SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING - AN OBSERVATIONAL STUDY

A Dissertation Submitted to

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY, CHENNAI

in partial fulfilment of the requirement for the award of the

Degree of M.D. (GENERAL MEDICINE) - BRANCH – I

REGISTRATION NO: 200120101503

MAY 2023

CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled **'SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING - AN OBSERVATIONAL STUDY'** is the bonafide work of Dr. A. Ashy Stephanie in partial fulfilment of the University regulations of The Tamilnadu Dr. M.G.R. Medical University, Chennai, for the award of Degree of Doctor of Medicine (M.D.) Branch- I - General Medicine examinations to be held in May 2023.

14.12.22

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DECLARATION

I, **Dr. A. Ashy Stephanie**, hereby declare that, I carried out this work entitled **'SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING - AN OBSERVATIONAL STUDY'** at Government Rajaji Hospital & Madurai Medical College, Madurai, under the guidance of Prof. Dr. S.C. Vivekananthan, Professor of Medicine, during the period of November 2021 to March 2022. I also declare that this bonafide work has not been submitted in part or full by me or any others for any award, degree or diploma to any other University or Board either in India or abroad. This is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the University rules and regulations for the award of Degree of Doctor of Medicine (M.D.) Branch- I-General Medicine.

Ashy Stephanie A

Place: Madurai

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Date: 14.12.2022

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to Prof. Dr. Rathinavel, M.S., M.Ch., Dean, Madurai Medical College, for having permitted me conduct this study and to use the hospital facilities at Madurai Medical College and Government Rajaji Hospital, Madurai.

I am greatly indebted to my beloved teacher Prof. Dr. M. Natarajan, M.D., Professor and Head, Department of Medicine for allowing me to do this study in the Department of Medicine. I also express my sincere thanks to him for giving me proper guidance, protocol and immense help and encouragement in conducting this study.

I express my gratitude to my Chief Dr. S.C. Vivekananthan M.D., D.T.C.D, Department of Medicine who immensely helped me in conducting this study.

I express my sincere and heartfelt gratitude to all Assistant Professors in the Department of Medicine, especially Dr. Naseema Banu M.D., Dr. Satheesh Kumar M.D. and Dr. Vinoth Kannan M.D. for their encouragement, kind guidance, constant support and cooperation in evaluating the patients.

I thank the Members, Secretary and Chairman of the Institutional Ethical committee, Madurai Medical College, Madurai.

I thank all the paramedical staff and other staff of the Madurai Medical College for all their help and cooperation in conducting this study.

I thank all my colleagues, Seniors, Juniors and friends for their constant encouragement and valuable criticism. I am extremely thankful to all my family members for their continuous support. Above all I thank God Almighty for His immense blessings. Finally my profound gratitude to all the patients, to whom I owe everything because this venture would not have been possible without them.

ABBREVIATIONS

TPE-Therapeutic Plasma Exchange

ALF-Acute Liver Failure

HSEC-Hepatic Sinusoidal Endothelial Cells

HSC-Hepatic Stellate Cells

AFP-Alpha Feto Protein

AST-Aspartate Aminotransferase

ALT-Alanine Aminotransferase

GGT-Gamma Glutamyl Transferase

DILI-Drug Induced Liver Injury

WBC-White Blood Cell

RBC-Red Blood Cell

WHC-West Haven Criteria

HE-Hepatic Encephalopathy

MAP-Mean Arterial Pressure

DIC-Disseminated Intravascular Coagulation

VLDL-Very Low Density Lipoprotein

ATP-Adenosine Tri Phosphate

YP-Yellow Phosphorus

ICP-Intra Cranial Pressure

KCHC-King's College Hospital Criteria

BBB-Blood Brain Barrier

MELD-Model for Endstage Liver Disease

MARS-Molecular Adsorbents Recyling System

LT-Liver Transplantation

OLT-Orthotopic Liver Transplantation

ADP-Adenosine Di Phosphate

UNOS-United Network of Organ Sharing

HBV-Hepatitis B Virus

IV -Intra Venous

TNF-Tumor Necrosis Factor

RES-Reticulo Endothelial System

VEGF-Vascular Endothelial Growth Factor

AKI-Acute Kidney Injury

ISHEN- International Society for Hepatic Encephalopathy and Nitrogen Metabolism.

PTT-Partial Thromboplastin Time

INR-International Normalised Ratio

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ABSTRACT

BACKGROUND OF THE STUDY

Yellow phosphorus, commonly used as rodenticide has a lethal dose of 1 milligram per kilogram, the most common mode of poisoning being ingestion. It causes periportal necrosis of liver leading to acute liver failure with the elevation of enzymes usually after 72 hours. After 72 hours the person develops coagulopathy, acute liver failure, which can also progress to MODS. Serum phosphorus level is considered as an important predictor of mortality in acetaminophen poisoning with acute liver failure. Hypophosphatemia occurs as a result of increased intracellular uptake of phosphorus to replenish high energy intermediates when there is brisk hepatocyte regeneration. Hence high serum phosphate level is associated with poor prognosis in patients with acute liver failure.

OBJECTIVES

To study the association between serum phosphorus and acute liver failure and to prognosticate the patients with acute liver failure with regard to serum phosphate level.

METHODOLOGY

Fifty patients admitted with consumption of toxic dose of Rat killer paste (yellow phosphorus) are segregated, they are then grouped on the basis of age and gender. Routine blood investigations are done. Serum phosphorus level at D1, D3 and D7 of poisoning are done along with serial monitoring of liver enzymes and PT- INR. The collected data is analysed by using Statistical Package for Social Sciences (SPSS) . The class intervals are fixed by using the formula, $I \geq (L^{-} S) / n.5 \leq n \leq 15$. Using Sturges' rule as a guide: $n = 1 + 3.322 \log10 (N)$, where N = Total number of observations.

RESULTS

In the study, it is found that there exists a correlation between the values of serum phosphorous and the patients' outcome irrespective of the treatment options.

CONCLUSION

In cases of acute liver failure presenting with coagulopathy and acute encephalopathy in yellow phosphorous poisoning, patients with transaminitis more than 2000 are associated with poor regenerative capacity of liver. In the study, survivors almost always had a dip in Serum phosphorus level on day 7 correlated as increased in regeneration of the liver which could compensate for the massive hepatic necrosis which occurred as a result of yellow phosphorous poisoning. The sensitivity of serum phosphorus in terms of prognostication is good in acute liver failure in yellow phosphorus poisoning.

SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING - AN OBSERVATIONAL STUDY

INTRODUCTION

Introduction

Yellow phosphorus commonly used rodenticide in the name ratol is a protoplasmic poison. The lethal dose is 1 milligram per kilogram. The most common mode of poisoning is ingestion which is either accidental or intentional. Being a protoplasmic poison it affects the ribosomal function and hence inhibits protein synthesis.

Liver receives major cardiac output. The common cause of Acute Liver Injury includes Infections-Hepatitis A,B,E,EBV, Ischemia, Wilson's disease, HELLP syndrome ,Vasoocclusive disease and toxins like paracetamol, yellow phosphorus etc. The main functions of Liver include Glucose Metabolism - Glycogenolysis, Gluconeogenesis, Glycolysis, fat and lipid metabolism, secretion of IGF, storage of Vitamins, detoxification, clotting factor synthesis etc.

Yellow Phosphorus causes periportal necrosis of liver leading to acute liver failure with the elevation of enzymes. Yellow phosphorus toxicity occur in the cellular organelles affecting protein synthesis hence resulting in reduced synthesis of VLDL , ATP and hence inhibits oxidation of fatty acid which results in diffuse fatty infiltration of the organs and cell death. The clinical manifestations of poisoning can be of three phases. In the first 24 hours there are only mild symptoms with gastrointestinal irritation. In the next 24 to 72 hours there is rise in bilirubin and liver enzymes. After 72 hours patient may develop coagulopathy, acute liver failure, hypotension and acute kidney injury.

Treatment for Yellow phosphorus poisoning includes gastric lavage and only supportive measures, as there is no specific antidotes for yellow phosphorus poisoning. In patients with acute liver failure due to toxins N-acetyl cysteine which replenishes

glutathione and that stabilizes the vasculature can be used. The candidates for liver transplantation following acute liver failure in yellow phosphorus poisoning is assessed using King's College Hospital Criteria. TPE is always used as bridge for ALF patients to liver transplantation. Serum phosphorus level is considered as an important predictor of mortality in acetaminophen poisoning with acute liver failure. Hypophosphatemia occurs as a result of increased intracellular uptake of phosphorus to replenish high energy intermediates when there is brisk hepatocyte regeneration. Hence high serum phosphate levels are associated with poor prognosis in patients with acute liver failure.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

- To study the association between Serum phosphorus and acute liver failure.
- To assess the prognosis of patients with acute liver failure with regards to Serum phosphate level.

REVIEW OF LITERATURE

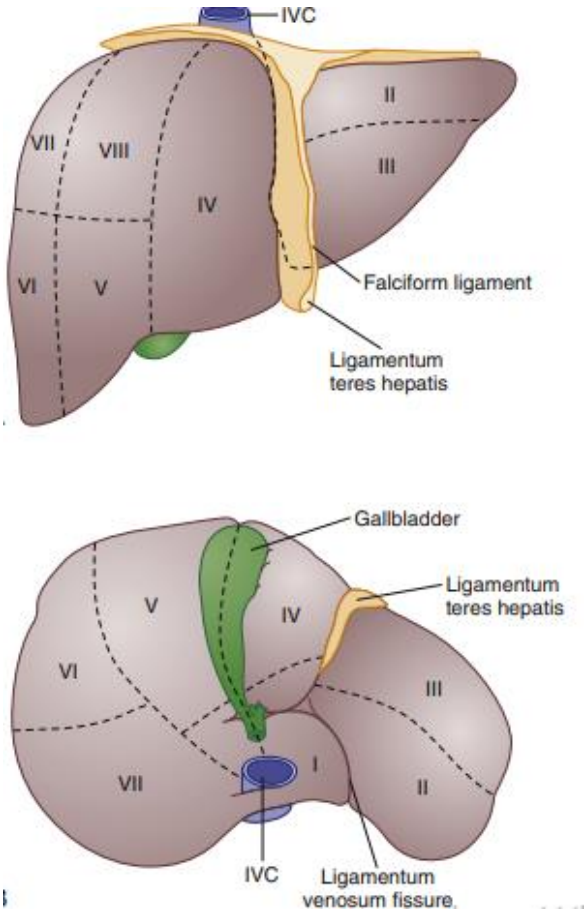
Review of Literature

LIVER

Liver has four lobes- right, left, caudate, and quadrate.[1,33] Anteriorly, the falciform ligament divides liver into the right and left anatomic lobes. Inferiorly, quadrate lobe is bounded by gallbladder fossa, porta hepatis and ligamentum teres hepatis. Caudate lobe is bounded by inferior vena cava groove, porta hepatis and ligamentum venosum fissure. [8]

The liver receives 40% of blood from the portal vein and 60% of blood from the hepatic artery.[34] Liver has 1-8 sub segments, with the caudate lobe as sub segment [4] and the others following in a clockwise pattern.

Figure : 1 Diagrammatic representation of lobes of liver

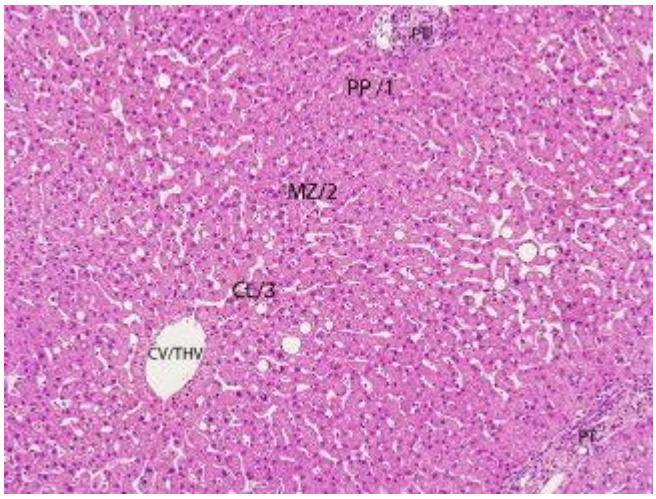


The liver is composed of different types of cells which includes- parenchymal cells -comprising of hepatocytes and cholangiocytes and non parenchymal cells which include kupffer cells, stellate cells, pit cells and sinusoidal endothelial cells. [35]

Hepatocytes are arranged in 3 different zones:

- Zone1 (periportal)
- Zone2 (midzonal)
- Zone3 (pericentral)

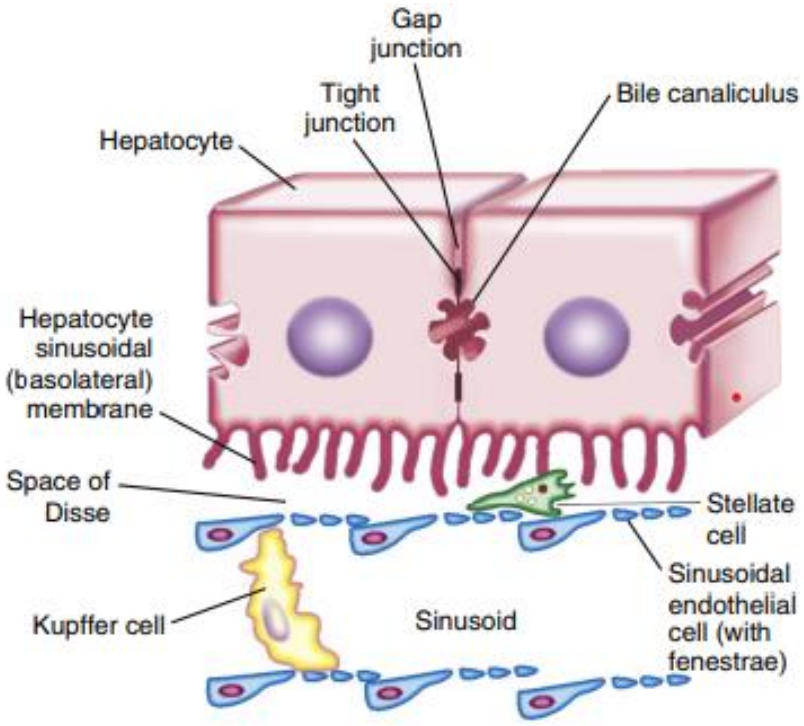
Figure : 2. Normal histology of liver[17]



The hepatocytes have capacity of regeneration following liver injury. The hepatocytes are principle cells which perform synthetic as well as metabolic functions of the liver. [40] The hepatocyte plasma membrane has got 3 surfaces with distinct action.

- Sinusoidal surface (basolateral) -close to sinusoidal epithelial cells
- Canalicular surface (apical)- close to biliary canaliculus
- Contiguous surface (lateral)

Figure : 3 Diagrammatic representation of different cells within a lobule of liver



Functional zones in liver

- Zone1-receives highly oxygenated blood, gluconeogenesis and urea cycle takes place in zone1
- Zone 2 - hepcidin production and iron regulation
- Zone 3- predominant glycolysis and xenobiotic metabolism

Kupffer cells : Specialised macrophages of reticuloendothelial system of liver found in sinusoidal lumen and they are active in pinocytosis and phagocytosis and close to the endothelial cells. They also secrete vasoactive and toxic cytokines and helps in immunity. Hence these cells are increased in inflammation - Toxic, Infection, Autoimmune conditions etc.

Sinusoidal endothelial cells: They are endothelial cells which differ from other systemic capillaries due to the presence of pores(fenestra) . [29] They arise from

hemangioblasts, sinus venous - endocardium.[36] HSEC act as barrier between blood and hepatocytes and also secretes cytokines-interleukin1, interferon, TNF alpha, endothelin, and hence regulates portal venous pressure in maintaining the vascular tone. They also secrete hepatocyte growth factor and stimulation by VEGF and helps in hepatocyte regeneration.[10]

Hepatic stellate cells (Cells of Ito) **:** These are mesenchymal cells which form elongated myofibroblasts and results in fibrosis post liver injury. They also acts as storage house of vitamin A. [23] HSCs also play an important role in inflammation and fibrotic remodelling by the production of TGF beta and increasing the expression of metalloprotienases, Extra cellular matrix proteins and cytokines. [38]

Pit cells :They are Natural Killer cells present in liver which are found within the sinusoids of liver, close to kupffer cells. They are associated with tumour cell killing activity and also apoptosis of virus infected hepatocytes. They also control the growth and hepatocytes differentiation.

Functions of liver

Protein metabolism : Liver produces several important proteins which are components of plasma- α1-Acid glycoprotein ,Albumin, AFP, α_1 Antichymotrypsin , ceruloplasmin, Complement C3, Complement C4 ,C-Reactive Protein, ferritin, fibrinogen, haptoglobin, Serum amyloid, transferrin. Both protein anabolism and catabolism takes place in liver, the most important urea cycle which detoxifies the ammonia also occurs in liver.

Fat metabolism: Fatty acid oxidation, production of lipoprotein and fatty acid synthesis occur in liver.

Carbohydrate metabolism: Glycogenolysis, gluconeogenesis occurs in the liver. Hence several metabolic pathways take place in liver (carbohydrates, protein, fat).

Liver Function Tests

Bilirubin: [27] Bilirubin is a byproduct of heme metabolism. Bilirubin metabolism occurs in the RES spleen (1st few steps).Bilirubin that is formed is bound to albumin and is taken by the liver where is conjugated by UDP Glucuronyl Transferase to form bilirubin mono glucuronide and di glucuronide. [6] It is then transported via Multidrug Resistant Protein [25](ATP dependent). In the gut, beta glucuronidases produced by bacteria then hydrolyse conjugated to unconjugated bilirubin further leading to urobilinogen production, which is excreted as urobilin , some amount is then reabsorbed in to venous portal system and excreted in feces.

Normal total serum bilirubin values -1.0-1.5 mg/dl.

Conjugated bilirubin-0.3mg/dl

Unconjugated bilirubin- 0.8 to 1.2 mg/dl

Icterus manifest only when the total serum bilirubin is at least 3mg/dl. Unconjugated hyperbilirubinemia is associated with acholuric jaundice, whereas in conjugated hyperbilirubinemia there occurs high coloured (tea coloured/cola coloured) urine. In evaluation of patients with jaundice, the initial step is to fractionate bilirubin to conjugated and unconjugated. If the conjugated bilirubin is less than 15 percent of total bilirubin then all the serum bilirubin is unconjugated.

Increased Unconjugated bilirubin occurs in

1. Increased Red cell haemolysis.

2. Disorders in bilirubin conjugation (rare)

3. Drugs that interfere with hepatic uptake of bilirubin

Table : 1 Causes of Hyperbilirubinemia

Cause	Mechanism
INDIRECT HYPERBILIRUBINEMIA	
Hemolytic Disorders	Overproduction of bilirubin
Inherited Red cell enzyme defects (e.g., glucose-6-phosphate dehydrogenase deficiency) Sickle cell disease Spherocytosis and elliptocytosis	
Acquired Drugs and toxins Hypersplenism Immune mediated Paroxysmal nocturnal hemoglobinuria Traumatic: macro- or microvascular injury	
Ineffective Erythropoiesis	Overproduction of bilirubin
Cobalamin deficiency Folate deficiency Profound iron deficiency Thalassemia	
Drugs: Rifampin, Probenecid	Impaired hepatocellular uptake of bilirubin
Inherited Conditions	Impaired conjugation of bilirubin
Crigler-Najjar syndrome types I and II Gilbert syndrome	
Other	
Hematoma and massive blood transfusion	Overproduction of bilirubin
DIRECT HYPERBILIRUBINEMIA	
Inherited Conditions	
Dubin-Johnson syndrome Rotor syndrome	Impaired excretion of conjugated bilirubin

Amino Transferases(AST and ALT)

AST: Present in mitochondria and cytoplasm. It is found in skeleton muscles, brain and pancreas, kidney, lungs, WBC, RBC. ALT-present in cytoplasm. It is more concentrated in liver and hence more specific indicator of liver injury. As a result of inflammation, alteration in membrane permeability occurs, which results in release of ALT and AST into blood, they are then cleared by Reticulo Endothelial System. AST cleared faster than ALT. [13,16]

Normal ranges: below 30 U/L for Males, 19U/L for Females

Elevation of Amino Transferases: [26,19]

(More than 1000U/L , ALT > AST):

1. Viral Hepatitis A to E
2. Toxin induced liver injury
3. DILI
4. Ischemic hepatitis
5. Autoimmune hepatitis
6. A cute Budd Chiari syndrome
7. Wilsons disease(ALF)
8. Acute biliary obstruction

(More than 1000 U/L, AST>ALT)

1. Acute rhabdomyolisis

2. Myopathy

3. Strenous exercise

4. Hypothyroidism

5. Toxin/medication - underlying alcohol liver disease

ALT >AST but less than 150 U/L

1. Alpha 1 antitrypsin deficiency

2. Chronic viral hepatitis

3. Steatosis and steato hepatitis

4. Wilson disease

5. Hyperthyroidism

Alkaline phosphatase

ALP is predominantly distributed in various organs of the body and produced from placenta, liver, small intestine and kidneys. The half life of ALP is 7 days. In liver it is produced on the canalicular membrane of hepatocytes, and increased serum ALP is associated with hepatobiliary disease, which in turn leads to the synthesis of enzyme and bile acid mediated leakage in to plasma. Increase in GGT and 5-nucleotidase correlate with the increase in hepatic source of ALP. [15] Intestinal ALP usually increase after a fatty meal. Bone ALP correlates with the age of increased bone growth (growth spurt). Low ALP is associated with Wilson's disease due to reduced activity of the enzyme as copper competitively inhibit zinc in its production.

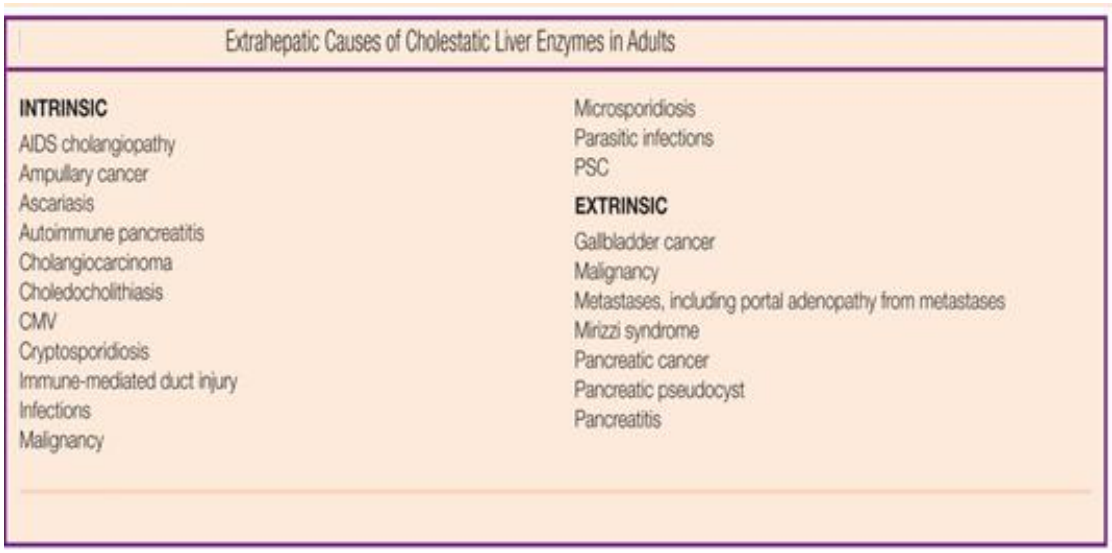
GGT : GGT is widely distributed in various organs in humans-kidneys, pancreas, spleen, seminal vesicles, heart, brain, liver(hepatocytes and cholangiocytes).The primary use of GGT in liver diseases is to establish both GGT and ALP increases in cholestatic jaundice and thus excludes other causes of increased ALP. [41] The other causes of increased GGT includes medications such as HAART and antiepileptics.

Table : 2 Causes of Cholestatic jaundice-Intrahepatic cholestasis

DRUGS[a]
Bland cholestasis
Anabolic steroids
Estrogens
Cholestatic hepatitis
Angiotensin-converting enzyme inhibitors: captopril, enalapril
Antimicrobials: amoxicillin-clavulanic acid, ketoconazole
Azathioprine
Chlorpromazine
NSAIDs: sulindac, piroxicam
Granulomatous hepatitis
Allopurinol
Antibiotics: sulfonamides
Antiepileptics: carbamazepine, phenytoin
Cardiovascular agents: hydralazine, procainamide, quinidine
Phenylbutazone
Vanishing bile duct syndrome
Amoxicillin-clavulanic acid
Chlorpromazine
Dicloxacillin
Flucloxacillin
Macrolides
PBC
PSC
GRANULOMATOUS LIVER DISEASE
Infections
Brucellosis
Fungal: histoplasmosis, coccidioidomycosis
Leprosy
Q fever
Schistosomiasis
TB, *Mycobacterium avium* complex, bacillus Calmette-Guérin
Sarcoidosis
Idiopathic granulomatous hepatitis
Other
Crohn disease
Heavy metal exposure: beryllium, copper
Hodgkin disease
VIRAL HEPATITIS
HAV
HBV and HCV, including fibrosing cholestatic hepatitis
HDV
HEV
EBV
CMV
IDIOPATHIC ADULTHOOD DUCTOPENIA
GENETIC CONDITIONS
Progressive familial intrahepatic cholestasis
Type 1 (formerly Byler disease)
Type 2
Type 3
Benign recurrent intrahepatic cholestasis
Type 1
Type 2
CF
MALIGNANCY
HCC
Metastatic disease
Paraneoplastic syndrome
Non-Hodgkin lymphoma
Prostate cancer
Renal cell cancer
INFILTRATIVE LIVER DISEASE
Amyloidosis
Lymphoma
INTRAHEPATIC CHOLESTASIS OF PREGNANCY
TPN
GRAFT-VERSUS-HOST DISEASE
SEPSIS

[a]Categorized by histologic pattern. Drug lists are not meant to be comprehensive.

Table : 3 Causes of Cholestatic jaundice-Extrahepatic cholestasis



Extrahepatic Causes of Cholestatic Liver Enzymes in Adults

INTRINSIC

AIDS cholangiopathy
Ampullary cancer
Ascariasis
Autoimmune pancreatitis
Cholangiocarcinoma
Choledocholithiasis
CMV
Cryptosporidiosis
Immune-mediated duct injury
Infections
Malignancy
Microsporidiosis
Parasitic infections
PSC

EXTRINSIC

Gallbladder cancer
Malignancy
Metastases, including portal adenopathy from metastases
Mirizzi syndrome
Pancreatic cancer
Pancreatic pseudocyst
Pancreatitis

Albumin: Albumin which maintains the plasma oncotic pressure is exclusively synthesised in the liver. Normally around 15gm /day is produced in humans. The half life of Albumin is 14-21 days and is degraded in skin, muscle, liver, kidney and in GIT by leakage. When serum levels are less than 3gm/dl in background of hepatitis, a chronic hepatic disease should always be ruled out. The synthesis of albumin in greatly influenced by nutritional status, hormones, systemic inflammation and osmotic pressure.[30]

Hypoalbuminemia: Causes

1. Malnutrition

2. Protien losing enteropathy

3. Nephrotic syndrome

4. Hormonal imbalances

5. Chronic systemic inflammatory conditions

Prothrombin time

Almost all clotting factors are synthesized in the liver except factor VIII which is secreted by vascular endothelial cells. Prothrombin time assess the extrinsic pathway of coagulation.[18] The extrinsic pathway includes clotting factors II, V, VII, X. Prothrombin time is prolonged in

1. Congenital deficiency of clotting factors

2. Vitamin K deficiency

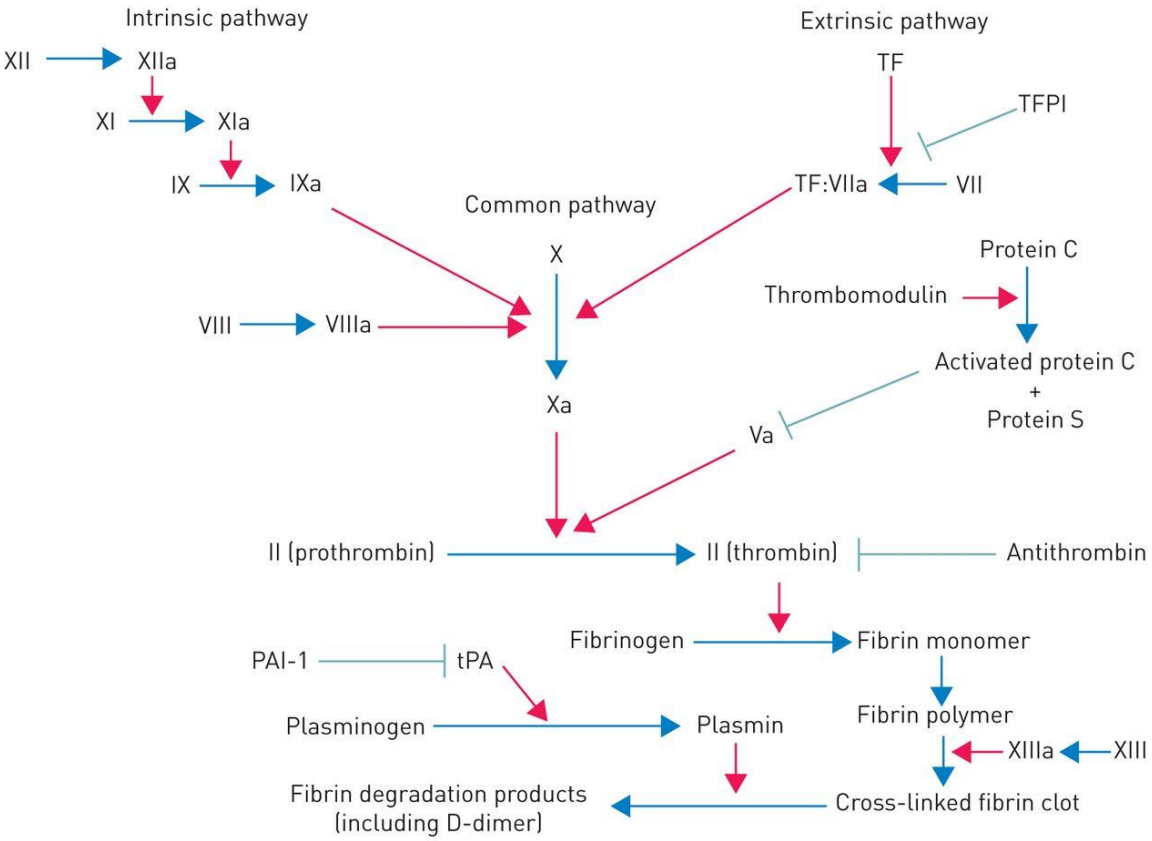
   (post translational modification of clotting factors II, VII, IX, X)

3. DIC

- Vitamin K deficiency: corrected by IV Vitamin K injection (more than 30 percent improvement with prothrombin time). IV is preferred over oral because it is not easily absorbed by intestine in patients with jaundice.
- DIC: diagnosed by reduced Factor VIII levels but normal in patients with liver disease. Factor VII has shortest half-life of 6 hours and hence Prothrombin time helps in assessment of acute hepatic impairment (ALF)

PTT which assesses the intrinsic pathway can also be deranged in patient with advanced liver disease but it is less sensitive.

Figure : 4 Diagrammatic representation of Coagulation cascade [22]



DIAGNOSTIC MODALITIES

ALF diagnosis is made in the clinical grounds of encephalopathy and coagulopathy with increased liver function test (transaminases). Encephalopathy can manifest as overt and can also be covert which is diagnosed clinically by psychometric testing. The commonly used scale for grading hepatic encephalopathy is West Haven Grading.

Table : 4 West-Haven criteria (WHC) for hepatic encephalopathy and clinical description[27]

WHC	ISHEN	Description	Suggested operative criteria	Comment
Unimpaired		No encephalopathy at all, no history of hepatic encephalopathy	Tested and proven to be normal	
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	Abnormal results of established psychometric or neuropsychological tests without clinical manifestations	No universal criteria for diagnosis local standards and expertise required

WHC	ISHEN	Description	Suggested operative criteria	Comment
Grade I		Trivial lack of awareness Euphoria or anxiety Shortened attention span Impairment of addition or subtraction Altered sleep rhythm	Despite oriented in time and space (see below), the patient appears to have some cognitive/ behavioral decay with respect to his or her standard on clinical examination or to the caregivers	Clinical findings usually not reproducible
Grade II	Overt	Lethargy or apathy Disorientation for time. Obvious personality change Inappropriate behavior Dyspraxia Asterixis	Disoriented for time (at least three of the following are wrong: day of the month, day of the week, month, season, or year) ± the other mentioned symptoms	Clinical findings variable, but reproducible to some extent

WHC	ISHEN	Description	Suggested operative criteria	Comment
Grade III		Somnolence to semistupor Responsive to stimuli Confused Gross disorientation Bizarre behaviour	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) ± the other mentioned symptoms	Clinical findings reproducible to some extent
Grade IV		Coma	Does not respond even to painful stimuli	Comatose state usually reproducible

All conditions are required to be related to liver insufficiency and/or portosystemic shunting.

Based on the cause the HE can be classified as 3 Types

- Type A – due to Acute Liver Failure
- Type B – due to portosystemic collaterals /shunting
- Type C – due to Cirrhosis

Liver enlargement occurs in Budd Chiari syndrome, malignant infiltration or alcohol-associated hepatitis.

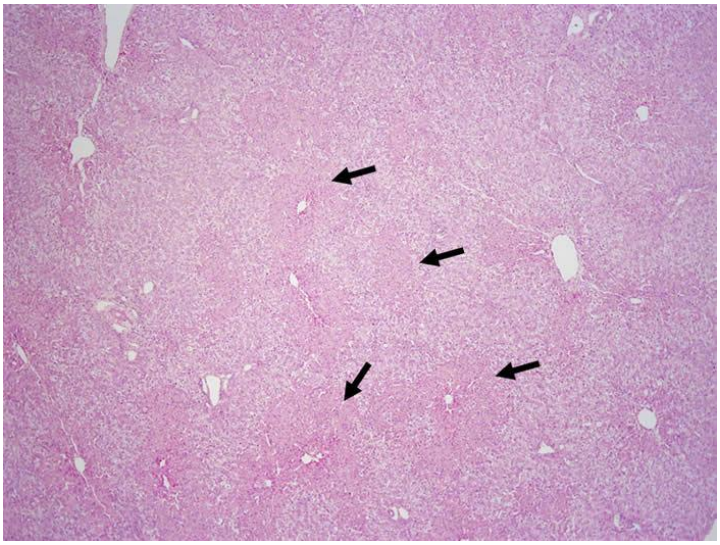
Liver imaging can be informative in pregnancy related ALF – shows fatty infiltration in acute fatty liver of pregnancy and decreased tissue perfusion in preeclampsia.

Liver biopsy-indicated in cases to rule out malignancy and alcoholic hepatitis[3]

In ALF it shows confluent necrosis, parenchymal collapse. As a result, liver biopsy is not performed routinely in patients with ALF. The findings are usually non-specific on biopsy, certain features which help in diagnosis –

- Inflammation - Autoimmune hepatitis
- Micro vesicular steatosis- Valproic acid toxicity
- Hepatocyte ballooning, Steatosis, Cirrhosis, Interface hepatitis- Wilson disease
- Fatty infiltration -Acute Fatty Liver of Pregnancy
- Fibrin micro thrombi, necrosis -Preeclampsia / Eclampsia
- Venous congestion, sinusoidal dilatation - Budd-Chiari syndrome

Figure 5 : Histology of Liver necrosis, arrows- shows zonal necrosis appearing darker pink ,normal viable hepatocytes are pale as a result of steatosis. [21]



Acute ischemic injury- common in older age and is associated with heart failure and cardiovascular diseases. They are usually common with right heart failure leading to liver congestion always or usually following hypotension. Usually the enzymes level are more than1000 and coagulopathy can also occur. It can also occur after trauma and surgical procedures which causes loss of vascular inflow to liver. Liver transplantation is not a good option in these patients.

Heamophagocytic lymphohistiocytosis, hematological malignancies, tropical diseases-dengue ,malaria, scrub typhus can also results in acute liver failure.

ALF can result in Hemodynamic instability presenting as hypotension and AKI, Cardiac complications such as arrhythmias can also occur which is usually triggered by hypo- or hyperkalemia, acidosis and hypoxia. Initially the patients have features of hyperdynamic circulation-increased cardiac output and reduced systemic vascular resistance which can then progress to hemodynamic instability progressing to reduced cardiac output and low MAP. Renal dysfunction occurs earlier in patients with Wilson disease, Amantia mushroom poisoning, and pregnancy-related ALF and is also precipitated by hypotension, infections leading to sepsis probably due to systemic inflammation and leukocyte dysfunction. Hypocortisolism can also occur.

In ALF, fibrinogen, prothrombin, and factors V, VII, IX, and X levels fall rapidly and increased consumption of these factors can result in DIC.

Table 5: Difference in presentation of Hepatotoxins – Acetaminophen and Phosphorus [43]

Phases of Illness after Ingestion of Various Hepatotoxins		
Phase	**Acetaminophen**	**Phosphorus**
I (1-24 H)		
Onset of toxicity	Immediate	Immediate
Anorexia, nausea, vomiting, diarrhea	+	++++
Shock	–	+
Neurologic symptoms	–	+
II (24-72 H)		
Asymptomatic latent period	+	±
III (>72 H)		
Jaundice	+	+
Hepatic failure	+	+
Renal failure	+	+
Maximum serum AST and ALT (×ULN)	1000	<10-100
Zonal necrosis	3	1
Steatosis	–	++++
Case-fatality rate (%)	5-15	25-50

ULN, upper limit of normal.

MANAGEMENT

Adequate fluid resuscitation and airway management in patients with encephalopathy. Metabolic acidosis when present is associated with poor prognosis and indicates severe toxicity.

N-Acetylcysteine is used in acetaminophen overdose and prevents liver injury when given within 15 hours of ingestion. Patients who are malnourished, alcoholics and patient on enzyme inducing drugs are associated with poor prognosis in ALF. Acute HBV infection-treated with antivirals and helps in clearance of viral load in blood. Amanita phalloides toxicity- Penicillin and silymarin can be used. Wilson disease D-

pencillamine can be used in acute hepatitis but has no role in encephalopathy. Autoimmune hepatitis-glucocorticoid therapy.

YELLOW PHOSPHORUS

The three forms of Phosphorus : Yellow, White and Red. Because red phosphorus is not soluble or absorbable, it is not hazardous when consumed. The only hazardous form of elemental phosphorus is yellow phosphorus (YP). It is a toxin which targets the protoplasm. In addition to making firecrackers, it is used as chemical that kills rats. Rodenticides are available as pastes and powders with 2-5% YP. It has an impact on various organ systems when ingested. [1]Although the commonly acknowledged lethal dose is 1 mg/kg body weight, even 15 mg can be fatal. It is easily absorbed in the digestive system and is fat-soluble. In the GI tract, it forms phosphine gas in diluted acid, causing signs and symptoms. After absorption, it can also cause immediate liver damage.

Yellow phosphorus is the chemical compound present in Ratol. Yellow phosphorus is the name given to white phosphorous that contains impurities. It is frequently sold as rat killer paste (3%) in South India. The Yellow phosphorous has a lethal dosage of 100 mg/kg body weight, and its toxicity rises when combined with a fatty dinner. Hepatotoxicity is caused by yellow phosphorus by the formation of phosphoric acid, which harms cells through free radicals. This poisoning is associated with high death rate and the likelihood of life after three days depends on the lowest possible increase in LFT. Altered sensorium, hypotension and hypoglycemia, metabolic acidosis and an increased prothrombin time are associated with poor prognosis.[25] The initial stage which occurs after 48 hours after ingestion include symptoms like vomiting, nausea, pain in the abdomen and smoking stools. In the next 12 hours there

is some reduction in symptoms and the third stage is characterised by elevated liver enzymes which manifests as acute liver failure and further progresses to Multi Organ Dysfunction Syndrome.

According to O. U. Fernandez,, L. L. Canizares, a study with 15 case, only two patients after poisoning with yellow phosphorous, had normal liver parameters and others had varied degrees of liver injury with only four presented with acute liver failure and of the complications, coagulopathy and marked elevations in hepatic enzymes are associated with worst prognosis.[11]

Yellow phosphorus toxicity occur in the cellular organelles affecting protein synthesis hence resulting in reduced synthesis of VLDL ,ATP and hence inhibits oxidation of fatty acid which results in diffuse fatty infiltration of the organs and cell death. [2]

During the hospital stay the patients who developed hemodynamic compromise are treated with IV fluids and ionotropes and vasopressors like Norepinephrine are avoided in patients with raised intracranial tension in Hepatic encephalopathy as it can cause further cerebral vasodilation resulting in further increase in ICP. In case of persistence of shock after resuscitation with vasopressors and IV fluids, steroids can be tried.[41]

In patients with acute liver failure due to toxins N-acetyl cysteine which replenishes glutathione and that stabilizes the vasculature can be used. The candidates for liver transplantation following acute liver failure in yellow phosphorus poisoning is assessed using kings college Hospital criteria.

Treatment for Yellow phosphorus poisoning includes gastric lavage and only supportive measures as there is no specific antidotes for yellow phosphorus poisoning TPE is used as bridge for ALF patients to liver transplantation. [14]Therapeutic plasma exchange in the setting of acute liver failure removes a toxin from the plasma and replenish the clotting factors in a study conducted with 43 patients. Therapeutic plasma exchange is highly beneficial in acute liver failure who do not fulfil KCHC where as in KCHC positive group benefits of therapeutic plasma exchange couldn't be well analysed.

In majority of ALF cases there occur severe hepatocyte necrosis and/or apoptosis, which will result in liver failure. ATP depletion results in cell enlargement and breakdown of the cell membrane, which leads to hepatocyte necrosis.[39] The blood-brain barrier (BBB) is altered as a result of inflammatory mediators activating microglia, accumulating neurotransmitter glutamine as a result of ammonia crossing the BBB and subsequent oxidative stress that results in the depletion of adenosine triphosphate (ATP) and guanosine triphosphate – pathogenesis behind the development of cerebral edema and astrocyte swelling and the resulting hepatic encephalopathy in ALF.

PROGNOSIS

The outcome depends on - underlying cause of ALF, age and grade of encephalopathy. Early hepatic encephalopathy is associated with poor prognosis. Prognostication can also be supported laboratory investigations.

PROGNOSTICATION CRITERIA FOR ALF

Table 6: King's College Hospital criteria for Acetaminophen and Non acetaminophen poisoning

King's College Hospital Indicators of a Poor Prognosis in ALF
ACETAMINOPHEN CASES
Arterial pH <7.25 more than 24 hr after drug ingestion*
All of the following:
Prothrombin time >100 sec or INR >6.5
Serum creatinine level >3.4 mg/dL (300 μmol/L) or anuria
Grade 3-4 encephalopathy
NONACETAMINOPHEN CASES
Prothrombin time >100 sec or INR >6.7
Any 3 of the following:
Unfavorable etiology (seronegative hepatitis or drug reaction)
Age <10 or >40 yr
Acute or subacute category (duration of jaundice >7 days)
Serum bilirubin level >17.5 mg/dL (300 μmol/L)
Prothrombin time >50 sec or INR >3.5
*Subsequent modification: arterial pH <7.25 or serum lactate >3.0 mmol/L after adequate fluid resuscitation.

Acute Liver Failure Study Group Index

Three classes of variables: Clinical (coma grade), laboratory (INR, serum bilirubin, serum phosphate), and a marker of apoptosis (M30).[32] MELD Score uses three parameters - S.bilirubin, INR, serum creatinine. It assess the mortality in patients with ALF and also helps to determine organ allocation by the United Network of Organ Sharing (UNOS)[42]

Table 7: MELD Score for ALF to determine the need for LT

Model for End-Stage Liver Disease (MELD) Score

MELD = 3.78 x $\log_e$ serum bilirubin (mg/dL) +
11.20 x $\log_e$ INR +
9.57 x $\log_e$ serum creatinine (mg/dL) +
6.43 (constant for liver disease etiology)

NOTES:

- If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0
- Any value less than one is given a value of 1 (i.e. if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)

Candidates selected for LT are based on the risk benefit ratio and whether a suitable donor is available for the patient. Organ donor allocation systems usually give priority for ALF patients which facilitate transplant in 48-72 hours.[32] Seronegative hepatitis or ALF without a definable cause was associated with a higher risk of primary graft nonfunction or early graft dysfunction.[28] Quirós-Tejeira et al. have studied that 39 children who recovered from ALF, from different causes without LT was found to have hypophosphatemia as the liver recovered from the insults of ALF. Also the values normalised after complete recovery of liver functions. Also 29 children who were followed up during the post transplant period after LT were also found to have normal phosphate levels after LT.

Baquerizo et al., in the study with 112 patients with ALF described the importance of phosphate administration in patients with hypophosphatemia in ALF.[7] It was postulated that low phosphate was associated with inadequate replenishment of ATP required for the hepatocyte regeneration and good outcomes post replenishment of phosphorous. It was also proved in the study by Schmidt and Dalhoff , showed that

low phosphorous was associated with rapid movement of phosphorous in liver resulting in ATP synthesis and hence phosphorous supplementation was associated with good outcome after surgery.[37]

Hypophosphatemia could be caused by a variety of factors, including decreased absorption (such as steatorrhea or the consumption of aluminium - or magnesium-containing antacids), increased excretion (such as hyperparathyroidism and vitamin D deficiency or resistance) and, perhaps most importantly, internal redistribution (e.g., refeeding syndrome, hyperventilation or cellular regeneration).[7]This had been indirectly demonstrated in animal studies, where transplanted livers in rats were found to exhibit large decreases in ATP and adenosine biphosphate (ADP) following surgery, with a nadir after 72 hours. In rat models rats that underwent partial hepatectomy and ischemic liver damage showed similar outcomes with respect to phosphorous values.

In the context of Fulminant liver failure, hypophosphatemia was one of the most common finding. In patients who underwent OLT, those who recovered from acute liver failure had lower serum phosphorus levels. Hypophosphatemia in hepatic recovery was due to brisk hepatocyte regeneration and intracellular phosphorus transported to replenish high-energy intermediates. Therefore, phosphorus level in patients with acute liver failure should be carefully monitored and aggressively replete. A blood phosphorus level of less than 2.5 mg/dL was associated with poor prognosis in ALF patients.

In severe liver injuries depletion of hepatocyte reserved to effect regeneration occurs, which prevented them from consuming phosphorus needed to create ATP and its high-energy intermediates. Another postulate was that the severe hepatocyte

necrosis might created a cytokine milieu that inhibited or delayed regenerative processes, possibly by altering hepatic microcirculation.

Trials of liver support devices had been used in patients as a bridge before LT in patients awaiting LT. Molecular Adsorbents Recyling System (MARS)- albumin dialysis circuit was commonly used. A randomized controlled trial, with 110 patients in a 3-year period. The survival rate was high in MARS group than in control group.[32].Another randomized controlled trail of TPE in ALF in 182 patients 11-year period. The survival rate was higher in TPE group than in controls.[9]

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN: Observational Study

STUDY SETTING: The study was conducted in the Department of General Medicine, Government Rajaji Hospital & Madurai Medical College, Madurai.

STUDY DURATION: The study was conducted for a period of 6 months.

STUDY POPULATION

The study was conducted on 50 patients with rat killer paste poisoning admitted in Toxicology and Medical wards in GRH, Madurai.

METHODS

- Patients admitted with consumption of toxic dose of Rat killer paste (yellow phosphorus) are segregated.
- Patients are grouped as per age, sex
- Routine blood investigations done
- Serum phosphorus level at D1(Day 1), D3(Day 3) and D7(Day 7) of poisoning are done
- Serial monitoring of Liver enzymes and PT- INR

INCLUSION CRITERIA

- Age : 15 – 40 years
- Both Males and Females
- Non-Alcoholics

- BMI-16-21
- VCTC, HbsAg and Anti HCV Negative
- Without prior suicidal attempts with Hepatotoxic agents
- Without comorbidities

EXCLUSION CRITERIA

- Age < 15 years > 40 years
- Non-Alcoholics
- VCTC, HbsAg and Anti HCV – Positive
- BMI <16 and >21
- Patients in shock, renal failure
- Patients with prior H/O jaundice

ETHICAL CONSIDERATION

Before the initiation of the study Institutional Ethical Committee approval of Madurai Medical College was obtained. Written informed consent was obtained on the day of admission explaining the enrolment in the study from the patients. The first degree relatives were also explained regarding the study and its use in research. The participants/ attenders were explained that the data collected in this study will be used only for research purposes. The participants of the study were told regarding the confidentiality of the study and they can be withdraw from the study at any time if there are not willing to participate in the study course.

STATISTICAL ANALYSIS

The collected data is analysed by using Statistical Package for Social Sciences (SPSS) package. The class intervals are fixed by using the formula ,

$I \geq (L - S) / n$

where I is the class interval, L is the greatest observed value, S is the smallest observed value, n is the length of the class interval.

Generally, $5 \leq n \leq 15$. Using Sturges' rule as a guide: $n = 1 + 3.322 \log_{10} (N)$, where

N = Total number of observations.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

The representative samples selected from the poisoning cases are analysed by taking into account their gender, age, Serum Bilirubin level, Phosphorous level, INR level, ALT and AST.

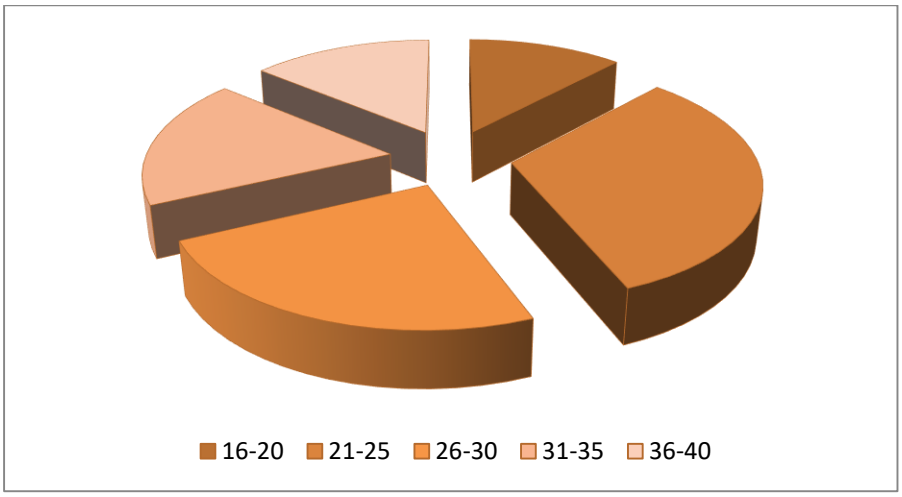
Out of the sample patients 23(46%) survived and 27(54%) patients died. The number of patients died is more than the number of patients survived. The probability of survival is 0.46.

Table : 8 Gender of the Patients

Sl. No.	Gender	No. of Patients	Total
1	Male	25	50
2	Female	25	50

Table : 8 depicts the gender wise classification of the patients. Fifty percentage are males and fifty percentage of the sample respondents are females. The proportion of males and females is demonstrated in the following diagram. The population in general also consists of equal number of males and females.

Figure : 6 Gender of the patients



Age Distribution of the Patients

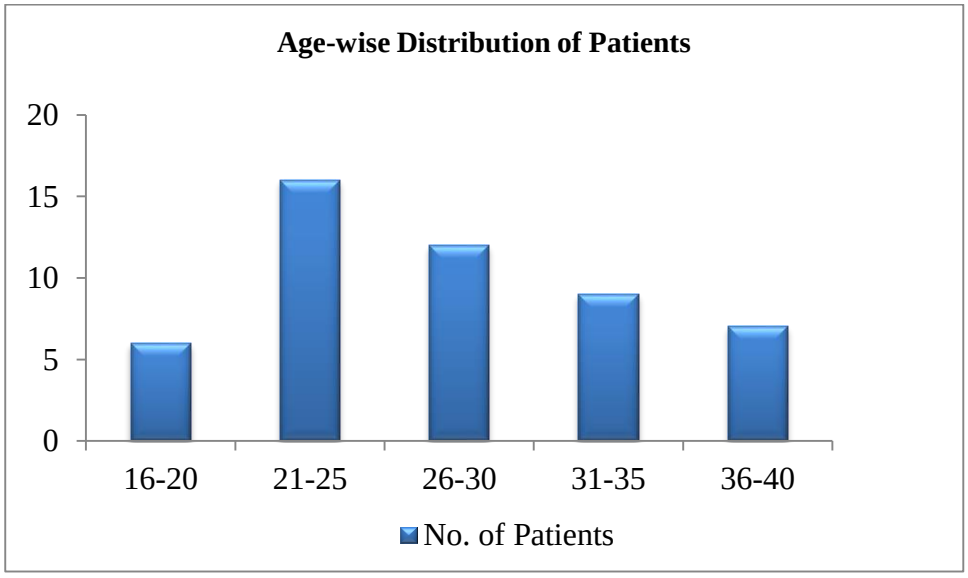
The patients are classified on the basis of their age and presented below.

Table : 9 Age Distribution of the Patients

Sl. No	Age	No. of Patients	Male	Female	Percentage
1	16-20	6	4	2	12
2	21-25	16	7	9	32
3	26-30	12	5	7	24
4	31-35	9	5	4	18
5	36-40	7	4	3	14

Table : 9 explains the age of the sample patients. The age varies from 17- 40. It is conveniently group under five different classes. This table confirms that the poison consumed cases are youth and middle agers. Sixteen cases (32%) are in the age group 21-25. The age group 16-20 has minimum number of cases(12%).The table also shows that as far as poisoning cases are concerned there is only marginal difference between the males and females in the different age groups. Another significant thing is all the patients are in the age group 16-40.

Figure : 7 Age wise Distribution of the Patients



Bilirubin which is conjugated in the liver, and excreted in bile, is grossly elevated in cases of hemolysis, hepatitis and in cholestasis. In Toxic hepatitis, the bilirubin is elevated >1000 and it also significantly influences the prognosis of the patients. From the lab investigations done the different levels bilirubin are segregated in groups and analysed.

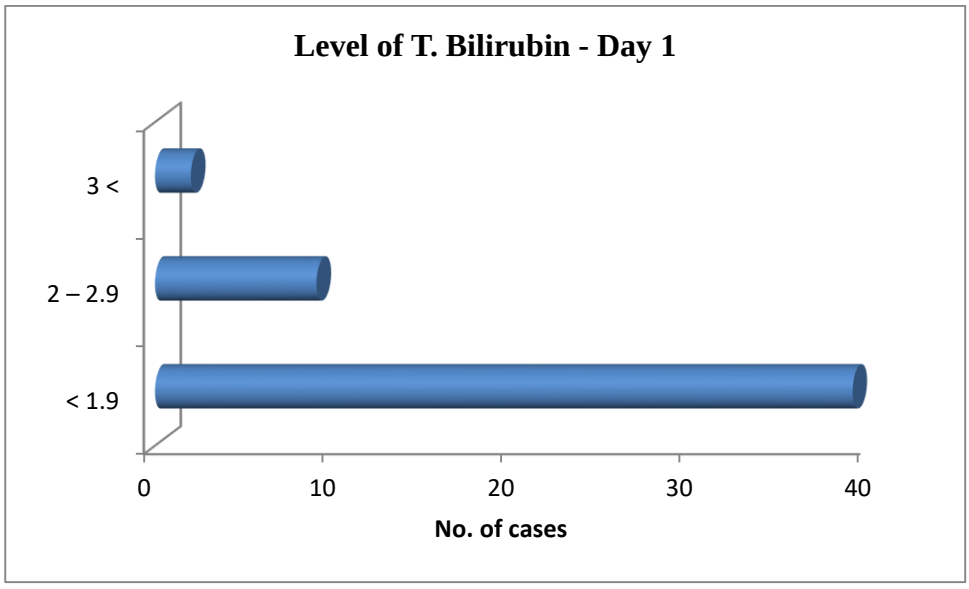
The total bilirubin level of the sample cases are analysed by comparing its level on the first day (D1), third day (D3) and seventh day (D7)

Table : 10 Total Bilirubin Level of the Patients on Day 1

Level of T. Bilirubin	No. of Patients	Percentage
< 1.9	39	78
2 – 2.9	9	18
3 >	2	4
Total	**50**	**100**

Table : 10 explains the total bilirubin level among the poisoning cases on the first day. It ranges from 1-3.5.The total bilirubin level of most of the poisoning cases (78%) are close to the normal. Only 11 patients have little higher than normal level.

Figure : 8 Total Bilirubin Level of the Patients on Day 1



The bilirubin level of the patients on the third day is given below to know the changes in the bilirubin level.

Table : 11 Total Bilirubin Level of the Patients on Day 3

Level of T. Bilirubin	No. of Patients	Percentage
< 6	29	58
6.1 – 8	12	24
8.1 – 10	8	16
10.1 >	1	2
Total	**50**	**100**

Table : 11 gives the total bilirubin level on the third day which ranges between 4.1 -11.1. All the patients crossed 4 and 21 exceeded 6. This shows that the bilirubin level is increasing everyday even after treatment.

Figure : 9 Total Bilirubin Level of the Patients on Day - 3

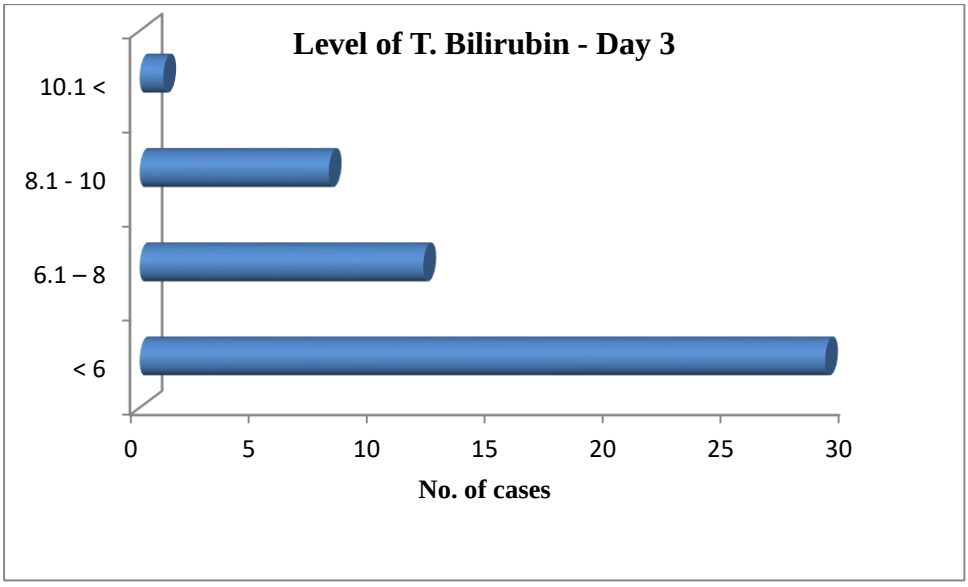


Table : 12 Total Bilirubin Levels of the Patients on Day 7

Level of T. Bilirubin	No. of Patients	Percentage
< 7.6	33	66
7.7 – 11.6	14	28
11.7- 15.6	2	4
15.7 >	1	2
Total	**50**	**100**

The pictorial representation of the total bilirubin level on the seventh day of treatment is given in the figure below.

Figure : 10 Total Bilirubin Level of the Patients on Day 7

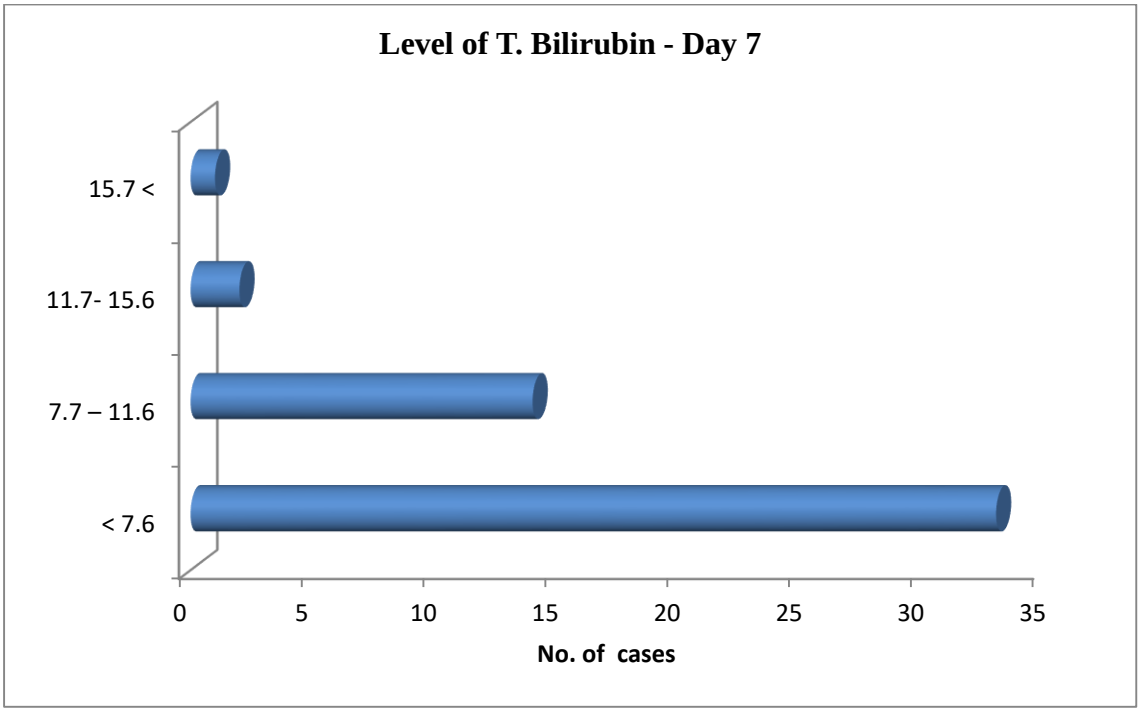


Table : 12 exhibits the total bilirubin level of the poisoning cases on the 7th day. It ranges between 3.7 – 18.9.The bilirubin level of 66% cases are less than 7.6.The bilirubin level of the survivors are 3.7-7.5 and for the dead it ranges from 5-18.9. It also shows that there is an association between bilirubin level and the number of deaths. If the bilirubin level increases the mortality also increases. On the other hand as it decreases the death decreases.

Figure : 11 Total Bilirubin Level on D1, D3 and D7

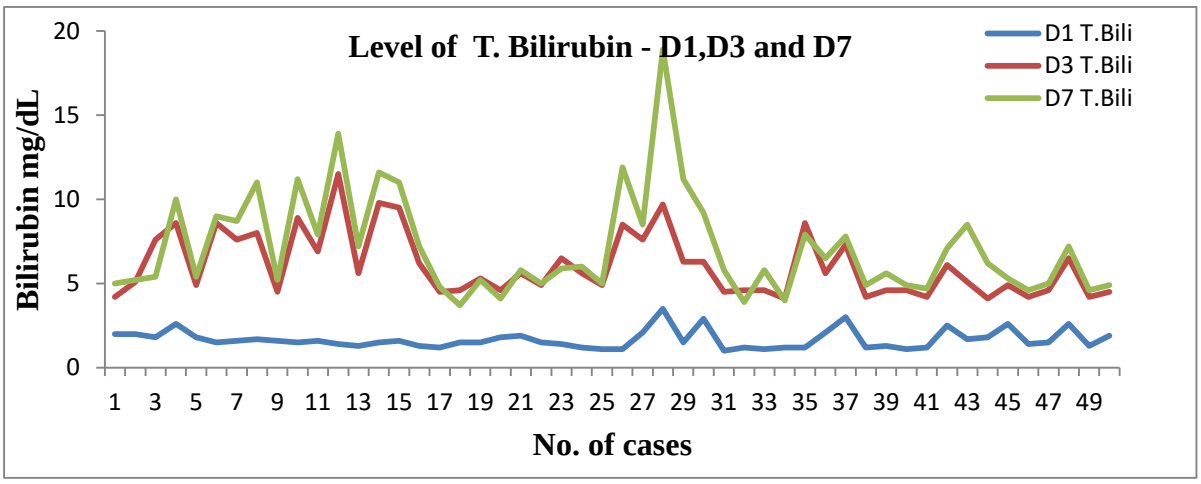


Figure : 12 Total Bilirubin Level of Discharge cases

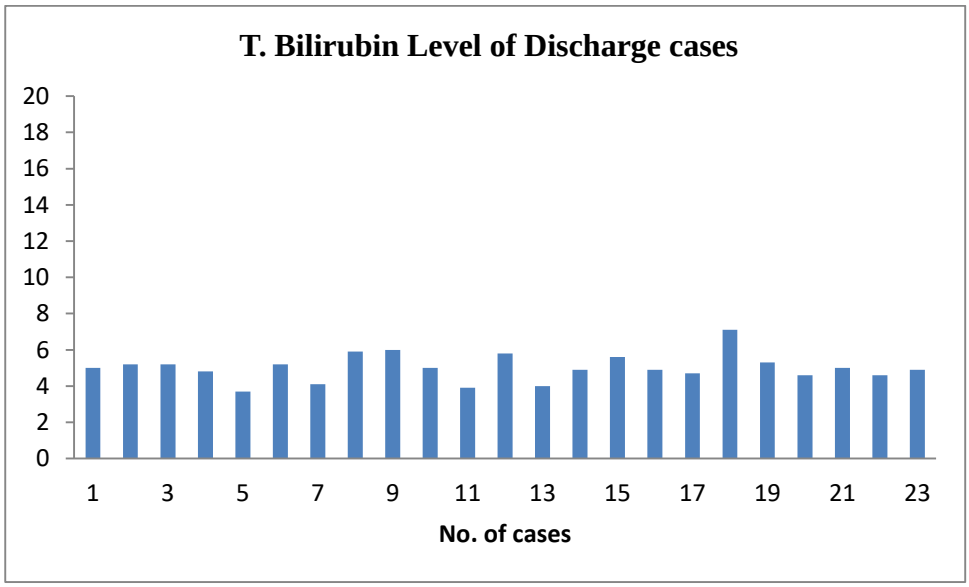
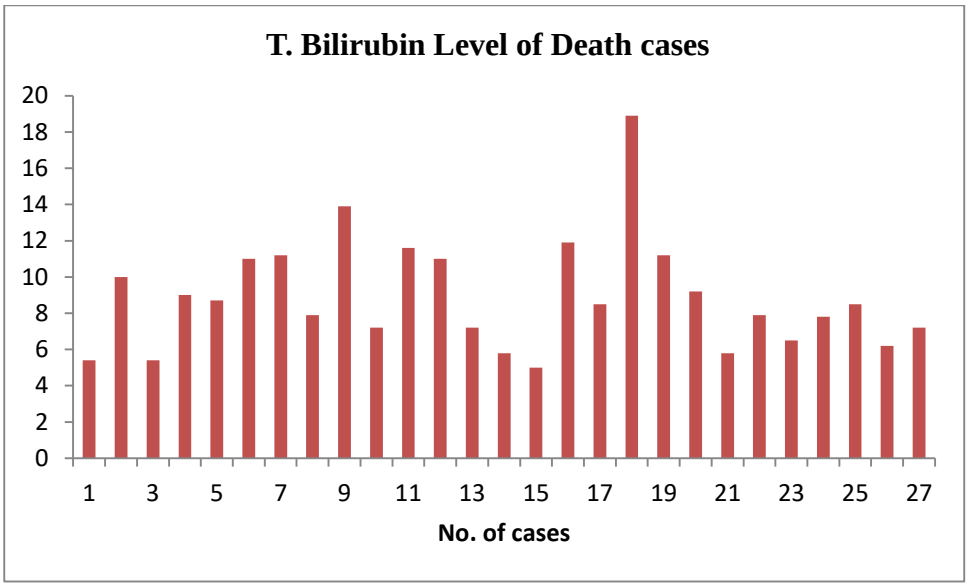


Figure : 13 Total Bilirubin Level of Death cases



Serum phosphorus is an important element in the body. Normal values are between 3.0-4.5 mg/ dL. The level of phosphorous falls as the hepatocytes regenerate following acute liver injury and hence is measured during the course of hospital stay and analysed.

The changes in the phosphorus level of the poisoning cases during treatment are analysed by measuring the level of phosphorous on day 1,3 and 7.

Table : 13 Phosphorus Level of Patients on Day 1

Level of PO4	No. of Patients	Percentage
2.8 – 3.2	16	32
3.3 - 3.7	8	16
3.8- 4.2	22	44
4.3-4.7	4	8
Total	50	100

Table :13 explains the phosphorus level of the poisoning cases on day 1. Between 2.8 and 3.2 there are 16 patients and in between 3.3 &3.7 there are only 8 cases. 44% of patients are in the range of 3.8-4.2 and only few are in the group 4.3-4.7.

Figure :14 Phosphorus Level of Patients on Day 1

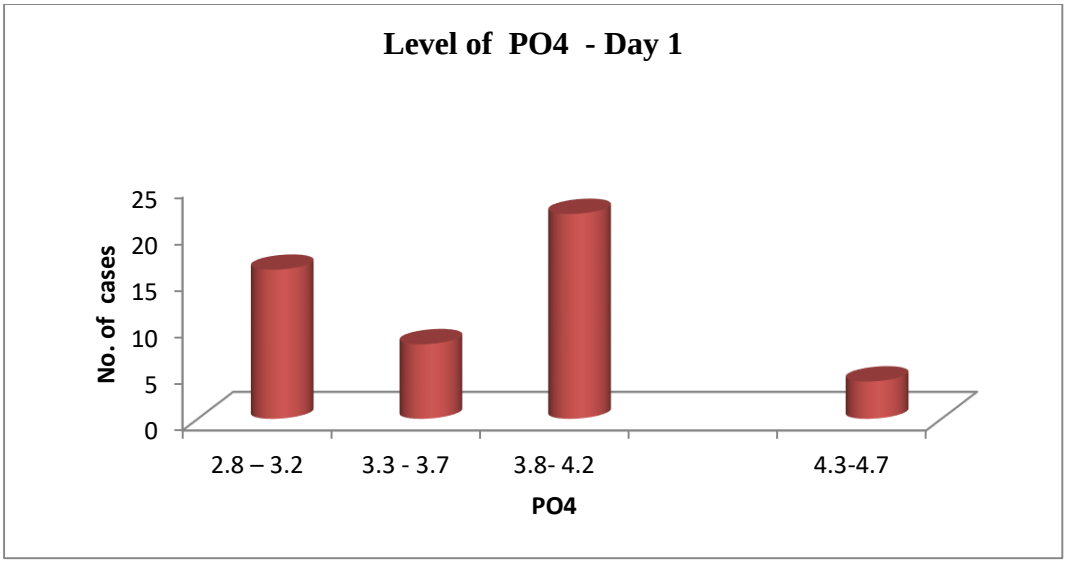


Table : 14 Phosphorus Level of Patients on Day 3

Level of PO4	No. of Patients	Percentage
1 - 3	12	24
3.1 – 5.1	18	36
5.2 – 7.2	11	22
7.3-9.3	9	18
Total	50	100

Table : 14 gives the changes in the phosphorus levels among the sample patients on the third day.58%patients are in between 3.1 & 7.2. 9 patients are in the range 7.3 & 9.3.There is a significant change in the phosphorus level on the third day as compared to the first day. 25 cases crossed the normal level and 18% cut across 7.3.

Figure : 15 Phosphorus Level of Patients on Day 3

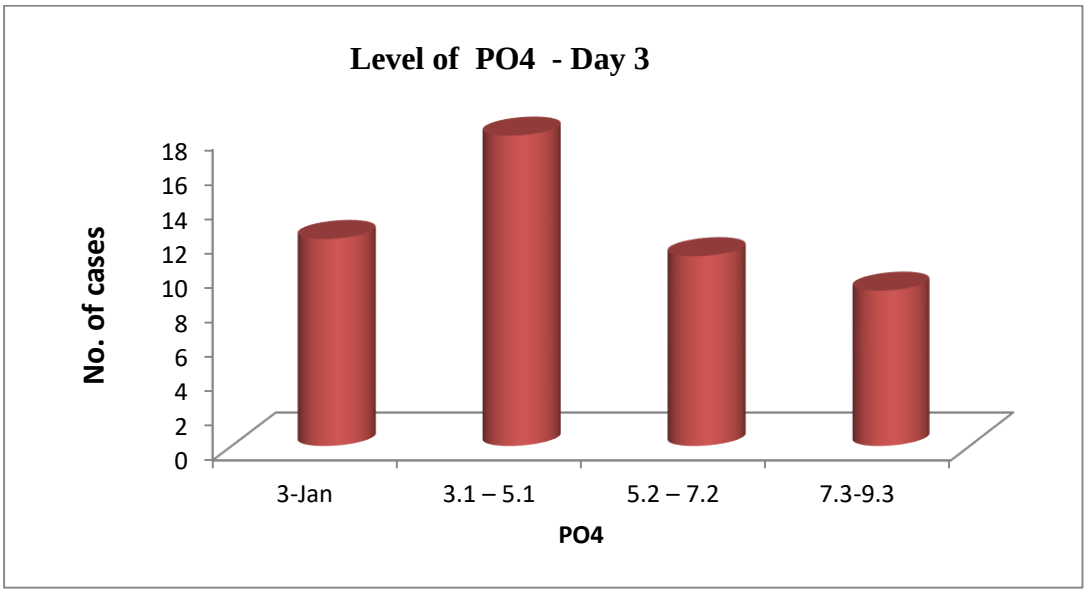


Table : 15 Phosphorus Level of Patients on Day 7

Level of PO4	No. of Patients	Percentage
1.8 – 3.5	18	36
3.6 – 5.3	10	20
5.4 - 7.1	17	34
7.2- 8.9	5	10
Total	50	100

Table :15 shows the phosphorous level of the sample cases on the seventh day. There is a steady increase in level of phosphorus.18 patients are in the group 1.8-3.5 and 17 patients in the group 5.2-7.1.The phosphorus level of 50% cases are more than 5.4.

Figure : 16 Phosphorus Level of Patients on Day 7

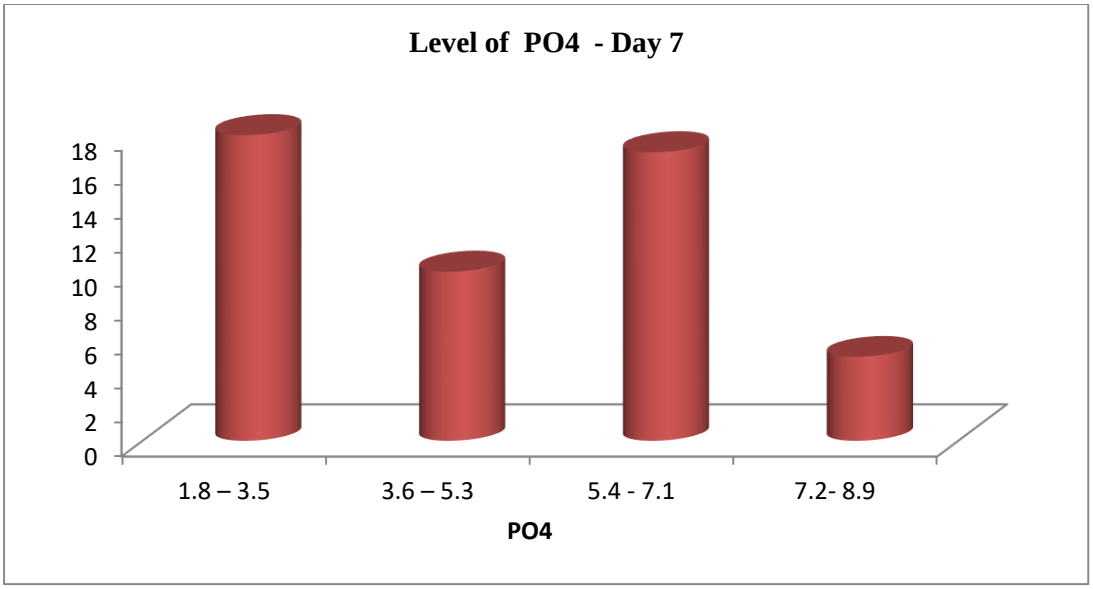


Figure : 17 Phosphorus Level of Patients on D1, D3 and D7

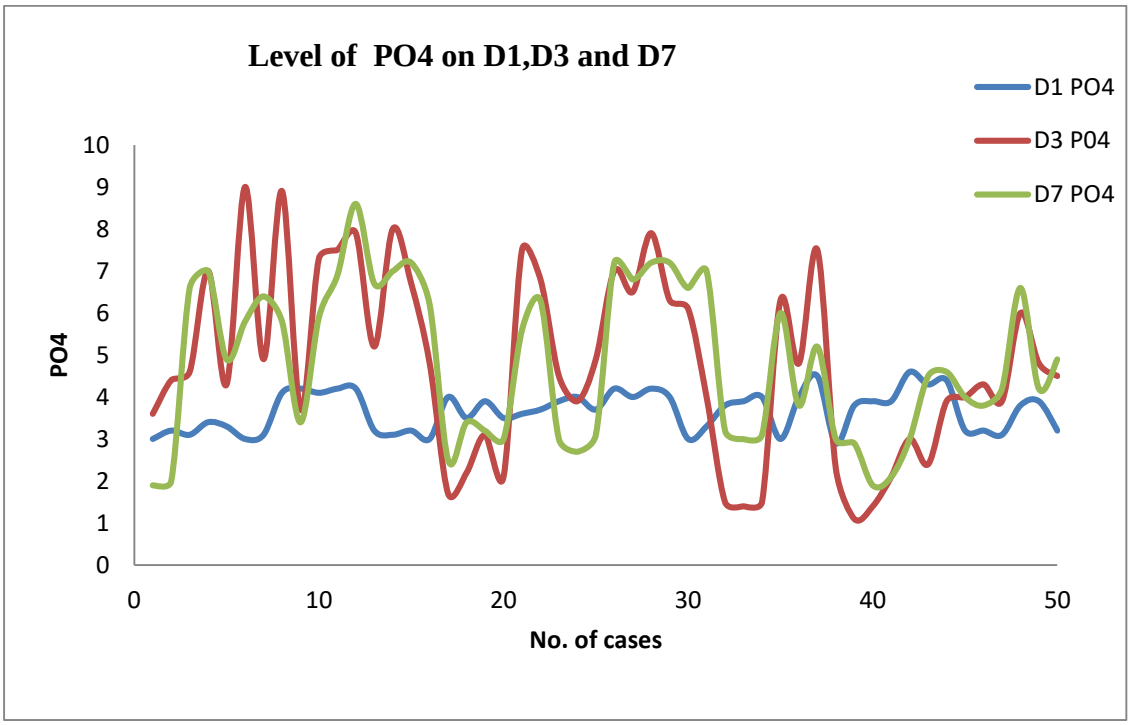


Figure : 18 Phosphorus Level of Discharge Patients

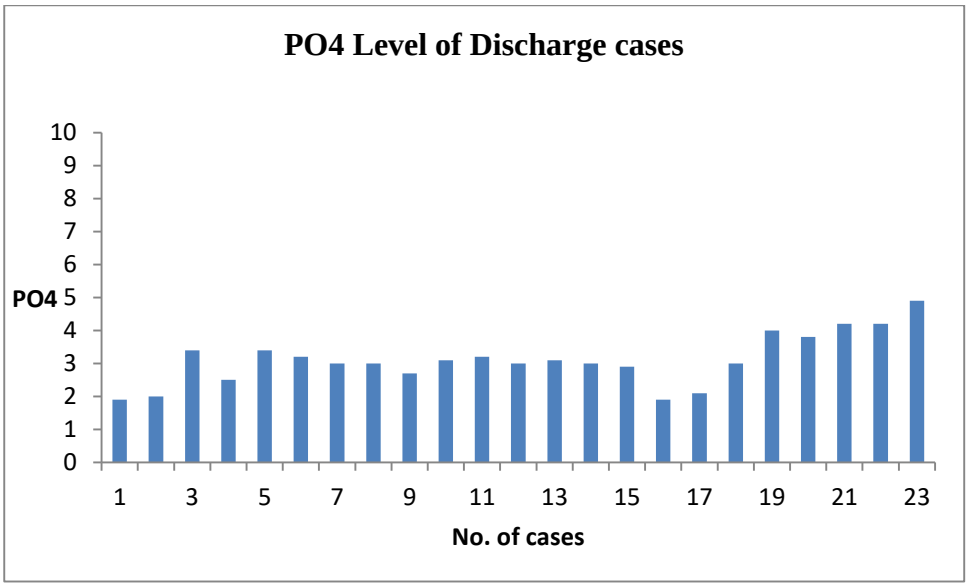
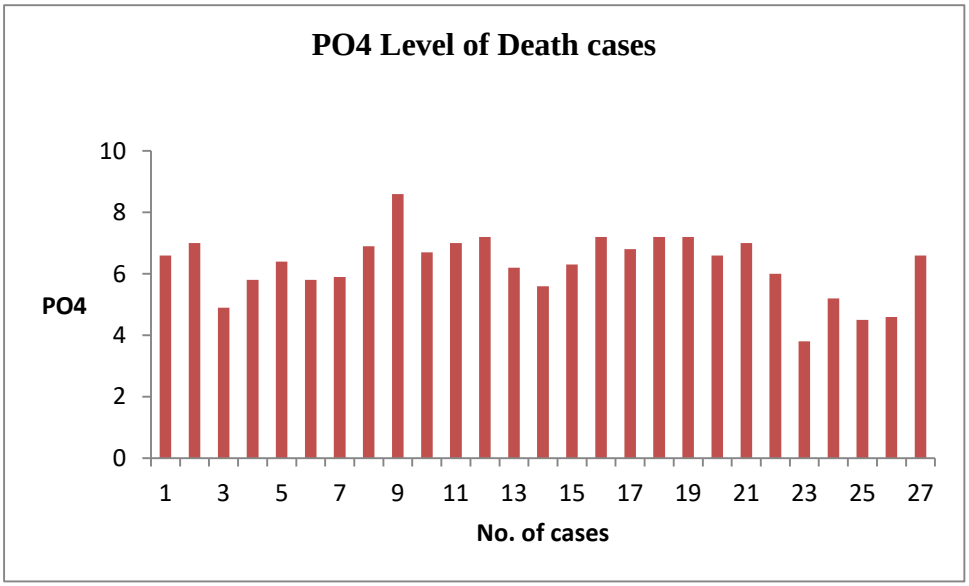


Figure : 19 Phosphorus Level of Dead Patients



INR gives the coagulability of the patients plasma. It represents the effectiveness coagulation cascade. In liver failure as the synthetic machinery is malfunctional, the patient's INR rises resulting in bleeding which can even progress to DIC due to consumption of coagulation factors.

The changes in the INR level of the patients who are representative samples are analysed by measuring the level of INR during the first day, third day and seventh day.

Table : 16 INR Level of Patients on Day 1

INR range	No. of Patients	Percentage
1 – 1.9	42	84
2 – 2.9	7	14
3 – 3.9	1	2
Total	**50**	**100**

Table :16 gives the various levels of INR of patients in the study. About 84% of the patients have INR below 2. In the entire study only 1 patient have INR between 3-3.9 and 7 patients in the INR range of 2 & 2.9.

Figure : 20 INR Level of Patients on Day 1

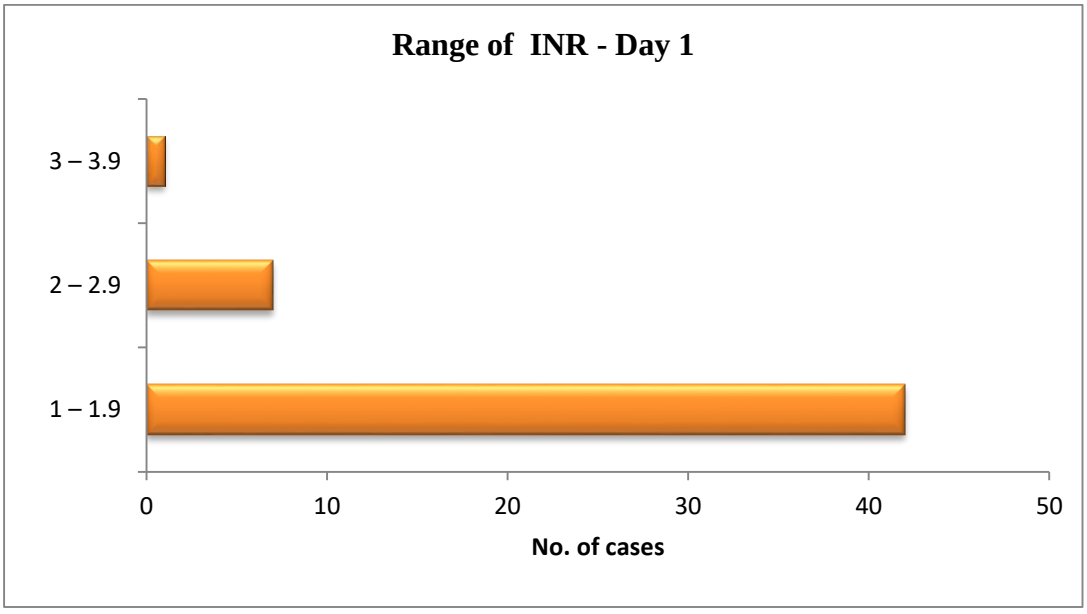


Table : 17 INR Level of Patients on Day 3

INR range	No. of Patients	Percentage
≤ 2.4	13	26
2.5 - 4.4	16	32
4.5 - 6.4	15	30
6.5 - 8.4	5	10
8.4 >	1	2
Total	**50**	**100**

The following figure describes the INR level of patients on the third day.

Figure : 21 INR Level of Patients on Day 3

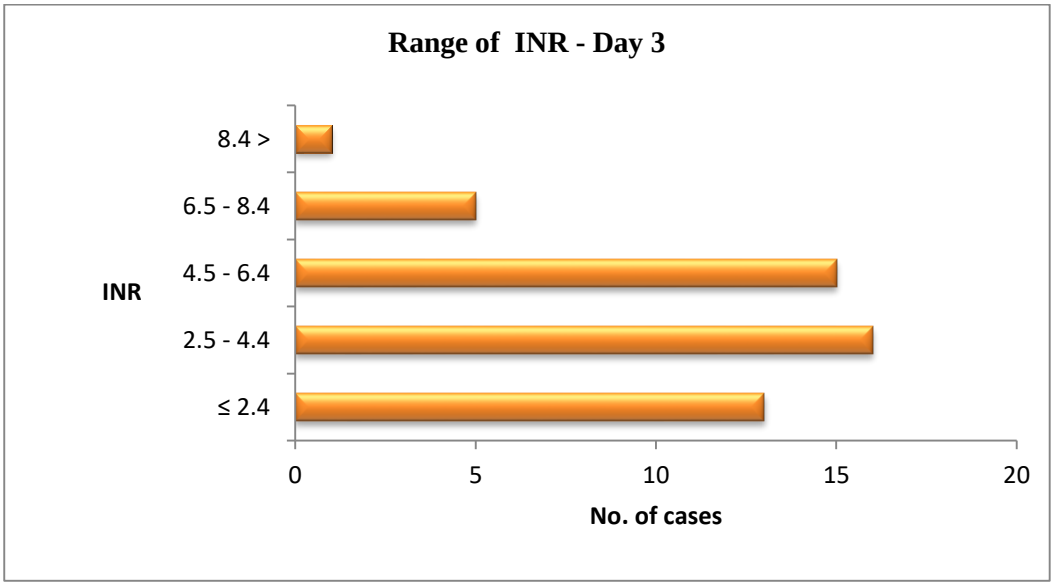


Table : 17 depicts the INR of patients on day 3,the INR of the patients drastically increased in day 3 probably as the result of liver failure. 62% patients have an INR of between 2.5 & 6.4. Five patients have an INR between 6.5-8.4, thirteen patients have INR less than 2.5.Only one patient has the INR value crossed 8.4

Table : 18 INR Level of Patients on Day 7

INR range	No. of Patients	Percentage
< 1.9	23	46
2 – 2.9	5	10
3 – 3.9	12	24
4 – 4.9	8	16
≥ 5	2	4
Total	**50**	**100**

Figure : 22 INR Level of Patients on Day 7

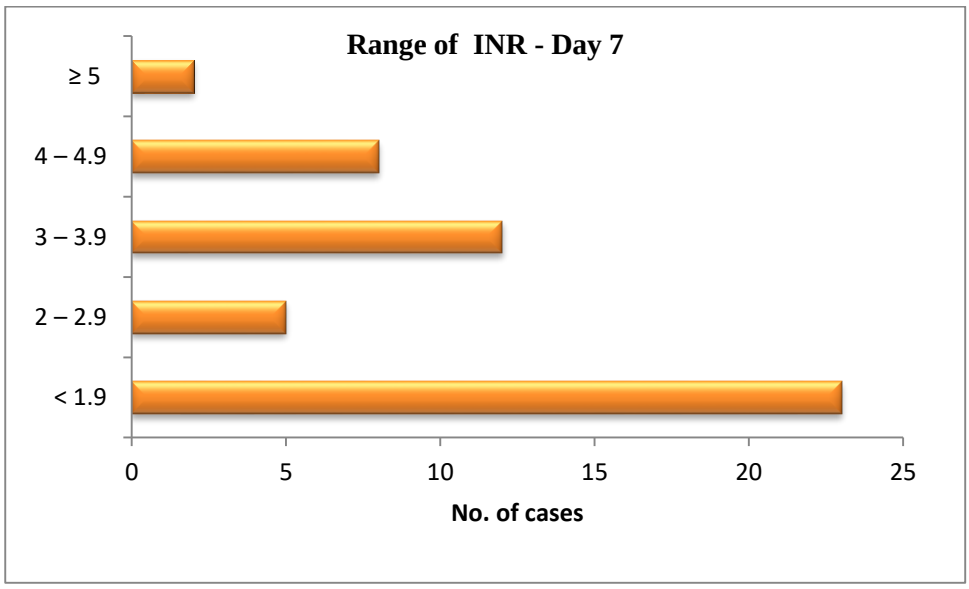


Table : 18 gives the INR level of patients on day 7. About 46 % patients have a fall in INR of less than 1.9 whereas in 20% patients it remains persistently elevated. About 17 patients have an INR in the intermediate range between 3 &4.9.

Figure : 23 INR Level of Patients on D1, D3 and D7

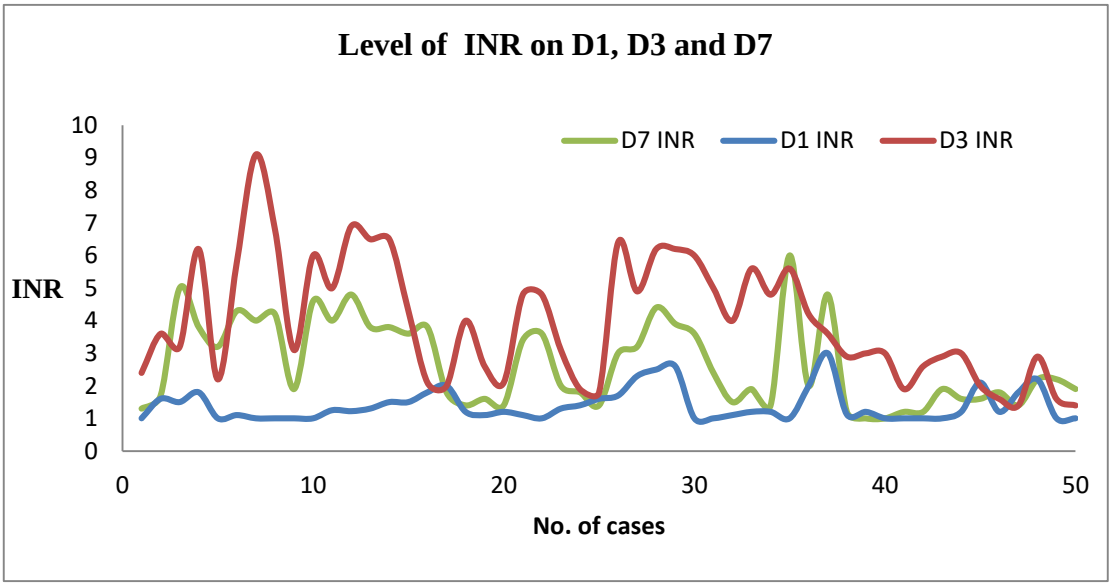


Figure : 24 INR Level of Discharge Patients

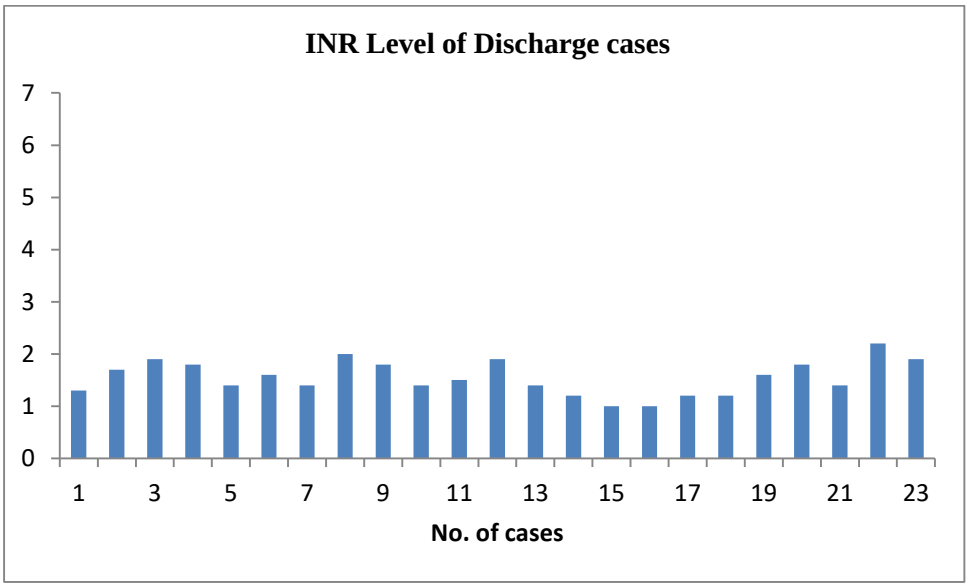
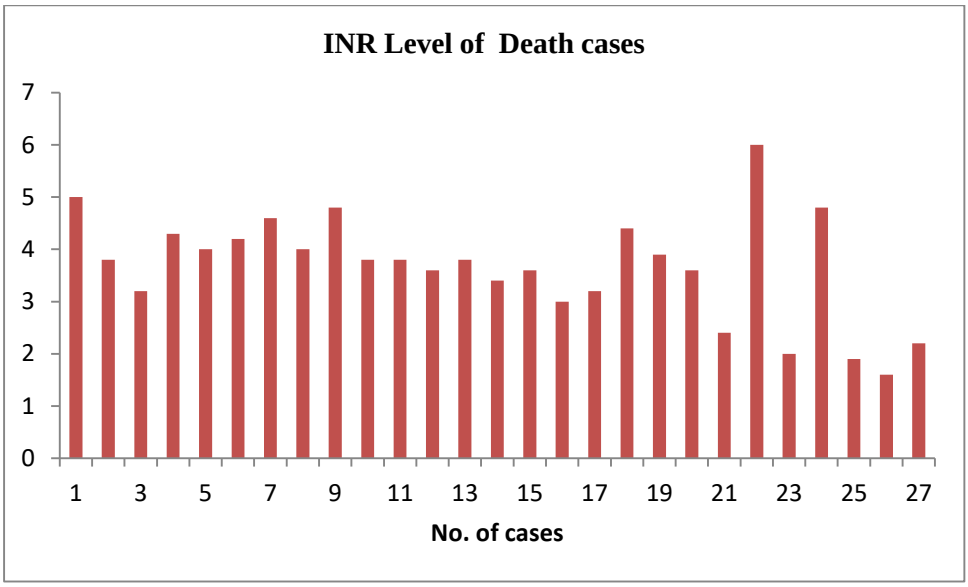


Figure : 25 INR Level of Dead Patients



AST values are collected during hospital stay. From the values collected on the serial days, analysis of the variables are made and finally a conclusion was driven that the level of AST increased gradually in patients who were deceased whereas the values were in a lower plateau range among the survives. Though the values of the enzymes do not a give a exact quantification of liver damage. Significant increase in transaminases are associated with poor prognosis.

Table : 19 AST Level of Patients on Day 1

Level of AST	No. of Patients	Percentage
18 - 232	42	84
233 - 447	6	12
448 - 662	1	2
663 - 877	1	2
Total	**50**	**100**

Table : 19 explains the AST level of the poisoning patients on the first day of treatment. Out of 50 patients the AST level of 42 patients are in between 18 and 232, 6 have upto 447 but not less than 233. Only two are in the range 448 to 877. This proves the fact that the AST level is normal on the first day.

Figure : 26 AST Level of Patients on Day 1

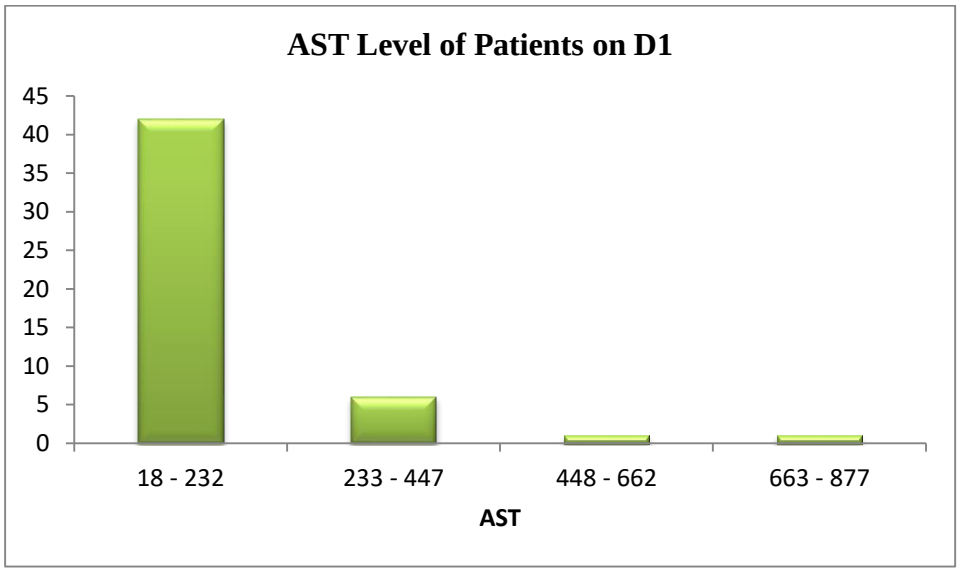


Table : 20 AST Level of Patients on Day 3

Level of AST	No. of Patients	Percentage
562 – 1165	28	56
1166 – 1769	8	16
1770 – 2373	9	18
2374 – 2977	2	4
2978 - 3581	3	6
Total	**50**	**100**

Table : 20 gives the AST level of patients on the third day. There is a sudden increase in the AST level as compared to the first day. Now, on the third day, AST level of 28 patients are between 562 to 1165, 8 are in between 1166 to 1769, 9 are in the group 1770 to 2373, 2 are in the range 2374 to 2977 and 3 patients have 2978 to 3581.

Figure : 27 AST Level of Patients on Day 3

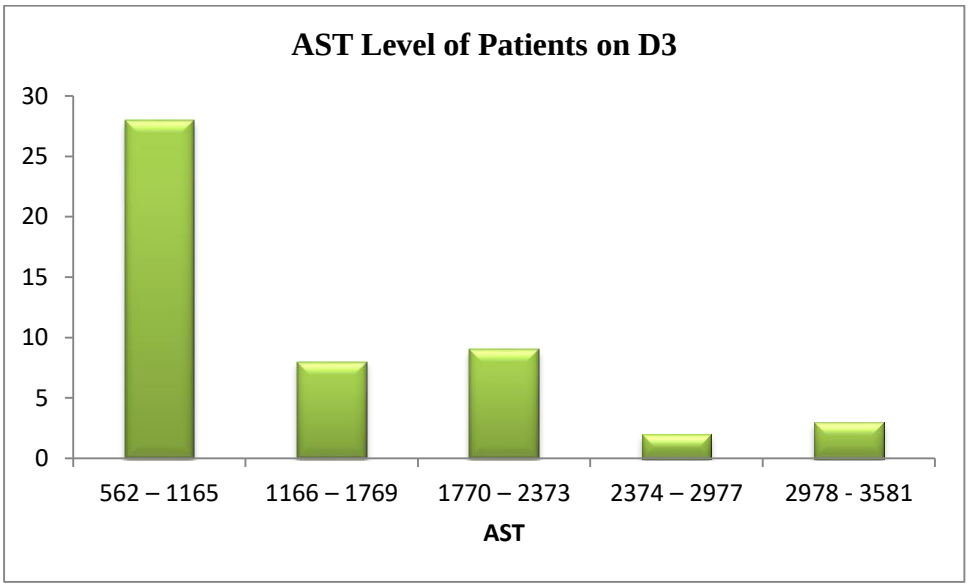


Table : 21 AST Level of Patients on Day 7

Level of AST	No. of Patients	Percentage
213 - 949	23	46
950 - 1686	4	8
1687 - 2423	9	18
2424 - 3160	6	12
3161 - 3897	8	16
Total	50	100

Table : 21 gives the AST level of patients on day 7, it is found that 23 patients have their AST levels more than 1700 on day 7 and 27 patients have them in the range between 213 &1700.8 patients who have values more than 3161 developed several other complications also during their hospital stay and all of them died.

Figure : 28 AST Level of Patients on Day 7

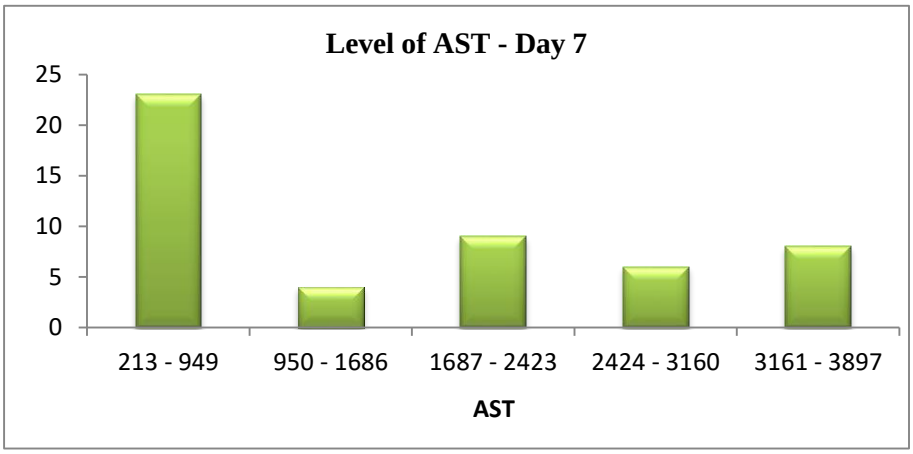


Figure : 29 AST Level of Patients on D1,D3 and D7

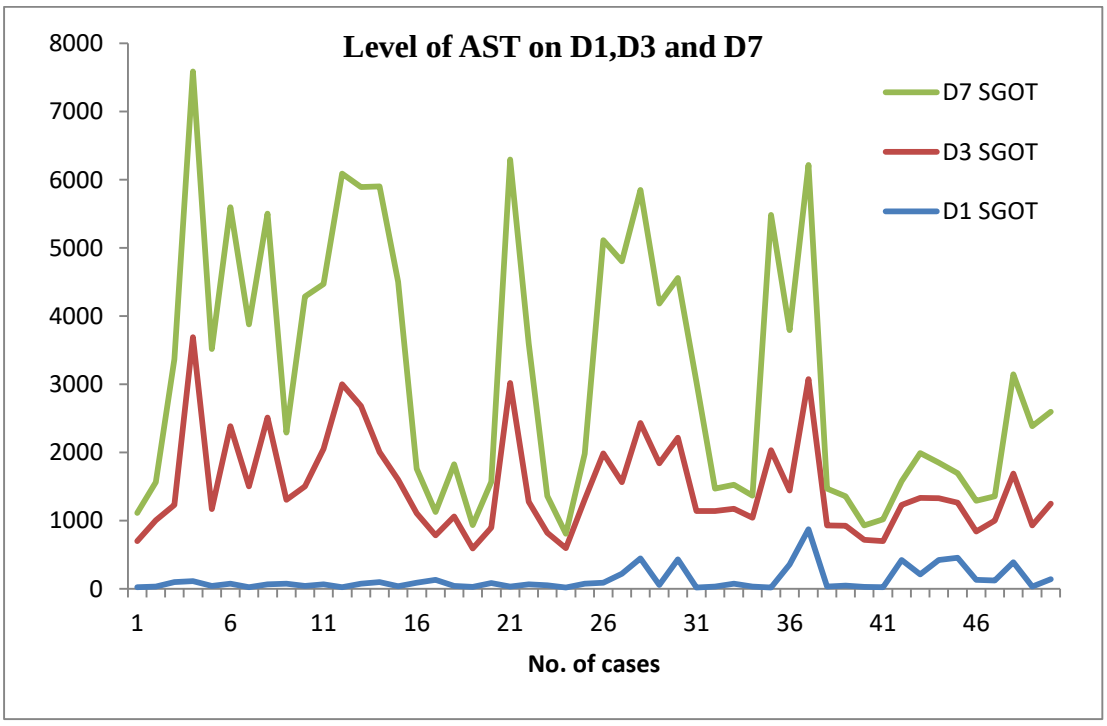


Figure : 30 AST Level of Discharge Patients

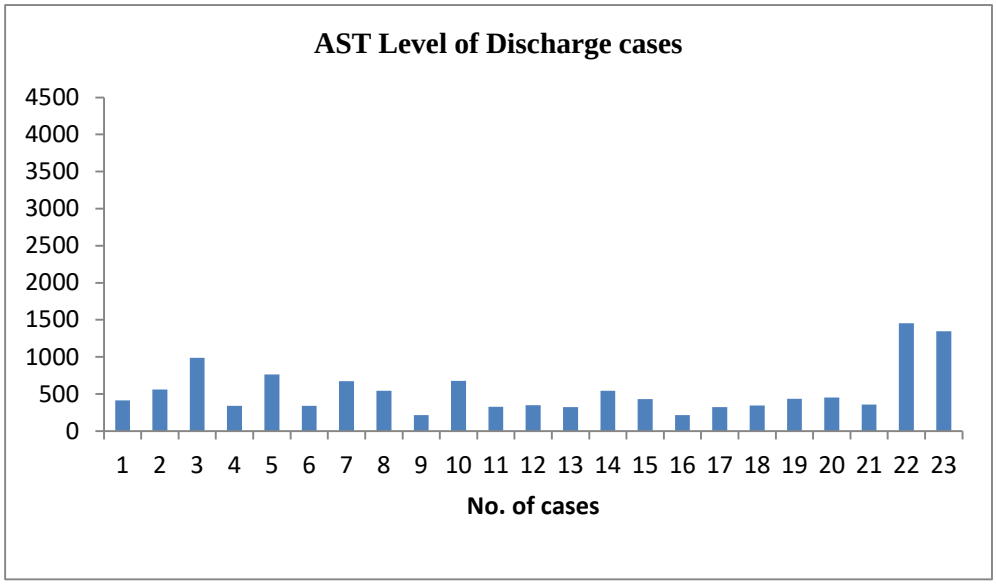
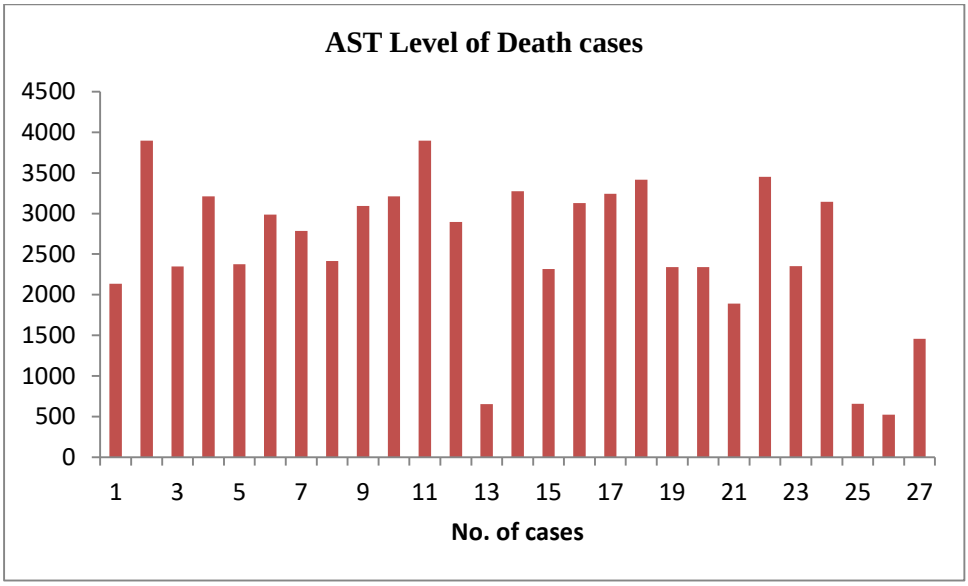


Figure : 30 depicts the AST level of discharge patients and all of them have values less than 1500 during their course in the hospital whereas most of the deceased have values more than 2000 which is depicted in figure : 31

Figure : 31 AST Level of Dead Patients



Alanine Transaminase(ALT)

Among the transaminases ALT is more specific to liver when compared to AST in liver injury as it is predominantly secreted by the liver. The other names are Alanine aminotransferase (ALT), Serum Glutamic-Pyruvic Transaminase (SGPT) and GPT. ALT/AST is of greater use in the diagnosis of alcohol related liver injuries. In the study hence both ALT and ALT are given more importance during data collection and are depicted as pictograms below.

Table : 22 ALT Level of Patients on Day 1

Level of ALT	No. of Patients	Percentage
28 - 203	37	74
204 - 379	4	8
380 - 555	6	12
556 - 731	2	4
732 - 907	1	2
Total	50	100

Table : 22 exhibits the ALT level of the poisoning cases of the first day. The ALT level of 37 patients are ranging from 28 and 203, 4 have more than203 but less than 379, 6 are in the group 380 to 555, 2 in the class 556 to 731 and only one is in between 732 and 907. This shows that the ALT level is normal or next to normal on the first day.

Figure : 32 ALT Level of Patients on Day 1

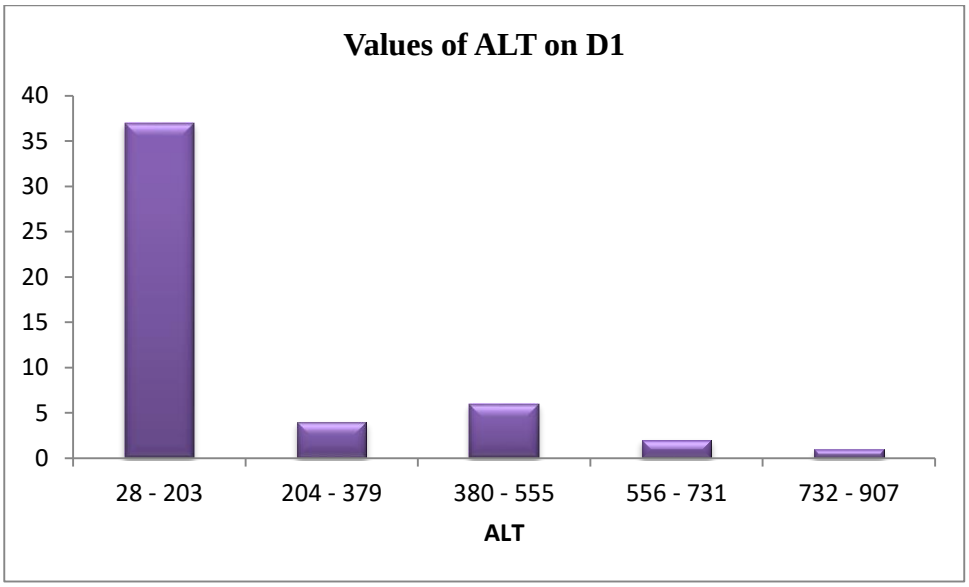


Table : 23 AST Level of Patients on Day 3

Level of ALT	No. of Patients	Percentage
454 - 1410	37	74
1411 - 2367	7	14
2368 - 3324	3	6
3325 - 4281	2	4
4282 - 5238	1	2
Total	50	100

Table : 23 gives ALT level of patients on the third day. The ALT level of 37 patients are 454 to 1410, 7 have in between 1411 and 2367, 3 are in the range 2368 to 3324, 2 in the class 3325 to 4281 and one crossed 4282. This also noted a significant fact that there is a sudden change in the ALT level in two days.

Figure : 33 ALT Level of Patients on Day 3

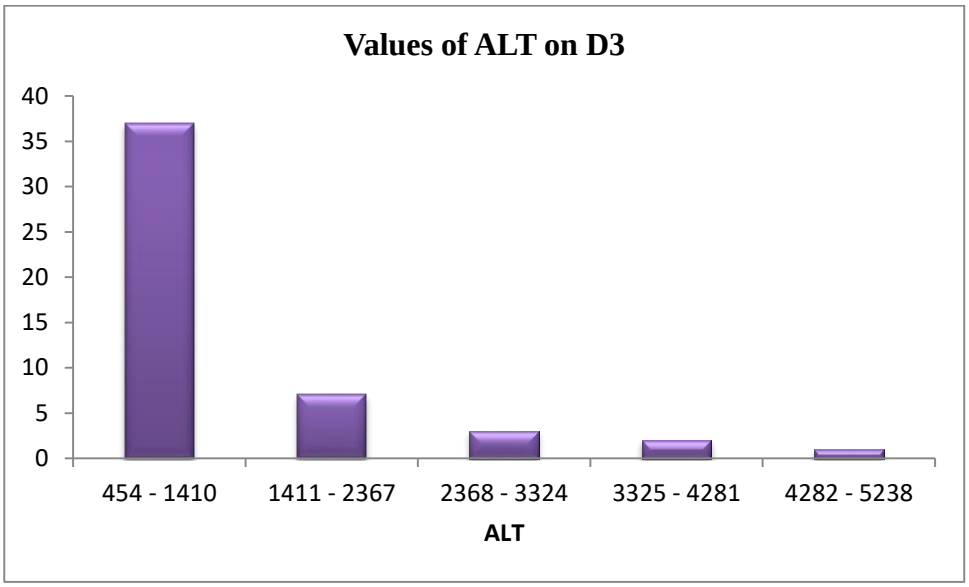


Table : 24 ALT values of Patients on Day 7

Level of ALT	No. of Patients	Percentage
215 – 1306	26	52
1307 - 2398	11	22
2399 - 3490	8	16
3491 - 4582	4	8
4583 - 5674	1	2
Total	**50**	**100**

Table : 24 gives ALT values of patients on their 7th day of hospital stay. Around 50 % patients have their values less than 1000 and others who have values more than 1000, who are associated with bad outcomes. Hence these values strongly correlates with the clinical outcome and the prognosis of the hospitalised patients.

Figure : 34 ALT Level of Patients on Day 7

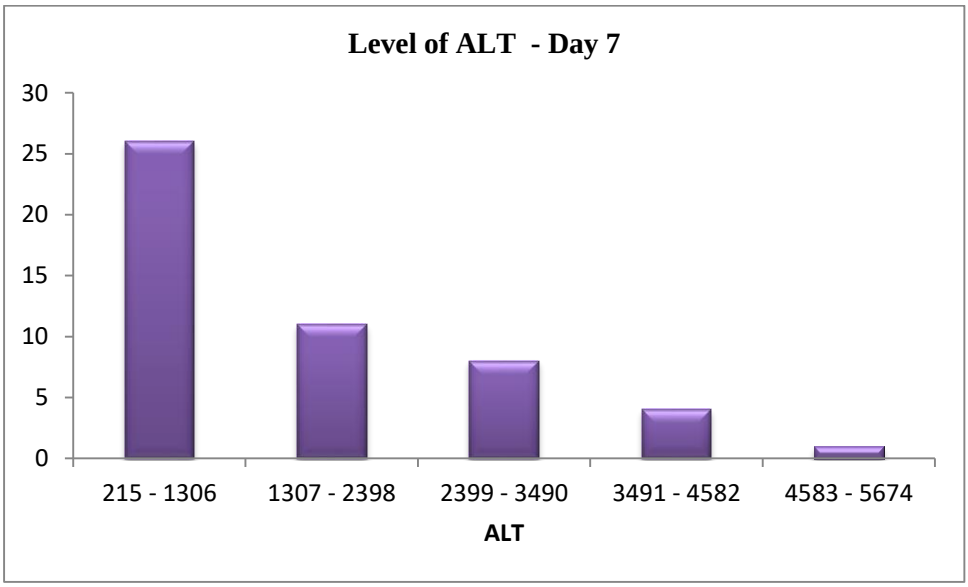


Figure : 35 ALT values of Patients on D1, D3 and D7

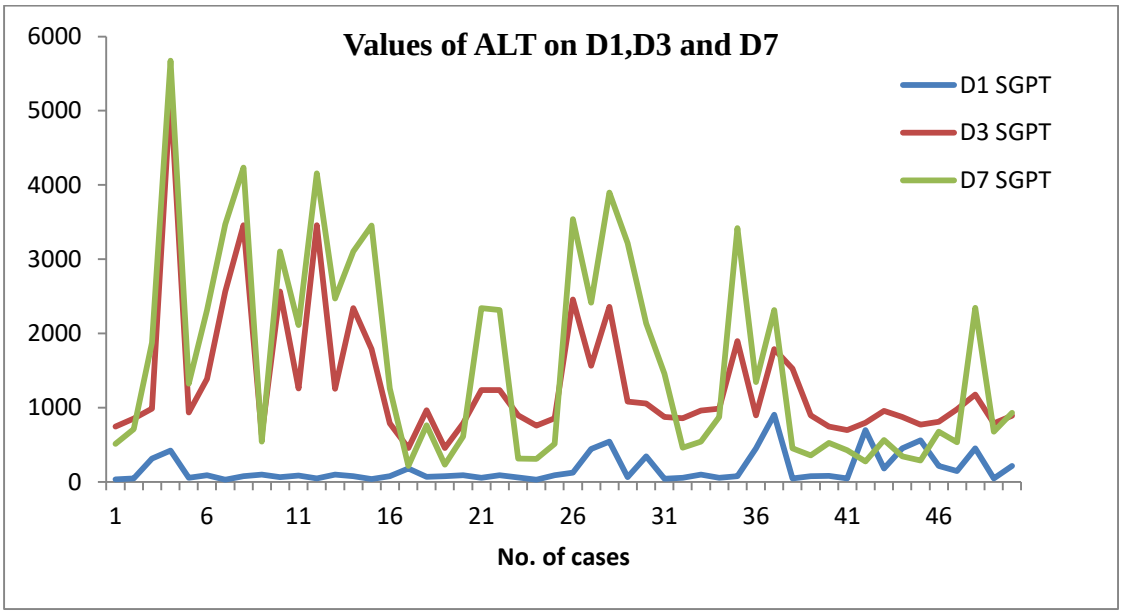


Figure : 36 ALT values of Discharge Patients

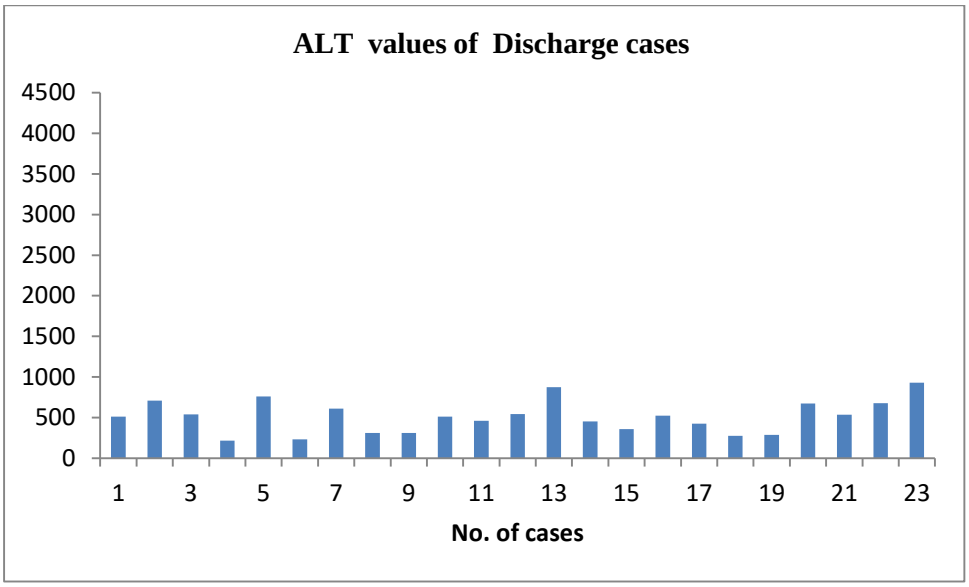
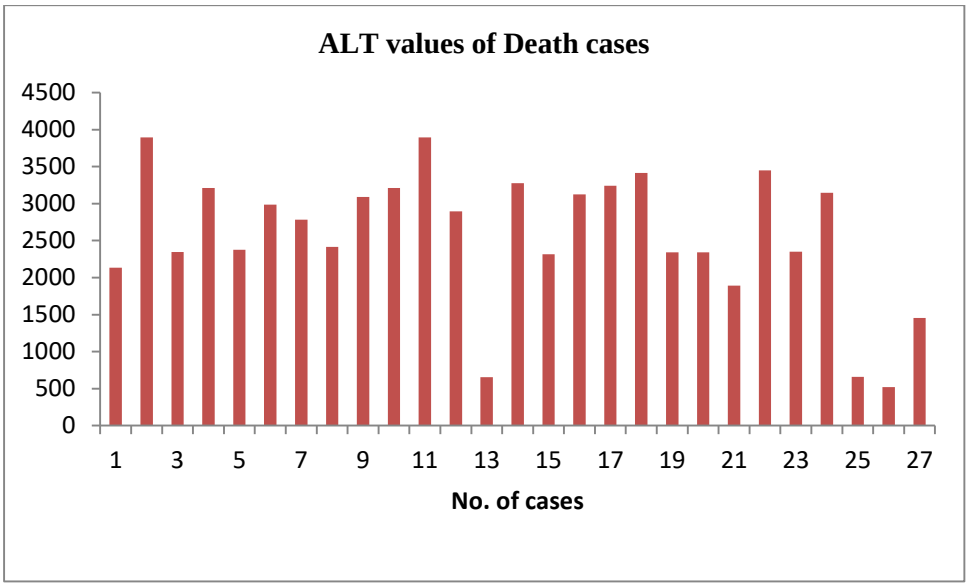


Figure : 37 ALT values of Dead Patients



ASSOCIATION BETWEEN CATEGORICAL VARIABLES

The chi-square for independence is used to study the relationship between

- Age and survival
- Gender and survival
- Serum bilirubin and phosphorus level
- Serum bilirubin and INR
- Serum bilirubin and AST level
- Serum bilirubin and ALT level
- Serum phosphorus and INR
- Serum phosphorus and AST
- Serum phosphorus and ALT

Table : 25 Association between Age and Survival

Age	Survival		
	Discharge	Death	Row Total
16-20	5 (2.76) [1.82]	1 (3.24) [1.55]	6
21-25	7 (7.36) [0.02]	9 (8.64) [0.01]	16
26-30	4 (5.52) [0.42]	8 (6.48) [0.36]	12
31-35	5 (4.14) [0.18]	4 (4.86) [0.15]	9
36-40	2 (3.22) [0.46]	5 (3.78) [0.39]	7
Column Total	23	27	50 (Total)

Null Hypothesis H_0: There is no association between age and survival.

The calculated value of the chi-square statistic is 5.3661 is less than 9.488, the table value of chi-square for 4 degrees of freedom at 5% level of significance. Hence there is no association between age and survival of patients. The null hypothesis is accepted. This affirms that the age and survival of poisoning cases are independent.

Table : 26 Association between Gender and Survival

Gender	Survival		
	Discharge	Death	Row Total
Male	13 (13.5) [0.02]	12 (11.5) [0.02]	25
Female	14 (13.5) [0.02]	11 (11.5) [0.02]	25
Column Total	27	23	50 (Total)

Null Hypothesis H_0: There is no association between gender and survival.

The calculated value of the chi-square statistic is 0.0805 is less than 3.841, the table value of chi-square for one degree of freedom at 5% level of significance. It is not significant. Hence there is no association between gender and survival of patients. The null hypothesis is accepted. This proves that gender and survival as far as poisoning cases are independent.

Table : 27 Association between Total Bilirubin and Serum Phosphorus

Level of Phosphorus	Level of Total Bilirubin			
	3.5-5	5.1-8	> 8	Row Total
Low < 3.5	10 (5.40) [3.92]	7 (7.20) [0.01]	1 (5.40) [3.59]	18
Normal 3.5-4.5	3 (1.80) [0.80]	2 (2.40) [0.07]	1 (1.80) [0.36]	6
High > 4.5	2 (7.80) [4.31]	11 (10.40) [0.03]	13 (7.80) [3.47]	26
Column Total	15	20	15	50 (Total)

Null Hypothesis H_0: There is no association between Total Bilirubin and Serum phosphorus

The calculated value of the chi-square statistic is 16.5456 is more than 9.488, the table value of chi-square for four degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and Serum phosphorus levels of patients. The null hypothesis is rejected. This affirms that the total bilirubin level and serum phosphorus level of poisoning cases are related.

Table : 28 Association between Total Bilirubin and INR

Level of INR	Level of Total Bilirubin			
	3.5-5	5.1-8	> 8	Row Total
< 1.5	9 (3.60) [8.10]	2 (5.04) [1.83]	1 (3.36) [1.66]	12
> 1.5	6 (11.40) [2.56]	19 (15.96) [0.58]	13 (10.64) [0.52]	38
Column Total	15	21	14	50 (Total)

Null Hypothesis H_0: There is no association between Total Bilirubin and INR

The calculated value of the chi-square statistic is 15.2517 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and INR of patients. The null hypothesis is rejected. This proves that the total bilirubin levels and INR levels as far as poisoning cases are concerned is associated.

Table : 29 Association between the Level of Total Bilirubin and AST level

Level of AST	Level of Total Bilirubin			
	3.5-5	5.1-8	> 8	Row Total
< 1000	12 (7.20) [3.20]	11 (10.08) [0.08]	1 (6.72) [4.87]	24
> 1000	3 (7.80) [2.95]	10 (10.92) [0.08]	13 (7.28) [4.49]	26
Column Total	15	21	14	50 (Total)

Null Hypothesis H_0: There is no association between Total Bilirubin and AST levels

The calculated value of the chi-square statistic is 15.6784 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and AST level of patients. The null hypothesis is rejected. This proves that the total bilirubin level and AST level are associated.

Table : 30 Association between the Level of Total Bilirubin and ALT Level

Level of ALT	Level of Total Bilirubin			
	3.5-5	5.1-8	> 8	Row Total
< 1000	14 (7.50) [5.63]	10 (10.50) [0.02]	1 (7.00) [5.14]	25
1000 >	1 (7.50) [5.63]	11 (10.50) [0.02]	13 (7.00) [5.14]	25
Column Total	15	21	14	50 (Total)

Null Hypothesis H_0: There is no association between Total Bilirubin and ALT levels

The calculated value of the chi-square statistic is 21.60 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and ALT level of patients. The null hypothesis is rejected. This proves that the total bilirubin level and ALT level are associated.

Table : 31 Association between the Phosphorus Level and INR

Level of Phosphorus	Level of INR		
	< 1.5	> 1.5	Row Total
Low < 3.5	10 (4.32) [7.47]	8 (13.68) [2.36]	18
3.5 - 4.5	1 (1.44) [0.13]	5 (4.56) [0.04]	6
High 4.5 >	1 (6.24) [4.40]	25 (19.76) [1.39]	26
Column Total	12	38	50 (Total)

Null Hypothesis H_0: There is no association between Serum phosphorus and INR

The calculated value of the chi-square statistic is 15.7932 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Phosphorus and INR of patients. The null hypothesis is rejected. This proves that the Phosphorus level and INR are associated.

Table : 32 Association between the Phosphorus level and AST level

Level of AST	Level of Phosphorus			
	Low	3.5-4.5	High > 8	Row Total
< 1000	17 (8.28) [9.18]	4 (2.76) [0.56]	2 (11.96) [8.29]	23
>1000	1 (9.72) [7.82]	2 (3.24) [0.47]	24 (14.04) [7.07]	27
Column Total	18	6	26	50 (Total)

Null Hypothesis H_0: There is no association between Serum phosphorus and AST.

The calculated value of the chi-square statistic is 33.398 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Serum Phosphorus and AST level of patients. The null hypothesis is rejected. This proves that the Phosphorus level and AST level are associated.

Table : 33 Association between the Level of Phosphorus and Level of ALT

Level of ALT	Level of Phosphorus			
	Low	3.5-4.5	High > 4.5	Row Total
< 1000	18 (9.50) [7.61]	5 (3.00) [1.33]	2 (12.50) [8.82]	25
> 1000	1 (9.50) [7.61]	1 (3.00) [1.33]	23 (12.50) [8.82]	25
Column Total	19	6	25	50 (Total)

Null Hypothesis H_0: There is no association between Serum phosphorus and ALT

The calculated value of the chi-square statistic is 35.5172 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Serum Phosphorus and ALT level of patients. The null hypothesis is rejected. This affirms that the Phosphorus level and ALT level are associated.

The chi-square tests reveal a fact that the bilirubin level, phosphorus level, INR, AST and ALT are increasing every day right from the first day till the seventh day. There is a

perfect relationship between them in case of died. For the survival cases there may be a progress in bilirubin level, INR, AST and ALT, but if the phospherou level do not increase or when there is no big change, the probability of survival is high.

DISCUSSION

DISCUSSION

Yellow phosphorus commonly used rodenticide, most commonly causes acute liver failure on ingestion. After the initial 48 -72 hours, the patients experiences vague abdominal symptoms and which then culminates to acute liver failure in the next 24 hours. In this study the participants are 50 and their course of hospital stay is observed. Routine blood investigations are done. The patients have a drastic increase in transaminase levels on the third day of ingestion of the poison and the patients who have the sustained elevation of the values on day 7. In the study the serum phosphorus values were also analysed on day 1,3 and7. In patients who had a dip in the values of serum phosphorus are associated with good prognosis and recovery. On the other hand in patients who had persistently elevated levels of serum phosphorus had a fatal outcome. From the meta-analysis of various studies, it was found that phosphorus was markedly lower in patients with acute liver failure of various reasons and it is postulated that the levels of serum phosphorous inversely correlates with the prognosis and is probably due to the increase uptake of phosphorus for ATP production which is used in hepatocyte regeneration after hepatic injury.

From the meta-analysis of various studies concerned with the post op recovery in patients after liver transplantation it is found that serum phosphorus plays an important role in the recovery of the patients after surgery. In some studies it is also proved among the paediatric population in acute liver injury following infections with hepatotropic viruses.

In this study 50 patients who were admitted in the medicine and toxicology wards of Madurai Medical College are segregated. They were holded up during their hospital stay and lab investigation such as Serum Bilirubin, AST, A

LT, INR, Serum Phosphorus values were tested and analysed. In addition to that the age and the gender of the poisoning cases are also considered.

Gender Distribution

In the study of 50 participants there are 25 males and 25 females. Hence there is no significant difference in the sex predilection of poisoning cases. It can be generalised because the total number of male patients and female patients admitted are more or less the same.

Age Distribution

In the study population, 6 are in the age group 16-20,16 in 21-25 age,12 in between 26-30, Between 31-35 there are 9 patients and 7 are in the age group 36-40.Most of the patients are middle aged. Among the middle aged 56% are in between 21-30.

This also communicate a message that the people who are above 40 are old are lesser in number admitted in the hospital.

Serum bilirubin

In the study it is found that the Serum bilirubin levels progressively increased in most of the cases from day 1 to day 7.It is found that 33 patients have their bilirubin levels upto 7.6,14 patients have the values between 7.7 and 11.6,2 patients are in between 11.7 & 15.6 and 1 crossed 15.7.

A noted significant fact is, the patients whose serum bilirubin level increases do not survive even after treatment.

Serum phosphorus

From the values of Serum phosphorus of patients enrolled in the study, 36% patients have low values of serum phosphorus in the range of 1.8-3.5,whereas the others had their values more than the normal range. It shows that 64% of patients have very high phosphorus levels by day 7.

This proves that the patients who have higher phosphorous level died and only few could be able to manage even if phosphorous level is high.

INR

In the study population 46% patients have INR values less than 2. 24% have 3 - 3.9. This confirms that the INR level are progressively elevated in most of the patient enrolled in the study. This shows that the patients with low level of INR or whose INR level do not progress so much are surviving.

AST

AST level of 46% patients are 213-949 and the remaining patients 54% have a significantly elevated level of AST more than 1000, which is associated with poor outcomes in the patients under study.

ALT

In the study population the patients in addition to AST have a significant increase in the levels of ALT as obtained from the reports.26 patients have their ALT values less than 1300 and the others have their value more than 1300.This also highlights the fact that ALT levels are also strong predictors of outcome. The AST level of the person also decides the probability of death and survival of the poisoning cases.

Association between Age and Gender with Survival

The calculated value of the chi-square statistic is 5.3611 is less than 9.488, the table value of chi-square for 4 degrees of freedom at 5% level of significance. Hence there is no association between age and survival of patients. Hence, we can conclude that the survival of poisoning patients does not depend on age. It depends upon the other factors.

The calculated value of the chi-square statistic is 0.0805 is less than 3.841, the table value of chi-square for one degree of freedom at 5% level of significance. It is not significant. Hence there is no association between gender and survival of patients. The age and gender are independent with regard to survival. Here also we can strongly believe that gender do not have any say in the survival of the poisoning cases. It may be based on the quantity of poison ingested. The age and gender are independent with regard to the survival.

Association between Serum Bilirubin and Phosphorus Level

The calculated value of the chi-square statistic is 16.5456 is more than 9.4848, the table value of chi-square for four degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and Serum phosphorus level of patients.

Association between Serum Bilirubin and INR

The calculated value of the chi-square statistic is 15.2517 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and INR levels of patients.

Association between Serum Bilirubin and AST level

The calculated value of the chi-square statistic is 15.6784 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and AST level of patients.

Association between Serum Bilirubin and ALT level

The calculated value of the chi-square statistic is 21.60 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Total Bilirubin and ALT level of patients.

Association between Serum Phosphorus and INR

The calculated value of the chi-square statistic is 15.7932 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Phosphorus and INR of patients.

Association between Serum Phosphorus and AST

The calculated value of the chi-square statistic is 33.398 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Serum Phosphorus and AST level of patients.

Association between Serum Phosphorus and ALT

The calculated value of the chi-square statistic is 35.5172 is more than 5.991, the table value of chi-square for two degrees of freedom at 5% level of significance. Hence there is association between Serum Phosphorus and ALT level of patients.

CONCLUSION

CONCLUSION

- In cases of acute liver failure presenting with coagulopathy and acute encephalopathy in yellow phosphorous poisoning, patients with transaminases more than 2000 are associated with poor regenerative capacity of liver. Hence patient have a grave outcome.
- Hypophosphatemia is frequently associated with regeneration of the liver as it negatively correlates with the ATP production required for hepatocyte regeneration.
- In the study, survivors usually had a dip in Serum phosphorus level on day 7 correlated as increased in regeneration of the liver, which could compensate for the massive hepatic necrosis, which occurred because of Yellow phosphorous poisoning.
- The amount of yellow phosphorus consumed also to some extent correlated with the prognosis of the patients and the individual susceptibility as a few patients who have consumed comparatively low amount of poison has resulted in poor outcome.
- Hence phosphorous levels can be used in prognostication in patients with acute liver failure in yellow phosphorus poisoning and also helpful in better selection of therapeutic options.
- The sensitivity of serum phosphorus in terms of prognostication is good in acute liver failure in yellow phosphorus poisoning but the specificity could not be well established.

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PROFORMA

Name:

Age / Sex:

In patient No:

Occupation:

Presenting complaints

- H/o Rat killer paste poisoning
- H/O Vomiting
- H/O pain in the abdomen
- H/O fever
- H/O jaundice
- H/O reduced urine output
- H/O malena/hematemesis
- H/O altered sleep Pattern
- H/O altered sensorium
- H/O constipation/ diarrhea
- H/O swelling of both legs
- H/O dyspnea

Past History

- H/o previous episodes of jaundice in the past
- H/o DM, HT, CKD, CAD, CLD, Autoimmune diseases, Tuberculosis, Malignancy

Personal History

H/o alcohol,smoking

H/o blood transfusion

H/o extramarital contact

Family History

History of jaundice in family members

General Examination

Consciousness

Pallor

Jaundice

Clubbing

Lymphadenopathy

Cyanosis

Pedal edema

Vitals

PR

BP

RR

SpO2

Systemic examination

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations

- CBC
- VCTC
- HbsAg and Anti HCV
- T.bilirubin, D.bilirubin, Ind.bilirubin
- SGOT,SGPT
- Serum Phosphorus
- Blood Urea,S.Creatinine

MASTER CHART

S.No	Name	Age	Sex	Amount ingested	Vomiting	Abdominal pain	Jaundice	Hb	TC	Urea	Creatinine	D1 T.Bili	D1 D.Bili	D1 In.Bili	D1 SGOT	D1 SGPT	D1 PO4	D1 INR	D1 E+/E-	D3 T.Bili	D3 D.Bili	D3 In.Bil	D3 SGOT	D3 SGPT	D3 P04	D3 INR	D3 E+/E-	D7 T.Bili	D7 D.Bili	D7 In.Bili	D7 SGOT	D7 SGPT	D7 PO4	D7 INR	D7 E+/E-	USG	Plasmapheresis	Dis / De
1	Krishna	19	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	2	1
2	Kurnal	22	1	1	0	1	1	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	3	0
3	Saipriya	21	0	2	1	1	0	0	0	0	1	0	0	0	0	1	0	0	0	2	1	0	1	0	0	0	1	1	0	0	1	1	1	0	1	0	3	0
4	Muthumari	23	0	3	0	0	1	0	0	0	0	1	0	0	0	1	0	1	0	2	1	0	0	0	1	1	1	2	1	1	1	1	1	0	0	1	2	1
5	Ponnamal	26	0	3	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0	1	0	0	0	0	1	2	1
6	Poovizhi	37	0	3	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2	1	0	0	0	1	1	1	2	1	0	1	1	1	0	1	1	3	0
7	Vellaraj	31	1	3	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	2	1	0	0	0	0	1	1	2	1	0	1	1	1	0	1	0	3	0
8	Thiloth	30	1	2	1	1	0	1	0	0	1	0	0	0	0	0	1	0	0	2	1	0	0	0	1	1	1	2	1	1	1	1	1	0	0	1	0	1
9	Kavitha	34	0	1	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	1	0	0	0	1	0	1	1	0	0	0	0	0	0	1	1	3	0
10	Jothi	25	0	3	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	2	1	1	0	0	1	1	1	2	1	1	1	1	1	0	0	1	2	1
11	Govindhammal	35	0	3	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	1	1	0	0	0	1	0	1	1	1	0	1	1	1	0	1	1	3	0
12	Kathamuthu	40	1	2	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	2	2	0	0	0	1	1	1	2	1	1	1	1	1	0	0	1	2	1

S.No	Name	Age	Sex	Amount ingested	Vomiting	Abdominal pain	Jaundice	Hb	TC	Urea	Creatinine	D1 T.Bili	D1 D.Bili	D1 In.Bili	D1 SGOT	D1 SGPT	D1 PO4	D1 INR	D1 E+/E-	D3 T.Bili	D3 D.Bili	D3 In.Bil	D3 SGOT	D3 SGPT	D3 P04	D3 INR	D3 E+/E-	D7 T.Bili	D7 D.Bili	D7 In.Bili	D7 SGOT	D7 SGPT	D7 PO4	D7 INR	D7 E+/E-	USG	Plasmapheresis	Dis / De
13	Dinesh	27	1	3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	1	1	1	1	0	1	1	1	0	1	0	4	0
14	Dharani	26	0	3	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	2	1	1	0	0	1	1	1	2	1	1	1	1	1	0	1	0	5	0
15	Megala	19	0	3	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	2	1	0	1	0	1	0	1	2	1	1	1	1	1	0	1	0	3	0
16	Sankar	22	1	3	1	0	0	2	1	1	1	0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	1	1	1	0	0	0	1	0	1	0	4	0
17	Anthony	32	1	1	0	1	0	2	1	1	1	0	0	0	0	0	1	1	0	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	3	0
18	Tharani	21	0	1	1	1	0	0	1	1	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	2	1
19	Krishnammal	25	0	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	2	0
20	Giri	27	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	4	0
21	Kasthuri	21	0	2	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	1	1	0	0	1	1	1	0	1	0	3	0
22	Arumugam	31	1	3	0	1	0	2	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	1	1	0	0	1	1	1	0	0	1	0	1
23	Brindha	27	0	1	1	0	0	0	0	1	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	3	0
24	Kadhampari	22	0	1	0	0	0	0	0	1	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	2	1
25	Nithya	20	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	1
26	Oorvasi	27	0	2	1	0	0	0	0	1	1	0	0	0	0	0	1	1	0	2	1	0	0	0	1	1	1	2	1	1	1	1	1	0	0	1	2	1

S.No	Name	Age	Sex	Amount ingested	Vomiting	Abdominal pain	Jaundice	Hb	TC	Urea	Creatinine	D1 T.Bili	D1 D.Bili	D1 In.Bili	D1 SGOT	D1 SGPT	D1 PO4	D1 INR	D1 E+/E-	D3 T.Bili	D3 D.Bili	D3 In.Bil	D3 SGOT	D3 SGPT	D3 P04	D3 INR	D3 E+/E-	D7 T.Bili	D7 D.Bili	D7 In.Bili	D7 SGOT	D7 SGPT	D7 PO4	D7 INR	D7 E+/E-	USG	Plasmapheresis	Dis / De
27	Krishna	23	1	3	1	1	1	2	0	0	0	1	0	0	1	1	1	1	0	2	1	0	0	0	1	0	1	2	1	0	1	1	1	0	0	1	2	1
28	Kandhasamy	24	1	3	1	0	1	2	1	0	0	1	0	0	1	1	1	1	0	2	1	0	0	0	1	1	1	2	2	1	1	1	1	0	0	1	3	1
29	Govinthammal	25	0	3	0	0	0	1	1	0	0	0	0	0	0	0	1	1	0	1	1	0	0	0	1	1	1	2	1	0	1	1	1	0	1	1	4	0
30	Bhuvaneshwari	38	0	2	0	1	1	0	0	0	1	1	1	0	1	1	0	0	0	1	0	0	1	0	1	1	1	2	1	1	1	1	1	0	1	0	3	0
31	Kunavathi	30	0	3	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	1	0	0	1	0	1	0	0	1	0	1
32	Kumar	36	1	1	1	0	0	2	0	0	1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	1	2	1
33	Jeyapandian	21	1	2	0	0	0	2	0	1	1	0	0	0	0	0	1	0	0	1	0	0	C	1	0	1	1	1	0	0	0	0	0	0	0	1	3	1
34	Suvetha	24	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1	0	4	0
35	Manoj	37	1	2	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	2	1	0	1	1	1	1	1	1	0	0	1	1	1	1	1	0	2	0
36	Abinaya	22	0	3	0	1	1	0	0	1	1	1	0	0	1	1	1	1	0	1	0	0	1	1	0	0	1	1	0	0	1	0	0	0	0	1	2	1
37	Sugadev	38	1	3	0	0	0	1	1	1	1	1	0	0	1	1	1	1	0	2	1	0	1	1	1	0	1	1	0	0	1	1	1	0	1	1	0	1
38	Padma	37	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	1	1	0	0	0	0	0	0	0	1	0	1
39	Chinnathambi	22	1	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	0	4	0
40	Periyasamy	17	1	1	1	1	0	2	0	1	1	0	0	0	0	0	1	0	0	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	3	1

S.No	Name	Age	Sex	Amount ingested	Vomiting	Abdominal pain	Jaundice	Hb	TC	Urea	Creatinine	D1 T.Bili	D1 D.Bili	D1 In.Bili	D1 SGOT	D1 SGPT	D1 PO4	D1 INR	D1 E+/E-	D3 T.Bili	D3 D.Bili	D3 In.Bil	D3 SGOT	D3 SGPT	D3 P04	D3 INR	D3 E+/E-	D7 T.Bili	D7 D.Bili	D7 In.Bili	D7 SGOT	D7 SGPT	D7 PO4	D7 INR	D7 E+/E-	USG	Plasmapheresis	Dis / De
41	Suresh	19	1	2	0	0	0	2	1	1	1	0	0	0	0	0	1	0	0	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	3	0
42	Ramasamy	35	1	1	1	0	1	1	0	1	0	1	0	0	1	1	1	0	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	0	1
43	Kannan	31	1	3	1	0	0	1	0	1	0	0	0	0	1	0	1	0	0	1	1	0	1	1	0	0	1	2	1	0	0	0	0	0	0	1	0	1
44	Rajesh	29	1	3	0	0	0	2	0	0	1	0	0	0	1	1	1	0	0	1	0	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	4	0
45	Deepak kumar	20	1	2	1	0	1	2	0	0	0	1	1	0	1	1	0	1	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	2	0
46	Dhivya	26	0	1	0	1	0	0	0	1	1	0	0	0	0	1	0	0	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	3	0
47	Sreelakshmi	31	0	1	0	1	0	1	0	1	1	0	0	0	0	0	0	1	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	0	1	3	1
48	Yuvaraj	28	1	3	0	0	1	2	0	0	1	1	0	0	1	1	0	1	0	1	1	0	1	1	1	0	1	1	0	0	0	1	1	0	1	0	2	0
49	Devaraj	30	1	1	0	1	0	0	1	0	1	0	0	0	0	0	1	0	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	3	0
50	Keerthi	32	0	1	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	1	1	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	2	0

KEY TO MASTER SHEET

➢ Sex	Male-1; Female-0
➢ Amount ingested:	5g -1 ; 10g - 2 ; 15g – 3
➢ Vomiting	Yes -1; No – 0
➢ Abdominal pain	Yes -1; No – 0
➢ Jaundice	Yes -1; No – 0
➢ Hb	9-11 - 0; 12-14 – 1; 15-16 – 2
➢ TC	≤ 8000 – 0; 8000 – 12000 -1
➢ Urea	16- 34 -0; 35-46 – 1
➢ Creatinine	0.4 - 1 – 0; 1.1 -3.5 – 1
➢ D1 T.Bili; D1 D.Bili; D1 In.Bili	1-2 – 0; 2.1-3.5 – 1
➢ D1 SGOT ; D1 SGPT	< 200 – 0; > 200 – 1
➢ D1 PO4	2.8 -3.8 – 0; 3.9 - 4.9 – 1
➢ D1 INR	1-1.5 – 0; 1.6-3 – 1
➢ D1 E+/E-; D3 E+/E- ; D7 E+/E-	E- - 0; E+ - 1
➢ D3 T.Bili ; D3 D.Bili ; D3 In.Bili	0-3.5 -0; 3.6-7 -1; 7.1-11.5 – 2
➢ D3 SGOT ; D3 SGPT	<1200 – 0; > 1200 – 1
➢ D3 PO4; D3 INR	1-5 - 0; 5.1-10 - 1
➢ D7 T.Bili ; D7 D.Bili ; D7 In.Bili	0-4 – 0; 4.1-8 -1; 8.1-19 -2
➢ D7 SGOT, D7 SGPT	<1500 – 0; > 1500 – 1
➢ D7 PO4, D7 INR	1-5 - 0; 6-10 - 1
➢ USG	AB - 0; N – 1

ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADURAI MEDICAL COLLEGE &GOVT.RAJAJI HOSPITAL, MADURAI
CDSCO: Reg. No. ECR/1365Inst/TN/2020 &DHR Reg.No.EC/NEW/INST/2020/484

Study Title	:	Serum Phosphorus as a Prognostic Indicator in Acute Liver Failure in Rat Killer Paste Poisoning- an observational study
Principal Investigator	:	**Dr.A.Ashy Stephanie**
Designation	:	PG in MD., General Medicine (2020-2023)
Guide	:	Dr.Vivekananthan.S.C, MD (GM),DTCD. Professor of General Medicine
Department	:	Department of General Medicine, Government Rajaji Hospital & Madurai Medical College, Madurai

The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on **04.10.2021** at GRH Auditorium, Govt. Rajaji Hospital, Madurai at 10.00 A.M

The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is **Approved.**

You should inform the IEC in case of any changes in study procedure, methodology, sample size investigation, Investigator or guide or any other changes.

1. You should not deviate from the area of work for which you had applied for ethical clearance.
2. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions. If encountered during from study.
3. You should abide to the rules and regulations of the institution(s)
4. You should complete the work within the specific period and if any extension is required, you should apply for the permission again for extension period.
5. You should submit the summary of the work to the ethical committee on completion of the study.
6. Serious Adverse Events occurred in the study should be intimated to the IEC within 24 hours of occurrence of the event.

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SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING -AN OBSERVATIONAL STUDY

INTRODUCTION Yellow phosphorus commonly used rodenticide in the name ratol is a protoplasmic poison. The lethal dose is 1 milligram per kilogram the most common mode of poisoning is ingestion which is either accidental or intentional. Being a protoplasmic poison it affects the ribosomal function and hence inhibits protein synthesis. Liver receives major cardiac output. The common cause of Acute Liver Injury includes Infections-Hepatitis A,B,E,EBV, Ischemia ,Wilson's disease, HELLP syndrome ,Vasoocclusive disease and toxins like paracetamol, yellow phosphorus etc. The main functions of Liver include Glucose Metabolism - Glycogenolysis, Gluconeogenesis, Glycolysis, fat and lipid metabolism, secretion of IGF, storage of Vitamins, detoxification, clotting factor synthesis. Yellow Phosphorus causes periportal necrosis of liver leading to acute liver failure with the elevation of enzymes. Yellow phosphorus toxicity occur in the cellular organelles affecting protein synthesis hence resulting in reduced synthesis of VLDL , ATP and hence inhibits oxidation of fatty acid which results in diffuse fatty infiltration of the organs and cell death. The clinical manifestations of poisoning can be of three phases. First 24 hours there are only mild symptoms with gastrointestinal irritation. In the next 24 to 72 hours there is rise in bilirubin and liver enzymes. After 72 hours patient may develop coagulopathy, acute liver failure, hypotension and acute kidney injury. Treatment for Yellow phosphorus poisoning includes gastric lavage and only supportive measures, as there is no specific antidotes for yellow phosphorus poisoning. In patients with acute liver failure due to toxins N-acetyl cysteine which replenishes glutathione and that stabilizes the vasculature can be used. The candidates for liver transplantation following acute liver failure in yellow phosphorus poisoning is assessed using King's College Hospital Criteria. TPE is always used as bridge for ALF patients to liver transplantation. Serum phosphorus level is considered as an important predictor of mortality in acetaminophen poisoning with acute liver failure. Hypophosphatemia occurs as a result of increased intracellular uptake of phosphorus to replenish high energy intermediates when there is brisk hepatocyte regeneration. Hence high serum phosphate levels are associated with poor prognosis in patients with acute liver failure. AIMS AND OBJECTIVES • To study the association between Serum phosphorus and acute liver failure. • To assess the prognosis of patients with acute liver failure with regards to Serum phosphate level.

ANTI PLAGIARISM CERTIFICATE

This is to certify that the dissertation entitled **'SERUM PHOSPHORUS AS A PROGNOSTIC INDICATOR IN ACUTE LIVER FAILURE IN RAT KILLER PASTE POISONING - AN OBSERVATIONAL STUDY'** of the candidate **Dr. A. ASHY STEPHANIE,** for the award of Degree of Doctor of Medicine (M.D) Branch- I - General Medicine personally verified the **urkund.com** website for the purpose of plagiarism check. I found the upload dissertation file contains pages from Introduction to conclusion and the result shows 1% of plagiarism in the dissertation.

Guide

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