

THE LIVER – AN UPDATE

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Abstract:

Dental practitioners are increasingly exposed to patients with medical problems these days. The liver disorder is one such group of disease which is associated with profound morbidity. There have been instances of neglect leading to transmission of infections in dental settings. It has also been observed that there are instances where dentists refuse to treat patients with certain illnesses due to ignorance of facts. It is mandatory for us to update our knowledge regularly. In this article, we will discuss the liver disorders and its implications in the practice of dentistry.

Clinical Relevance: Dentists should be able to manage/treat patients with liver disorders effectively.

Objective Statement: The reader should understand the various disorders that commonly affect the liver, oral manifestation of liver disorders and clinical implications. They should be able to make appropriate measures to prevent cross infection.

Keywords: liver disorder/Classification, hepatitis, liver disorders/dental care.

Introduction:

Dental practitioners are increasingly exposed to patients with medical problems these days. While most of the medical illness are disclosed, a large majority, especially infections of chronic nature may be undisclosed or in certain condition's undiagnosed. It has also been observed that there are instances where dentists refuse to treat patients with certain illnesses due to ignorance of facts. At the same time, there have been instances of neglect leading to transmission of infections in dental settings. It is, therefore, mandatory for us to update

our knowledge in order to provide evidence-based care

In this article, we will discuss the liver disorders and its implications in the practice of dentistry.

Functions:

The liver is the largest internal organ and has many essential functions. Liver synthesizes most essential serum proteins (albumin, transporter proteins, some of the blood coagulation factors, as well as many enzymes and growth factors)

Produces bile and its transporters (bile acids, cholesterol, lecithin, phospholipids)

Intervenes in the regulation of nutrients (glucose, glycogen, lipids, cholesterol, amino acids), and metabolites and conjugates lipophilic compounds (bilirubin, cations, drugs) to facilitate their excretion in bile or urine.

Liver dysfunction alters the metabolism of carbohydrates, lipids, proteins, drugs, bilirubin and hormones [1, 2]. The liver disease presents a number of concerns for the delivery of medical and dental care.

Liver disorders:

Liver disease can be classified as

Acute - characterized by rapid resolution and complete restitution of organ structure and function once the underlying cause has been eliminated

Chronic- characterized by persistent damage, with progressively impaired organ function.

They can also be classified as

Infectious such as Hepatitis A, B, C, D and E, infectious mononucleosis, secondary syphilis and tuberculosis or

Non-infectious due to substance abuse such as alcohol and drugs

Hepatitis

Hepatitis is inflammation of the liver, most commonly caused by a viral infection. There are five main hepatitis viruses, referred to as types A, B, C, D and E. These viruses belong to a different family and have little in common except the target organ they infest. Types B and C lead to chronic disease, together, are the most common cause of liver cirrhosis and cancer [3].

Hepatitis B is a DNA virus. Its prevalence is highest in sub-Saharan Africa and East Asia. Most people in these regions become infected with the hepatitis B virus during childhood and between 5–10% of the adult population are chronically infected. In the Middle East and the Indian subcontinent, an estimated 2–5% of the general population is chronically infected. [4] A blood-borne disease, Hep B is hundred times more infectious than HIV, mainly transmitted by

exposure to an infected individual's blood, semen, saliva or vaginal discharge [5].

Hepatitis C is an RNA virus. It is similar to Hep B in behavior. The incubation period ranges from 2 weeks – 6 months. It is estimated that about 3% of the world population is infected with Hepatitis C virus (HCV) [5]. Its prevalence is more common in the developing countries of the world. About 1.5 million deaths occur per year due to HCV [6,7].

Hepatitis D (delta) virus (HDV) is a small, defective RNA virus that requires HBsAg for transmission. In general, the highest rates of HDV infection are in areas where HBV is endemic. Acquiring HBV and HDV during the same exposure (HBV/HDV coinfection) is associated with more severe acute hepatitis and higher mortality. [7]

Hepatitis E virus (HEV) is an RNA virus. Five genotypes have been identified; the first four of which infect humans. HEV is endemic in many countries of Asia, Central America, and Africa. Classic epidemic HEV infection is due to the most common cause of acute hepatitis in endemic areas. Epidemic HEV infection is transmitted via the fecal-oral route and is associated with large waterborne outbreaks. It typically occurs in adolescents and young adults and is clinically associated with a high rate of jaundice and cholestasis [7].

Alcoholic liver disease (ALD)

ALD presents as a broad spectrum of disorders, ranging from simple fatty liver to more severe forms of liver injury, including alcoholic hepatitis (AH), cirrhosis, and hepatocellular carcinoma (HCC). Fatty liver is an early response to alcohol consumption and it develops in heavy drinkers. About 30% of heavy drinkers develop more severe forms of ALD, such as advanced fibrosis and cirrhosis. Patients with underlying ALD and heavy alcohol intake may develop alcoholic hepatitis. AH may lead to severe complications related to liver failure and portal hypertension and also has high short-term mortality [8].

Non-alcoholic fatty liver disease (NAFLD)

Non-alcoholic fatty liver disease (NAFLD) also ranges from simple steatosis to nonalcoholic steatohepatitis (NASH), leading to fibrosis and potentially cirrhosis, and it is one of the most common causes of liver disease worldwide. NAFLD is associated with medical conditions such as metabolic syndrome, obesity, cardiovascular disease and diabetes. NASH is usually diagnosed through liver biopsy, recent research has enabled noninvasive techniques to identify patients at risk. Weight loss through improved diet and increased physical activity is the cornerstone therapy of NAFLD. [9].

Hepatocellular carcinoma (HCC)

Hepatocellular carcinoma (HCC) is the 6th most common cancer worldwide and the 3rd leading cause of cancer-related death [10]. Most of the cases are due to chronic hepatitis B and C infection. The disease is most common in Asia and Africa. The first line of treatment consists of the surgical resection or liver transplantation. HCC is characterized by fast tumor cell growth, early metastasis, and multidrug resistance. The 5-year survival rate is in the range of 5%.

Oral manifestation of liver disease:

The only manifestation of advanced liver disease in the oral mucosa is jaundice, which is the yellow pigmentation that results from the deposition of bilirubin in the submucosa. Jaundice manifests at serum levels greater than 2.5-3 mg/dL. The mucosa on the soft palate and in the sublingual region are thinner hence often first to reveal a yellow hue. With time, the yellow changes can be visible at any mucosal site. In some patients, impaired hemostasis can be manifested as petechiae or excessive gingival bleeding with minor trauma. [1, 5, 11].

Recent studies have drawn attention to some extrahepatic manifestations of HCV infection localized in the oral cavity, such as lichen planus, xerostomia, and sialadenosis, Sjogren syndrome [2, 12]. The association

between hepatitis C and oral lichen planus is controversial. This association is greater in Europe and Asia. Studies have proven that the link between the two conditions is tenuous and not sufficient to warrant screening for hepatitis C infection in all patients with lichen planus [12, 13]. Tongue hyperpigmentation in a number of patients undergoing treatment with pegylated interferon for Hep C has also been reported [15].

Dental management

For any walk-in patient a detailed clinical evaluation involving extra-oral and intra-oral examinations may pick up signs of liver disease [15]. If the patient reports a history of liver disease, the dentist should consult with the patient's medical practitioners to ensure that a safe and appropriate dental treatment plan is established in light of the liver dysfunction [5]

Liver disease is often associated with a reduction in clotting factors, which results in an impaired hemostasis. In a patient with liver disease, the risk for the dentist is related to the extent of the liver disease, medications, the type of dental treatment planned and the presence of co-morbidities [15].

- Invasive treatment should be avoided for patients with acute liver failure and acute hepatitis.
- Emergency treatment should be provided in a hospital setting.

If invasive treatment is planned, the following blood tests may be required:

- Complete blood examination
- International Normalized Ratio: INR (> 1.7 indicated a serious risk of bleeding)
- Coagulation tests (prothrombin time, activated partial thromboplastin time)
- Liver function tests

If test results are significantly abnormal then any dental treatment must be provided only after consultation with either the relevant medical specialist or by referral to a specialist in oral medicine or oral and maxillofacial surgery [15,16].

Local hemostatic measures such as compression, sutures, dressings of oxidized cellulose, and antifibrinolytic agents such as tranexamic acid will be required after surgical procedures. Pre-operative optimization with vitamin K therapy or transfusions may be necessary. Where immune impairment is present, antibiotic prophylaxis is advised. Attention should be paid to minimize trauma [15].

Prescribing Medications in Liver Disease

The liver plays a central role in the pharmacokinetics of the majority of drugs. The physiological changes that accompany hepatic impairment alter drug disposition [17].

There is no simple endogenous marker to predict hepatic function. The semi-quantitative Child-Pugh score has been used to assess the severity of liver function impairment, but it only offers the physician a rough guidance for dosage adjustment. Currently, The Food and Drug Administration (FDA) and the European Medicines Evaluation Agency (EMA) have undertaken a study of the effect of liver disease on the pharmacokinetics of drugs which is aimed at generating, specific dosage recommendations for patients with hepatic dysfunction [18].

Most analgesics, antibiotics, and local anesthetics are well tolerated by the patient with early stage liver disease. However, where liver disease is advanced it may be necessary to reduce the dose or avoid some medications completely:

- Tetracycline causes liver damage hence should not be used.
- Erythromycin and Metronidazole inhibit the cytochrome P450 liver enzyme resulting in the delayed metabolism of other drugs and can also cause direct damage to liver tissues.
- Metabolism of Clindamycin is prolonged. Ketoconazole and fluconazole are also metabolized in the liver and should be avoided [16].

- Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) are metabolized in the liver it may increase the risk of gastrointestinal bleeding. They should be avoided.
- Paracetamol should be avoided where there is advanced liver disease and should not be prescribed if alcohol abuse is identified, but the short-term use of this drug at reduced doses i.e 2 grams/day is found to be safe in patients with non-alcoholic liver disease [19]
- Benzodiazepines should be given at lower dose with a longer interval between doses
- Sedatives and opiates may trigger encephalopathy.

Local anesthesia

Local anesthesia is not entirely safe in patients with hepatic impairment. Most of the amide local anesthetics used in dental practice undergo biotransformation in the liver. Articaine is metabolized partly in plasma and prilocaine receives some metabolism in the lungs. However, the liver is the main site of metabolic activity. All of an injected dose of local anesthetic reaches the circulation and if metabolism is affected the concentration in plasma increases. Only about 2% of the drug will be excreted unchanged. This may lead to signs of CNS toxicity with relatively low doses of the anesthetic[1,5,15].

Total anesthetic dosage should be reduced and the interval of time between subsequent injections may be extended. In these cases, initial injection with rapid-onset anesthetics such as lidocaine or mepivacaine followed by injection with a long-acting anesthetic like etidocaine or bupivacaine may be the best protocol for limiting total anesthetic dosage while achieving adequate pain control [15].

Occupational Transmission

Transmission of hepatitis infection is a source of major concern. According to WHO report, most of the hepatitis infections are acquired in the health-care setting [4]. It

is more important in developing countries where the rate of hepatitis-infected individuals is higher. Researchers have observed the practice of local private medical and dental practitioners and found that most of them were using unsterilized needles and syringes. [22,23] Most of the patients diagnosed with Hep C (76 %) had a history of treatment/injections from these doctors. Unsafe injection practices such as improper sterilization, repeat usage of single-use needles and syringes, inappropriate administration techniques and hazardous means of disposal pose the greatest threat to developing nations.

In general, transmission of infectious agents in healthcare settings can occur [3,6,7]

1. from patient to patient (because of improper infection control practices),
2. from patient to provider (as a result of needle sticks)
3. From provider to the patient (during surgery).

The risk of transmission depends on factors related to the agent, the host, and the environment. After the percutaneous injury, the risk of contracting HBV infection is 6%-30%. The virus can survive in dry blood for at least a week. HCV can survive in the environment for 16 hours on a dry surface and in water at low temperatures for up to five months, and it can be detected in saliva [6,7]. Disinfectants that inactivate Hep B virus also will kill HCV on environmental surfaces, and commercial hand antiseptics are effective in inactivating the virus on hands.

From 2008 through 2012, the Centre for disease control (CDC), United States received notice of 15 outbreaks of health care-associated transmission of HCV in non-dental ambulatory care settings [20]. An event that occurred in 2001 has been elaborated wherein a person with acute hepatitis B had none of the traditional risk factors but reported having recent oral surgery done. On investigating the oral surgery practice where the patient received

dental treatment revealed that another surgical patient seen earlier on that same day was on the state's reportable disease registry for HBV. Molecular epidemiologic techniques indicated transmission of HBV between the two patients. The investigators speculated that a lapse in cleanup procedures had occurred after the source patient had left an area contaminated with blood [20].

Although most studies have not found dental treatment to be a risk for HBV and HCV, the above instances are an evidence that it may still pose a risk [21].

Studies have also shown that the knowledge and attitude toward Hep B and C infection among the health-care workers was highly dissatisfactory [24, 25].

Standard precautions are recommended for the care and treatment of all patients, regardless of their perceived or confirmed Infectious status, and in the handling of all body fluids, non-intact skin, and mucous membranes.

Infection Control

All dental clinics should adhere to recommended infection control practices such as operational oversight of infection control practices training in prevention of bloodborne pathogens transmission HBV vaccination for staff. Use of appropriate personal protective equipment, effective sterilization and disinfection procedures [6]

Two important but neglected source of infection in the dental setting are impressions and stainless steel crowns in pediatric patients. Dasgupta et al [23] have pointed out that pre-procedural oral prophylaxis and mouth rinses are highly efficient in reducing the overall microbial load intraorally as well as on alginate impression surface.

Stainless steel crown (SSC) falls in the category of the critical instrument (A critical instrument is one which penetrates soft tissue or bone, contacts blood stream or other sterile tissue). All critical dental instruments that are heat stable, sterilization by steam under pressure is advocated.

Farhin K²⁴ et al have suggested, try-in SSC can be reduced by prior measuring of mesiodistal width of the concerned tooth and selecting a crown of the corresponding size by correlating it with the conversion chart provided by the manufacturer. They recommend three-step process which has been routinely followed by orthodontic bands, without any known complications. Initially, wiping and immersion of SSC in 3% sodium hypochlorite or 2% glutaraldehyde solution for 10 min, which will dissolve the organic contaminants like saliva and blood, followed by ultrasonic cleaning of SSC for 15 min. The chemical disinfection is necessary as ultrasonic cleaning does not completely eliminate the organic contaminants from the tried-in SSCs. Finally, autoclaving the SSC would provide complete decontamination of SSC prior to its reuse.

Needle-Stick Injury and Blood Spills

The risk of HCV and HBV transmission through a needle-stick injury from a known source depends on the viral load of the source patient, the first aid administered and the instruments involved. [5].

Immediate Management of a Needle-Stick Injury

- Wash the skin with soap and water at the site of exposure, then cover
- Rinse your mouth, nose, and eyes well with water or saline if exposed
- Report the incident and follow your local workplace Occupational Exposure Protocol

If the health care worker is vaccinated for HBV and has HBV Ab on testing no treatment is recommended. However, if the vaccine status is not known or not found to have HBV Ab and the source is positive for HBSAg then HBIG 0.06 ml/Kg is administered ASAP and revaccination should be done.

There is no post-exposure prophylaxis for HCV. Direct viral testing for HCV RNA by PCR before 6 weeks will aid in early

identification. HCV antibody testing should be done at 4-6 months to rule out infection.

Care of patients undergoing Liver Transplantation

Orofacial complications such as oral mucositis and opportunistic infections are expected with organ transplantation and these are usually managed in phases (pre-transplantation, peri-transplantation (during) and post-transplantation/supportive care).

An active dental disease that could cause disseminated infection such as abscessed teeth and advanced periodontal disease should be treated prior to transplantation. Supportive care is usually performed in a hospital setting by trained dental specialists in liaison with the liver transplant team.

The treatment aims of supportive care are to:

- Eliminate or stabilize sites of oral infection
- Extract unrestorable teeth
- Provide oral hygiene instruction so the transplant recipient can maintain their oral health.

After the transplantation no elective treatment should be carried out for 3–6 months. Treatment post-transplant should only occur after consultation with patient's specialist [28].

Avoiding Discrimination

Healthcare workers should respect the rights of people with hepatitis, regardless of how they were infected. Everyone living with hepatitis/liver disease should have access to care and services regardless of transmission route, gender, race, culture, sexual orientation or lifestyle issues. Discrimination and stigmatizing behaviors can be avoided by:

Health care worker education and continuing medical education
Ensuring standard infection-control procedures are followed, thus reducing the need for disclosure or differential treatment
Ensuring people's privacy and confidentiality are protected.

Conclusion

Liver disease does pose a challenge in providing effective dental treatment. Hepatitis is prevalent worldwide and chronic cases may be undiagnosed or undisclosed. However, with the use of standard precaution and following of safety control protocol and continuous education regarding these diseases, health care providers can provide appropriate dental care for patients. We can also limit the spread of infection that may occur in a dental setting by strictly adhering to infection control and universal precaution.

References

1. Golla K, Epstein JB, and Cabay RJ; Liver disease: Current perspectives on medical and dental management. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;98:516-21
2. Cruz-Pamplona M, Margaix-Muñoz M, Gracia Sarrión-Pérez MG. Dental considerations in patients with liver disease. *J Clin Exp Dent*. 2011;3(2): e127-34.
3. Price. Update on HBV, HDV, and HEV. *Top Antivir Med*. 2014;21(5):157-163
4. www.who.int/features/qa/76/en
5. Little, Falace, Miller, Rhodus. Dental management of the medically comprised patient. 7th edition. Mosby Elsevier.
6. R. Monina K levels and Anne C. Moorman. Hepatitis C virus: An overview for dental health care providers. *JADA* 2013; 144(12):1340-1347.
7. Pol S. Hepatitis C virus: 25 years-old, the end? *Med Sci (Paris)*. 2013 ;29(11):998-1003.
8. Gao B and Bataller R. Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets. *Gastroenterology*. 2011; 141(5): 1572–1585.
9. Schwenger KJ and Allard JP. Clinical approaches to non-alcoholic fatty liver disease. *World J Gastroenterol*. 21, 2014; 20(7): 1712–1723.
10. Scaggiante B, Kazemi M, Pozzato G, Dapas B, Farra R, Grassi M, Zanconati F, and Grassi F. Novel hepatocellular carcinoma molecules with prognostic and therapeutic potentials. *World J Gastroenterol*. 7, 2014; 20(5): 1268–1288.
11. Rodica Ghiuru, D, Munteanu. Oral manifestation of liver disease. *Romanian Journal of Oral Rehabilitation*. Vol. 3, No. 1, January 2011
12. Alavian SM, Mahboobi N, Mahboobi N, Karayiannis P. Oral conditions associated with Hepatitis C virus infection. *Saudi J Gastroenterol* 2013;19: 245-51
13. Kumar K P M, Jois HS, Hallikerimath S, Kale AD. Oral Lichen Planus as an Extra-hepatic Manifestation of Viral Hepatitis-Evaluation in Indian Subpopulation. *J Clin Diagn Res*. 2013;7(9):2068-9.
14. Tsilika K, Tran A, Trucchi R, Pop S, Anty R, Cardot-N, Lacour JP, Ortonne JP, Passeron T. Secondary Hyperpigmentation During Interferon Alfa Treatment for Chronic Hepatitis C Virus Infection. *JAMA Dermatol*. 2013;149(6):675-677
15. Aparna Dalal and John D. Jr. Lang (2013). Anesthetic Considerations for Patients with Liver Disease, <http://www.intechopen.com/books/hepatic-surgery/anesthetic-considerations-for-patients-with-liver-disease>
16. www.ashm.org.au/
17. Verbeeck RK. Pharmacokinetics and dosage adjustment in patients with hepatic dysfunction. *Eur J Clin Pharmacol*. 2008; 64(12):1147-61.
18. Bosilkovska M, Walder B, Besson M, Daali Y, Desmeules J. Analgesics in patients with hepatic impairment: pharmacology and clinical implications. *Drugs*. 2012. 20; 72(12):1645-69.
19. Mike Mitka, MSJ FDA Asks Physicians to Stop Prescribing High-Dose Acetaminophen Products *JAMA*. 2014; 311(6):563.
20. www.cdc.gov/hepatitis

21. Nima Mahboobi1, Stephen R Porter, Peter Karayiannis, Seyed-Moayed Alavian. Dental Treatment as a Risk Factor for Hepatitis B and C Viral Infection. A Review of the Recent Literature. *J Gastrointestin Liver Dis.* 2013; 22: 1: 79-86
22. Verma R, Behera B K, Jain R B, Arora V, Chayal V, Gill P S. Hepatitis C: A silent threat to the community of Haryana, India: A community-based study. *AMJ* 2014; 7: 1, 11-16.
23. Thakral B, Marwaha N, Chawla YK, Saluja K, Sharma A, Sharma RR, et al. Prevalence & significance of hepatitis C virus (HCV) seropositivity in blood donors. *Indian J Med Res.* 2006; 124: 431–8.
24. S Setia, RS Gambhir, V Kapoor, G Jindal, S Garg, and S Setia. Attitudes and Awareness Regarding Hepatitis B and Hepatitis C Amongst Health-care Workers of a Tertiary Hospital in India. *Ann Med Health Sci Res.* 2013; 3(4): 551–558
25. Mehta A, Gupta M, Upadhyaya N. Status of occupational hazards and their prevention among dental professionals in Chandigarh, India: A comprehensive questionnaire survey. *Dent Res J (Isfahan).* 2013; 10(4):446-51.
26. Dasgupta D, Sen SK, Ghosh S, Bhattacharyya J, Goel P. Effectiveness of mouth rinses and oral prophylaxis on the reduction of microorganisms count in irreversible hydrocolloid impression: an in vivo study. *J Indian Prosthodont Soc.* 2013; 13(4):578-86.
27. Farhin K, Abhinav S, Thejokrishna P, Sajjad M. Stainless steel crowns reuse and decontamination techniques: A survey among Indian pediatric dentists. *J Indian Soc Pedod Prev Dent* 2013;31:265-9
28. Glassman P, Wong C, Gish R. A review of liver transplantation for the dentist and guidelines for dental management. *Spec Care Dentist.* 1993; 13(2):74-80.