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Outcome of Liver Transplantation in Patients with HCV Related Liver Cirrhosis: Review Article

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ABSTRACT

Background: Hepatitis C virus (HCV)-related liver cirrhosis is a leading indication for liver transplantation (LT) globally. Despite advances in antiviral therapies, recurrence of HCV post-transplant remains a significant challenge, impacting graft survival and case outcomes. The introduction of direct-acting antivirals (DAAs) has revolutionized hepatitis C virus management, improving post-transplant prognosis by achieving sustained virological response (SVR) and reducing the burden of reinfection. However, challenges such as donor organ availability, immunosuppressive management, and comorbid conditions continue to influence LT success. Additionally, HCV-associated with cirrhosis was associated with increased possibility of hepatocellular carcinoma (HCC), further complicating patient selection and prognosis.

Objective: This review explored the outcomes of LT in cases with HCV-related cirrhosis, highlighting the recurrence rates, graft survival, and long-term complications. **:** This review also examines the effect of HCV recurrence on graft function, fibrosis progression, & overall survival rates compared to other indications for LT.

Methods: Data were collected from online review articles and papers from the PubMed, Science direct and Google scholar. We searched for Liver Cirrhosis, HCV, and Liver Transplantation. The authors also reviewed references from pertinent literature, however only the most recent or comprehensive studies from 2006 to 2024 were included. Documents in languages other than English were disqualified due to lack of translation-related sources. Papers such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations that were not part of larger scientific studies were excluded.

Conclusion Emerging therapeutic strategies, including antiviral prophylaxis and innovative immunosuppressive regimens, offer promising avenues for improving outcomes. Ultimately, while LT extends survival in HCV-related cirrhosis, long-term management remains critical to optimizing graft function and patient quality of life. Future investigation should focus on refining treatment protocols and addressing the evolving tests of hepatitis C virus in the post-transplant site.

Keywords: Outcome, Liver cirrhosis, HCV, Liver transplantation.

INTRODUCTION

Hepatitis C virus (HCV) infection is a primary etiology of end-stage hepatic disorder requiring transplantation of liver. Major centers indicate that roughly twenty-five to thirty percent of their candidate pools include cases infected with HCV. Currently, around four million Americans are infected with the virus, with an anticipated twenty to thirty percent of these cases likely to develop to cirrhosis. A shortage of donors is the primary cause for organ transplantation, requiring the use of inadequate organs. The prevalence of HCV-positive organ donors makes the effects of utilizing such organs a critical and crucial question. Until recently, the only therapy available for HCV infection involved interferon (IFN) combined with ribavirin, which was effective in only a minority of cases and produced significant treatment-limiting side effects. Recurrence of HCV is common following liver transplantation; among cases with adequate follow-up, virtually all cases transplanted for HCV exhibited biopsy-confirmed cirrhosis within five years. Moreover, early HCV cholestatic recurrence, which restricts graft historically, has traditionally impacted approximately ten percent of liver transplants for HCV. The recurrence of HCV also led to markedly reduced graft & case survival in a comparison with liver transplantation for other causes, such as nonalcoholic steatohepatitis (NASH). Liver transplantation for HCV thus prolonged recipients' lives but ultimately didn't cure them of liver disorder [(1)].

Hepatitis C virus (HCV) infection

Hepatitis C virus (HCV) is a significant health burden, impacting around one hundred and seventy million cases worldwide. Unfortunately, the majority of people infected with Hepatitis C are unable to remove the virus & progress to chronic infection. This rate is greater in cases infected with human immunodeficiency virus (HIV) & diminished in women & kids. Cirrhosis, hepatic decompensation, portal hypertension & hepatocellular carcinoma has been documented as outcomes of chronic HCV infection, with a reported annual mortality exceeding three hundred thousand attributed to HCV infection. Over fifty percent of HCC cases in endemic populations are attributed to chronic HCV infection, which accounts for above six percent of global cirrhosis cases [(2)].

➢ HCV life cycle

Hepatitis C virus is a small encircled RNA virus classified into family Flaviviridae & the genus

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Hepacivirus. Hepatitis C virus (HCV) genomic RNA was single-stranded & of positive division, enveloped by core protein & surrounded by a bilayer of lipid that included 2 glycoproteins of virus (E1 & E2), so constituting the virion. Although sequence of nucleotide distinctions between genotypes, all presently recognized hepatitis C genotypes are pathogenic & hepatotropic [3].

Hepatitis C virus lifecycle begins by binding of a virion to its particular receptors on hepatocytes. To currently, the identified receptors of cells that initiate the bending phase of hepatitis C infection are receptor of high-density lipoprotein scavenger receptor class B type I, tetraspanin CD81, tight junction protein claudin-1, & occludin. The virus is proposed to interact with its receptor complex, be suppressed, & release the nucleocapsid inside the cytoplasm. The virus subsequently initiates uncovering to secrete its RNA genome, utilized for both polyprotein conversion & reproduction within the cytoplasm. Replication of HCV occurs inside the "replication complex," which comprises viral cellular proteins & non-structural proteins. The NS5B protein catalyzes hepatitis C virus replication. Nonetheless, further viral nonstructural proteins are equally significant. The NTPase/helicase domain of the NS3 protein performs multiple critical activities for replication of virus, involving RNA-activated NTPase activity, binding RNA, & RNA unwinding units with significant 2ry structure. NS4B induces the formation of a replication complex that facilitates replication of hepatitis C virus. The NS5A protein has an essential regulatory function in viral replication. New direct-acting antivirals (DAAs), particularly created to block the NS5B RNA-dependent RNA polymerase, are increasingly become accessible. Many recent direct-acting antivirals (e.g., NS5A protein inhibitors) have demonstrated potential in clinical trials [4].

Several cellular components are included in replication of hepatitis C virus, including cyclophilin A, which is necessary for HCV replication by interacting with NS5B & NS5A, & microRNA-122, which facilitates hepatitis C virus replication by binding to the 5' untranslated region (5' UTR) of the hepatitis C virus genome. Consequently, host variables may serve as prospective targets for anti-HCV therapy. Currently, a minimum of 2 host-targeted medicines (HTAs) have reached clinical improvement, involving selective suppressors of cyclophilin A & antagonists of microRNA-122 [5].

Pathogenesis of HCV Infection:

The molecular pathways behind chronic infection development have been intensively examined however remain inadequately comprehended. Some investigations indicate that the removing of infection relates with the initial emergence of antibody with broad neutralizing reactions through severe HCV infection, while a delayed stimulation of these antibodies in the later stages is associated with chronic HCV infection. Conversely, other investigations have found no correlation among neutralizing antibodies and infection clearance. In addition to antibody reactions, cellular immune reactions play a protecting goal in the result of acute HCV infection, with strong & polyfunctional Hepatitis C virus-specific T cell reactions facilitating spontaneous infection clearance, while weak or restricted T cell reactions result in long-lasting infection [6].

The functional part of cytotoxic T lymphocyte (CTL) reactions indicates that CD4+ T cells are essential for reducing immune evasion & initiating effective memory cytotoxic T lymphocyte in the resolution of severe hepatitis C virus infections in humans & experimentally infected chimpanzees. In contrast, through long-lasting hepatitis C virus infection, both CD4+ & CD8+ T cells experience rapid exhaustion due to diminished interleukin-2 (IL-2) production & heightened appearance of the programmed death 1 (PD-1) molecule, correspondingly. Following the launch of 1st generation, direct-acting antiviral drugs in 2011, the preservation of immune cells, such as natural killer cell activity, is achieved via interferon-free therapy. Moreover, an elevated frequency of CD8+ T cells & a partial reversion of exhaustion indicators on HCV - specific T cells were seen in cases with chronic HCV. Nevertheless, other investigations indicate that CD8+ T cell expansion exerts a restricted influence following the eradication of HCV. These investigations indicate that host genetic diversity affects hepatitis C virus pathogenesis, involving the onset of chronicity & immunological responses to the infection [7].

Clinical and histopathologic features of hepatitis C:

Acute hepatitis C virus infection frequently occurs sub-clinically, with a substantial percentage of patients staying without symptoms. The initial phase of acute HCV may occur in certain infected cases, presenting symptoms typical of acute viral hepatitis, such as malaise, lethargy, nausea, anorexia, abdominal pain, dark urine, jaundice, & pale feces. Fulminant hepatitis, characterized by a severe & quick decline in function of liver, occurs infrequently in the context of hepatitis C virus. The duration from hepatitis C virus exposure to onset of symptoms or laboratory indicators of liver damage (time of incubation) may range significantly, spanning from 2 - 20 weeks, with a typical manifestation occurring around seven weeks. The principal laboratory indicator of acute hepatitis C virus infection is often high alanine aminotransferase (ALT) & aspartate aminotransferase (AST) values, signifying hepatocyte destruction. Post-hepatitis C virus infection, viremia is rapidly identifiable,

increasing between hundred thousand & ten million IU/mL within several weeks [8].

A reduction in viral load frequently occurs 1-2 weeks later, corresponding with a significant elevation in alanine aminotransferase & aspartate aminotransferase concentrations. This pattern illustrates the immune system's reaction to hepatitis C virus infection, which facilitates hepatocyte death & significantly affects the pace of spontaneous viral clearance. Thus, elevated initial hepatitis C virus viremic concentrations & more severe acute HCV manifestations are associated with increased risks of spontaneous clearance. Spontaneous resolution of HCV generally occurs in 6 months of infection. A greater possibility of viral clearance was noted in cases with symptoms, women, & younger cases. In contrast, spontaneous remission of HCV infection is less probable in those co-infected with human immunodeficiency virus, intravenous drug users, or those of black ethnicity. The recognition of particular alleles adjacent to the IL28B gene, which encodes interferon-lambda 3 (IFNλ3), produced significant visions into the genetic factors affecting HCV infection outcomes. These alleles are similarly indicative with spontaneous healing from severe hepatitis C virus. Spread of the protective IL28B genotype (CC genotype against CT/TT genotypes) demonstrates significant racial differences, become more common in Asian cases & considerably fewer so in cases of African origin. In common of cases (sixty percent to eighty-five percent) who don't experience spontaneous clearance of HCV infection, prolonged infection develops as a highly varied illness, marked by a range of clinical symptoms & rates of progression. Significant morbidity & mortality generally occur after the infection progresses to cirrhosis or last-stage liver disorder, perhaps leading to hepatocellular carcinoma (HCC) [9].

Among chronically infected HCV cases, the concentration of HCV RNA in blood are mostly consistent over time, usually changing, & may range above one million IU/mL. Several characteristics correspond with elevated loads of virus, involving HIV co-infection, advanced age, male sex, and elevated BMI. In contrast, cases with dual hepatitis B virus infection or more severe liver disorder typically show reduced viral levels. Chronic HCV virus infection produces a range of histological alterations in the liver, mainly marked by varying degrees of prolonged inflammation & steatosis. Frequent periportal lymphocytic infiltrates are observed, although they don't reliably forecast the development of hepatic disorder progression. In prolonged HCV, a difference in the progression of substantial fibrosis is observed, with some persons displaying pronounced fibrotic alterations following extended viral infection, while others demonstrate minimal impacts, the underlying cause of which remains to be fully clarified. Fibrosis arises from an imbalance in matrix dynamics outer cells, characterized by synthesis of collagen more than its degradation, commencing in the periportal regions. The process of fibrosis can either stabilize or progress to more severe structural changes, involving development of septae that connect nearby lobules. Progressing outside this phase results in cirrhosis, marked by significant scarring & nodular regrowth of the liver. As cirrhosis progresses, problems such portal HTN arise, increasing the possibility of hepatocellular carcinoma because of neoplastic changes in the liver parenchyma. Comprehending the pathophysiological mechanisms leading to end-stage hepatic disorder is essential for prompt & efficient therapeutic measures to hinder or reverse fibrosis in chronic HCV infection. The possibility of hepatocellular carcinoma (HCC) in prolonged HCV infection is substantial, requiring vigilant screening techniques for cirrhosis & hepatocellular carcinoma. This proactive strategy of HCV screening is essential because chronic hepatitis C virus often progresses asymptomatically until cases reach severe stages [10].

The goal of HCV in the direct introduction of oncogenic procedures is still being examined. Increasing data indicates that hepatitis C virus-C protein participates in oncogenic modulation by stimulating proto-oncogenes & inhibiting pathways of apoptotic. Nonetheless, it is plausible that prolonged inflammation characteristic of persistent HCV infection significantly facilitates oncogenesis, resulting in the emergence of HCC. Ultimately, chronic HCV infection is associated with numerous extrahepatic symptoms, primarily of an inflammatory nature. These signs complicate clinical therapy of hepatitis C virus, indicating necessity to define the larger systemic implications of prolonged infection of HCV [11].

Liver cirrhosis:

Cirrhosis is defined by fibrosis & nodule formation in the liver, leads to persistent damage that affects the normal lobular liver structure. Different incidents may harm the liver, involving viral infections, chemicals, autoimmune mechanisms, or genetic disorders. With every insult, the liver develops scar tissue (fibrosis), firstly retaining its functionality. Following a protracted insult, the majority of liver tissue becomes fibrotic, resulting in functional impairment & the onset of cirrhosis [12].

- **Incidence in Egypt:** Liver disorders in Egypt are prevalent, with several documented etiologies involving parasitic, viral, bacterial, & metabolic origins. According to the Egyptian demographic health census, the estimated prevalence of liver illnesses among Egyptians aged one to sixty-nine years was 2.9%. Prior to the HCV pandemic, schistosomiasis represented a significant public health

issue in Egypt. Over the decades, HCV has been prominent among Egyptians, exhibiting the highest rate globally. In 2015, the prevalence of HCV viraemia within the population was approximately 4.4%. Hepatocellular carcinoma, arising as a consequence of liver cirrhosis, has emerged as the predominant cancer in Egyptian males & the 2nd most prevalent cancer in Egyptian females [13].

- **Etiology:** Chronic liver disorders typically develop to cirrhosis. In industrialized nations, the predominant etiologies of cirrhosis are hepatitis C virus, alcoholic liver disease, & nonalcoholic steatohepatitis, whereas in underdeveloped nations, HBV & HCV are the primary etiologies. Additional etiologies of cirrhosis involve AIH, 1ry cholangitis of bile duct, 1ry sclerosing cholangitis, Wilson's disease, hemochromatosis, deficiency of alpha-1 antitrypsin, drug-induced liver cirrhosis, Budd-Chiari syndrome & chronic right-sided heart failure. Cryptogenic cirrhosis is characterized as cirrhosis of indeterminate origin [13].

- **Mechanism of liver cirrhosis:** Many types of cells produce hepatic cirrhosis, involving hepatocytes & sinusoidal covering cells like hepatic stellate cells (HSCs), sinusoidal endothelial cells (SECs), & Kupffer cells (KCs). Hepatic stellate cells constitute a constituent of the liver sinusoidal wall, & their role is to store vitamin A. Upon exposure to inflammatory cytokines, these cells become stimulated, separated into myofibroblasts, & initiate collagen deposition, leading to fibrosis. Sinusoidal endothelial cells form covering of endothelium & are distinguished by fenestrations they create in the wall, facilitating the exchange of nutrients & liquid among hepatocytes & sinusoids. Defenestration of the sinusoidal wall may occur as a consequence of chronic alcohol consumption, leading to fibrosis in perisinusoidal region. Kupffer cells are satellite macrophages that also border the walls of sinusoids. Investigation primarily utilizing animal models has demonstrated their involvement in liver fibrosis through the release of harmful mediators upon exposure to damaging substances & their function as antigen-presenting cells for viruses. Hepatocytes contribute to the pathophysiology of cirrhosis by releasing reactive oxygen species & inflammatory mediators upon injury, which may activate hepatic stellate cells & induce liver fibrosis [15].

The primary etiology of mortality & morbidity in cirrhotic cases is a start of portal HTN & hyperdynamic circulation. Portal HTN arises as a result of fibrosis & changes in vasoregulation, both intrahepatically & systemically, leading to the development of collateral circulation & hyperdynamic circulation. Intrahepatically, sinusoidal endothelial cells release both endothelin-1 (ET-1) & nitric oxide (NO), which affect hepatic stellate cells, resulting in either contraction or relaxation of sinusoids, so regulating sinusoidal blood flow. In cases with cirrhosis, there is an elevation in production of endothelin-1, accompanied by increased receptor sensitivity & a decrease in nitric oxide production. This results in heightened intrahepatic vasoconstriction & resistance, hence commencing portal HTN. The contractile actions of hepatic stellate cells in the sinusoids facilitate vascular remodeling, hence enhancing vascular resistance. Collateral circulation is established to reduce the rise in intrahepatic pressure. In systemic & splanchnic circulation, an elevation in nitric oxide generation occurs, causing vasodilation & a reduction in resistance of systemic vessels. This stimulates the activation of the renin-angiotensin-aldosterone system (RAAS), causing water & salt retention, which results in a hyperdynamic circulation. In cirrhosis accompanied by portal HTN, there is a reduction of vasodilators, mainly nitric oxide (NO), within the liver, whereas an elevation of NO exists outer the liver in the splanchnic & systemic circulation, resulting in sinusoidal vasoconstriction & splanchnic (systemic) vasodilation. The collaterals enhance hyperdynamic circulation trough elevating venous return to the heart. [16].

- **Diagnosis**

The medical history & physical examination may show cases with or at possibility for cirrhosis. Cases with cirrhosis often suffer from muscle cramps (64% prevalence), pruritus (39%), inadequate sleep quality (63%) & sexual dysfunction (53%). Risk factors, including diabetes & alcohol consumption, together with symptoms like muscle cramps, pruritus, sleep disturbances, & sexual dysfunction lack both sensitivity & specificity for diagnosing cirrhosis. Most physical examination findings lack sensitivity for cirrhosis. However, some exhibit specificity exceeding ninety percent, involving Terry's nails (characterized by white discoloration, absent lunula, & dark pink tips), gynecomastia, facial telangiectasia, caput medusae, palmar erythema, reduced body hair, testicular atrophy, & jaundice [17].

Imaging and hepatic biopsy:

Various imaging modalities are utilized in conjunction with laboratory tests to assist in the identification of cirrhosis. These modalities involve ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), & transient elastography (FibroScan). **Ultrasonography** is an economical, noninvasive, & accessible method for assessing cirrhosis. It may identify nodularity and heightened echogenicity of the liver, indicative of cirrhosis. Nevertheless, these results are nonspecific as

they may also arise in fatty liver disease. It may also regulate the rate of caudate lobe width to width of right lobe, which naturally elevates in cirrhosis. Also, it assists as an effective screening instrument for hepatic cell carcinoma in cases with cirrhosis. Duplex Doppler US facilitates the evaluation of the patency of hepatic, portal, & mesenteric veins. **CT & MRI** with contrast may identify hepatocellular carcinoma & vascular injuries, with MRI demonstrating superiority over computed tomography. Magnetic resonance imaging can also identify iron & fat deposition concentrations in the liver for steatosis & hemochromatosis, in addition to blockage of bile duct when an MRC (magnetic resonance cholangiography) is conducted. Magnetic Resonance Imaging (MRI) is, however, costly & not easily accessible [(18)].

Transient elastography (FibroScan): Is a non-invasive technique utilizing high-frequency US pulses to assess stiffness of liver, which is indicative of fibrosis. In cirrhosis, a scan of colloid liver-spleen utilizing technetium-99m sulfur colloid can demonstrate heightened colloid uptake in the bone marrow & spleen relative to the liver. The existence of esophageal varices or stomach on esophagogastroduodenoscopy (EGD) recommends portal hypertension. **Liver biopsy** is the gold standard for detecting cirrhosis in addition to determining the inflammation degree (grade) & fibrosis (stage) of the disease. However, it may miss the diagnosis at times because of sampling mistakes. The identification of cirrhosis via biopsy involves the identification of fibrosis & nodules. The nodular pattern might be macronodular, micronodular, or mixed with the micronodular pattern being an independent risk factor for greater hepatic venous pressure gradient (HVPG) & more severe illness. Noninvasive assays utilizing direct & indirect serum indicators were utilized to differentiate cases with substantial fibrosis or cirrhosis from those with no or mild fibrosis [(17)].

➢ Complications

Complications associated with hepatic cirrhosis may involve [(19)]:

• Portal HTN. • Swelling in the belly & lower extremities. • Jaundice. • Hepatic encephalopathy. • Splenomegaly. • Hemorrhage. • Infections.

➢ Treatment/Management

Liver damage is irreversible. However, further liver harm should be prevented to arrest the development of the disease. General treatment to inhibit prolonged hepatic disease involves prevention of alcohol, immunization for hepatitis B virus & hepatitis C virus, proper nutrition with a balanced food, reduction of weight, & early management of progressing causes such as hypotension, dehydration, & infections. This is accomplished through regular assessment of volume status, renal function, variceal progression, & development to hepatocellular carcinoma. Particular therapy typically addresses the underlying causes, such as antiviral agents for hepatitis of virus, corticosteroids & immunosuppressants for AIH, ursodeoxycholic a` & obeticholic a` for 1ry biliary cholangitis, chelation of copper for Wilson's disorder, & iron chelation along with hemochromatosis phlebotomy. A minimum weight reduction of seven percent is advantageous in non-alcoholic steatohepatitis (NASH), & complete abstinence from alcohol is essential in alcoholic cirrhosis [(20)].

Liver Transplantation

Liver transplantation (LT) can be curative or extend life for properly chosen cases with acute liver failure, severe cirrhosis, hepatic malignancies, or congenital metabolic abnormalities. Recent developments in surgical procedures, organ preservation & procurement, & immunosuppressive have led to significant enhancements in liver transplantation, evidenced by improved case survival rates, graft longevity, & overall quality of life. **Duffy *et al.*** [(21)] stated a twenty-year actuarial survival rate of fifty-two percent for cases & forty-two percent for grafts following transplantation. They additionally documented enhanced health-related quality of life in twenty-year survivors than control cases with chronic liver disease, diabetes, or congestive heart failure. LT is now considered a reliable surgical procedure and is the preferred treatment for certain disorders that significantly impair hepatic function.

Indications:

Liver transplantation may be required in cases of acute & chronic end-stage hepatic disorder when medical treatment has proven ineffective. Cases having hepatic decompensation, involving variceal hemorrhage, hepatic encephalopathy, or ascites, should undergo medical treatment, & a thorough evaluation for liver transplantation must commence for suitable candidates. As much as eighty percent of liver transplantations result from decompensated cirrhosis. Cases with cirrhosis are typically classified based on the Child-Turcotte-Pugh score (CTP score). This score has been initiated by integrating biochemical assays & clinical data (serum albumin, serum bilirubin, international normalized ratio (INR), encephalopathy and ascites) to assess prognosis [(22)].

Particular indications for hepatic transplantation [(23)]:

1 Graft failure is a significant sign for hepatic transplantation. Hyper acute rejection resulting in thrombosis of hepatic artery & failure of graft happens rapidly through the postoperative period. While re-

transplantation is possible, the results are lower compared to that of the initial transplant.

2 Chronic hepatitis C leading to cirrhosis was a predominant reason for transplantation of liver until 2015. Since 2016, decompensated cirrhosis resulting from prolonged hepatitis C infection has emerged as the greatest 3rd prevalent indication for transplantation of liver, surpassed associated with alcohol-induced hepatic disorder & NASH. To prevent re-infection following hepatic transplantation & subsequent failure of graft, it was essential to eliminate prolonged HCV infection before to the procedure. Nonetheless, new direct antiviral medicines have emerged in the past decade, facilitating chronic HCV treatment following liver transplantation.

3 Hepatitis B infection traditionally led to a rising incidence of chronic hepatic disorder; however, the utilization of Hepatitis B Immunoglobulins (HBIG) & the advent of antiviral therapies has contributed to a reduction in liver transplantation rates. Additionally, controlling and managing the infection is essential to prevent re-infection following the transplant. Hepatitis B may lead to hepatocellular cancer, which is an important factor for transplantation of the liver.

4 Autoimmune hepatitis (AIH) may causes liver cirrhosis & failure, despite prolonged corticosteroid & immunosuppressive therapy. Liver transplantation should be considered in acute hepatic failure resulting from AIH or in cases of chronic cirrhosis attributable to AIH. Poor prognoses & the necessity for transplantation of the liver may be anticipated based on the following indicators: youthful age, a MELD score exceeding twelve recurrent relapses, & a protracted decline in aminotransferase concentrations post-treatment.

5 Cases of primary biliary cirrhosis (PBC) exhibiting severe pruritus or decompensated cirrhosis unresponsive to alternative medical treatments necessitate transplantation of the liver. Over the years, the necessity for transplantation of the liver has diminished due to the administration of Ursodeoxycholic a` for the treatment of PBC, which decelerates disease progression.

6 Liver transplantation is contemplated for early-stage cholangiocarcinoma cases featuring nonresectable perihilar lesions (below three centimeters in diameter) or associated parenchymal liver disease, like 1ry sclerosing cholangitis with cirrhosis. Liver transplantation must be performed with regimens of neoadjuvant chemotherapy to achieve increased survival rates compared to transplantation of liver conducted without neoadjuvant therapy. Cases receive a MELD exception upon meeting the requirements for qualifying for the UNOS waiting list.

7 NASH is regarded as primary causes for hepatic transplantation. Nonalcoholic steatohepatitis is part of the continuum of nonalcoholic fatty liver disorder, which ranges from isolated steatosis to NASH with concurrent cirrhosis. Liver problems are associated with metabolic syndrome, characterized by elevated body mass index (BMI) & obesity. Liver transplantation has been increasing because of nonalcoholic steatohepatitis, as there is currently no effective management for nonalcoholic steatohepatitis or fibrosis. Cases diagnosed with nonalcoholic steatohepatitis, both with & without cirrhosis, exhibit an elevated risk of developing hepatic cell carcinoma.

8 Liver transplantation is required for cases with severe liver failure resulting from Wilson syndrome or in patients of decompensated cirrhosis unresponsive to all medicinal treatments. Transplantation of liver in Wilson disease provides favorable results, even in patients with metabolic problems such as kidney failure, which resolves post-transplantation. Heterozygous parent's cases may participate in living donor liver transplantation (LDLT), producing good outcomes.

9 Other problems associated with cirrhosis, including hepatopulmonary syndrome & portopulmonary hypertension, also warrant liver transplantation.

10 Liver transplantation is required in cases of decompensated cirrhosis or in cases with hepatocellular carcinoma who have hereditary hemochromatosis (HH). Cirrhosis resulting from hereditary hemochromatosis has the greatest likelihood for the development of hepatocellular carcinoma compared to all other etiologies of cirrhosis. Iron reduction therapy via phlebotomy before to transplantation has led to enhanced results following liver transplantation.

Technique

Any liver transplant technique contains 2 components, the recipient & the donor:

Recipient operations: Are accomplished with the complete excision of the case's native liver following the division of the hepatic ligamentous attachments & hilar structures. The inferior vena cava (IVC) must be enclosed to make sure sufficient blood regulator. Donors are classified as either deceased or living [24].

Deceased donor liver transplantation (DDLT): (It isn't applied in Egypt). The liver of donor is typically organized on a distinct table, & following the body of recipient is ready, the liver of donor is transferred to table, where anastomoses are subsequently performed. Initially, the suprahepatic inferior vena cava is got involved, subsequently the infra hepatic inferior vena cava, and finally the portal vein. Following completion of these

stages, the clamps are detached, & the portal vein starts the influx of blood to perfuse the liver. The hepatic arteries of both the receiver & donor are joined around the gastroduodenal artery anastomoses, followed by the reconstruction of the bile duct. In 2003, the initial effort at a split graft has been executed, wherein the liver from a reduced donor is separated for transplantation into 2 receivers; right lobe is utilized as an allograft in absence of middle hepatic vein, identical to the improved procedure utilized in living donor liver transplantation (LDLT) for grafts of right lobe, while left segment of liver, including of the common hepatic artery & the IVC, is also utilized [(24)].

Living Donor Liver Transplantation (LDLT): Once, living donors were exclusively utilized in pediatric situations necessitating liver transplantation. Given the rising demand for liver transplants & the scarcity of reduced donors, living donors are also utilized in adult cases. Liver transplantation from living donors is more intricate & necessitates meticulous dissection.

A living donor graft is partial, in contrast to the complete transplant obtained from a reduced donor. A graft of living donor shows a significantly smaller hepatic artery, portal vein, & hepatic vein that require implantation. Thus, it is essential to create sufficient space by incising the hepatic vein laterally to facilitate sufficient causes of arterial hepatic, portal, & reconstruction of bile duct [(24)].

The anastomosis is conducted for the hepatic vein, requiring sufficient length for the procedure, followed by the portal vein, & lastly the hepatic artery, which presents challenges because of numerous short branches. Finally, duct-to-duct anastomosis is carried out for the bile duct. Grafts obtained from a living donor involve left lateral sector, accounting for twenty percent of the total volume of liver; the left lobe, representing forty percent of the capacity; and the right lobe, constituting the remaining sixty percent of the hepatic volume.

Occasionally, dual grafting is utilized, whereas two left lobes from separate donors are transplanted into a single recipient. Every donors having hepatectomy exhibit a distinctive incision in the right subcostal area that continues into midline, hence preserving division of the rectus muscle bilaterally. In patients of right hepatic lobe donation, left lobe must be fixed to the anterior wall of abdomen prior to closure of wound [(25)].

➢ Complications

Complications are either late or early post-hepatic transplantation [(23)] :

- **Early complications:** • 1ry non-function of the hepatic allograft. • Acute cell rejection. • Thrombosis of hepatic artery. • Infection. • Biliary complications.
- **Late complications:** • Complications associated with immunosuppression. • Recurrent disease after transplantation of the liver. • De novo malignancy.

CONCLUSION

Emerging therapeutic strategies, including antiviral prophylaxis and innovative immunosuppressive regimens, offer promising avenues for improving outcomes. Ultimately, while LT extends survival in HCV-related cirrhosis, long-term management remains critical for optimizing graft function and patient quality of life. Future investigation should focus on refining treatment protocols and addressing the evolving tests of hepatitis C virus in the post-transplant site.

Ethical Considerations: The research ethics committee of the El-Sahel Teaching Hospital, General Surgery Department, accepted the research protocol with following the Helsinki Declaration (2013). Informed written consents were obtained, ensuring data confidentiality and the right to withdraw at any time. Patients incurred no costs, were informed of all results, received appropriate care, and had direct contact with the researcher.

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