REVIEW OF LAB DIAGNOSIS IN MODERN ERA, CURRENT INSTRUMENTS USED FOR DIAGNOSIS OF HEPATITIS

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ABSTRACT

Viral hepatitis is a global public health problem, particularly in developing countries due to its persistent circulation in the environment. The improved sanitary condition, increase in awareness of personal hygiene and other precautionary measures have led to the marked reduction in transmission of hepatitis. There are various causes for different types of hepatitis. Hepatitis B and hepatitis C are more prevailing types of hepatitis. Various types of diagnostic tests are being performed including serologic tests (to detect antibody in serum) and molecular tests (to analyze biological markers in the genome and proteome), which vary with the type of hepatitis. The development of detection techniques possessing the requisite sensitivity and specificity for the practical routine monitoring purposes is of great importance necessary for the protection of public. Mostly PCR and ELISA are used for performing diagnostic tests. PCR are very expensive techniques and used by higher labs and hospitals.

Keywords: Hepatitis, Diagnostic tests, Serologic markers, Viral load, Lab instruments

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INTRODUCTION

The word "Hepatitis" derived from the ancient Greek word "hepar" (root word "hepat") meaning liver and the Latin word "itis" meaning inflammation [1]. The breakthrough understanding of hepatitis came in 1963 when Dr. Baruch Blumberg discovered an antigen that detected the presence of hepatitis B (HBV) in blood samples [2]. Hepatitis is an inflammation of the liver. It can be self-limiting or can progress to fibrosis (scarring), cirrhosis or liver cancer. Viruses are the major cause of hepatitis in the world, but other infections, toxic substances (e.g. alcohol, certain drugs) and autoimmune diseases can also cause hepatitis [3]. There are mainly five types of hepatitis that are caused by a virus A, B, C, D, and E - plus type G [4]. In case of chronic hepatitis, symptoms usually not developed in the beginning. Signs and symptoms of acute hepatitis appear quickly including fatigue, flulike symptoms, dark urine, pale stool, abdominal pain, loss of appetite, unexplained weight loss, yellow skin and eyes [5]. There are different types of tests performed for diagnosis of hepatitis including enzyme immunoassay, virus RNA assays, Liver biopsy (hepatitis C), physical examination, liver biopsy, liver function test, ultrasound, blood tests, viral antibody testing [5, 6]. Chronic hepatitis type B and C can often

lead to serious health issues like chronic liver disease, cirrhosis, liver cancer, bleeding disorders, kidney failure, hepatic encephalopathy, hepatocellular carcinoma. Practicing good hygiene (avoid drinking dirty local water, alcohol, seafood and use clean healthy fruit and vegetables) and avoiding contact with contaminated blood (avoid sharing drug needles, razors, others toothbrush, touching spilled blood) helps to avoid contracting hepatitis [5]. The options of treatment are determined by type of hepatitis as well as the severity of hepatitis either acute or chronic. There is no treatment for hepatitis A other than supportive care. Antiviral medications and Liver transplant for hepatitis B treatment. Combination therapy is preferred treatment choice in hepatitis C. People with chronic hepatitis B and hepatitis C should have a medical evaluation for liver disease every 6-12 months. Alpha interferon (a medication) used for hepatitis D treatment. For hepatitis E no special medication, however, rest, more fluid intake and some antivirals used. Vaccination available for hepatitis type A and type B, but there is no vaccine for hepatitis C [7, 8].

METHOD

Lab Diagnosis-Sample Collection and Transportation

1. The specimen of choice is Blood. 2. 3-5 ml of venous blood is to be collected in a sterile dry and labeled vial. Avoid hemolysis of samples as it may interfere with the ability of tests to accurately test the markers. 3. To avoid degradation of viral nucleic acid in the specimen, serum should be removed from clotted blood within 4 hrs of collection and stored at -20 to -70°C. 4. In case of outbreak of hepatitis A and hepatitis E (transmitted by fecal-oral route), in addition to blood samples from patients, water samples and sewage samples may also be collected for RT-PCR . 5. Serum samples can be kept at 4-8°C for maximum of 7 days and if required to store the serum samples for longer duration, it should be frozen at -2°C or lower and transported to the testing lab on frozen ice-packs. 6. Sewage and water samples are transported at room temperature [9].

HEPATITIS A

Lab Tests

Liver biopsy has a minimal role in acute HAV infection. It may play a part in chronic relapsing HAV infection or in situations where the diagnosis is uncertain. Other investigations (e.g., serum acetaminophen) may be necessary, depending on findings from the history and clinical examination. Molecular diagnostic techniques performed on blood and feces for HAV RNA are purely research tools at present.

Kodani have developed a NAT-based (nucleic acid test) assay that may be able to detect five viral genomes of hepatitis simultaneously are HAV RNA, HBV DNA, HCV RNA, HDV RNA, and HEV RNA. Independent validation would have potential clinical implications for wider patient surveillance, donor specimens screening, and use in the setting of outbreaks [10].

Liver Function Tests

Liver Enzymes

Rises in the levels of ALT (Alanine aminotransaminase) and aspartate aminotransferase (AST) are sensitive for hepatitis A. Levels may exceed 10000 mIU/mL with ALT levels generally greater than AST levels. These levels usually return to reference ranges over 5-20 weeks.

Rises in alkaline phosphatase accompany the acute disease and may progress during the cholestatic phase of the illness following the rises in transaminase levels **[11]**.

Hepatic Synthetic Function

Bilirubin level rises soon after the onset of bilirubinuria and follows rises in ALT and AST levels. Levels may be impressively high and can remain

elevated for several months persistence beyond 3 months indicates cholestatic HAV infection.

Older individuals have higher bilirubin levels. Both direct and indirect fractions increase because of hemolysis, which often occurs in acute HAV infection. Modest falls in serum albumin level may accompany the illness [11,12].

Serologic Tests

Anti-Hepatitis A Virus Immunoglobulin M

The diagnosis of acute HAV infection is based on serologic testing for immunoglobulin M (IgM) antibody to HAV. Test results for anti-HAV IgM are positive at the time of onset of symptoms and usually accompany the first rise in the alanine aminotransferase (ALT) level.

Anti-Hepatitis A Virus Immunoglobulin G

Anti-HAV immunoglobulin G (IgG) appears soon after IgM and generally persists for many years. The presence of anti-HAV IgG in the absence of IgM indicates past infection or vaccination rather than acute infection. IgG provides protective immunity [13, 14].

Ultrasonography

Imaging studies are usually not indicated in HAV infection. However, Ultrasonography may be required when alternative diagnoses must be excluded. The goals should be to assess vessel patency and to evaluate any evidence supporting the presence of unsuspected underlying chronic liver disease. Ultrasound scanning is essential in patients with FHF (Fulminant Hepatic Failure).

Histologic Findings

Histopathology reveals pronounced portal inflammation early in the illness, which is consistent with viral hepatitis. Focal necrosis and acidophilic bodies are less pronounced than infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) [15, 16].

Guidance for the Interpretation of the Test Results

- **IgM negative / IgG negative:** Most persons with these results have never contracted hepatitis A. Antibodies of the IgM variety develop five to ten days prior to the onset of symptoms.
- **IgM positive / IgG negative:** This result indicates acute hepatitis A.
- **IgM positive / IgG positive:** This result indicates that acute hepatitis A occurred within the last six months. By six months, the IgM reverts to negative.
- **IgM negative / IgG positive:** Persons with this result are immune to hepatitis A. They have either been infected with the virus months or years in the past (with or without symptoms), or they have been vaccinated for hepatitis A. However, if they

are currently ill, it is not likely to be due to hepatitis A [16].

HEPATITIS B

Selection of Individuals

Individual or groups of individuals which are at highrisk for infection should be tested including health care workers and emergency personnel, partners or individuals living in close household contact with infected person, individuals who have had multiple sex partners or who have been diagnosed with an STD (sexually transmitted disease), injection drug users, men who have sex with men, individuals who received a blood transfusion prior to 1992, individuals who have tattoos or body piercings, individuals who travel to countries where hepatitis B is common (Asia, Africa, South America, the Pacific Islands, Eastern Europe, and the Middle East), individuals emigrating from countries where hepatitis B is common, or who are born to parents who emigrated from such countries and all pregnant women should be tested for hepatitis B infection[17].

Laboratory Tests

Hepatitis B serologic testing involves measurement of several HBV-specific antigens and antibodies. Various serologic markers or combinations of markers are used to identify the different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection/vaccination, or is susceptible to infection [18].

Hepatitis B Serologic Test

Hepatitis B Surface Antigen (HBsAg)

A protein on the surface of hepatitis B virus, it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.

Hepatitis B Surface Antibody (HBsAb or anti-HBs)

The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti-HBs also develop in a person who has been successfully vaccinated against hepatitis B. Someone who is surface antibody positive is not infected, and cannot pass the virus on to others.

Total Hepatitis B Core Antibody (HBcAb or anti-HBc)

Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame. This test is often used by blood banks to screen blood donations [11, 12].

IgM Antibody to Hepatitis B Core Antigen (IgM anti-HBc)

Positivity indicates recent infection with hepatitis B virus. Its presence indicates acute infection [17, 18, 19].

Tests	Results	Interpretation
HBsAg anti-HBc anti-HBs	Negative Negative Negative	Susceptible
HBsAg anti-HBc anti-HBs HBsAg anti-HBc anti-HBs	NegativeImmune due to naturalPositiveinfectionPositiveImmune due toNegativeImmune due toNegativehepatitis B vaccinationPositiveImmune due to	
HBsAg anti-HBc IgM anti- HBc anti-HBs	Positive Positive Positive Negative	Acutely infected
HBsAg anti-HBc IgM anti- HBc anti-HBs	Positive Positive Negative Negative	Chronically infected
HBsAg anti-HBc anti-HBs	Negative Positive Negative	Interpretation unclear as four possibilities: 1. Resolved infection (most common), 2. False-positive anti- HBc, thus susceptible, 3. "Low level" chronic infection, 4. Resolving acute infection.

HBeAg (e-antigen)

This is a protein produced by the virus when it is actively replicating. If this test is positive, it indicates that there is a lot of virus in the blood, which means that you can more easily spread the virus to others [20, 21].

Anti-HBe (e-antibody)

Often as the virus stops replicating in the body and the e-antigen disappear from the blood, the e-antibody appears. This can happen spontaneously or after treatment. It appears with recovery from acute infection. In chronic infection it is generally a marker of reduced viral reproduction (or replication) indicating a less infectious state **[19, 20]**.

Molecular Tests

Molecular tests for diagnosis of hepatitis B includes Hepatitis B DNA Test (HBV-DNA)

It is a highly sophisticated blood test that checks for the presence of hepatitis B virus DNA in the bloodstream. This test indicates how much virus is present in the blood. HBV DNA level in the blood is used to detect active HBV infection and to monitor response to antiviral therapy [21].

Hepatitis B Drug Resistance, Genotype, and BCP/PreCore Mutation

This blood test is not commonly ordered. A liver specialist may order the test to determine a patient's hepatitis B virus genotype (A-H) for research purposes and to detect a viral mutation that may be associated with resistance to current treatments. This is a Polymerase Chain Reaction test, which again, is not readily available or used outside large teaching hospitals [22].

Liver Function Tests (LFTs)

These are a group of blood tests that helps to find out how well the liver is working. The most important test includes ALT.

Alanine Aminotransferase (ALT)

This is an enzyme that is released from liver cells into the bloodstream when the liver is injured. ALT levels are included in the regular monitoring of all chronic hepatitis B patients and this test can also be useful in deciding whether a patient would benefit from therapy, or for evaluating how well a current treatment is working. This test sometimes called SGPT. An elevated ALT level indicates that the liver is not functioning properly and that there is a risk of permanent liver damage. During acute hepatitis B infection, ALT levels can be temporarily elevated, but this rarely leads to long-term liver problems. In chronic hepatitis B, ALT levels can be either periodically or consistently increased, indicating a higher risk of long-term liver damage.

AST (Aspartate Aminotransferase)

It is found in the liver, heart and muscle so is less accurate than the ALT in measuring liver damage. But this enzyme is often ordered to help monitor potential liver damage from the hepatitis B virus [22, 23].

Liver Biopsy

It involves the removal of a small piece of tissue from the liver using a special needle. Tissue is examined under a microscope to look for inflammation or liver damage. Liver biopsy is considered gold standard method to stage liver disease and assess for the degree of fibrosis, but it is not widely used in resource-limited settings because of its high cost, invasiveness, patient discomfort, risk of complications, sampling error, as well as the need for expert histological interpretation **[24]**.

HEPATITIS C

Laboratory Tests

Two categories of virological assays are in practice used for the diagnosis and management of hepatitis C virus (HCV) infection, including serological and molecular biology-based assays. Serological assays includes screening tests based on enzyme immunoassays (EIAs); supplemental "analytical" assays based on immunoblot testing and serological assays detecting genotype-specific antibodies for the serological determination of HCV genotype, so-called "serotyping" assays.

Molecular assays includes qualitative assays, detecting HCV RNA in body fluids, quantitative assays measuring HCV viral load, a parameter that estimates the level of HCV replication in the liver and tests analyzing the sequence of HCV genomes (genotyping assays) [25].

Serologic Assays

Enzyme Immunoassay

Anti-HCV is detected by enzyme immunoassay (EIA). The third-generation test (EIA-3) used today is more sensitive and specific. However, as with all enzyme immunoassays, false-positive results are occasionally a problem with the EIA-3. Additional or confirmatory testing is often helpful. The presence of HCV RNA in serum indicates an active infection. Testing for HCV RNA is also helpful in patients in whom EIA tests for anti-HCV are unreliable. For instance, immune-compromised patients may test negative for anti-HCV despite having HCV infection because they may not produce enough antibodies for detection with EIA [26, 27].

Recombinant Immuno-blot Assay

Immuno-blot assays are used to confirm anti-HCV reactivity, too. These tests are also called "Western blots"; serum is incubated on nitrocellulose strips on which four recombinant viral proteins are blotted. Color changes indicate that antibodies are adhering to the proteins. An immune-blot is considered positive if two or more proteins react and is considered indeterminate if only one positive band is detected. If the immune-blot test is negative, the EIA result was probably a false positive. Immuno-blot tests are routine in blood banks when an anti-HCV-positive sample is found by EIA. Immuno-blot assays are highly specific and valuable in verifying anti-HCV reactivity **[28]**.

Molecular Assays

PCR Amplification

It can detect low levels of HCV RNA in serum. Testing for HCV RNA by PCR is particularly useful when aminotransferases are normal or only slightly elevated, when anti-HCV is not present, or when several causes of liver disease are possible. Thus, the reliability and specificity of the PCR technique are not standardized. In addition, it is expensive and prone to technical or laboratory error [29].

Quantification of HCV RNA in Serum

Several methods are available for measuring the titer or level of virus in serum, which is an indirect assessment of viral load. These methods include a quantitative PCR and a branched DNA (b DNA) test. In addition, serum levels of HCV RNA can vary spontaneously by 3- to 10-folds over time. Viral load does not correlate with the severity of the hepatitis or with a poor prognosis (as it seems to in HIV infection); but viral load does correlate with the likelihood of a response to antiviral therapy. Rates of response to a course of alpha interferon and ribavirin are higher in patients with low levels of HCV RNA. There are several definitions of a "low level" of HCV RNA, but the usual definition is below 2 million copies per milliliter (mL) **[30, 31]**.

Genotyping of HCV

There are 6 known genotypes and more than 50 subtypes of hepatitis C. The genotype of infection is helpful in defining the epidemiology of hepatitis C. Knowing the genotype or serotype (genotype-specific antibodies) of HCV is helpful in making recommendations and counseling regarding therapy. Patients with genotypes 2 and 3 are almost three times more likely to respond to therapy with alpha interferon or the combination of alpha interferon and ribavirin. For these reasons, testing for HCV genotype is often clinically helpful. Once the genotype is identified, it need not be tested again; genotypes do not change during the course of infection [**32**, **33**].

Immunostaining

Immunostaining using polyclonal or monoclonal antibodies to detect HCV antigens in the liver has been reported to be useful. However, these tests are not commercially available, and, even in the hands of research investigators, immunostaining detects HCV antigens in liver tissue in only 60 to 70 percent of patients with chronic hepatitis C--largely in those with high levels of HCV in serum. This test also requires special handling of liver tissue and thus is not appropriate for routine clinical use **[34, 35]**.

Biochemical Indicators for Hepatitis C Virus Infection

1. In chronic hepatitis C, increases in the alanine and aspartate aminotransferases range from 0 to 20 times (but usually less than 5 times) the upper limit of normal. 2. Alanine aminotransferase levels are usually higher than aspartate aminotransferase levels, but that finding may be reversed in patients who have cirrhosis. 3. Alkaline phosphatase and gamma glutamyltranspeptidase are usually normal. If elevated, they may indicate cirrhosis. 4. Rheumatoid factor and low platelet and white blood cell counts are frequent in patients with cirrhosis, providing clues to the presence of advanced disease. 5. The enzymes lactate dehydrogenase and creatinine kinase are usually normal. 6. Albumin levels and prothrombin time are normal until late-stage disease. 7. Iron and ferritin levels may be slightly elevated [36].

Testing Availability and Selection

Two main technologies exist for assessing HCV RNA levels or viral load. Quantitative PCR is the most sensitive test for determining hepatitis C viral load, whereas the branched-chain DNA test appears to be the most precise method. Major limitations of the current tests are inadequate dynamic range and high variability of PCR-based assays, and poor sensitivity of the branched-chain DNA test.

HEPATITIS D

Laboratory Studies

The following serum test results are present in patients with co-infection with hepatitis D virus (HDV) and hepatitis B virus (HBV):

- Results are positive for HDV antigen in 20%
- Results are positive for HDV ribonucleic acid (RNA) in 90%; reverse transcriptase polymerase chain reaction assay is currently the most sensitive assay for the detection of HDV viremia.
- Results for anti-HDV immunoglobulin M (IgM) are positive initially and then are positive for anti-HDV immunoglobulin G (IgG); the finding of antigen A antibody to HDV is almost exclusively associated with chronic HDV infections

HCV Antibody	HCV RNA	HCV Infection
Negative	Negative	No infection or too early after exposure for the test to be accurate; if suspicion remains high, retesting at a later time may be required.
Positive/Indeterminate	Negative	Past infection or no infection (false-positive screen); additional testing if indicated.
Positive/Weak/ Indeterminate	Positive	Current infection

Table 2: Qualitative analysis of serologic tests of hepatitis C.

Test Results Not Infected **HDV Co-infection HDV Super-infection** Hepatitis D antibody (HDV Ab) Negative Positive Positive Hepatitis B surface antigen Positive/Negative Positive Positive (HBsAg) Hepatitis B core IgM antibody Negative Positive Negative (HBc IgM Ab)

Table 3: Interpretation of serologic tests of hepatitis D.

- Results for anti-HB core IgM are positive, except with super-infection, in which anti-HB core IgM is absent
- A hepatic panel may show alanine aminotransferase and aspartate aminotransferase levels greater than 500 IU/L
- For synthetic liver function markers, an international normalized ratio greater than 1.5 or a pro-thrombin time greater than 17 seconds may be the first evidence of fulminant liver failure

Hepatitis B surface antigen (HBsAg) is required for HDV replication but may be suppressed to undetectable levels with active HDV replication.

Imaging Studies

Right upper quadrant ultrasonography helps in the evaluation for biliary obstruction and hepatocellular carcinoma. Perform cholescintigraphy (hydroxyliminodiacetic acid) to exclude acute cholecystitis, if clinically indicated.Perform computed tomography (CT) scanning or magnetic resonance imaging (MRI) if hepatocellular carcinoma is suggested. (An alpha-fetoprotein [AFP] level greater than 250 ng/ml is highly suggestive of hepatocellular carcinoma [HCC] **[37, 38]**.

Procedures and Histologic Findings

Results from liver biopsy in patients with acute disease are consistent with acute hepatitis, and, generally, a biopsy is not indicated. Consider liver biopsy if the serologic diagnosis of hepatitis is inconclusive. In patients with chronic liver disease, liver biopsy is indicated to evaluate for the presence of fibrosis and cirrhosis. HDV antigen immunohistochemical analysis of liver tissue is the criterion standard for establishing a diagnosis of persistent HDV infection. Histologic features are very similar to those observed in patients with HBV infection. Acidophilic bodies and degeneration of hepatocytes with acidophilic cytoplasm are present. The few inflammatory cells (lymphocytes) likely represent the direct cytotoxicity of HDV. Results of immuno-histochemical staining for HDV antigen are positive. With super-infection, staining often reveals that HBsAg is suppressed [39, 40].

Indications for Testing

Abrupt onset of nausea, anorexia or jaundicewith known chronic hepatitis B virus (HBV) with worsening liver disease [41].

HEPATITIS E

The commonly used tests for HEV infection include detection of IgM and IgG anti-HEV antibodies and detection of HEV RNA. IgM anti-HEV antibodies can be detected during the first few months after HEV infection, whereas IgG anti-HEV antibodies represent either recent or remote exposure. The presence of HEV RNA indicates current infection, whether acute or chronic. Although several diagnostic assays for anti-HEV antibodies are available, they have undergone fairly limited testing and often provide discordant results, particularly for IgG antibodies. Additional tests include reverse transcriptase polymerase chain reaction (RT-PCR) to detect the hepatitis E virus RNA in blood and/or stool; this assay requires specialized laboratory facilities. This test is particularly needed in areas where hepatitis E is infrequent, and in cases with chronic HEV infection [42-44].

Hepatitis B PCR Quantitative Blood Test

This test is used to look for the presence of Hepatitis B viral genetic material in the blood. The results for this test are quantitative, meaning they provide a numerical result rather than a simple positive or negative. Because Viral DNA is often detectable sooner than antibodies developed in response to an infection, Hepatitis B PCR testing can be used as a screening for people who have had a recent exposure. This test can also be used a confirmatory test for a previous positive result or to assist in monitoring the effects of antiviral therapy.

Hepatitis B is a viral liver infection which is spread through exposure to infected blood or bodily fluids. It is the most common cause of acute viral Hepatitis. Hepatitis B infections often show no symptoms but when symptoms do occur they are often described as flu-like. Common symptoms include abdominal pain, fever and loss of appetite, nausea, joint pain, fatigue, jaundice, and dark colored urine. Chronic Hepatitis B infections can cause serious health complications like cirrhosis and liver cancer [45, 46].

This test is typically ordered by people: 1. Who require a screening for Hepatitis B but may not yet be at a point after exposure where a Hepatitis B surface Antigen test will be accurate., 2. Are receiving treatment for Hepatitis B and wish to monitor their viral levels to see how effective their course of treatment is., 3. Require a highly sensitive test to confirm the results of a previous Hepatitis B test. Results for this test are quantitative. People who require a Hepatitis B PCR test but only desire a positive or negative result may order the Hepatitis B PCR Qualitative test. People who wish to order a Hepatitis B screening but do not require an early exposure test should consider the Hepatitis B surface Antigen test or the Hepatitis B Panel as they are highly accurate at 3-12 weeks or greater after exposure. Turnaround time for the Hepatitis B PCR quantitative test is typically 5-7 business days. The Hepatitis B PCR test can typically detect the virus 3 weeks from exposure or any time after. Some people may be detectable earlier. This Hepatitis B testing does not have any special requirements [47, 48]

ELISA Test

An enzyme-linked immune-sorbent assay, also called ELISA or EIA, is a test that detects and measures antibodies in your blood. This test can be used to determine if you have antibodies related to certain infectious conditions. Antibodies are proteins that

REFERENCES

- Ki Tae Suk, Dong Joon Kim. Drug-induced liver injury: present and future. Clinical and Molecular Hepatology, 18(3), 249-257, 2012.
- 2. The global burden of disease, 2004 update. World Health Organization, 2004.
- 3. Steven K Herrine. Liver Structure and Function. Merck manuals. Last full review/revision May 2016.
- Wasley A, Grytdal S, Gallagher K. Surveillance for acute viral hepatitis--United States, 2006. MMWR Surveill Summ. 57(2), 1-24, 2008.
- Heidelbaugh J, Sherbondy M. Cirrhosis and chronic liver failure: Part II. Complications and Treatment. Am Fam Physician. 74(5),767-776, 2006.
- Scott JD, Gretch DR. Molecular diagnostics of hepatitis C virus infection: a systemic review. JAMA, 297(7), 724-32, 2007.
- Smedile A, Casey JL, Cote PJ. Hepatitis D viremia following orthotopic liver transplantation involves a typical HDV virion with a hepatitis B surface antigen envelope. Hepatology., 27(6), 1723-9, 1998.
- Rizzetto M, Verme G. Delta hepatitis--present status. J Hepatol. 1(2):187-93, 1985.
- 9. Longatti A. The dual role of exosomes in hepatitis A and C virus transmission and viral immune activation. Viruses. 7(12):6707-15, 2015.
- Liu W, Zhai J, Liu J, Xie Y. Identification of recombination between subgenotypes IA and IB of hepatitis A virus. Virus Genes. 40(2), 222-4, 2010.
- 11. Kodani M, Mixson-Hayden T, Drobeniuc J, Kamili S. Rapid and sensitive approach to simultaneous detection of genomes

your body produces in response to harmful substances called antigens.

A field trial of an enzyme-linked immune-sorbent assay (ELISA) for the detection of the hepatitis Be markers is reported. It is simple to perform, is designed to be read by eye and does not require any expensive apparatus. When compared with a commercially available RIA kit for the detection of the same markers, ELISA was shown to be as sensitive as RIA for the detection of anti-HBe but slightly less sensitive for the detection of HBeAg. However if all specimens negative for both HBeAg and anti-HBe by ELISA are considered to be potentially infectious, the ELISA should prove to be as useful as RIA for determining the "e" status of HBsAg-positive patients and, therefore, provide a reliable indication of the risk of secondary spread of hepatitis B infection to contacts by needle stick accident, close personal contact or perinatal transmission. A blood test, called Hepatitis C Antibody test is used to find out if someone has ever been infected with Hepatitis C.

CONCLUSION

We studied all types of hepatitis tests. Mostly type hepatitis B & Hepatitis C observed in patients and causing agents includes viruses (HBV, HCV). Diagnostic tests performed on PCR, ELISA and doing blood screening. PCR are very expensive techniques and used by higher labs and hospitals. For hepatitis A and hepatitis B vaccination available, whereas, no vaccination to prevent HCV infection.

of hepatitis A, B, C, D and E viruses. J ClinVirol. 61(2), 260-4, 2014.

- Flehmig,B. A solid phase radioimmunoassay for Detection of IgM Antibodies to Hepatitis A Virus; The Journal Of Infectious Diseases, 140, 169-175, 1979.
- Lemon, S.M., et al. Immunoglobulin M Response to Hepatitis A Virus Determined by Solid Phase Radioimmunoassay; Infection and Immunity, 28, 927-936, 1980.
- Roque-Afonso AM, Desbois D, Dussaix E: Hepatitis A virus: serology and molecular diagnostics. Future Virology, 5(2), 233-242, 2010.
- 15. De Paula VS: Laboratory diagnosis of hepatitis A. Future Virology 7(5), 461-472, 2012.
- Ljungstrom I, Engvall E, Ruitenberg EJ. Proceedings: ELISA, enzyme-linked immunosorbent assay—a new technique for sero-diagnosis of trichinosis. Parasitology, 69, 1974
- 17. Runyon BA. and the Practice Guidelines Committee, American Association for the Study of Liver Diseases Management of adult patients with ascites due to cirrhosis. Hepatology. 39, 841–56, 2004.
- Cordoba J, Lopez-Hellin J, Planas M, Sabin P, Sanpedro F, Castro F, et al. Normal protein diet for episodic hepatic encephalopathy: results of a randomized study. J Hepatol. 41, 38–43, 2004.
- Schuurs AHWM, van Weemen BK. Enzyme-immunoassay: a powerful analytical tool [Review]. J Immunoassay 1, 229-249, 1980.
- Sartori M, La Terra G, Aglietta M. Transmission of hepatitis C via blood splash into conjunctiva [letter] Scand J Infect Dis. 25, 270–1, 1993.

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- Ippolito G, Puro V, Petrosillo N. Simultaneous infection with HIV and hepatitis C virus following occupational conjunctival blood exposure [letter] JAMA. 280, 28, 1998.
- 22. Watson KJ. Surgeon, test (and heal) thyself: sharps injuries and hepatitis C risk. Med J Aust. 181:366–7, 2004.
- 23. Bean P. Latest discoveries on the infection and coinfection with hepatitis D virus. Am Clin Lab. 21(5), 25-7, 2002.
- John D. Scott, David R. Gretch, Molecular Diagnostics of Hepatitis C Virus Infection , JAMA. 297(7), 724-732, 2007.
- 25. Sonal Asthana, Norman Kneteman, Operating on a patient with hepatitis C , PMC, 2724804.
- 26. World Health Organization Hepatitis C. Geneva: The Organization; 2009. Initiative for vaccine research.
- Sherman M, Shafran S, Burak K. Management of chronic hepatitis C: consensus guidelines. Can J Gastroenterol. 21, 25–34, 2007.
- Wong JB, McQuillan GM, McHutchison JG. Estimating future hepatitis C morbidity, mortality, and costs in the United States. Am J Public Health. 2000; 90: 1562–9.
 Albright JE, Cook SE. Projecting future complications of chronic hepatitis C in the United States. Liver Transpl. 9, 331, 2003.
- Dienstag JL, McHutchison JG. American Gastroenterological Association technical review on the management of hepatitis C. Gastro-enterology. 130, 231–64, 2006.
- Mast EE, Hwang LY, Seto DS, et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. J Infect Dis. 192, 1880– 9, 2005.
- Strader DB, Wright T, Thomas D. Diagnosis, management, and treatment of hepatitis C. Hepatology. 39:1147–71, 2004.
- Puro V, De Carli G, Cicalini S, et al. European recommendations for the management of healthcare workers occupationally exposed to hepatitis B virus and hepatitis C virus. Euro Surveill. 10, 260–4, 2005.
- 33. Thorburn D, Roy K, Cameron SO. Risk of hepatitis C virus transmission from patients to surgeons: model based on an unlinked anonymous study of hepatitis C virus prevalence in hospital patients in Glasgow. Gut. 52, 1333–8, 2003.
- Thorburn D, Roy K, Wilson K, et al. Anonymous pilot study of hepatitis C virus prevalence in liver transplant surgeons. Liver Transpl. 12, 1084–8, 2006.
- 35. Gunson RN, Shouval D, Roggendorf M, et al. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections in health

care workers (HCWs): guidelines for prevention of transmission of HBV and HCV from HCW to patients. J ClinVirol. 27, 213–30, 2003.

- Thornburn D, Dundas D, McCruden EA. A study of hepatitis C prevalence in healthcare workers in the West of Scotland. Gut. 48, 116–23, 2001.
- Alfaiate D, Deny P, Durantel D. Hepatitis delta virus: from biological and medical aspects to current and investigational therapeutic options. Antiviral Res. 122, 112-29, 2015.
- Braga WS, Castilho Mda C, Borges FG. Hepatitis D virus infection in the Western Brazilian Amazon - far from a vanishing disease. Rev Soc Bras Med Trop. 45(6), 691-5, 2012.
- Heidrich B, Deterding K, Tillmann HL, Raupach R, Manns MP, Wedemeyer H. Virological and clinical characteristics of delta hepatitis in Central Europe. J Viral Hepat. 16(12), 883-94, 2009.
- Makuwa M, Mintsa-Ndong A, Souquiere S, Nkoghe D, Leroy EM, Kazanji M. Prevalence and molecular diversity of hepatitis B virus and hepatitis delta virus in urban and rural populations in northern Gabon in central Africa. J ClinMicrobiol. 47(7), 2265-8, 2009.
- Ordieres C, Navascues CA, Gonzalez-Dieguez ML. Prevalence and epidemiology of hepatitis D among patients with chronic hepatitis B virus infection: a report from Northern Spain. Eur J Gastroenterol Hepatol. 29(3),277-83, 2017.
- 42. Aggarwal R, Jameel S: Hepatitis E. Hepatology, 54(6), 2218-2226, 2011.
- 43. Hoofnagle JH, Nelson KE, Purcell RH: Hepatitis E. New Engl J Med 367, 1237-1244, 2012.
- 44. Aggarwal R: Diagnosis of hepatitis E. Nat Rev Gastroenterol Hepatol, 10, 24-33, 2013.
- 45. HU, Gray JW. A programmable system to perform the polymerase chain reaction. DNA. 7(6), 441–7, 1988.
- Van Guilder HD, Vrana KE, Freeman WM. Twenty-five years of quantitative PCR for gene expression analysis. BioTechniques. 44(5), 619–26, 2008.
- Stahlberg A, Thomsen C, Ruff D, et al. Quantitative PCR analysis of DNA, RNAs, and Proteins in the same single cell. Clin Chem. 58, 1682–1691, 2012.
- Dobrovolskaia, E., Gam, A., and Slater, J.E. Competition enzyme-linked immunosorbant assay (ELISA) can be a sensitive method for the specific detection of small quantities of allergen in a complex mixture. Clin Exp Allergy. 36, 525– 530, 2006.