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Edge Innovations in Liver Disease Diagnosis and Treatment

Dhumane S*, Gangurde M, Patil U, Raut H and Udavant P

MET's Institute of D. Pharmacy, India

***Corresponding author:** Srushti Dhumane, MET's Institute of D. Pharmacy, Adgaon, Nashik, India, Email: amitkakad12@gmail.com

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Abstract

Although the liver performs a variety of functions, its role in the body's metabolism is the most crucial. A liver disease is any condition that affects liver function and has the potential to cause inflammation of the liver or damage to liver tissue. Hepatologists are now more excited than ever due to a plethora of new facts regarding liver disease. Liver disease might be difficult to diagnose in its early stages due to its mild symptoms. Many times, the signs appear too late. Liver disease is a serious condition for which there are now no specific treatment options. This makes the situation worse despite advances in the goods used to treat it. A new perspective on the various cell sources under investigation has been provided by the recent discoveries in the significant interest in using haematopoietic stem cells for regenerative medicine. There are currently a wide range of naturally derived products on the market that have potent hepatoprotective qualities against serious liver diseases. Many novel procedures have recently been created for the purposes of diagnosis and treatment.

Keywords: Liver Cirrhosis; Silymarin; Hepatic Ultrasonography; Liver Inflammation

Abbreviations

CT: Computed Tomography; LS: Liver Stiffness; MRI: Magnetic Resonance Imaging; SVM: Support Vector Machine; 3D: Three-Dimensional; DCE: Dynamic Contrast-Enhanced; ROS: Reactive Oxygen Species; MSCs: Mesenchymal Stem/Stromal Cells; NAFLD: Non-Alcoholic Fatty Liver Disease; ALD: Alcoholic Liver Disease.

Introduction

People's livers undergo a range of changes as they age, which may have an effect on their clinical characteristics and prognoses. Our liver's volume and blood flow both sharply decrease with ageing. These changes and decreased cytochrome P450 performance may affect medication metabolism and raise the risk of drug-induced liver injury. Elderly people may be more vulnerable to autoimmune illnesses because of compromised dendritic cell maturation and a decrease in regulatory T cells, but they may have reduced immune responses to infections or malignant cells. These changes in immune function could affect the pathogenesis of viral hepatitis, autoimmune liver diseases, and the development of hepatocellular carcinoma. Furthermore, several organs' reserve functions have significantly declined in older adults, which All together, elderly adults exhibit a variety of liver and other organ alterations that may have an impact on the management and clinical features of liver illnesses in these patients [1]. The clinical course and therapy of liver illnesses in the elderly may differ in various areas from those in younger persons, despite the fact that there are no liver diseases that are particular to senior age.

Over the past ten years, a wealth of fresh information about liver disease has increased hepatologists' excitement. On the other hand, it is becoming more and more challenging to validate and integrate information to be used in clinical practice due to the emergence of new developing disorders (such non-alcoholic steatohepatitis) and novel therapeutic approaches. Certain liver illnesses, especially hepatocellular carcinoma, chronic hepatitis C, alcoholic liver disease, and non-alcoholic fatty liver disease, should be reexamined in older adults. Certain treatment modalities, including liver transplantation and antiviral medication, ought to be explored with particular cohorts of senior patients as well [2]. Every year, liver disease is the leading cause of death. Over 30 million Americans have liver illnesses, and over 29 million people have chronic liver conditions. In England, the leading causes of death are respiratory illnesses, cancer, and stroke, with liver ailment coming in fifth [3]. NIDDK responds to questions and provides liver disease information to those with the illness, their families, healthcare providers, and the general public through the NIDDK Health Information Centre [4].

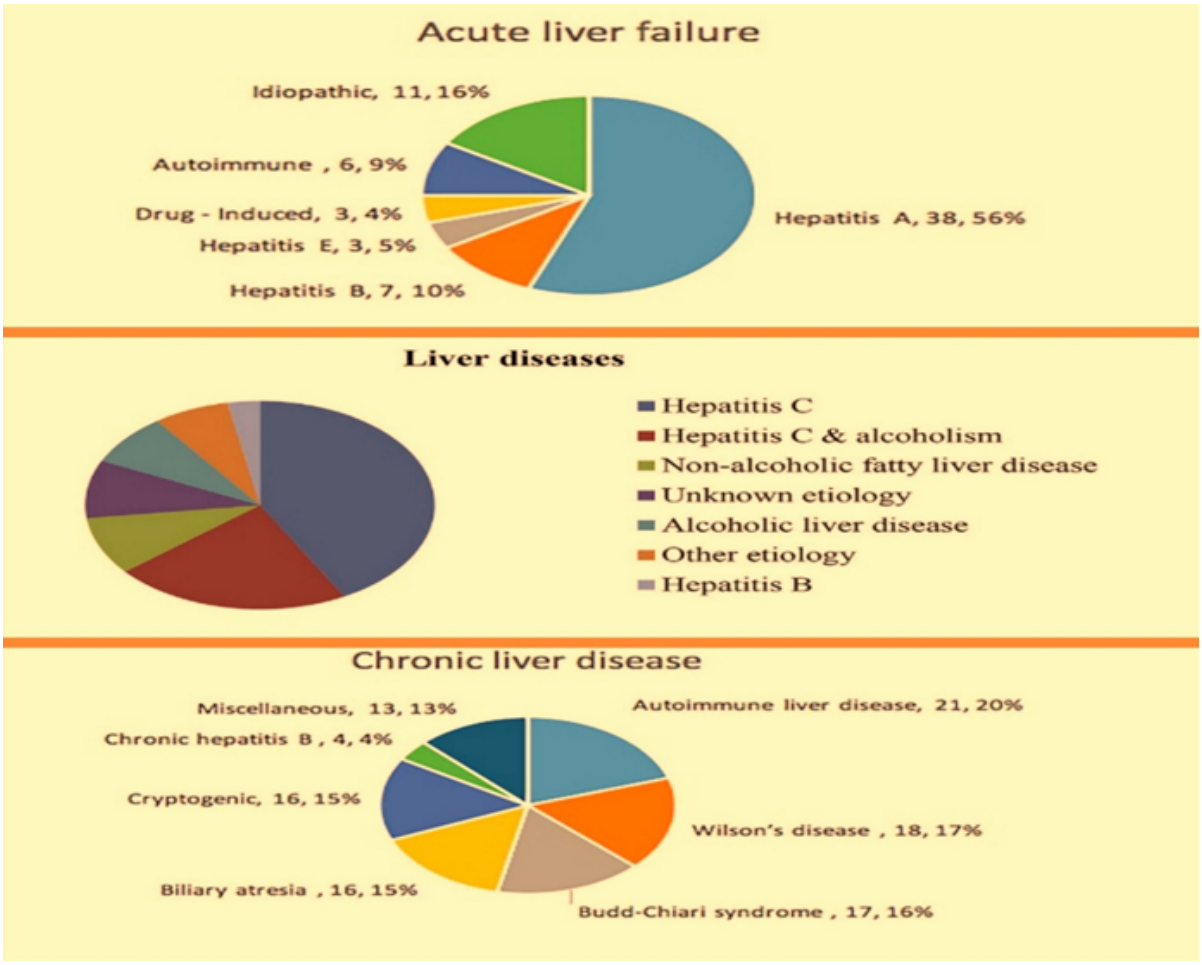

Figure 1: Diagrammatic representation of percentage of people suffering from liver disease [5,6].

The median survival for 151 individuals with NAFLD and 94 individuals with AFLD was 20 years and 24 years, respectively. In the NAFLD group, cirrhosis developed in 10/151 patients (7%) and in the AFLD group in 19/94 patients (20%).

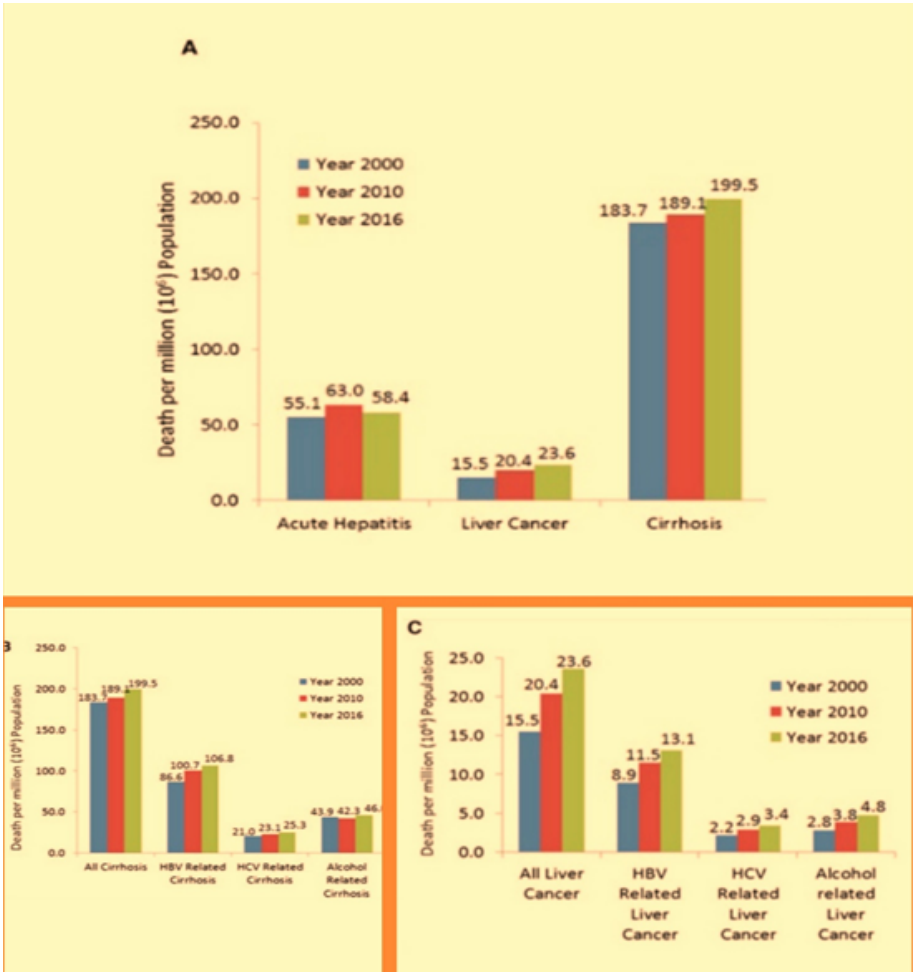

Figure 2: Diagramatic representation of liver diseased people death rate [7].

Biochemical Diagnosis of Liver Diseases

Clinical chemists and pathologists in particular need to be able to recognise abnormal liver function test results and understand the clinical consequences of such findings. Many important metabolic activities are regulated by the liver. Damage to the liver causes distortions in these metabolic pathways. It is possible to evaluate and diagnose hepatic disease using the blood concentrations of many serum analytes. Serum analytes can aid in the biochemical diagnosis of liver disease in a variety of ways. This paper's analysis primarily focusses on the analytes associated with end-stage liver disease, cholestasis, poor excretion, and decreased synthetic function. The significant forms of liver disease will be associated with these serum analyte abnormalities [8]. In India, liver diseases cause more than 2.4% of fatalities annually. Because of its modest symptoms, liver disease can be challenging to diagnose in its early stages. The symptoms frequently show up when it's too late. The goal of this work is to enhance the diagnosis of liver illnesses through the investigation of two identification techniques: patient parameters and genome expression. The study outlines drawbacks and goes over the computational methods that can be used to the previously outlined methodology. It suggests ways to increase these algorithms' effectiveness [9].

Active hepatic inflammation plays a critical role in the inflammation-necrosis-regeneration pathway that leads to liver cirrhosis and hepatocellular carcinoma. The prognosis of liver cirrhosis may be influenced by several factors, such as the cause, severity, and co-occurring conditions of the liver disease. The prognosis for advanced cirrhosis drops to a year or two. Accurate advanced diagnosis and targeted treatment with various molecules may aid in comprehending the pathophysiological mechanisms of cirrhosis, the meticulous approach to more successful therapeutic treatments, and the mechanisms of fibrogenesis [10].

Automatic Liver and Lesion Segmentation: A Primary Step in Diagnosis of Liver Diseases

Computed tomography (CT) imaging is frequently used for two purposes: the diagnosis of liver diseases and the assessment of liver volume for liver transplantation and surgery. Segmenting the liver and lesion is considered to be one of the most crucial initial steps in computer-aided diagnosis of liver diseases. Lesion alone cannot be automatically segmented from the abdominal CT image since there are tissues outside the liver that are equally intensity to the lesions.

Consequently, in order to precisely segment the lesion from the liver, the liver must first be segmented. This research proposes an automatic and efficient method for liver and lesion segmentation from CT images required for computer-aided liver diagnosis. The technique uses Alternative Fuzzy C-Means clustering for lesion segmentation and confidence connected region growth, which is enabled by preprocessing and postprocessing operations, for automatic liver segmentation. By contrasting the automatic and manual segmentation results based on volume measurement inaccuracy, figure of merit, spatial overlap, false positive, false negative, and visual overlap, the method is quantitatively assessed [11].

Multiparametric Magnetic Resonance for the Non-Invasive Diagnosis of Liver Disease

Reliable approaches for diagnosing and staging liver pathology are urgently needed in clinical practice due to the rising frequency of liver disease worldwide. The current gold standard, liver biopsy, is invasive and subject to observer dependent variability and sampling issues. The objective of this investigation was to evaluate the diagnostic precision of an innovative magnetic resonance technique for characterizing liver tissue.

We performed a prospective research to compare liver biopsy with our magnetic resonance technology. Proton spectroscopy, T1 mapping, and T2 mapping were the distinct parts of the scanning technique that measured liver fibrosis, steatosis, and hemoiderosis, respectively. Adult patients who were not chosen and were referred for a liver biopsy as part of their regular care were gathered. Physicians blinded to the histology results analyzed the scans done before the liver biopsy. Assessments were made of the relationships between histological characteristics and magnetic resonance imaging. Additionally, evaluations of receiver-operating characteristics were performed.

For 79 individuals, paired magnetic resonance imaging and biopsy data were acquired. Strong correlations were seen between magnetic resonance measurements and histology (rs = 0.68 p <0.0001 for fibrosis, rs = 0.89 p <0.001 for steatosis, and rs = -0.69 p <0.0001 for hemosiderosis). The diagnosis of any degree of fibrosis, steatosis, and hemosiderosis had area under the receiver operating characteristic curves of0.94, 0.93, and 0.94, respectively. The innovative scanning technique presented here offers excellent diagnostic precision in evaluating liver fibrosis, steatosis, and hemosiderosis and may eventually supplant liver biopsy in numerous cases. This is the first instance of a non-invasive test being used to distinguish between a healthy liver and the early stages of fibrosis [12].

Liver Stiffness: An Innovative Metric for Identifying Liver Illness

Liver disease diagnosis, particularly liver cirrhosis, has been transformed by the noninvasive quantification of liver stiffness (LS) utilizing ultrasound-based transient elastography with FibroScan®. Other methods, including magnetic resonance elastography or acoustic radiation impulse frequency imaging, are presently being researched. LS out performs all other noninvasive methods for detecting cirrhosis and is a great surrogate marker of advanced fibrosis (F3) and cirrhosis (F4). Less than 6 kPa is regarded as normal and does not indicate the presence of active liver disease. The generally accepted cut-off values for F3 and F4 fibrosis are 8 and 12.5 kPa, respectively. Esophageal varices are likely at levels >20 kPa, and LS has a strong correlation with portal pressure." "There are numerous other causes that can also cause liver swelling, include tumor cell infiltration, mast cell infiltration (mastocytosis), inflammatory cell infiltration (all types of hepatitis), or amyloidosis. Furthermore, LS is elevated during mechanical cholestasis and directly connected with venous pressure (e.g., during liver congestion). Consequently, it is imperative to always interpret LS in light of clinical, imaging, and laboratory results. Ultimately, liver fibrosis's molecular causes have become clearer because to LS. The unique hypothesis of the pressure-stiffness-fibrosis sequence is presented [13].

Other Techniques for Diagnosis of Liver Disease

For the detection, characterization, and evaluation of the response to treatment of focal and diffuse liver disorders, hepatic ultrasonography and magnetic resonance imaging (MR) are being utilized more and more .While elastography and dynamic contrast-enhanced (DCE) studies are still the first-choice evaluation, ultrasonography has lately become more capable [14].

Feature extraction and 3D reconstruction of CT scans are done by computer processing technologies in three-dimensional (3D) display. It is a tool that provides stereoscopic, accurate, and intuitive ways for clinical decision-making by showing,

characterizing, and understanding the 3D anatomy and morphological aspects of organs. It has become more and more important in the identification and treatment of liver disorders. In the meantime, the combination of 3D models and hydrodynamic analysis has emerged as a novel non-invasive technique for the diagnosis and detection of portal hypertension. Over the past ten years, the safe and effective use of 3D simulation software for pre-hepatectomy assessment, virtual hepatectomy, and measurement of liver volumes in blood flow areas of the portal vein has been demonstrated [15].

The Support Vector Machine (SVM) is a supervised learning model that identifies patterns in data through related learning techniques. Using two datasets of liver patients with various feature combinations, such as SGOT, SGPT, and Alkaline Phosphates, support vector machines are used to classify liver disease. The accuracy, error rate, sensitivity, prevalence, and specificity of a support vector machine classifier are measured to assess its performance. In comparison to the BUPA dataset, the results indicate that the ILPD dataset has the best accuracy, error rate, and prevalence at the first six ordered characteristics. This can be attributable to the fact that the ILPD liver dataset has more valuable properties than the BUPA dataset, which diagnoses liver disease, such as total bilirubin, direct bilirubin, albumin, gender, age, and total proteins [16].

Recent Advances in Products Used for Treatment of Liver Disease

Advances in products used for treatment of liver disease are a grave illness, and the situation is made worse by the absence of exact treatment plans. The current treatments for liver diseases are inappropriate, and their long-term usage is hampered by systemic toxicity. Because the toxicity factor seems to be on the lower side, medicinal plants have been utilized historically for ages to treat liver ailments [17].

Any ailment that impairs liver function and may lead to liver inflammation or tissue damage is considered a liver disease. Liver illnesses have traditionally been treated with natural compounds found in fruits, vegetables, insects, plants, herbs, and animals. These are chemical substances that are typically biologically active and are used in drug design and discovery. Numerous natural products with strong hepatoprotective properties against major liver ailments are now commercially available. The present state of scientific, clinical, and translational research on natural products as potential treatments for a range of liver illnesses is summed up in this overview. In addition, our attention will be directed towards the identification and biological assessment of natural compounds that exhibit promise as novel therapeutic agents for liver ailments. There should be more prospective, controlled trials conducted on glycyrrhizin, an herbal treatment with many components that has intriguing hepatoprotective effects in individuals with subacute liver failure. Prospective research on the antifibrotic/ fibrolytic activity of interferon is necessary, as it has demonstrated intriguing antifibrotic effects in both people and animals. Curcumin, resveratrol, and thalidomide are three recently identified substances that have shown great promise in treating experimental liver illnesses. Their mode of action is linked to their capacity to reduce profibrotic and pronecrotic cytokines as well as down-regulate NF-κB. Unfortunately, there isn't enough clinical research. Other promising medications used mostly for cholestasis include silymarin and sulfoadenosylmethionine, but further controlled trials could increase their benefits [18].

Liver illnesses have traditionally been treated with natural compounds found in fruits, vegetables, insects, plants, herbs, and animals. These are chemical substances that are typically biologically active and are used in drug design and discovery. Numerous natural products with strong hepatoprotective properties against major liver ailments are now commercially available. The present state of scientific, clinical, and translational research on natural products as potential treatments for a range of liver illnesses is summed up in this overview. In addition, our attention will be directed towards the identification and biological assessment of natural compounds that exhibit promise as novel therapeutic agents for liver ailments [19].

Role of Silymarin

The rising incidence of liver illnesses like cirrhosis and chronic hepatitis highlights the need for effective and affordable therapies. It is still up for debate whether silymarin, which is derived from the seeds of milk thistle or *Silybum marianum*, can be useful in the treatment of liver disorders. Thus, the goal of this review is to evaluate silymarin's clinical efficacy and safety using a methodical methodology. At concentrations found in clinical conditions, silymarin has effects on metabolism and cell regulation. These effects include scavenging reactive oxygen species (ROS) of the R-OH type, inhibiting the 5-lipoxygenase pathway, controlling cell membrane permeability through carrier-mediated regulation, and suppressing nuclear factor (NF)-κB, which can affect DNA expression. A significantly significant difference in mortality observed in favor of silibinin, the major isomer included in silymarin, was observed in pooled data from case record studies comprising 452 patients with Amanita phalloides poisoning (mortality 9.8% vs. 18.3% with standard treatment; $p < 0.01$). Valid conclusions regarding the value of silymarin cannot be taken from the few available trials in patients with toxic (solvents, for example) or iatrogenic (antispychotic, tacrine, etc.) liver

disorders because they are underpowered and the trials are generally obsolete. An enhanced clinical tolerance to tacrine is the exception. Despite some encouraging outcomes in individuals with acute viral hepatitis, silymarin's usefulness in treating these infections cannot be conclusively established [20].

In addition to promoting hepatocyte regeneration and having antioxidant and membrane-stabilizing properties, silymarin also lowers inflammatory responses and prevents fibrogenesis in the liver. Clinical and experimental trials have validated these findings. Open trials have shown that silymarin treatment extended the survival period of patients with alcohol-induced liver cirrhosis. Silymarin has the ability to dramatically lower insulin resistance, angiogenesis, and tumor cell proliferation. Moreover, it inhibits tumor necrosis factor-alpha-induced protein synthesis and mRNA expression because of adhesion molecules and has an anti-atherosclerotic activity. Numerous research employing in vitro and in vivo techniques have demonstrated the chemopreventive effect of silymarin on HCC; by interfering with cytokines, it can have a positive influence on the balance between cell survival and apoptosis [21].

Treatment by Cell Transplantation

Cell treatments have been effectively used to treat a variety of liver disorders at locations all over the world, including hereditary metabolic liver diseases, acute liver failure, and acute-on-chronic liver failure. Additionally, cell treatments may be widely used to treat non-inherited liver illnesses, liver cancer, and other liver diseases. They may help increase the effectiveness of liver transplantation [22].

The liver has several jobs to do, but its part in the body's metabolism is the most important one. Although medicinal care can partially restore hepatic insufficiency-related impairment of this function, OLT is still the gold standard of therapeutic intervention. Other options, like LCT, are suggested because they aren't usually stated or accessible. This operation is completely reversible, less costly, and less invasive than OLT. To date, this treatment has helped over 50 patients. There were other indications, such as FHF, decompensated end-stage cirrhosis, acute on chronic illnesses, and inborn errors of metabolism. As a result, LCT has reached the clinical application stage, and the current indications and protocols are specified. Research topics that are still being explored include stem cell biology, cell quality, and rejection avoidance [23].

Recent developments in the intense interest in using hematopoietic stem cells for regenerative medicine have given us a fresh perspective on the other cell sources that are being studied. In a variety of experimental and therapeutic applications, the main disadvantages and benefits of xenogenic primary cells, tumor-derived cell lines, immortalized hepatocytes, and stem cells are discussed. The convergence of advancements in liver biology, bioengineering, and the development of mechanical components for artificial devices will create exciting opportunities for treating patients with liver failure by customizing the therapeutic choice based on the aetiology and stage of liver disease, even though none of them currently represent a gold standard" in clinical practice [24].

In small animal models, mesenchymal stem cells, also known as multipotent mesenchymal stromal cells (MSCs), have been thoroughly studied for the treatment of both acute and chronic liver damage. Their ability to develop into hepatocyte-like cells, to lower inflammation, and to improve tissue regeneration at the site of injury are some possible mechanisms of action, albeit these are not fully understood. There is a lack of evidence in large animals for this problematic strategy. There have been reports of MSC infusion side effects in experimental settings, including the contribution to a fibrotic process. Still, MSCs made a swift transition from the lab to the bedside, and over 280 registered clinical trials-28 of which are liver disease-focused-have been conducted with the cell. Long-term advantages are still unknown if there haven't been any serious adverse effects reported to date [25].

Herbal Drugs in Treatment of Liver Diseases

The usage of herbal medications has grown significantly in popularity. There is a lack of conclusive evidence supporting the effectiveness of herbal remedies in liver illnesses, and licensing laws and pharmacovigilance related these items are still lacking. However, certain herbal remedies have demonstrated potential efficacy, such as silymarin for treating antifibrosis, phyllantus amarus for treating chronic hepatitis B, glycyrrhizin for treating chronic viral hepatitis, and several herbal combinations from China and Japan that warrant further investigation in suitable research [26].

Numerous plant species and their extracts have demonstrated hepatoprotective properties. The Indian medical system has around 300 treatments for treating chronic liver disorders including jaundice. Worldwide, there are about 600 commercial herbal preparations being offered that claim to have hepatoprotective properties. Numerous plants have been shown to contain the active phytochemical component that confers hepatoprotective effect. It is possible to separate these phytochemicals and create medications with just one ingredient that meet the quality and requirements of contemporary medicine. The main issues with herbal products are their consistency and quality control. The medicinal plant's nutritional status, seasonal variations,

climatic conditions, natural and genetic mutations, and batch-to-batch variances can all lead to variations in efficacies [27].

This study examines a variety of herbal remedies, including milk thistle (Silymarin), licorice (Glycyrrhizaglabra), Liv-52, Camellia sinensis (green tea), and FuzhengHuayu, that are believed to protect the liver. The growing popularity of herbal remedies is a reflection of both the perception that these treatments are safe since they are "natural" and their perceived efficacy in treating and preventing disease. This study offers a general overview of the mechanisms underlying the actions of herbal medicines and assesses the effectiveness of herbal extracts in the treatment of liver illnesses [28].

Animal Models

In order to better understand human etiology and to test new medications and identify therapeutic targets, researchers rely heavily on animal models.

Chronic Liver Disease: Rat models of liver disease in humans are being created. But as of now, no model is able to fully capture the "corresponding" human illness. Limiting variables include the length of time it takes for a particular liver illness to manifest in people as well as the fact that rats' immune systems differ from humans' and that their differing metabolic rates have an impact on liver homeostasis. These characteristics explain why it is challenging to create suitable mouse models for researching the course of diseases and testing novel medications before they are introduced into clinical settings. However, both old and novel potential animal models that replicate specific characteristics of chronic liver illnesses are being utilized to expand our knowledge of the fundamental mechanisms underlying various liver disorders [29].

Using cloned hepatitis B virus DNA as a transgenic in a severely combined immunodeficient host, a model for hepatitis B virus-associated chronic liver disease has been created. These mice reliably facilitate the expression and replication of viral genes. These mice acquired chronic liver illness after adoptively transferring unprimed, syngeneic splenocytes, which eliminated the virus from their liver and serum. In the absence of tolerance, this model will allow the determination of the roles played by the virus and the host in chronic liver disease [30].

Animal Models for Fatty Liver Disease: Globally, non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD) are the primary causes of chronic liver illnesses. A wide range of liver abnormalities, including simple steatosis, fibrosis, cirrhosis, and superimposed hepatocellular carcinoma, are included in ALD and NAFLD [31].

Rats with non-alcoholic fatty liver disease (NAFLD) had various characteristics of the disease, such as inflammation, necrosis, elevated oxidative stress, mismatch between pro- and antioxidant enzyme mRNAs, decreased adiponectin levels, and increased levels of pro-inflammatory mediators. We suggest that a very helpful model for studying non-alcoholic fatty liver disease (NAFLD) is female rats fed a diet rich in highly unsaturated fatty acids [32].

Lately, mesenchymal stem/stromal cells (MSCs) have been suggested as a promising effector in cell-based therapy for ALD and NAFLD. Applications for MSC therapy include hepatoprotection, control over the inflammatory process, and angiogenesis, especially in pre-clinical disease models of ALD and NAFLD. According to recent research, hepatospecific MSC-based treatments may help liver disorders by improving liver function and reducing fibrosis and inflammation. Similar to solid-organ transplantation, the enormous number of cells and donor availability provide challenges for MSC methods, as does cell entrapment in the lungs. In this article, we address the utilization of MSCs as a treatment strategy for ALD and NAFLD based on recent developments, and we present the data that is now available to build a framework for a possible clinical application [33].

Conclusion

The study aims to enhance liver disease diagnosis through patient parameters and genome expression, highlighting drawbacks and suggesting ways to increase their effectiveness. Accurate advanced diagnosis and targeted treatment can help understand the pathophysiological mechanisms of cirrhosis, the precise approach to successful therapeutic treatments, and the mechanisms of fibrogenesis. The research proposes an automatic and efficient method for liver and lesion segmentation from CT images for computer-aided liver diagnosis. Older adults should re-examine certain liver diseases, such as hepatocellular carcinoma, chronic hepatitis C, alcoholic liver disease, and non-alcoholic fatty liver disease, and explore treatment modalities like liver transplantation and antiviral medication.

References

1. Tajiri K, Shimizu Y (2013) Liver physiology and liver diseases in the elderly. World Journal of Gastroenterology 19(46): 8459-8467.

2. Floreani A (2007) Liver Diseases in the Elderly: An Update. Digestive Diseases 25(2): 138-143.

3. Sivakrishnan S, American liver foundation, HEPAMAP, World Health Organization (2019) Liver Diseases-An Overview. World Journal of Pharmacy and Pharmaceutical Sciences 8(1): 1385-1387.

4. National Institutes of Health (NIH) Liver Disease-Research, NIDDK.

5. (2020) Etiology of liver disease in the patients enrolled in the study.

6. (2020) Liver disease.

7. Mondal D, Das K, Chowdhury A (2022) Epidemiology of Liver Diseases in India. Search life-sciences literature 19(3): 114-117.

8. Wolf PL Department of Pathology, University of California and Veteran's Administration Medical Centers (1999) Biochemical Diagnosis of Liver Disease. In Indian Journal of Clinical Biochemistry, pp: 59-90.

9. Sontakke S, Lohokare J, Dani R (2017) Diagnosis of liver diseases using machine learning. International Conference on Emerging Trends & Innovation in ICT (ICEI), pp: 129-133.

10. Romanelli RG, Stasi C (2016) Recent advancements in diagnosis and therapy of liver cirrhosis. Current Drug Targets 17(15): 1804-1817.

11. Kumar SS, Moni RS, Rajeesh J (2013) Automatic liver and lesion segmentation: a primary step in diagnosis of liver diseases. SIViP 7: 163-172.

12. Banerjee R, Pavlides M, Tunnicliffe EM, Piechnik SK, Sarania N, et al. (2014) Multiparametric magnetic resonance for the non-invasive diagnosis of liver disease. Journal of Hepatology 60(1): 69-77.

13. Mueller S, Sandrin L (2010) Liver stiffness: a novel parameter for the diagnosis of liver disease. Hepatic Medicine 2: 49-67.

14. Van Beers BE, Daire J, Garteiser P (2015) New imaging techniques for liver diseases. Journal of Hepatology 62(3): 690-700.

15. Fang C, An J, Bruno A, Cai X, Fan J, et al. (2020) Consensus recommendations of three-dimensional visualization for diagnosis and management of liver diseases. Hepatology International 14(4): 437-453.

16. Hashem EM, Mabrouk MS (2014) A study of Support Vector Machine Algorithm for liver disease diagnosis. In American Journal of Intelligent Systems 4(1): 9-14.

17. Ghosh N, Ghosh R, Mandal V, Mandal SC (2011) Recent advances in herbal medicine for treatment of liver diseases. Pharmaceutical Biology 49(9): 970-988.

18. Muriel P, Rivera-Espinoza Y (2007) Beneficial drugs for liver diseases. Journal of Applied Toxicology 28(2): 93-103.

19. Zhang A, Sun H, Wang X (2013) Recent advances in natural products from plants for treatment of liver diseases. European Journal of Medicinal Chemistry 63: 570-577.

20. Saller R, Meier R, Brignoli R (2001) The use of silymarin in the treatment of liver diseases. In Drugs 61(14): 2035-2063.

21. Feher J, Lengyel G (2012) Silymarin in the prevention and treatment of liver diseases and primary liver cancer. Current Pharmaceutical Biotechnology 13(1): 210-217.

22. Yu Y, Fisher JE, Lillegard JB, Rodysill B, Amiot B, et al. (2012) Cell therapies for liver diseases. In Liver Transplantation 18(1): 9-21.

23. Smets F, Najimi M, Sokal EM (2008) Cell transplantation in the treatment of liver diseases. Pediatric Transplantation 12(1): 6-13.

24. Campli CD, Gasbarrini G, Gasbarrini A (2003) Review article: a medicine based on cell transplantation is there a future for treating liver diseases. Alimentary Pharmacology & Therapeutics 18(5): 473-480.

25. Meier RP, Muller YD, Morel P, Gonelle-Gispert C, Buhler LH (2013) Transplantation of mesenchymal stem cells for the treatment of liver diseases, is there enough evidence. Stem Cell Research 11(3): 1348-1364.

26. Stickel F, Schuppan D (2007) Herbal medicine in the treatment of liver diseases. Digestive and Liver Disease 39(4): 293-304.

27. Girish C, Pradhan S C (2011). Indian herbal medicines in the treatment of liver diseases: problems and promises. Fundamental & Clinical Pharmacology 26(2): 180-189.

28. Rajaratnam M, Prystupa A, Lachowska-Kotowska P, Załuska W, Filip R (2014) Herbal medicine for treatment and prevention of liver diseases. Journal of Pre-Clinical and Clinical Research 8(2): 55-60.

29. Liu Y, Meyer C, Xu C, Weng H, Hellerbrand C, et al. (2013) Animal models of chronic liver diseases. American Journal of Physiology Gastrointestinal and Liver Physiology 304(5): G449-G468.

30. Larkin J, Clayton M, Sun B, Perchonock CE, Morgan JL, et al. (1999) Hepatitis B virus transgenic mouse model of

chronic liver disease. Nature Medicine 5(8): 907-912.

31. Bertola A (2018) Rodent models of fatty liver diseases. Liver Research 2(1): 3-13.

32. Tipoe G, Ho C, Liong EC, Leung T, Lau T, et al. (2009). Voluntary oral feeding of rats not requiring a Very high fat diet is a clinically relevant animal Model of non-alcoholic fatty liver disease (NAFLD). Histol Histopathol 24(9): 1161-1169.

33. Korkida F, Stamatopoulou A, Roubelakis MG (2023) Recent advances in mesenchymal Stem/Stromal Cell-Based therapy for Alcohol-Associated liver disease and non-alcoholic fatty liver disease. Stem Cells Translational Medicine 13(2): 107-115.