidote Therapy:** Intravenous N-acetylcysteine (NAC) infusion was initiated immediately based on the serum acetaminophen level and time since ingestion. The standard 21-hour protocol was followed: Loading dose: 150 mg/kg over 1 hour Maintenance doses: 50 mg/kg over 4 hours, followed by 100 mg/kg over 16 hours.

**Supportive Care:** Intravenous fluids to maintain hydration. Monitoring of liver and renal function. Psychiatric Consultation: Psychiatry was consulted for evaluation and management of underlying psychological stressors.

**Outcome:** Over the next 48 hours, the patient's symptoms improved, and liver function tests showed stabilization. No signs of progressive liver failure were noted. She was discharged in stable condition on day 4 with a follow-up plan for psychiatric care and liver function monitoring.

**DISCUSSION**

Acetaminophen poisoning is one of the most common causes of drug-related toxicity worldwide, accounting for a significant number of hospital admissions for overdose. While it is generally safe at therapeutic doses, acetaminophen can cause severe hepatotoxicity in overdose situations due to saturation of normal metabolic pathways and the resultant accumulation of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI). This case underscores the critical importance of prompt identification, timely intervention, and multidisciplinary management. In this case, the patient presented 12 hours after ingestion, a timeframe that is critical for decision-making regarding treatment with N-acetylcysteine (NAC). The patient's elevated serum acetaminophen levels and initial signs of hepatotoxicity (elevated liver enzymes and a mildly increased INR) reinforced the need for immediate antidotal therapy. NAC, a precursor of glutathione, acts by replenishing glutathione stores, thereby facilitating the detoxification of NAPQI. Initiation of NAC within 8–24 hours post-ingestion has been shown to significantly reduce the risk of severe hepatotoxicity and acute liver failure. This case highlights the importance of the Rumack-Matthew nomogram in assessing the need for NAC administration.

The nomogram, based on plasma acetaminophen levels and time since ingestion, serves as a guideline to determine the risk of hepatotoxicity and the need for intervention. In patients who present late or have unclear timelines of ingestion, clinical judgment and laboratory findings become pivotal for decision-making. The clinical course of this patient was consistent with early-stage acetaminophen toxicity, classified by initial gastrointestinal symptoms followed by biochemical evidence of liver injury. The absence of co-ingestion of other substances and the lack of prior liver disease were favorable factors in this case, reducing the risk of severe outcomes such as acute liver failure. In addition to the medical management, the psychiatric evaluation and intervention were integral components of care. This patient's overdose was a deliberate act linked to psychological distress, underscoring the need for addressing the underlying mental health issues. Without proper psychological care, the risk of recurrent self-harm or overdose remains high. A multidisciplinary approach involving emergency medicine, hepatology, and psychiatry ensures comprehensive care for such patients.

**CONCLUSION**

This case illustrates the essential steps in managing acute acetaminophen poisoning: early recognition, timely initiation of antidotal therapy, and integration of mental health support. The successful outcome in this patient was due to the rapid administration of NAC, effective supportive care, and close monitoring of liver function. Acetaminophen poisoning continues to be a global health concern, necessitating widespread awareness among healthcare providers regarding its pathophysiology, diagnostic criteria, and management protocols. The Rumack-Matthew nomogram remains an invaluable tool for risk stratification and treatment planning. Lastly, this case underscores the importance of a holistic approach to treatment, which not only addresses the physical consequences of overdose but also targets the psychological factors driving such behaviour. Ensuring long-term follow-up and mental health support is critical for preventing future harm and improving overall patient outcomes. **REFERENCES**

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