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Review Article

Hepatotoxicity: A comprehensive review

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ABSTRACT

Liver is the primary site of digestion for drugs and different exogenous mixes. As most medications are taken orally the liver is the entrance to the tissues for such mixes following ingestion from the gastrointestinal tract. The biggest organ in the body is being advanced to keep up the body's inward milieu and furthermore shield itself from the difficulties it faces during its working. It is a fundamental organ having different capacities. It assumes a significant job in the digestion, combination and capacity yet additionally in the detoxification of numerous endogenous and exogenous mixes and changing them over to less harmful substances for excretion. Hepatotoxicity suggests substance driven liver harm. Medication induced liver injury is a reason for intense and constant liver sickness. The liver assumes a focal part in changing and clearing synthetic compounds and is helpless to the harmfulness from these specialists. Other chemicals or natural chemicals agents (e.g., microcystins) and herbal remedies can also induce hepatotoxicity.

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1. Introduction

The liver assumes a significant part in the digestion and expulsion of medications. Detoxification of medications and xenobiotic in the liver by drug utilizing chemicals (DMEs) is a significant wonder in the securing of homeostasis.¹ The liver is an imperative organ and its key area and multidimensional capacities uphold pretty much every other organ in the body. Liver is likewise the primary organ for digestion and disposal of medications.² Poisonous hepatitis is the most extreme antagonistic response to antituberculosis drugs, it as a rule starts in the initial not many long stretches of treatment alongside liver rot, which may advance to encephalopathy and demise. Alcoholic liver illnesses with cirrhosis (development of stringy tissue in liver) brought about by unreasonable liquor utilization is a typical event. Liver can once in a while be harmed by certain synthetic substances called hepatotoxins.³ Drug-induced liver injury (DILI) is the most continuous sign for drug withdrawal from

the drug market because of its relationship with noteworthy antagonistic impacts, dismalness, and mortality.⁴ DILI is liable for most of intense liver disappointment cases and is currently the main source for liver transplantation among patients.⁵ It is critical to perceive that DILI is generally named characteristic (or direct) versus particular. Natural DILI is regularly portion related and happens in a huge extent of people presented to the medication (unsurprising) and beginning is inside a brief timeframe length (hours to days).⁶

2. Types of liver diseases and its symptom

There are various types of liver disease mentioned below in the table.^{8–10}

3. Conclusion

Drug induced Liver Injury harm goes from the unusual and non-portion identified with that happening typically after overdoses. It may include digestion to harmful, receptive intermediates, obstruction, with film transport or with

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Table 1: Types of drug induced liver injury⁷

Types	Prognosis	Enzymatic Profile
Hepatocellular	More Severe prognosis	Alanine transaminase >2ULN, Serum ALT/Serum Alk.
Cholestatic	More prone to chronic disease	Alk phos > 2 Upper limit of normal, Serum Alanine transaminase, serum Alk.
Mixed	More prone to chronic disease	Alanine transaminase > 2 Upper limit of normal, Phos between 2 & 5

Table 2: Types of liver diseases and its symptom

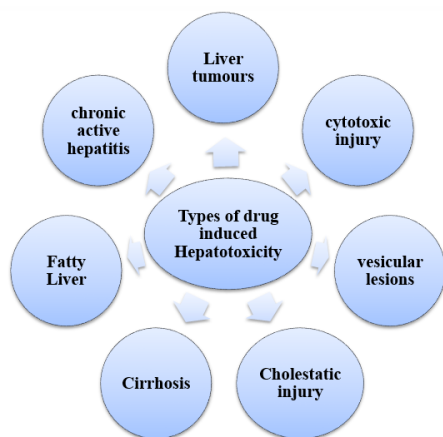
Liver Disease	Characterization	Causes/Conditions of Disease
Acute liver failure	Reduction in liver function	Drugs, toxic chemicals, various liver diseases
Autoimmune related	Development of antibodies against self-liver cells, Inappropriate immune response against hepatic cells	Primary biliary cirrhosis, Primary sclerosing cholangitis, Autoimmune hepatitis
Genetic disease	Gene mutations that causes liver injury	Hemochromatosis, Wilson's disease, deficiency of α -1 antitrypsin
Liver infections	Infections that leads to several type of liver damage and blockage of bile ducts	Viral hepatitis (Hepatitis A, B, C, D and E), Parasitic infections (yellow fever virus, herpes viruses)
Hepatitis (A,B,C,D and E)	Acute or chronic liver damage	Hepatotropic viruses, alcohol assumption, drugs, xenobiotics, autoimmune disease, non-alcoholic fatty liver disease (NAFLD)
Liver cancer	Cancerous tumour in the liver	Increased risk of chronic Hepatitis ; hepatocellular carcinoma (HCC)
Hepatic vein obstruction	Blood clots obstruct , blood flow from the liver; development of symptoms such like jaundice enlarged liver, ascites, and abdominal pain	Hypercoagulable disorders, thrombosis of the hepatic vein, hepatic cancer, parasitic infection
Bile ducts obstruction	Blockage of bile ducts	Tumours, Gallbladder stones, inflammation, sudden physical injury

Table 3: Types of drug induced liver disease and its mechanism

Liver diseases	Drugs	Mechanism
Zonal necrosis	Paracetamol, carbon tetrachloride, Amatoxins	Cessation of protein synthesis due to the inhibition of RNA synthesis, largely confined to a particular zone of the liver lobule ¹
Cholestasis	Chlorpromazine, estrogen, erythromycin and its derivatives ¹¹	Impairment of bile flow, itching and jaundice. Injury to canalicular membrane and transporters (Kaplowitz; 2004).
Steatosis	Carbamazepine ¹²	Triglyceride accumulation which leads to either small droplet [micro vesicular] or large droplet [macro vesicular] fatty liver
Micro vesicular fats Non-alcoholic steatohepatitis Lactic acidosis	Didanosine, tetracycline, acetylsalicylic acid, valproic acid Amiodarone, tamoxifen Zidovudine, riboflavin, metformin	Altered mitochondrial respiration, β - oxidation leads to lactic acidosis and triglyceride accumulation ¹²
Granuloma	Diltiazem, sulfa drugs, quinidine	Granulomas located in periportal or portal areas and show features of systemic vasculitis and hypersensitivity, Macrophages, lymphocytes infiltrate hepatic lobule.
Vascular lesions/collapse ¹³	Nicotinic acid, cocaine, methylenedioxymeth amphetamine	Injury to the vascular endothelium/ Causes ischemic or hypoxic injury.
Oncogenesis Veno- occlusive ¹⁴	Oral contraceptives, androgens Busulfan, cyclophosphamide	Encourages tumor formation ¹³ Injury to the hepatic venous endothelium.

Table 4: Therapeutic agents causing hepatotoxicity.^{15,16}

Antimicrobial	Anti- epileptics	Analgesics and Anti-Tuberculosis drug	Immunomodulator	Others
Amoxicillin Isoniazid	Phenytoin Lamotrigine	NSAIDs Rifampicin, Rifabutin	Interferon- β Interferon- α	Methotrexate Androgen- containing steroids
Sulfamethoxazole	Valproic Acid	Pyrazinamide	Anti-TNF agents Azathioprine	Amiodarone
Trimethoprim	Carbamazepine	Prothionamide	Cyclophosphamide	Inhaled anaesthetics

**Fig. 1:** Types of drug induced Hepatotoxicity⁷

cell natural chemistry, for example, protein amalgamation, or immunological instruments and contrasts in resistant responsiveness, hereditary, dietary and different variables. The liver is dependent upon expected harm from a gigantic exhibit of drug operators, Natural poisons, metals and metalloids, mycotoxins, endotoxins.

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5. Conflicts of Interest

All contributing authors declare no conflicts of interest.

6. Source of Funding

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