International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 1 Jan-Feb 2021, pp: 1062-1072 www.ijprajournal.com ISSN: 2249-7781

Treatment of Liver Cancer

Anuja Anil Burande, Mr. L.D. Hingane, Mr. Hingane L.D.
Aditya pharmacy college, beed

Date Of Submission: 15-02-2021 Date Of Acceptance: 02-03-2021

ABSTRACT: Deaths from liver cancer are common, especially in East Asia and Pacific, South Asia, and parts of Sub-Saharan Africa, largely as a result of infection decades ago. As the toll from other cancers is likely to climb in the coming decades, however, liver cancer incidence and mortality rates should fall, as generations vaccinated against the hepatitis B virus (HBV)—the cause of most liver cancers globally—reach middle and old age. Much still needs to be done and it is feasible and affordable to hasten the decline. Much can also be done to address other causes of liver cancer—including some on the rise, in particular, obesityrelated non-alcoholic fatty liver disease (NAFD)—in the coming years and decades. The latter half of the twentieth century witnessed the identification of the main causes of liver cancer and deployment of the first cancer prevention vaccine for humans. All of the risk factors that lead to cirrhosis cause at least as many noncancer deaths as cancer deaths. Controlling these risk factors would not only reduce the incidence of liver cancer; it would also reduce the incidence of cirrhosis and its other complications, notably, end-stage liver disease and portal hypertension.

I. INTRODUCTION

"Cancer is when cells in the body change and grow out of control. Your body is made up of tiny building blocks called cells".

Normal cells grow when your body needs them, and die when your body does not need them any longer.

Cancer is made up of abnormal cells that grow even though your body doesn't need them. In most cancers, the abnormal cells grow to form a lump or mass called a tumor. If cancer cells are in the body long enough, they can grow into (invade) nearby areas. They can even spread to other parts of the body (metastasis)

"Liver cancer is cancer that starts in your liver. This is also called primary liver cancer".

Primary liver cancer is not the same as cancer that started somewhere else in the body and then has spread (metastasized) to the liver. Cancer that starts in another organ, such as the colon, breast, or lung, and then spreads to the liver is called secondary liver cancer. Secondary liver cancer is more common in the U.S. than primary liver cancer. Cancer that has spread to the liver from somewhere else is treated like the original cancer. For instance, lung cancer that has spread to the liver is treated like lung cancer.

Description Of Liver

The liver is a large, pyramid-shaped organ that lies behind the ribs on the right side of the body. It's under the right lung. It is divided into right and left lobes.The liver helps break down nutrients. These include sugars, starch, fats,and proteins. It also stores some of these. The liver also makes proteins, such as albumin. This helps the body balance fluids. It also makes clotting factors, which help blood thicken or clot when a person is bleeding. Bile made in the liver is important for digesting food and for other bodily functions.One of the liver's most important jobs is to filter out and destroy toxins in the body. When the liver isn't working well, chemicals can build up inside the body and cause damage.

The liver is located in the upper right-hand portion of the abdominal cavity, beneath the diaphragm, and on top of the stomach, right kidney, and

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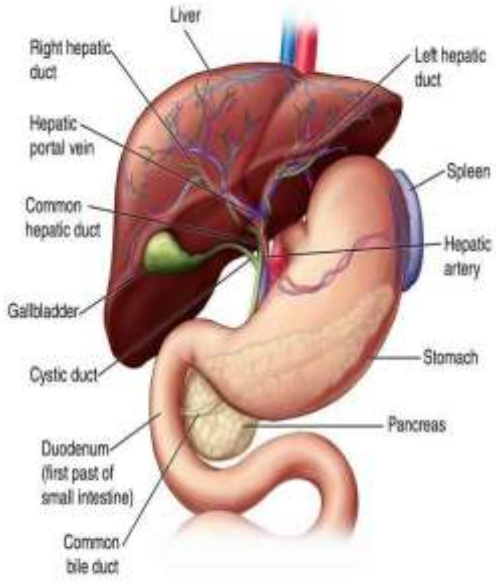
intestines.Shaped like a cone, the liver is a dark reddish-brown organ that weighs about 3 pounds.
There are 2 distinct sources that supply blood to the liver, including the following:
Oxygenated blood flows in from the hepatic artery
Nutrient-rich blood flows in from the hepatic portal vein

The liver holds about one pint (13%) of the body's blood supply at anygiven moment. The liver consists of 2 main lobes. Both are made up of 8 segments that consist of 1,000 lobules (small lobes). These lobules are connected to small ducts (tubes) that connect with larger ducts to form the common hepatic duct. The common hepatic duct transports the bile made by the liver cells to the gallbladder and duodenum (the first part of the small intestine) via the common bile duct.

Functions of the liver

The liver regulates most chemical levels in the blood and excretes a product called bile. This helps carry away waste products from the liver. All the blood leaving the stomach and intestines passes through the liver. The liver processes this blood and breaks down, balances, and creates the nutrients and also metabolizes drugs into forms that are easier to use for the rest of the body or that are nontoxic. More than 500 vital functions have been identified with the liver. Some of the more well-known functions include the following:Production of bile, which helps carry away waste and break down fats in the small intestine during digestion.
Production of certain proteins for blood plasma.
Production of cholesterol and special proteins to help carry fats through the body.
Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy) and to balance and make glucose as needed .
Regulation of blood levels of amino acids, which form the building blocks of proteins.
Processing of for use of its iron content (the liver stores iron).
Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine).
Clearing the blood of drugs and other poisonous substances
Regulating blood clotting.
Resisting infections by making immune factors and removing bacteria from the bloodstream.
Clearance of bilirubin, also from red blood cells. If there is an accumulation of bilirubin, the skin and eyes turn yellow.

When the liver has broken down harmful substances, its by-products are excreted into the bile or blood. Bile by-products enter the intestine and leave the body in the form of feces. Blood by-products are filtered out by the kidneys, and leave the body in the form of urine.



Liver

Symptoms

- Most people don't have signs and symptoms in the early stages of primary liver cancer. When signs and symptoms do appear, they may include:
- Losing weight without trying.
- Loss of appetite.
- Upper abdominal pain.
- Nausea and vomiting.
- General weakness and fatigue.
- Abdominal swelling.
- Yellow discoloration of your skin and the whites of your eyes (jaundice).
- White, chalky stools.
- Swelling or fluid build-up in the abdomen (belly)Itching.

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Transmission

The cells in our bodies have a regulated system of growth and division. New cells are formed to replace older cells as they die. Occasional DNA damage results in abnormal cell production. But our immune system does a pretty good job of keeping them under control. It's a system that serves us well.Cancer cells don't follow these regulations. Part of their abnormality is that they continue to reproduce even though old cells aren't dying off.This uncontrolled growth of abnormal cells is what forms a tumor. And because they keep reproducing, they can metastasize (spread) locally and to distant sites. Liver cancer, like other types of cancer, can spread in three ways.
Through
Tissue. Cancer cells break off from the primary tumor in the liver and form
New tumors in nearby tissues.
In the
Lymph system. Cancer cells make their way into nearby lymph nodes. Once in
The lymph system, cancer cells can be transported to other areas of the body.
Through
The circulatory system. Cancer cells get into the bloodstream, which
Carries them throughout the body. Anywhere along the way, they can establish
New tumors and continue to grow and spread.
No matter where your metastatic tumors form, it's still liver cancer and will be treated as such.

Liver Stages

The stage of a cancer tells you its size and whether it has spread. It helps your doctor decide which tr eatment you need.
The tests and scans you have to diagnose your cancer give some information about the stage. There are different staging systems that doctors can use to stage cancer that started in the liver (primary liver cancer).
The stage of a cancer tells you its size and whether it has spread. This is important because your doctor uses this information to help decide which treatment you need. The tests you have after being diagnosed with liver cancer help stage your cancer.
There are different staging systems your doctor can use. The staging systems used to describe the size and position of liver cancer are the:
1.TNM staging system
2.Number staging system
1.TNM stands for Tumour, Node, Metastasis. It describes:
The size of the primary tumour (T)
Whether the cancer has spread to the lymph nodes (N)
Whether the cancer has spread to another part of the body (M)
The TNM system is used for cancer staging all over the world. It is important for doctors to use the same staging system because then they can be sure they are all talking about the same situation when they are comparing notes or carrying out research.
2.Number staging systems use the TNM system to divide cancers into stages. Most types of cancer have 4 stages, numbered from 1 to 4. Doctors often write the stage down in Roman numerals. So they may write stage 4 as stage IV.
Here is a brief summary of what the stages mean for most types of cancer:
Stage 1 usually means that a cancer is small and contained within the organ it started in

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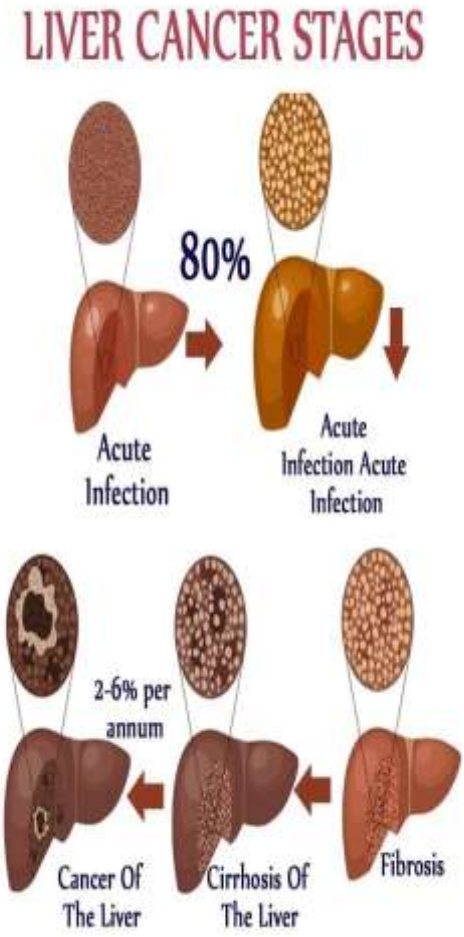
Stage 2 usually means that the tumour is larger than in stage 1 but the cancer hasn't started to spread into the surrounding tissues. Sometimes stage 2 means that cancer cells have spread into lymph nodes close to the tumour. This depends on the particular type of cancer

Stage 3 usually means the cancer is larger. It may have started to spread into surrounding tissues and there are cancer cells in the lymph nodes nearby.



Diagnosis

A thorough and accurate cancer diagnosis is the first step in developing a liver cancer treatment plan. Your team of liver cancer experts will use a variety of tests and tools designed for diagnosing liver cancer, evaluating the disease and developing your individualized treatment plan. Throughout your treatment, we'll use imaging and laboratory tests to track the size of the tumors, monitor your response to treatment, and modify your plan when needed.

Examples of procedures for diagnosing liver cancer include:

Biopsy: Once liver cancer has been diagnosed, your doctor will obtain a tissue sample to determine the type and stage of the disease, choosing from several biopsy methods, including fine needle aspiration (FNA) biopsy, core needle biopsy or laparoscopic biopsy. Laparoscopy is a minimally invasive method of obtaining a tissue sample without the risks of surgery.Bone scan: If you are experiencing bone pain or blood tests reveal elevated calcium levels, your radiation oncologist may perform a bone scan to detect whether liver cancer has spread to the bone.

CT scan: A CT scan can provide precise information about the size, shape and position of tumors in the liver or elsewhere in the abdomen, as

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well as nearby blood vessels. CT scans may also be used to guide a biopsy needle precisely into a suspected tumor (CT-guided needle biopsy).

Lab tests: To diagnose liver cancer, your doctor will perform a variety of liver function tests to assess the function of the liver by measuring the level of certain proteins or waste products in the blood. These tests may also be used to develop a treatment plan and evaluate your response to it.

MRI: These scans may help distinguish between benign and malignant tumors. They may also be used to examine blood vessels in and around the liver.

PET/CT: This test may help doctors determine whether the liver cancer has spread to areas such as the bones or lungs.

Ultrasound: This test may be recommended every six to 12 months to assess the progress of treatment.

Treatment

The appropriate liver cancer treatment plan is created only after the patient's health and the progression of cancer is determined. The oncologist may use one or more treatment methods for liver cancer.

1.Surgery

The doctor removes the cancerous tissue, in case of preliminary stage cancer

2.Hyperthermia

The doctor uses heat therapy to kill the cancerous cells

3.Percutaneous ethanol injection

Alcohol is injected into the tumor to destroy it

4.Radiation therapy

High energy X rays are used to kill cancer cells.

5.Chemotherapy / Target therapy

Chemotherapy and target therapy drugs are used to kill cancer cells.

1.Surgery

Surgery is the removal of the tumor and some surrounding healthy tissue during an operation. It is likely to be the most successful disease-directed treatment, particularly for patients with good liver function and tumors that can be safely removed from a limited portion of the liver. Surgery may not be an option if the tumor takes up too much of the liver, the liver is too damaged, the tumor has spread outside the liver, or the patient has other serious illnesses. A surgical oncologist is a doctor who specializes in treating cancer using surgery. A hepatobiliary surgeon also has specialized training in surgery on the liver and pancreas. Sometimes, liver transplant surgeons are involved in these operations. Before surgery, talk with your health care team about the possible side effects from the specific surgery you will have. Learn more about the basics of cancer surgery.

Two types of surgery are used to treat HCC:

Hepatectomy: When a portion of the liver is removed, the surgery is called a Ahepatectomy can be done only if the cancer is in 1 part of theliver and the liver is working well. The remaining section of liver takes over the functions of the entire liver. The liver may grow back to its normal size within a few weeks. A hepatectomy may not be possible if the patient has advanced cirrhosis, even if the tumor is small.

The side effects of a hepatectomy may include pain, weakness, fatigue, and temporary liver failure. The health care team will watch for signs of bleeding, infection, liver failure, or other problems that need immediate treatment.

Surgery

Liver transplantation: Sometimes, a liver transplantation can be done. This procedure is possible only when specific criteria are met, including tumor size and number and whether a suitable donor is found. These criteria usually are a single tumor that is 5 cm or smaller or 3 or fewer tumors, all of which are smaller than 3 cm. It is important to understand that the number of available donor livers is very limited, so transplantation is not always an option.

After a transplant, the patient will be watched closely for signs that the body might be rejecting the new liver or that the tumor has come

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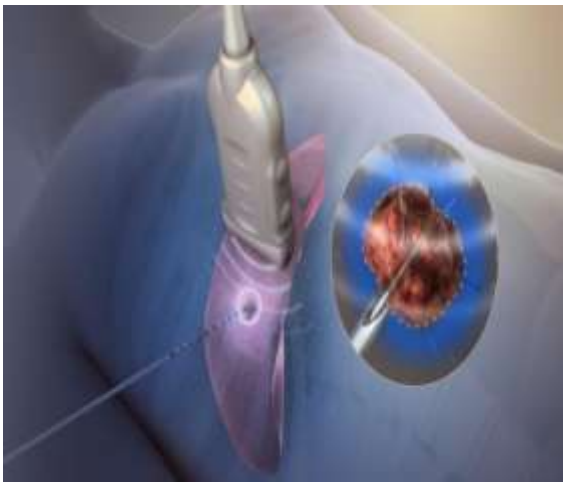
back. The patient must take medication to prevent rejection. These drugs can cause side effects, such as puffiness in the face, high blood pressure, or increased body hair. Liver transplant has significant risks of serious complications, including death from infection or the body's rejection of the donor liver.

Liver transplantation is a particularly effective treatment for people with a small tumor because transplantation removes the tumor and the damaged liver. However, there are few donors, and people waiting for a liver transplant may have to wait for a long time before a liver becomes available.

During this time, the disease may get worse. The transplant center will advise you on how long the wait is likely to be and what rules are used to prioritize people on the waiting list.

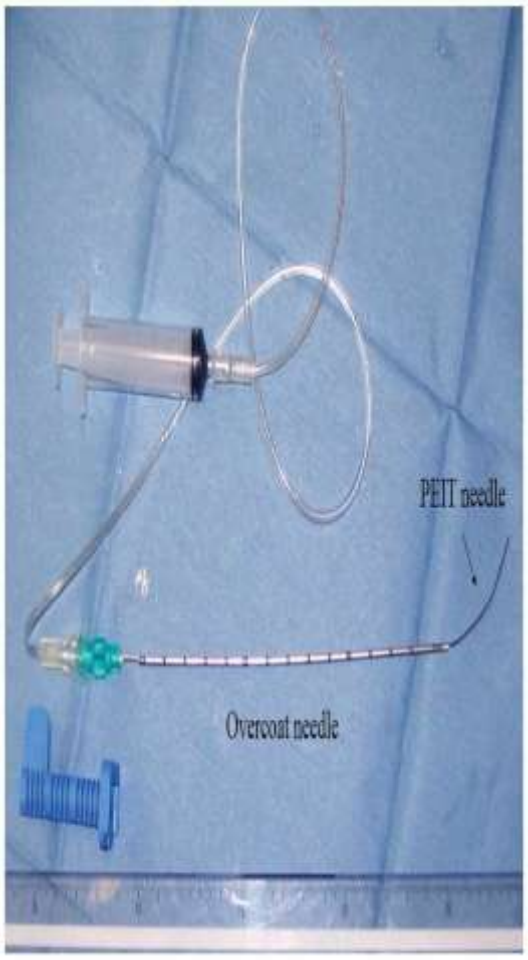
2.Radiofrequency ablation (RFA)

RFA and microwave therapy both use heat to destroy cancer cells. They may be given through the skin, through laparoscopy, or during a surgical operation while a patient is sedated. Sedation is giving medication to become more relaxed, calm, or sleepy. This treatment approach is also called thermal ablation.



RFA

3.Percutaneous ethanol injection Percutaneous ethanol injection is when alcohol is injected directly into the liver tumor to destroy it. Side effects include fever and pain after the procedure. In general, the procedure is simple, safe, and particularly effective fora tumor smaller than 3 cm. However, if the alcohol escapes from the liver, a person may have brief but severe pain. This option is rarely used and has been largely replaced by RFA .



Injection

4.Radiation therapy

Radiation therapy is the use of high-energy x-rays or other particles to destroy cancer cells. A doctor who specializes in giving radiation therapy to treat cancer is called a radiation oncologist.

Stereotactic body radiation therapy (SBRT). SBRT is a term that describes several methods of delivering high doses of radiation therapy to a tumor while limiting the amount of radiation to nearby healthy tissue. This is important because healthy liver tissue can be damaged by radiation. SBRT effectively treats tumors that are about 5 cm or smaller. However, it is still considered investigational compared to RFA (see above) because there is not much available information about its long-term effectiveness.

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Radiation therapy

5.Systemic therapy

Systemic therapy is the use of medication to slow the growth of or kill cancer cells. Medications circulate through the body and therefore can reach cancer cells throughout the body. Systemic therapies are generally prescribed by a medical oncologist, a doctor who specializes in treating cancer with medication. Common ways to give systemic therapies include an intravenous (IV) tube placed into a vein using a needle, an injection into a muscle or under the skin, or in a pill or capsule that is swallowed (orally).

The types of systemic therapies used for advanced f include:

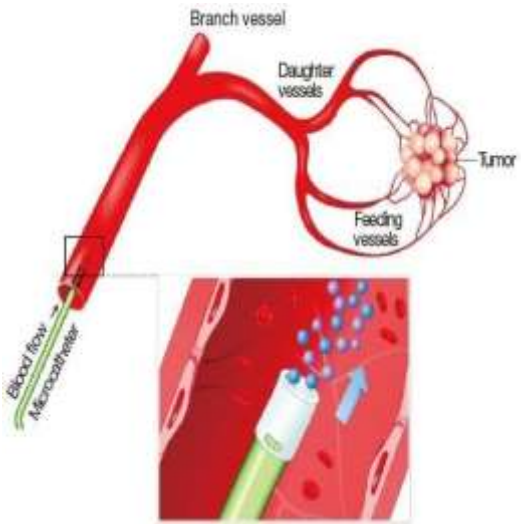
- **Targeted therapy**
- **Immunotherapy**

Targeted therapy

Targeted therapy is drug treatment that targets the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment blocks the growth and spread of cancer cells while limiting damage to healthy cells.Recent studies show that not all tumors have the same targets. To find the most effective treatment, your doctor may run tests to identify the genes, proteins, and other factors in your tumor. This helps doctors better match each patient with the most effective treatment whenever possible. In addition, many research studies are taking place now to find out more about specific molecular targets and newtreatments directed at them. Learn more about the basics of targeted treatments.

For HCC, anti-angiogenesis drugs are the most common type of targeted therapy. Antiangiogenesis therapy is focused on stopping angiogenesis, which is the process of making new blood vessels. Because a tumor needs the nutrients delivered by blood vessels to grow and spread, the goal of anti-angiogenesis therapies is to "starve" the tumor.

Some anti-angiogenesis therapies are for people with unresectable HCC. Unresectable means that surgery is not an option.



Immuno therapy

Immunotherapy, also called biologic therapy, is designed to boost the body's natural defenses to fight the cancer. It uses materials made either by the body or in a laboratory to improve, target, or restore immune system function. One common type of immunotherapy is called an immune checkpoint inhibitor. Immune checkpoint inhibitors work by blocking the pathways that would otherwise allow the cancer to hide from the immune system.

Immunotherapies include:

Nivolumab (Opdivo). In 2017, the FDA approved an immunotherapy called nivolumab for the treatment of HCC. Nivolumab can be used to treat people who have already been treated with sorafenib, which is a type of targeted therapy.

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Pembrolizumab. In 2018, the FDA approved the immunotherapy pembrolizumab for the treatment of people with HCC. Like nivolumab, pembrolizumab can be used to treat people who have previously been treated with sorafenib. Pembrolizumab is an immune checkpoint inhibitor.

Nivolumab with ipilimumab (Yervoy). In 2020, the FDA approved the use of the combination of nivolumab with another immunotherapy drug called ipilimumab (Yervoy) to treat patients with HCC who have already been treated with sorafenib. Both nivolumab and ipilimumab are immune checkpoint inhibitors.

Atezolizumab with bevacizumab. In 2020, the FDA approved the use of the combination of atezolizumab, an immunotherapy drug, with bevacizumab, a targeted therapy drug, for people with unresectable or metastatic HCC who have not received previous cancer treatment using medications. Unresectablemeans surgery is not an option. Atezolizumab is an immune checkpoint inhibitor, and bevacizumab is an anti-angiogenesis therapy (see "Targeted therapy" above).Other immunotherapy drugs are still being studied in clinical trials. Different types of immunotherapy can cause different side effects. Common side effects include skin reactions, flu-like symptoms, diarrhea, and weight changes.

Talk with your health care team about possible side effects for the immunotherapy recommended for you. Learn more about the basics of immunotherapy.

Drugs Of Liver Cancer

This lists of cancer drugs approved by the Food and Drug Administration (FDA) for liver cancer. The list includes generic names and brand names. The drug names link to NCI's Cancer Drug Information summaries. There may be drugs used in liver cancer that are not listed here.

Drugs Approved for Liver Cancer-
Atezolizumab
Avastin (Bevacizumab)
Bevacizumab
Cabometyx (Cabozantinib-S-Malate)
Cabozantinib-S-Malate
Cyramza (Ramucirumab)
Keytruda (Pembrolizumab)
LenvatinibMesylate
Lenvima (LenvatinibMesylate)
Nexavar (SorafenibTosylate)
Nivolumab
Opdivo (Nivolumab)
Pemazyre (Pemigatinib)
Pembrolizumab
Pemigatinib
Ramucirumab
Regorafenib
SorafenibTosylate
Stivarga (Regorafenib)
Tecentriq (Atezolizumab)

Risk factors

A risk factor is anything that increases a person's chance of developing cancer. factors often influence the development of cancer, most do not directly cause cancer. Some people with several risk factors never develop cancer, while others with no known risk factors do. Knowing your risk factors and talking about them with your doctor may help you make more informed lifestyle and health care choices.

The following factors can raise a person's risk of developing HCC. The main risks in the United States are cirrhosis of the liver and nonalcoholic fatty liver disease (NAFLD).

Cirrhosis. Cirrhosis develops when liver cells are damaged and replaced by scar tissue. Most cirrhosis in the United States is caused by alcohol abuse. Other causes are NAFLD, viral hepatitis (types B and C, as described below), too much iron in the liver from a disease called hemochromatosis, and some other rare types of chronic liver disease. Combined alcohol abuse and hepatitis virus infection puts people at high risk of cirrhosis and HCC.

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Obesity, NAFLD, and diabetes. Obesity causes fat to be deposited in the liver, which leads to a condition known as NAFLD. Over the past decade, strong evidence has emerged suggesting that NAFLD and diabetes, a related disorder, are increasingly important risk factors for HCC in the United States.

Viral hepatitis. Hepatitis viruses are viruses that infect the liver. The 2 common types are hepatitis B and hepatitis C. Viral hepatitis is the largest risk factor for liver cancer worldwide. Hepatitis C has become much more common than hepatitis B because there is no vaccine to prevent hepatitis C.

Viral hepatitis can be passed from person to person through exposure to blood or bodily fluids. This can happen through physical injury or trauma, by sharing needles during drug use or the tattooing process, or by sexual contact. In the case of hepatitis B, an unborn baby or infant can get the virus if the mother has it. This can be avoided by vaccinating the baby.

If you develop acute hepatitis B or C and then "clear the virus," you recover completely from the acute infection. Only people who do not clear the virus and have a persistent infection have an increased risk. Your doctor will be able to perform blood tests that tell if you have cleared the virus.

Age. In the United States, adult primary liver cancer occurs most often in people older than 60.

Gender. Men are more likely than women to develop liver cancer.

Environmental factors. Some environmental factors may increase the risk of liver cancer, such as exposure to certain chemicals or eating

food contaminated with aflatoxin. Aflatoxin is a toxin made by a mold that can grow on stored nuts and grains. There is less risk of this in the United States.

Risk factors are cumulative. This means that having more than 1 risk factor increases the risk of developing liver cancer even more. For instance, a person who carries both hepatitis B and C has a higher risk than a person carrying 1 type of the virus. Similarly, a person with hepatitis C who also drinks alcohol has a higher risk.

Prevention

Many liver cancers could be prevented by reducing exposure to known risk factors for this disease.

Avoid and treat hepatitis B and C infections

Worldwide, the most significant risk factor for liver cancer is chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV). These viruses can spread from person to person through sharing contaminated needles (such as in drug use) through unprotected sex, and through childbirth, so some liver cancers may be avoided by not sharing needles and by using safer sex practices (such as always using condoms).

Limit alcohol and tobacco use Drinking alcohol can lead to cirrhosis, which in turn, can lead to liver cancer. Not drinking alcohol or drinking in moderation could help prevent liver cancer.Since smoking also increases the risk of liver cancer, not smoking will also prevent some of these cancers. If you smoke, quitting will help lower your risk of this cancer, as well as many other cancers and lifethreatening diseases.

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Get to and stay at a healthy weight

Avoiding obesity might be another way to help protect against liver cancer. People who are obese are more likely to have fatty liver disease and diabetes, both of which have been linked to liver cancer.

Limit exposure to cancer-causing chemicals

Changing the way certain grains are stored in tropical and subtropical countries could reduce exposure to cancer-causing substances such as aflatoxins. Many developed countries already have regulations to prevent and monitor grain contamination.

Treat diseases that increase liver cancer risk

Certain inherited diseases can cause cirrhosis of the liver, increasing a person's risk for liver cancer. Finding and treating these diseases early in life could lower this risk. For example, all children in families with hemochromatosis should be screened for the disease and treated if they have it. Treatment regularly removes small amounts of blood to lower the amount of excess iron in the body

II. CONCLUSION

Liver cancer is the second leading cause of cancer-related death and an alarming number of new liver cancer cases are expected each year. Chemotherapy is the best treatment choice for liver cancer treatment due to its noninvasiveness and ability to completely kill cancer cells. Effective clinical results of cancer chemotherapy cannot be achieved owing to various physicochemical and biological barriers. Chemotherapeutic agents are nonspecific in nature and result in off-target or systemic toxicities. The emergence of resistance to anticancer drugs leads to lower cellular uptake of the drugs, resulting in the inferior clinical outcomes of the drugs. Moreover, poor solubility of these drugs results in their lower pharmacokinetics. Nanocarrier-based targeted delivery has been the best alternative for overcoming these barriers. Nanocarriers surface-functionalized with targeting ligands are capable of delivering increased concentrations of drugs selectively to tumors, achieving chemotherapeutic effects with lower off-target toxicities. Liver cancer cells overexpress various receptors that recognize some specific ligands. Nanocarrier systems surface-functionalized with targeting ligands have been reported for active delivery of receptor-based drugs in liver cancer treatment. Stimulus-responsive nanocarrier systems have also been used for selective delivery of anticancer drugs to liver cancer cells. The current status of liver cancer−targeted drug delivery through ligand-functionalized nanocarriers shows that such nanoformulations will certainly lead to their marketability with superior effects on liver cancer treatment.

III. RESULT

The project on treatment of Liver cancere was prepared and submitted successfully.

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