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SUICIDAL ACUTE IRON POISONING IN ADOLESCENT FEMALES – A CASE SERIES.

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Abstract:

Acute iron toxicity in adolescents and adults is rare and usually results from intentional ingestion in suicidal attempts. Only a handful of cases of acute iron toxicity with clinical and autopsy-pathological findings have been previously reported in the literature. We report five fatal cases of acute iron toxicity in adolescent females died with suicidal ingestion of 20-60 iron or iron-folic. Cases were reported for autopsy in the year 2015 to 2023. Autopsies were performed and tissue samples were preserved for toxicological analysis and histopathological studies for accurate identification of the cause of death. Common autopsy findings were edema, multiple confluent patechial hemorrhages in internal organs with pale parenchyma. Microscopic findings revealed, edema ininternal organs, surface mucosal necrosis, erosion of stomach and intestinal mucosa with lymphoid aggregates and hemosiderin pigments deposition in sub-mucosa, diffuse hepatic, portal necrosis and focal hemorrhages in sinusoids and granular hemosiderin pigments deposit in the hepatocytes, diffuse acute tubular necrosis, intravascular hemorrhages and hemosiderin pigments depositions in glomeruli and renal tubules, dilated, congested blood vessels, parenchymal necrosis, pigments depositions and lymphoid aggregates in spleen, lung parenchyma with diffuse necrosis and pigments depositions, brain cell necrosis irregular cellular aggregates, congested blood vessels and foci with brown hemosiderin pigments depositions in stroma and around blood vessels. In all cases, the viscera were found positive for iron preparations. Present
report clearly described specific gross and histopathological features of acute iron poisoning. Though essential micronutrientits knowledge as a poison and monitored and supervised use is the key to prevent iron toxicity.

Keywords: Acute Iron poisoning, Suicide, Autopsy, Histopathology

Introduction:

Iron is the most abundant trace element in the body and is essential for most biological systems. The total content of iron in the body is about 3–5 g, with most of it found in the blood and the rest in the liver, bone marrow, and muscles in the form of heme [1]. An adult human's body contains approximately 4 g (0.005% body weight) of iron, which is mostly found in hemoglobin and myoglobin. These two proteins play crucial roles in vertebrate metabolism, transporting oxygen through the blood and storing oxygen in muscles, respectively. Human iron metabolism requires a minimum amount of iron in the diet to sustain the necessary levels. Iron is also the metal at the active site of many important redox enzymes in plants and animals that deal with cellular respiration, oxidation, and reduction [2]. Nonionic forms of iron are converted to ferrous iron in the stomach by gastric acid under normal physiological conditions. After that, ferrous iron is absorbed in the small intestine and oxidised into ferric iron before being released into the bloodstream. The presence of free iron in the blood is toxic to the body because it disrupts normal cell function, causing harm to organs such as the liver, stomach, and cardiovascular system [3]. Acute iron poisoning is not uncommon in children. Accidental ingestion of iron supplements and/or over-the-

counter vitamins is often the cause. In fact, ferrous sulphate has been one of the leading causes of accidental poisoning in children over the past half century. Thanks to preventive packaging and improved labelling and warnings, accidental iron ingestion by children has decreased dramatically [4]. Acute iron toxicity in adults and adolescents is rare and usually results from intentional ingestion in suicidal attempts. Ingestion of large amounts of iron preparations can cause acute gastrointestinal damage, acute liver necrosis, hemorrhagic shock, multisystem organ failure, coagulopathy, and death [5]. A case report and a review of literature by Yu D. and Giffen MA reported that the main autopsy findings were iron encrustations over the gastric rugae, superficial stainable iron deposits overlying areas of mucosal necrosis, and underlying sub-mucosal fibrin thrombi. While no significant stainable iron was present in the liver [6]. In the Indian context, no such autopsy-based report was available in the literature that drove us to report all these cases.

Clinical presentation of cases:

Case 1:

A dead body of a 13-year-old female child was brought for autopsy to the department of Forensic Medicine and Toxicology at Gandhi Medical College, Bhopal, on July 15, 2015. Her father found her in a drowsy state with complaints of severe nausea and vomiting at home. Her parents took her immediately to a nearby private hospital. She was given primary treatment for vomiting with no suspicion of poisoning. After two hours of treatment in the hospital, her father left her against medical advice as she improved slightly. Later in the night, she suddenly developed acute abdominal pain, nausea, severe vomiting, and diarrhea and became unconscious. She was subsequently brought to the tertiary care hospital. On examination, she was unconscious; her BP was 90/60 mm of Hg, her pulse was 104 per minute, and her temperature was subnormal with cold extremities. After an hour of intensive care treatment, she was declared dead in the early hours of the morning. No lab investigations were possible, nor was any definite medical diagnosis concluded due to the short hospital stay. An autopsy was conducted to determine the cause of death and revealed multiple confluent hemorrhagic patches over the surface of the stomach, intestine, liver, heart, lungs, and both kidneys, as well as a yellowish-brownish-colored mottled liver that was hard to cut [Fig. 1]. The stomach showed mucosal erosion and contained greenish-blackish material mixed with mucous and eroded, congested mucosal tissue [Fig. 1]. An opinion regarding the cause of death was kept pending, and a visceral sample was preserved for chemical analysis. Tissue samples were preserved and fixed in 10% formalin for histopathological examination. Later on in the police investigation, history revealed that the girl had argued with her mother over watching TV, and in a sudden rage, she consumed 20 iron pills lying in her mother's room. Her mother used to take prenatal iron supplements. Two strips of iron tablet wrapper were found under the bed. A FSL report of viscera was found positive for ferrous sulphate.

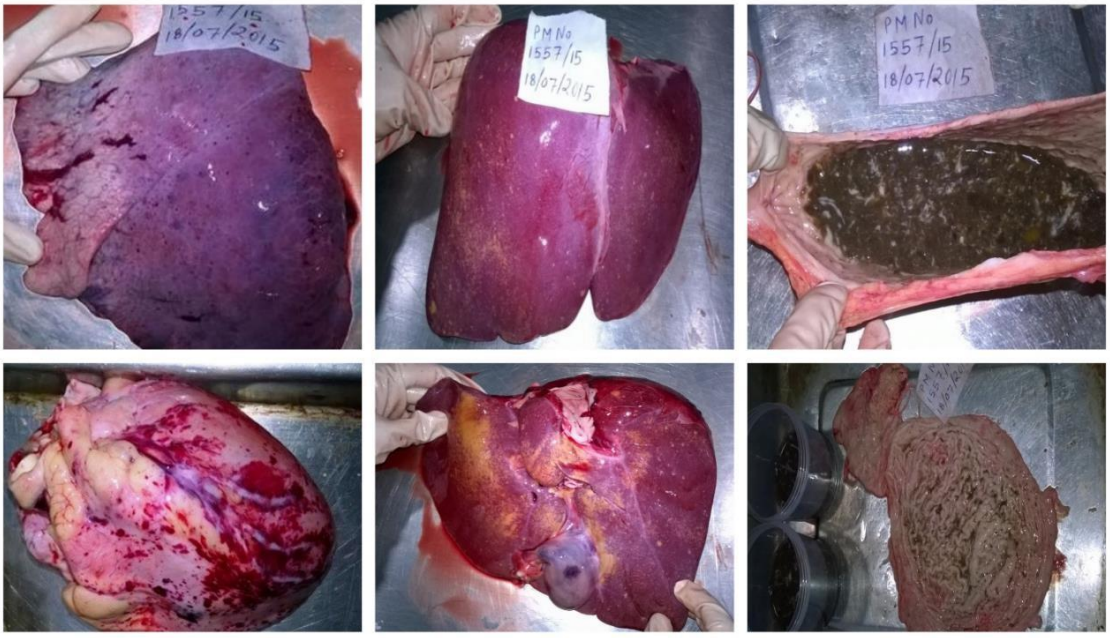

Fig. 1 Showing confluent multiple patechial hemorrhages on the lung and heart. Yellowish brownish color mottled liver on the anterior and posterior surfaces. Stomach showing congested mucosa with mucosal erosion and prominent ruggocities Stomach containing greenish-blackish material mixed with mucous (Case 1).

Case 2:

A 19-year-old female BSc first-year student living in a private hostel was brought to the Hamidiya hospital in Bhopal on February 17, 2017, with complaints of breathlessness, severe abdominal pain, vomiting, and bloody diarrhea. During conversation with her friend and roommate, she admitted the ingestion of three strips and 30 tablets of iron after an argument with her boyfriend. The girl used to take an iron tablet once a day for the treatment of anemia due to severe menorrhagia. On examination, she was semiconscious and in a gasping state. Pulse rate: 100 per min; BP: 90/50 mm Hg; blood sugar: 290 mg/dl. Treatment was given with IV fluids, oxygen, and ionotropic support. After three hours of intensive care treatment and a total of twelve hours of survival after the ingestion of iron tablets, she lost her battle for life. An autopsy was conducted in the mortuary of Gandhi Medical College, Bhopal, on the next day after the arrival of her parents. Findings revealed generalized pallor, bluish discolorations of finger nails, and vaginal bleeding. Multiple petechial hemorrhages, edema, and extreme pallor were found in internal organs [Fig. 2]. Death was opined to be due to poisoning and its complications. Viscera samples were preserved for chemical analysis and were found positive for ferrous fumarate.

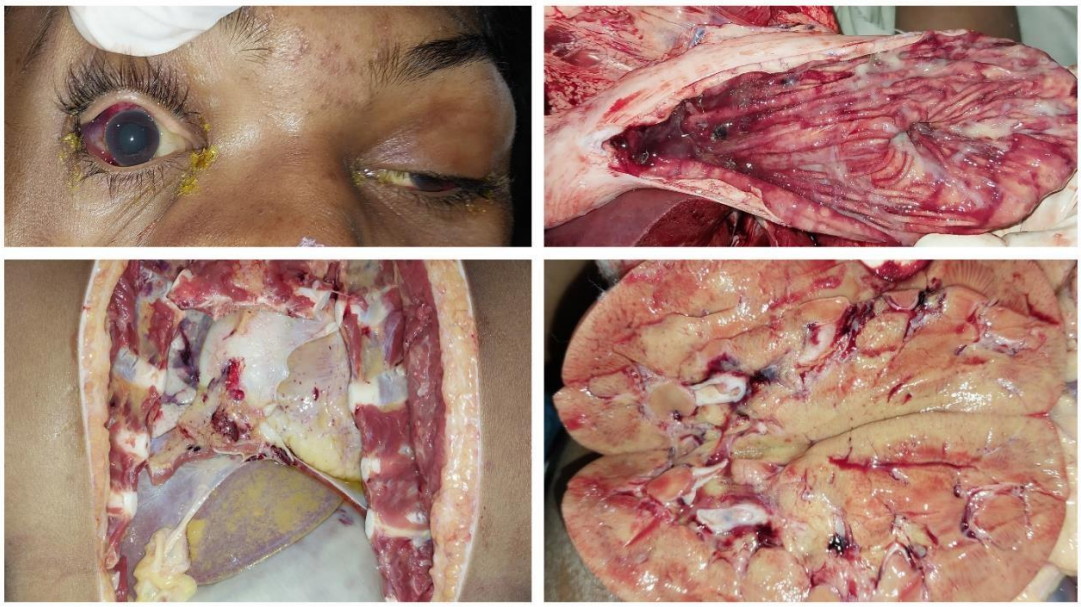

Fig. 2 Showing yellowish discoloration of skin and a dried yellow color tear flow mark near the canthus of both eyes. Multiple patechial hemorrhages and yellowish discoloration of internal organs and body fluids. Severely congested, hemorrhagic, and eroded stomach mucosa and prominent ruggocities. Petechial hemorrhages, congestion, and yellowish discoloration of the kidney (Case 5).

Case 3:

A 20-year-old female who was a lab technician by profession and working in a private hospital lived alone in a rented house near the same hospital. One morning after her night duty, she did not respond to doorbells and phone calls made by her landlord, who then broke open the door and found her lying unconscious in her bathroom. She was subsequently admitted to the same nearby hospital where she worked. Upon admission, her BP was 96/58 mmHg, her pulse rate was 82 per minute, and her RBS was 314 mg/dl by glucometer. Her condition further deteriorated, and she suddenly collapsed within an hour; despite multiple resuscitation efforts, she could not be revived. She was then brought for autopsy to the department of forensic medicine and toxicology at Gandhi Medical College, Bhopal, in August 2018. A thorough inspection of the room of the lady revealed a suicide note and five empty wrappers of ferrous sulphate medications on the side table alongside. At autopsy, all internal organs showed multiple confluent hemorrhages with edema and congestion. The stomach contained about 300 ml of brownish material with hemorrhagic, severely congested, and edematous mucosa. The opinion regarding the cause of death was poisoning and its complications, and a viscera sample was preserved for chemical analysis, which was sent to FSL, where it was found positive for ferrous fumarate.

Case 4:

A dead body of a 15-year-old female student of 9th standard was brought for autopsy to the department of forensic

medicine and toxicology at Gandhi Medical College, Bhopal, on November 20, 2020. She was found dead in theearly hours of the morning, at home, in her bed, lying in a pool of black vomitus and faecal material. She was brought to the Hamidiya Hospital in Bhopal by her parents. She was admitted to the emergency room with complaints of being drowsy and not responding to painful stimuli. Upon admission, her BP was 80/50 mmHg, her pulse rate was 90 per minute, and her RBS was 286 mg/dl by glucometer. Blood work was made available in this case, revealing metabolic acidosis with a high anion gap, and a diagnosis of unknown substance ingestion with refractory shock, respiratory failure, and aspiration was made. She was given IV fluids for maintenance, IV antibiotics, IV vasopressors, and gastric lavage with KMnO4. But in spite of all treatment measures, her life could not be saved, and she was declared dead within 24 hours of admission. At autopsy, external and internal findings were similar to those in case number 3, except for findings in the brain showing severe edema, congestion, and multiple confluent patechial hemorrhages on both the cerebral and more cerebellar regions. The blood vessels of the brain parenchyma revealed hemorrhage and edema. Stomach containedabout100 ml of mucoid fluid material. Mucosa is congested, sloughed, and edematous, with multiple hemorrhagic areas seen at places more in the pyloric region. Stomach ulcers were prominent. The cause of death was opined to be poisoning, and a visceral sample was sent for chemical analysis. Later on, about 6 to 7 empty wrappers of ferrous sulphate tablets with 10 tablets each were later found hidden under her mattress by the investigating officer upon completing the on-site investigation. The FSL report was later found positive for ferrous sulphate upon follow-up of the case.

Case 5:

A dead body of a 17-year-old female was brought for autopsy to the department of forensic medicine and toxicology at Gandhi Medical College, Bhopal, on February 20, 2023. She developed breathlessness, acute abdominal pain, nausea, and bloody diarrhea at home. Upon questioning by her parents, she admitted to having consumed about 60 iron-folic acid pills from an Anganwadi/courtyard shelter held at her home. The girl and her mother got into a heated argument about cooking a meal for the entire family. Her parents took her to a primary care center, were further referred from there to the secondary higher centers, and were subsequently brought dead to Hamidiya Hospital, Bhopal. Her total survival time was approximately 20 hours. No investigations were made in this case, as the majority of the time was spent being transported to the higher centers. The autopsy revealed a well-nourished body with pallor present all over and swollen ankles and eyelids. Dried yellow-colored tear flow marks are present near the canthus of both eyes [Fig. 2]. On internal examination, multiple patechial hemorrhages were present over the surface of the stomach, intestine, peritoneum, heart, lungs, and the entire gastrointestinal tract. All internal organs and body fluids were pale, having yellowish discoloration [Fig. 2]. Stomach contained 200 ml of brownish pasty material mixed with mucoid fluid. The mucosa was severely congested, edematous, and hemorrhagic all over. The lung and brain were grossly edematous. The urinary bladder was full of dark yellow urine. Death was opined to be due to poisoning and its complications. A viscera sample was preserved for chemical analysis and found positive for ferrous sulphate and folic acid preparations.

Histopathological examination:

During the autopsy of all cases, tissue samples were preserved in 10% formalin for histopathological examination. Prior written informed consent was obtained from the close relative of the deceased present at the time of the postmortem examination and concerned police personnel for the preservation and histopathological examination of tissue samples. The relatives have signed informed consent regarding publishing their data and photographs. Ethical approval was waived by the local institutional ethics committee in view of the retrospective reporting of the cases and the fact that all the procedures being performed were part of routine work. Tissues were processed and slides stained with H&E in the Department of Pathology, Gandhi Medical College, Bhopal. Findings revealed surface mucosal erosions and necrosis in the stomach and intestine with generalized edema, congestion, and lymphoid aggregates, along with brownish hemosiderin pigment depositions in the sub-mucosa (Fig. 3a, b, and c). The liver showed portal and peri-portal necrosis of hepatocytes, along with focal hemorrhages, edema, and hemosiderin pigment depositions (Fig. 3d, e, and f). Acute tubular necrosis, intravascular hemorrhage, and tubular congestion were found in both kidneys (Fig. 4a, b). Spleen showing lymphoid aggregates with pigment depositions (Fig. 4c) Lung tissues showed congestion, edema, and diffuse necrosis of pneumocytes (Fig. 4d); brain tissue revealed necrosis, irregular cellular aggregates, congested blood vessels, and foci of brown pigment deposition around the blood vessels (Figs. 4e, f).

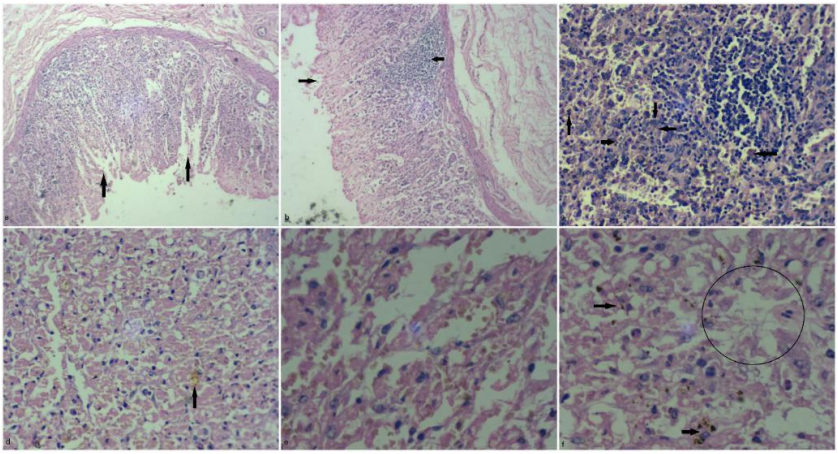

Fig. 3 Photomicrograph showing

a. Stomach mucosa showing surface mucosal necrosis, erosion, and lymphoid aggregates. 10x.
b. Section of the intestine with mucosal erosion and lymphoid aggregates 10x.
c. Lymphoid aggregates in the intestine with pigment deposition and necrosis. 40x.
d. Diffuse hepatic necrosis with brownish pigment deposition, focal haemorrhages, and edema 20x.
e. Hepatic necrosis with haemorrhage. 40 x.
f. Hepatic portal and peri-portal necrosis with brownish pigment deposition. 40x.
g.

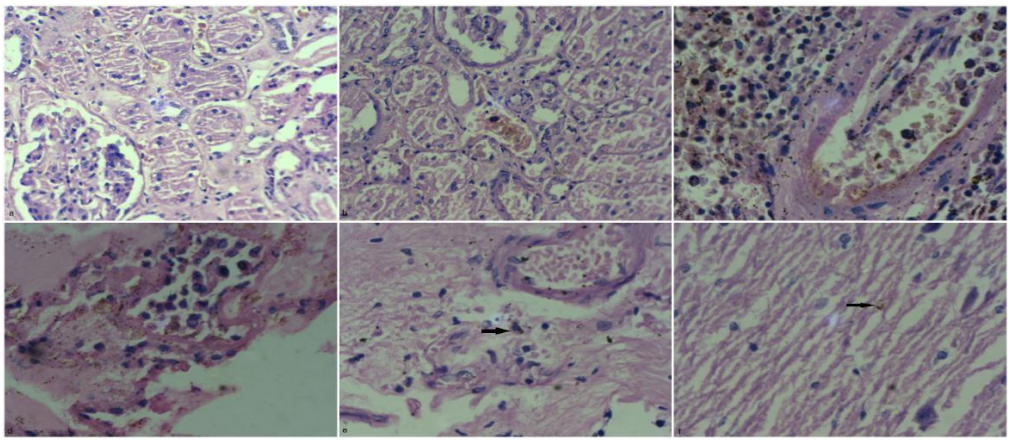

Fig. 4 Photomicrograph Showing

a. Section of the kidney showing acute tubular necrosis with haemorrhage and glomerular congestion 20x.
b. Section of the kidney with a brownish pigment deposit and intravascular haemorrhage. 20x.
c. Section of congested, dilated splenic blood vessels with an abundance of brownish pigment depositions and necrosis. 40x.
d. Section of lung with marked oedema, brownish pigment depositions, and necrosis. 40x.
e. Section of the brain showing necrosis and brown pigment deposits in the brain around the vessels. 10x.
f. Section of the brain showing brownish pigments 40x.

Discussion:

Iron deficiency anemia is a common problem in India, especially in adolescent and pregnant females, and can often be treated through dietary changes and oral medication with iron salts. Various iron preparations are available, most commonly in the form of iron salts, including ferrous gluconate, ferrous sulphate, and ferrous fumarate. Ferrous sulphate is the most frequently used iron supplement and is easily available free of charge in government supply. Iron is crucial for the majority of biological systems because it helps carry oxygen and aids

in cellular respiration. It is an ideal mediator of diverse biological redox reactions. Iron poisoning is common in children, mostly accidental; though uncommon in adolescents and adults, it is ingested with suicidal intent. In the event of an iron excess, the GI mucosa sustains corrosive damage, which may result in acute hemorrhagic gastritis, among other things. Third spacing causes enormous fluid loss, hemorrhage, and shock, all of which further lead to increased iron absorption [7]. Ingestion of toxic doses of iron preparations affects the mitochondria intracellularly, which disrupts oxidative phosphorylation, resulting in anaerobic metabolism, which causes metabolic acidosis along with increased capillary permeability. Iron also contributes to coagulopathy, arteriolar dilatation, severe acidosis, and shock [8]. Free radicals and lipid peroxidation damage the myocardium, which can further lead to cardiac failure, peri-portal hepatic necrosis, pancreatitis, kidney damage, and pulmonary damage [9].

Due to the scarcity of fatal cases of acute iron overdose, the gross and histopathological findings described in the literature are limited. Here we are reporting five cases of suicidal acute iron poisoning in adolescent females belonging to the age group of 13–20 years, reported in the mortuary of Gandhi Medical College, Bhopal, between 2015 and 2023. Who have ingested 20–60 iron tablets containing ferrous sulphate in cases 1 and 4, ferrous fumarate in cases 2 and 3, and 60 iron-folic acid tablets in case 5. External autopsy findings were nonspecific except in case 5, in which the skin all over the body is looking yellowish in color with a dried yellow tear mark present near the canthus of both eyes (Fig. 2). Gross internal autopsy findings were almost similar in all the cases, which are enumerated as multiple confluent petechialhemorrhages with contrast pale parenchyma in all internal organs, that is, the heart, liver, kidneys, lungs, and peritoneum (Fig. 1). Stomach mucosa is sloughed with prominent rugosities (Fig. 1), severely congested, and hemorrhagic (Fig. 2).

Histopathological examination revealedsurface mucosal erosions and necrosis in the stomach and intestine with generalized edema, congestion, and lymphoid aggregates, along with brownish hemosiderin pigment depositions in the sub-mucosa (Fig. 3a, b, and c). The liver showed portal and peri-portal necrosis of hepatocytes, along with focal hemorrhages, edema, and hemosiderin pigment depositions (Fig. 3d, e, and f). Acute tubular necrosis, intravascular hemorrhage, and tubular congestion were found in both kidneys (Fig. 4a, b). Spleen showing lymphoid aggregates with pigment depositions (Fig. 4c) Lung tissues showed congestion, edema, and diffuse necrosis of pneumocytes (Fig. 4d); brain tissue revealed necrosis, irregular cellular aggregates, congested blood vessels, and foci of brown pigment deposition around the blood vessels (Figs. 4e, f).

A case report and a review of literature by Yu D, Giffen MA reported a 25-year-old man ingested large quantity of Iron salt tablets with suicidal intend and died 65.5 hours later [6]. Clinical course and gross internal autopsy findings were similar in our cases; however, laboratory tests indicating hepatic and renal compromise were not possible in our cases due to the short survival time, which was within 24 hours of ingestion. Previous reports have described gastric and intestinal mucosal necrosis and ulceration [10]. Similarly found in our cases, however, visible iron encrustation of the gastro-esophageal mucosa, which is found to be specific for acute toxicity, was not seen in our cases. Similar findings were reported by Sane MR, in which a 20-year-old female allegedly consumed some tablets with suicidal intention and died within 48 hours of admission due to multi-organ failure [5]. The dose of iron tablets was not mentioned.

Literature describes five clinical stages of iron poisoning [5]. These stages of the clinical course may not be found in all patients, and in cases of massive overdose, the patient may present in shock. [11]. The clinical course of all cases represents stage I and rapidly progresses to stage III. Stage II is a dormant stage in which gastrointestinal symptoms disappear and apparent clinical improvement occurs. This is usually seen in some of the earliest cases of iron poisoning, but after 24 hours, they had serious illnesses and died [12]. Similarly found in our case 1. Stage III denotes systemic toxicity, clinically present with pallor, chilly extremities, tachycardia, and tachypnoea as concomitant indications of hypoperfusion; hypotension presents as hypovolemic shock and positive anion-gap metabolic acidosis [13]. Similar clinical presentations were also seen in our cases, which represent stage III. High anion gap metabolic acidosis was seen in our case. Available literature describes hepatic damage in the form of edema and peri-portal hepatic necrosis in acute iron intoxication [14,15,16]. Similar findings were seen in our cases. These clinical signs and symptoms describe the pathophysiology of iron poisoning.

Iron is an essential mineral that plays an important role in transporting oxygen throughout the body; however, like many other nutrients, it is harmful in high amounts. Iron deficiency anemia is common among women. Many national government programs are running for the prevention and treatment of iron deficiency anemia by prescribing iron tablets. In our cases, all females somehow had easy access to iron tablets through Anganwadi, private hospitals, and at home, where they were kept carelessly. In this case report, we recommend that people know that iron tablets are a poison. Though they are also good for pregnant women, they can be extremely dangerous. Its knowledge as a poison and its monitored and supervised use are the keys to preventing iron toxicity. The pharmacist should educate parents on keeping all iron tablets in locked cabinets and out of reach of children.

It is important to educate patients that empirical consumption of iron without any medical indication is not recommended

Statements and Declarations:

Consent to participate and/or consent to publish: Written informed consent was obtained from the close relative of the deceased present at the time of the postmortem examination and concerned police personnel for the preservation and histopathological examination of tissue samples. The relatives have signed informed consent regarding publishing their data and photographs.

Competing interests and Funding: The authors have no competing interests to declare that are relevant to the content of this article. No funding was received to assist with the preparation of this manuscript.

Ethical approval: Ethical approval was waived by the local institutional ethics committee in view of the retrospective reporting of the cases and the fact that all the procedures being performed were part of routine work.

Author's contribution statements: All authors contributed in reporting the cases. Material preparation, samples collection were performed by Dr Sangita Chaurasia, Dr Rajneesh Kumar Pandey and Dr Saagar Singh. Tissue samples processing and Histo-pathological examination was performed by Dr Sangita Chaurasia. The first Draft of the manuscript was written by Dr Saagar Singh and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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