RECOMMENDATIONS

According to this study, the following recommendations could be suggested:

1. Further studies should be done to clarify the efficacy of serum HA in determining the severity of liver fibrosis using larger sample size to be able to detect cut off values for HA in diagnosing liver fibrosis.

2. Further studies are required to estimate the role of serum HA in estimating response to the current HCV treatment lines.

3. The studies will be conducted to evaluate the changes in HA level in response to treatment should be before and after study rather than two different groups study.

4. Further studies are required to evaluate HA in other causes of liver fibrosis as HBV, NASH and in patients with HBV/HIV co infection.

REFERENCES

1. Ryan KJ, Ray CG. Sherris medical microbiology. 4thed. New York: McGraw Hill; 2004.

2. Maheshwari A, Ray S, Thuluvath PJ. Acute hepatitis C. Lancet 2008; 372 (9635): 321–32.

3. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet 2011; 378 (9791): 571–83.

4. Rosen HR. Clinical practice: chronic hepatitis C infection. N Engl J Med 2011; 364 (25): 2429–38.

5. Fauci AS, Braunwald E, Isselbacher KJ. Harrison´s principles of internal medicine. 14thed. Singapore: McGraw-Hill; 1998.

6. Nakano T, Lau GM, Sugiyama M, Mizokami M. An updated analysis of hepatitis C virus genotypes and subtypes based on the complete coding region. Liver Int 2011; 32 (2): 339–45.

7. Van Soest H, Boland GJ, Van Erpecum KJ. Hepatitis C: changing genotype distribution with important implications for patient management. Netherland J Med 2006; 64: 96-9.

8. Kessler HH, Stelzl E, Raggam RB, Haas J, Kirchmeir F, Hegenbarth K, et al. Effects of storage and type of blood collection tubes on hepatitis C virus level in whole blood samples. J Clin Microbiol 2001; 39: 1788-90.

9. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57(4):1333-42.

10. World Health Organization (WHO). Hepatitis C. Geneva: WHO; 2011.

11. Alter MJ. Epidemiology of hepatitis C virus infection. World J Gastroenterol 2007; 13 (17): 2436–41.

12. Wilkins T, Malcolm JK, Raina D, Schade RR. Hepatitis C: diagnosis and treatment. Am Fam Physician 2010; 81 (11): 1351–7.

13. Highest rates of hepatitis C virus transmission found in Egypt. Al Bawaaba [Cited On: 9 Aug, 2010]. Available from: http://www.albawaba.com/news/highest-rates-hepatitis-c-virus-transmission-found-egypt.[Accessed On: 5 Nov, 2014].

14. Xia X, Luo J, Bai J,Yu R. Epidemiology of HCV infection among injection drug users in China: systematic review and meta-analysis. Public health 2008; 122 (10): 990–1003.

15. Tohme RA, Holmberg SD. Is sexual contact a major mode of hepatitis C virus transmission?. Hepatology 2010; 52 (4): 1497–505.

16. Mast EE. Mother-to-infant hepatitis C virus transmission and breastfeeding. Advances in Experimental Medicine and Biology 2004; 554: 211–6.

17. Jafari S, Copes R, Baharlou S, Etminan M, Buxton J. Tattooing and the risk of transmission of hepatitis C: a systematic review and meta-analysis. Int J Infect Dis 2010; 14 (11): 928–40.

18. Wong T, Lee SS. Hepatitis C: a review for primary care physicians. CMAJ 2006; 174 (5): 649–59.

19. Pondé RA. Hidden hazards of HCV transmission. Medical Microbiol Immunol 2011; 200 (1): 7–11.

20. Lindenbach B, Rice C. Unravelling hepatitis C virus replication from genome to function. Nature 2005; 436 (7053): 933–8.

21. Penin F, Dubuisson J, Rey FA, Moradpour D. Structural biology of hepatitis C virus. Hepatology 2004;39:5-19.

22. Marcellin P. Hepatitis C: clinical spectrum of the disease. J Hepatol 1999; 31 (Suppl. 1): 9-16.

23. Gonzalez-Peralta RP, Davis GL, Lau JY. Pathogenetic mechanisms of hepatocellular damage in chronic hepatitis C virus infection. J Hepatol 1994; 21: 255-9.

24. Lerat H, Berby F, Trabaud MA, Vidalin O, Major M, Trépo C, et al. Specific detection of hepatitis C minus strand RNA in haematopoietic cells. J Clin Invest 1996; 97: 845-51.

25. Pileri P, Uematsu Y, Campagloni S, Galli G, Falugi F, Petracca R, et al. Binding of hepatitis C virus to CD81. Science 1998; 282: 938 - 41.

26. Shimizu YK, Hijikata M, Iwamoto A, Alter HJ, Purcell RH, Yoshikura H. Neutralizing antibodies against hepatitis C virus and the emergence of neutralization escape mutant viruses. J Virol 1994; 68: 1494 - 500.

27. Bukh J, Miller RH, Purcell RH. Genetic heterogeneity of hepatitis C virus: quasispecies and genotypes. Semin Liver Dis 1995; 15: 41- 63.

28. Weiner AJ, Brauer MJ, Rosenblatt J, Richman KH, Tung J, Crawford K, et al. Variable and hypervariable domains are found in the regions of HCV corresponding to the flavivirus envelope and NSl proteins and the pestivirus envelope glycoproteins. Gastroenterology 1999; 117: 408-13.

29. Neumann AU, Lam NP, Dahari H, Gretch DR, Wiley TE, Layden TJ, et al. Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon alfa therapy. Science 1998; 282: 103-7.

30. Moser M, Murphy KM. Dendritic cell regulation of Th1-Th2 development. Nat Immunol 2001, 1:199–203.

31. Zeuzem S, Franka A, Lee JH, Herrmann G, Ruster B, Roth WK. Phylogenetic analysis of hepatitis C virus isolates and their correlation to viremia, liver function tests, and histology. Hepatology 1996; 1003 - 9.

32. Féray C, Caccamo L, Alexander GJ, Ducot B, Gugenheim J, Casanovas T, et al. European collaborative study on factors influencing outcome after liver transplantation for hepatitis C. Gastroenterology 1999; 117: 619-25.

33. Soriano V, Garcia-Samaniego J, Rodriguez-Rosado R. Hepatitis C and HIV infection: biological, clinical, and therapeutic implications. J Hepatol 1999; 31 (Suppl.1): 119-23.

34. Wiley TE, McCarthy M, Breidi L, MC Carthy M, Layden TJ. Impact of alcohol on the histological and clinical progression of hepatitis C infection. Hepatology 1998; 28: 805 - 9.

35. Pagliaro L, Peri V, Linea C. Camma C, Guinta M, Magrin S. Natural history of chronic hepatitis C. Ital J Gastroenterol Hepatol 1999; 31: 28 - 44.

36. Gremion C, Cerny A. Hepatitis C virus and the immune system: a concise review. Rev Med Virol 2005; 154:235-68.

37. Zavaglia C, Martinetti M, Silini E, Bottelli R, Daielli C, Asti M, et al. Association between HLA class II alleles and protection from or susceptibility to chronic hepatitis C. J Hepatol 1998; 281:1-7.

38. Rehermann B, Chang KM, McHutchison JG, Kokka R, Houghton M, Chisari FV. Quantitative analysis of the peripheral blood cytotoxic T lymphocyte response in patients with chronic hepatitis C virus infection. J Clin Invest 1996;98: 1432-40.

39. Taylor DR, Shi ST, Lai MM. Hepatitis C virus and interferon resistance. Microbes Infect 2000; 2:1743-56.

40. Mangia A, Santoro R, Piattelli M, Pazienza V, Grifa G, Iacobellis A, et al. IL-10 haplotypes as possible predictors of spontaneous clearance of HCV infection. Cytokine.2004; 253:103-9.

41. Bellentani S, Pozzato G, Saccoccio G, Crovatto M, Crocè LS, Mazzoran L, et al. Clinical course and risk factors of hepatitis C virus related liver disease in the general population: report from the Dionysos study. Gut 1999; 446:874-80.

42. Lepe R, Layden-Almer JE, Layden TJ, Cotler S. Ethnic differences in the presentation of chronic hepatitis C. J Viral Hepat 2006; 132:116-20.

43. Friedman SL. Liver fibrosis-from bench to bedside. J Hepatol 2003; 38(Suppl. 1):S38-53.

44. Pinzani M. Liver fibrosis. Springer Semin Immunopathol 1999; 21:475–90.

45. Arthur MJ. Fibrogenesis II metalloproteinases and their inhibitors in liver fibrosis. Am J Physiol Gastrointest Liver Physiol 2000; 279:G245-9.

46. Gabele E, Brenner DA, Rippe RA. Liver fibrosis: signals leading to the amplification of the fibrogenic hepatic stellate cell. Front Biosci 2003; 8: D69-77.

47. Marra F. Hepatic stellate cells and the regulation of liver inflammation. J Hepatol 1999; 31:1120-30.

48. Lindquist JN, Marzluff WF, Stefanovic B. Fibrogenesis III posttranscriptional regulation of type I collagen. Am J Physiol Gastrointest Liver Physiol 2000; 279:G471-6.

49. Sato M, Suzuki S, Senoo H. Hepatic stellate cells: unique characteristics in cell biology and phenotype. Cell Struct Funct 2003; 28:105-12.

50. Magness ST, Bataller R, Yang L, Brenner DA. A dual reporter gene transgenic mouse demonstrates heterognity in hepatic fibrogenic cell populations. Hepatology 2004; 40:1151-9.

51. Suskind DL, Muench MO. Searching for common stem cells of the hepatic and hematopoietic systems in the human fetal liver: CD34+ cytokeratin 7/8+ cells express markers for stellate cells. J Hepatol 2004; 40: 261-8.

52. Higuchi H, Gores GJ. Mechanisms of liver injury: an overview. Curr Mol Med 2003; 3:483-90.

53. Canbay A, Friedman S, Gores GJ. Apoptosis: the nexus of liver injury and fibrosis. Hepatology 2004; 39:273-8.

54. Zaltron S, Spinetti A, Biasi L, Baiguera C, Castelli F. Chronic HCV infection: epidemiological and clinical relevance. BMC Infect Dis 2012; 12 (Suppl 2): S2.

55. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidence and risk factors. J Gastroenterology 2004; 127: 35–50.

56. Zignego AL, Ferri C, Pileri SA, Caini P, Bianchi FB. Extrahepatic manifestations of hepatitis C virus infection: A general overview and guidelines for a clinical approach. Dig Liver Dis 2007; 391:2-17.

57. Manns MP, Rambusch EG. Autoimmunity and extrahepatic manifestations in hepatitis C virus infection. J Hepatol 1999; 31:39-42.

58. Pascual M, Perrin L, Giostra E, Schifferli JA. Hepatitis C virus in patients with cryoglobulinemia type II. J Infect Dis 1990;162 (2): 569–70.

59. Johnson R, Gretch D, Yamabe H, Hart J, Bacchi CE, Hartwell P, et al. Membranoproliferative glomerulonephritis associated with hepatitis C virus infection. N Engl J Med 1993; 328 (7) : 465–70.

60. Alter MJ, Seeff LB, Bacon BR, Thomas DL, Rigsby MO, Di Bisceglie AM. Testing for hepatitis C virus infection should be routine for persons at increased risk for infection. Ann Intern Med 2004;141:715-7.

61. Centers for Disease Control and Prevention (CDC). Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV related chronic disease. MMWR Recomm Rep 1998;47:1-39.

62. Colin C, Lanoir D, Touzet S, Meyaud-Kraemer L, Bailly F, Trepo C. Sensitivity and specificity of third-generation hepatitis C virus antibody detection assays: an analysis of the literature. J Viral Hepat 2001;8:87-95.

63. Thio CL, Nolt KR, Astemborski J, Vlahov D, Nelson KE, Thomas DL. Screening for hepatitis C virus in human immunodeficiency virus-infected individuals. J Clin Microbiol 2000;38:575-7.

64. Kalantar-Zadeh K, Miller LG, Daar ES. Diagnostic discordance for hepatitis C virus infection in hemodialysis patients. Am J Kidney Dis 2005; 46: 290-300.

65. Alter MJ, Kuhnert WL, Finelli L. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Centers for Disease Control and Prevention. MMWR Recomm Rep 2003; 52:1-15.

66. Scott JD, Gretch DR. Molecular diagnostics of hepatitis C virus infection: a systematic review. JAMA 2007;297:724-32.

67. Saldanha J, Lelie N, Heath A. Establishment of the first international standard for nucleic acid amplification technology (NAT) assays for HCV RNA: WHO collaborative study group. Vox Sang 1999;76:149-58.

68. Germer JJ, Rys PN, Thorvilson JN. Determination of hepatitis C virus genotype by direct sequence analysis of products generated with the Amplicor HCV test. J Clin Microbiol 1999;37:2625-30.

69. Proceedings of the international workshop on epidemiology, diagnosis and management of hepatitis c infection. Med Community 1996; 6-7:1-32.

70. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology 2009; 49(4):1335-74.

71. Ruiz-Moreno M, Leal-Orozco A, Millàn A. Hepatitis C virus infection in children. J Hepatol 1999, 31:124-9.

72. Silva MA, Hegab B, Hyde C, Guo B, Buckels JA, Mirza DF. Needle track seeding following biopsy of liver lesions in the diagnosis of hepatocellular cancer: a systematic review and meta-analysis. Gut 2008; 57 (11): 1592–6.

73. Bedossa P, Dargere D, Paradis V. Sampling variability of liver fibrosis in chronic hepatitis C. Hepatology 2003; 38: 1449-57.

74. Guido M, Rugge M. Liver biopsy sampling in chronic viral hepatitis. Semin Liver Dis 2004; 24: 89-97.

75. Al KB, Shiffman M. Percutaneous liver biopsy in clinical practice. Liver Int 2007; 279:1166–73.

76. Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68, 276 biopsies. J Hepatol 1986; 22:165–73.

77. Knodell RG, Ishak KG, Black WC, Chen TS, Craig R, Kaplowitz N, et al. Formulation and application of a numerical scoring system for assessing histological activity in asymptomatic chronic active hepatitis. Hepatology1981;15:431-5

78. Schmid M, Flery R, Buhler H, Havelka J, Grob PJ, Heitz PU. Chronic viral hepatitis B and C: an argument against the conventional classification of chronic hepatitis. Virchows Arch 1994; 425: 221-8.

79. Ishak K, Baptista A, Bianchi L. Histologic grading and staging of chronic hepatitis. J Hepatol 1995;24:289-93.

80. Bedossa P, Poynard T. An algorithm for grading activity in chronic hepatitis C. Hepatology 1996;24:289-93.

81. Poynard T, Ratziu V, Benmanov Y, Di Martino V, Bedossa P, Opolon P. Fibrosis in patients with chronic hepatitis C: detection and significance. Semin Liv Dis 2000;20:47-55.

82. French METAVIR Cooperative Study Group. Intraobserver and inter-observer variations in liver biopsies in patients with chronic hepatitis C. Hepatology 1994;20:15-20.

83. Zhou K, Lu LG. Assessment of fibrosis in chronic liver diseases. J Dig Dis 2009; 10(1):7-14

84. Afdhal NH, Nunes D. Evaluation of liver fibrosis: a concise review. Am J Gastroenterol 2004; 99: 1160-74.

85. Grigorescu M. Noninvasive biochemical markers of liver fibrosis. J Gastrointestin Liver Dis 2006; 15(2):149-59.

86. Pinzani M, Rombouts K, Colagrande S. Fibrosis in chronic liver disease: diagnostic and management. J Hepatol 2005; 42: S12-36.

87. Bataller R, Brenner DA. Liver fibrosis. J Clin Invest 2005; 115(2):209–18.

88. Gelse K, Poschl E, Aigner T. Collagens—structure, function, and biosynthesis. Adv Drug Deliv Rev 2003; 55(12):1531–46.

89. Rosenberg WM, Voelker M, Thiel R, Becka M, Burt A, Schuppan D, et al. Serum markers detect the presence of liver fibrosis: a cohort study. Gastroenterology 2004; 127(6):1704–13.

90. Teare JP, Sherman D, Greenfield SM, Simpson J, Bray G, Catterall AP, et al. Comparison of serum procollagen III peptide concentrations and PGA index for assessment of hepatic fibrosis. Lancet 1993; 342(8876):895–8.

91. Giannini E, Caglieris S, Ceppa P, Risso D, Lantieri PB, Testa R. Serum pro-collagen III peptide levels are related to lobular necrosis in untreated patients with chronic hepatitis C. Eur J Gastroenterol Hepatol 2001;13(2):137–41.

92. Lohr M, Hummel F, Martus P, Cidlinsky K, Kröger JC, Hahn EG, et al. Serum levels of extracellular matrix in acute pancreatitis. Hepatogastroenterology 1999; 46(30):3263–70.

93. Tebib JG, Viguier P, Noel E, Colson F, Barbier Y, Bouvier M. Serum N terminal procollagen III fragment: a predictive marker of joint destruction in rheumatoid arthritis? Clin Rheumatol 1992;11(4):502–7.

94. Gabrielli GB, Corrocher R. Hepatic fibrosis and its serum markers: a review. Dig Dis 1991;9(5):303–16.

95. Leeming DJ, Nielsen MJ, Dai Y, Veidal SS, Vassiliadis E, Zhang C, et al. Enzyme-linked immunosorbent serum assay specific for the 7S domain of Collagen Type IV (P4NP 7S): A marker related to the extracellular matrix remodeling during liver fibrogenesis. Hepatol Res 2012; 42(5):482-93.

96. Schytte S, Hansen M, Moller S, Junker P, Henriksen JH, Hillingsø J, et al. Hepatic and renal extraction of circulating type I procollagen aminopropeptide in patients with normal liver function and in patients with alcoholic cirrhosis. Scand J Clin Lab Invest 1999;59(8):627–33.

97. McHutchison JG, Blatt LM, De Medina M, Craig JR, Conrad A, Schiff ER, et al. Measurement of serum hyaluronic acid in patients with chronic hepatitis C and its relationship to liver histology. J Gastroenterol Hepatol 2000;15(8):945–51.

98. Berres ML, Papen S, Pauels K, Schmitz P, Zaldivar MM, et al. A functional variation in CHI3L1 is associated with severity of liver fibrosis and YKL-40 serum levels in chronic hepatitis C infection. J Hepatol 2009; 50(2):370–6.

99. Leroy V, Monier F, Bottari S, Trocme C, Sturm N, Hilleret MN, et al. Circulating matrix metalloproteinases 1, 2, 9 and their inhibitors TIMP-1 and TIMP-2 as serum markers of liver fibrosis in patients with chronic hepatitis C: comparison with PIIINP and hyaluronic acid. Am J Gastroenterol 2004;99(2):271–9.

100. Boeker KH, Haberkorn CI, Michels D, Flemming P, Manns MP, Lichtinghagen R. Diagnostic potential of circulating TIMP-1 and MMP-2 as markers of liver fibrosis in patients with chronic hepatitis C. Clin Chim Acta 2002; 316(1–2):71–81.

101. Moreno M, Bataller R. Cytokines and renin-angiotensin system signaling in hepatic fibrosis. Clin Liver Dis 2008; 12(4):825–52.

102. Kanzler S, Baumann M, Schirmacher P, Dries V, Bayer E, Gerken G, et al. Prediction of progressive liver fibrosis in hepatitis C infection by serum and tissue levels of transforming growth factor-beta. J Viral Hepat 2001; 8(6):430–7.

103. Breitkopf K, Godoy P, Ciuclan L, Singer MV, Dooley S. TGF-beta/Smad signaling in the injured liver. Z Gastroenterol 2006; 44(1):57–66.

104. Bonner JC. Regulation of PDGF and its receptors in fibrotic diseases. Cytokine Growth Factor Rev 2004; 15(4):255–73.

105. Zhang BB, Cai WM, Weng HL, Hu ZR, Lu J, Zheng M, et al. Diagnostic value of platelet derived growth factor-BB, transforming growth factor-beta1, matrix metalloproteinase-1, and tissue inhibitor of matrix metalloproteinase-1 in serum and peripheral blood mononuclear cells for hepatic fibrosis. World J Gastroenterol 2003; 9(11):2490–6.

106. Gressner OA, Lahme B, Demirci I, Gressner AM, Weiskirchen R. Differential effects of TGF-beta on connective tissue growth factor (CTGF/CCN2) expression in hepatic stellate cells and hepatocytes. J Hepatol 2007; 47(5):699–710.

107. Gressner OA, Gressner AM. Connective tissue growth factor: a fibrogenic master switch in fibrotic liver diseases. Liver Int 2008; 28(8):1065–79.

108. Kovalenko E, Tacke F, Gressner OA, Zimmermann HW, Lahme B, Janetzko A, et al. Validation of connective tissue growth factor (CTGF/CCN2) and its gene polymorphisms as noninvasive biomarkers for the assessment of liver fibrosis. J Viral Hepat 2009; 16(9):612–20.

109. Dufour DR, Lott JA, Nolte FS, Gretch DR, Koff RS, Seeff LB. Diagnosis and monitoring of hepatic injury. I. Performance characteristics of laboratory tests. Clin Chem 2000; 46(12):2027–49.

110. Park GJ, Lin BP, Ngu MC, Jones DB, Katelaris PH. Aspartate aminotransferase: alanine aminotransferase ratio in chronic hepatitis C infection: is it a useful predictor of cirrhosis? 1. J Gastroenterol Hepatol 2000;15(4):386–90.

111. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C 1. Hepatology 2003;38(2):518–26.

112. Shaheen AA, Myers RP. Diagnostic accuracy of the aspartate aminotransferase-to-platelet ratio index for the prediction of hepatitis C-related fibrosis: a systematic review 5. Hepatology 2007;46(3):912–21.

113. Lin ZH, Xin YN, Dong QJ, Wang Q, Jiang XJ, Zhan SH, et al. Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis 1. Hepatology 2011; 53(3): 726-36.

114. Poynard T, Imbert-Bismut F, Munteanu M. Overview of the diagnostic value of biochemical markers of liver fibrosis (FibroTest, HCV FibroSure) and necrosis (ActiTest) in patients with chronic hepatitis C. Comp Hepatol 2004;3(1):8-23.

115. Castra L, Foucher J, Bertet J, Couzigou P, de Ledinghen V. FibroScan and FibroTest to assess liver fibrosis in HCV with normal aminotransferases1. Hepatology 2006;43(2): 373-4.

116. Rockey DC, Bissell DM. Noninvasive measures of liver fibrosis 4. Hepatology 2006; 43(2 Suppl 1):S113–20.

117. Halfon P, Imbert-Bismut F, Messous D, Antoniotti G, Benchetrit D, Cart-Lamy P, et al. A prospective assessment of the interlaboratory variability of biochemical markers of fibrosis FibroTest and activity test ActiTest in patients with chronic liver disease. Comp Hepatol 2002; 1(1):3.

118. Patel K, Gordon SC, Jacobson I, Hézode C, Oh E, Smith KM, et al. Evaluation of a panel of non-invasive serum markers to differentiate mild from moderate-to advanced liver fibrosis in chronic hepatitis C patients. J Hepatol 2004;41: 935-42.

119. Romero-Gomez M, Gomez-Gonzalez E, Madrazo A, Vera-Valencia M, Rodrigo L, Pérez-Alvarez R, et al. Optical analysis of computed tomography images of the liver predicts fibrosis stage and distribution in chronic hepatitis C. Hepatology 2008; 47: 810-6.

120. Ganne-Carrié N, Ziol M, de Ledinghen V, Douvin C, Marcellin P, Castera L, et al. Accuracy of liver stiffness measurement for the diagnosis of cirrhosis in patients with chronic liver diseases. Hepatology 2006; 44: 1511-7.

121. Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, et al. Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. Gastroenterology 2008; 134: 960-74.

122. Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Gonçales FL Jr, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. N Engl J Med 2002;347:975-82.

123. American Association for the Study of Liver Diseases and Infectious Diseases Society of America. Recommendations for testing, managing, and treating hepatitis C. HCV guidelines 2014. Available from: http://www.hcvguidelines.org/full-report-view. [Accessed On: 14 Dec, 2014].

124. Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. Ann Intern Med 2012;156(4):271-8.

125. Lawitz E, Sulkowski MS, Ghalib R, Rodriguez-Torres M, Younossi ZM, Corregidor A, et al. Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naive patients: the COSMOS randomised study. Lancet 2014;384(9956):1756-65.

126. de Weerd NA, Samarajiwa SA, Hertzog PJ. Type I interferon receptors: biochemistry and biological functions. J Biol Chem 2007; 282 (28): 53–7.

127. Liu YJ. IPC: professional type 1 interferon-producing cells and plasmacytoid dendritic cell precursors. Annu Rev Immunol 2005 ; 23: 275–306.

128. Hermant P, Michiels T. Interferon-λ in the context of viral infections: production, response and therapeutic implications. J Innate Immun 2014; 17: 35-9.

129. Sharieff KA, Duncan D, Younossi Z. Advances in treatment of chronic hepatitis C: 'pegylated' interferons. Cleve Clin J Med 2002; 69 (2): 155–9.

130. Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. Lancet 2001; 358(9286):958-65.

131. Hadziyannis SJ, Sette H Jr, Morgan TR, Balan V, Diago M, Marcellin P, et al. Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. Ann Intern Med 2004; 140(5): 346-55.

132. Ascione A, De Luca M, Tartaglione MT, Lampasi F, Di Costanzo GG, Lanza AG, et al. Peginterferon alfa-2a plus ribavirin is more effective than peginterferon alfa-2b plus ribavirin for treating chronic hepatitis C virus infection. Gastroenterology 2010; 138(1):116-22.

133. NIH Consensus Statement on Management of Hepatitis C: 2002. NIH Consens State Sci Statements 2002; 19(3):1-46.

134. Zylberberg H, Chaix ML, Brechot C. Infection with hepatitis C virus genotype 4 is associated with a poor response to interferon-alpha. Ann Intern Med 2000;132:845-6.

135. Koshy A, Marcellin P, Martinot M, Madda JP. Improved response to ribavirin interferon combination compared with interferon alone in patients with type 4 chronic hepatitis C without cirrhosis. Liver 2000;20: 335-9.

136. Kamal SM, El Tawil AA, Nakano T, He Q, Rasenack J, Hakam SA, et al. Peginterferon alpha-2b and ribavirin therapy in chronic hepatitis C genotype4: impact of treatment duration and viral kinetics on sustainedvirological response. Gut 2005; 54: 858-66.

137. Okanoue T, Sakamoto S, Itoh Y, Minami M, Yasui K, Sakamoto M, et al. Side effects of high-dose interferon therapy for chronic hepatitis C. J Hepatol 1996; 25: 283-91.

138. Lawitz E, Mangia A, Wyles D, Rodriguez-Torres M, Hassanein T, Gordon SC, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med May 2013; 368(20):1878-87.

139. Jacobson IM, Gordon SC, Kowdley KV, Yoshida EM, Rodriguez-Torres M, Sulkowski MS, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med 2013; 368(20):1867-77.

140. Afdhal N, Reddy KR, Nelson DR, Lawitz E, Gordon SC, Schiff E, et al. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. N Engl J Med 2014; 370(16):1483-93.

141. Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. N Engl J Med 2014; 370(20):1889-98.

142. Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, et al. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med 2014; 370(20):1879-88.

143. Naggie S, Sulkowski M, Lalezari J, Fessel WJ, Mounzer K, Shuhart M, et al. All-oral therapy with sofosbuvir plus ribavirin for the treatment of HCV genotype 1, 2, and 3 infection in patients Co-infected with HIV (PHOTON-1). Presented In: 21stConference on Retroviruses and Opportunistic Infections. March 3-6, 2014 . Boston, MA; 2014

144. Douek DC, Roederer M, Koup RA. Emerging concepts in the immunopathogenesis of AIDS. Annu Rev Med 2009; 60: 471-84.

145. Arthos J, Cicala C, Martinelli E, Macleod K, Ryk DV, Wei D. HIV-1 envelope protein binds to and signals through intergrin, the gut mucosal homing receptor for peripheral Tcells. Nat Immunol 2008; 9: 301-9.

146. Plantier JC, Leoz M, Dickerson JE, De Oliveria F, Cordonnier F, Lemee V. A new human Immunodeficiency virus derived from gorillas. Nat Med 2009; 15: 871-2.

147. Gelderblom HR, Gentile M, Scheidler A. Zur Struktur und Funktion bei HIV. AIFO 1993; 5: 231.

148. Orenstein JM. Ultrastruture of HIV/AIDS. Pathol 2002; 26: 245-50.

149. Ferguson MR, Rojo DR, von Lindern JJ. HIV-1replication cycle. Clin Lab Med 2002; 22: 611-35.

150. Berger EA, Murphy PM, Farber JM. Chemokine receptors as HIV-1 coreceptors: Roles in viral entry, tropism, and disease. Annu Rev Immunol 1999; 17:657-700.

151. Mage'rus-Chatinet A, Yu H, Garcia S, Ducloux E. Galactosyl ceramide expressed on dendritic cells can mediate HIV-1 transfer from monocyte derived dendritic cells to autologous T cells. Virol 2007; 362: 67-74.

152. Pantaleo G, Demarest JF, Schacker T, Vaccarezza M, Cohen OJ, Daucher M, et al. The qualitative nature of the primary immune response to HIV infection is a prognosticator of disease progression independent of the initial level of plasma viremia. Proc Natl Acad Sci USA 1996; 94 (1): 254–8.

153. Mehandru S, Poles MA, Tenner-Racz K, Horowitz A, Hurley A, Hogan C, et al. Primary HIV-1 infection is associated with preferential depletion of CD4+ T lymphocytes from effector sites in the gastrointestinal tract. J Exp Med 2004; 200(6): 761–70.

154. UNAIDS. UNAIDS report on the global AIDS epidemic. UNAIDS 2013. Available from:http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/20131120_UNAIDS_Global_Report_2013_en.pdf [Accessed On: 2 Dec, 2014].

155. Global AIDS Response Progress Report 2012 Arab Republic of Egypt. National Aids Program. 2012. 4-12. Available from: http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/ce_EG_Narrative_Report%5B1%5D.pdf [Accessed On: 28 Mar, 2014].

156. Barrada M. In Brief: epidemic update in Egypt. UNAIDS 2012. Available from: http://www.un.org.eg/docs/UNAIDS%20NEWSLETTER_Egypt_Issue%201_EN.pdf. [Accessed On: 2 Dec, 2014].

157. Hollingsworth TD, Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. J Infect Dis 2008; 198:687-93.

158. Boily MC, Baggaley RF, Wang L. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies. Lancet Infect Dis 2009; 9:118–29.

159. Public Health Agency of Canada (PHAC). HIV Transmission risk: a summary of evidence. Public Health Agency of Canada. PHAC 2013. Available from: http://www.phac-aspc.gc.ca/aids-sida/publication/hivtr-rtvih-eng.php.[Accessed on 21 Mar, 2013].

160. Brooks M. Eliminating HIV/HCV among injection drug users is possible. Medscape Medical News from the: International Conference on Viral Hepatitis (ICVH) 2012. Available from: http://www.medscape.com/viewarticle/761011.[Accessed On: 13 Dec, 2012].

161. Mofenson LM. Prevention in neglected subpopulations: prevention of mother-to-child transmission of HIV infection. Clin Infect Dis 2010; 50 (Suppl 3): S130-48.

162. De Cock KM, Fowler MG, Mercier E, de Vincenzi I, Saba J, Hoff E, et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. JAMA 2000; 283(9):1175-82.

163. Walkely A. Africa: HIV Transmission Via Transfusions in Continent Remains High. All Africa 2009. Available from: http://allafrica.com/stories/201001050140.html [Accessed on January 23, 2013].

164. Beltrami EM, Williams IT, Shapiro CN, Chamberland ME. Risk and management of blood-borne infections in health care workers. Clin Microbiol Rev 2000; 13(3):385-407

165. Hecht FM, Busch MP, Rawal B, Webb M, Rosenberg E, Swanson M, et al. Use of laboratory tests and clinical symptoms for identification of primary HIV infection. AIDS 2002;16(8):1119-29.

166. Giles M, Workman C. Clinical manifestations and the natural history of HIV. In: Hoy J, Lewin S, Post JJ, Street A (eds). HIV management in Australasia: a guide for clinical care. Sydney: Australasian Society for HIV Medicine; 2009. 125-7.

167. World Health Organization (WHO): Case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva: WHO; 2007.

168. Jackson BR, Busch MP, Stramer SL, AuBuchon JP. The cost-effectiveness of NAT for HIV, HCV, and HBV in whole-blood donations. Transfusion 2003;43:721-9.

169. Drosten C, Panning M, Drexler JF, Hänsel F, Pedroso C, Yeats J, et al. Ultrasensitive monitoring of HIV-1 viral load by a low-cost real-time reverse transcription-PCR assay with internal control for the 5`long terminal repeat domain. Clin Chem 2006; 52: 1258-66.

170. Gazzard BG, Anderson J, Babiker A, Boffito M, Brook G, Brough G, et al. British HIV Association Guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. HIV Med 2008;9(8):563-608.

171. WHO Health Organization (WHO). Antiretroviral therapy. Geneva: WHO; 2010.

172. Simon V, Ho DD, Abdool Karim Q. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. Lancet 2006; 368:489-504.

173. Hammer SM, Eron JJ, Reiss P, Schooley RT, Thompson MA, Walmsley S. Antretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. JAMA 2008; 300: 555-70.

174. Graham CS, Baden LR, Yu E, Mrus JM, Carnie J, Heeren T, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. Clin Infect Dis 2001;33(4):562-9.

175. Greub G, Ledergerber B, Battegay M, Grob P, Perrin L, Furrer H, et al. Clinical progression, survival, and immune recovery during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV Cohort Study. Lancet 2000; 356(9244):1800-5.

176. Ragni MV, Nalesnik MA, Schillo R, Dang Q. Highly active antiretroviral therapy improves ESLD-free survival in HIV-HCV co-infection. Haemophilia 2009; 15(2):5 52-8.

177. Soriano V, Puoti M, Sulkowski M, Cargnel A, Benhamou Y, Peters M, et al. Care of patients coinfected with HIV and hepatitis C virus: 2007 updated recommendations from the HCV-HIV International Panel. AIDS 2007;21(9):1073-89.

178. Halfon P, Bourliere M, Penaranda G, Deydier R, Renou C, Botta-Fridlund D, et al. Accuracy of hyaluronic acid level for predicting liver fibrosis stages in patients with hepatitis C virus. Comp Hepatol 2005;4:6.

179. Murray RK, Granner DK, Mayes PA, Rodwell VW. Harper's illustrated biochemistry. 26thed. New York: McGraw-Hill; 2003.

180. Necas J, Bartosikova L, Brauner P, Kolar J. Hyaluronic acid (hyaluronan): a review. Vet Med 2008;53(8):397–411.

181. Kopke-Aguiar LA, Martins JR, Passerotti CC, Toledo CF, Nader HB, Borges DR. Serum hyaluronic acid as a comprehensive marker to assess severity of liver disease in schistosomiasis. Acta Trop 2002;84(2):117–26.

182. Gressner OA, Weiskirchen R, Gressner AM. Biomarkers of hepatic fibrosis, fibrogenesis and genetic predisposition pending between fiction and reality. J Cell Mol Med 2007; 115: 1031-51.

183. Montazeri G, Estakhri A, Mohamadnejad M, Nouri N, Montazeri F, Mohammadkani A, et al. Serum hyaluronate as a non-invasive marker of hepatitic fibrosis and inflammation in HBeAg negative chronic hepatitis B. BMC Gastroenterol 2005, 5:32

184. Stickel F. Serum hyaluronate correlates with histological progression in alcoholic liver disease. Eur J Gastroenterol Hepatol 2001; 8: 42-50.

185. Suzuki A, Angulo P, Lymp J, Li D, Satomura S, Lindor K. Hyaluronic acid, an accurate serum marker for severe hepatic fibrosis in patients with non-alcoholic fatty liver disease. Liver Int 2005; 25: 779-86.

186. Crawford DHG, Murphy TL, Ramm LE, Fletcher LM, Clouston AD, Anderson GJ, et al. Serum hyaluronic acid with serum ferritin accurately predicts cirrhosis and reduces the need for liver biopsy in C282Y Hemochromatosis. Hepatology 2009; 492: 418-42.

187. Nishiura T, Watanabe H, Ito M, Matsuoka Y, Yano K, Daikoku M, et al. Ultrasound evaluation of the fibrosis stage in chronic liver disease by the simultaneous use of low and high frequency probes. Br J Radiol 2005; 78927:189-97.

188. Puoti M, Moiodi MC, Travi G, Rossotti R. The burden of liver disease in HIV infected patients. Semin Liver Dis 2012; 32: 103-13.

189. Bica I, McGovern B, Dhar R, Stone D, McGowan K, Scheib R, et al. Increasing mortality due to endstage liver disease in patients with human immunodeficiency virus infection. Clin Infect Dis 2001; 32:492–7.

190. Mohsen AH, Easterbrook PJ, Taylor C, Portmann B, Kulasegaram R, Murad S, et al. Impact of human immunodeficiency virus (HIV) infection on the progression of liver fibrosis in hepatitis C virus infected patients. Gut 2003; 52:1035–40.

191. Rancinan C, Neau D, Saves M, Lawson-Ayayi S, Bonnet F, Mercié P, et al. Is hepatitis C virus co-infection associated with survival in HIV-infected patients treated by combination antiretroviral therapy? AIDS 2002; 16:1357–62.

192. Chung RT, Evans SR, Yang Y, Theodore D, Valdez H, Clark R, et al. Immune recovery is associated with persistent rise in hepatitis C virus RNA, infrequent liver test flares, and is not impaired by hepatitis C virus in co-infected subjects. AIDS 2002; 16:1915–23.

193. Liang TJ, Rehermann B, Seeff LB, Hoofnagle JH. Pathogenesis, natural history, treatment, and prevention of hepatitis C. Ann Intern Med 2000;132:296-305.

194. Myers RP, Fong A, Shaheen AA. Utilization rates, complications and costs of percutaneous liver biopsy: a population-based study including 4275biopsies. Liver Int 2008; 28(5): 705–12.

195. Korner T, Kropf J, Gressner AM. Serum laminin and hyaluronan in liver cirrhosis: markers of progression with high prognostic value. J Hepatol 1996; 25(5):684-8.

196. Imbert-Bismut F, Ratziu V, Pieroni L, Charlotte F, Benhamou Y, Poynard T. Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. Lancet 2001; 357(9262):1069-75.

197. Poynard T, Imbert-Bismut F, Ratziu V, Chevret S, Jardel C, Moussalli J, et al. Biochemical markers of liver fiborsis in patients infected by Hepatitis C virus: Longitudinal validation in a randomized trial. J Viral Hepat 2002; 9:128-33.

198. Abo Al-Azm A and El-Sheikh M. Prevalence of hepatitis C and B viruses in Gharbia Governorate rural area in comparison with a group of blood donors. JHGID1996; 4(4): 31-9.

199. Pinzani M. Pathogenesis of hepatic fibrosis in liver disease from bench to bedside. Massachusetts: American Association for the Study of Liver Disease; 2004.

200. Jam S, Ramezani A, Sabzvari D, Moradmand-Badie B, Seyedalinaghi S, Jabbari H, et al. A cross-sectional study of anemia in human immunodeficiency virus-infected patients in Iran. Arch Iran Med 2009; 12(2):145-50.

201. Enawgaw B, Alem M, Addis Z, Melku M. Determination of hematological and immunological parameters among HIV positive patients taking highly active antiretroviral treatment and treatment naïve in the antiretroviral therapy clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study. BMC Hematol 2014; 14(1):8.

202. Toson ESA, EL- Bendary MM, El-Mezayen HA, Sahyon HA. Longitudinal evaluation of hyaluronic acid and its degrading enzymes and degradation products in Egyptian patients with chronic hepatitis C. Paper Presented In: International Conference on Advances in Agricultural, Biological & Environmental Sciences (AABES-2014) Oct 15-16, 2014 Dubai (UAE); 2014.

203. Saitou Y, Shiraki K, Yamanaka Y, Yamaguchi Y, Kawakita T, Yamamoto N, et al. Noninvasive estimation of liver fibrosis and response to interferon therapy by a serum fibrogenesis marker, YKL-40, in patients with HCV-associated liver disease. World J Gastroenterol 2005; 11(4): 476–81.

204. Arain SA, Meo SA, Jamal Q. Serum hyaluronic acid level does not reliably differentiate minimal and significant liver disease in chronic hepatitis C. Saudi Med J 2011;32(12):1241–5.

205. Guéchot J, Loria A, Serfaty L, Giral P, Giboudeau J, Poupon R. Serum hyaluronan as a marker of liver fibrosis in chronic viral hepatitis C: effect of α-interferon therapy J Hepatol 1995; 221:22-6.

206. Patel K, Lajoie A, Heaton S, Pianko S, Pianko S, Behling CA, Bylund D, et al. Clinical use of hyaluronic acid as a predictor of fibrosis change in hepatitis C. J Gastroenterol Hepatol 2003;18(3):253–7.

207. Valva P, Casciato P, Diaz Carrasco JM, Gadano A, Galdame O, Galoppo MC, et al. The role of serum biomarkers in predicting fibrosis progression in pediatric and adult hepatitis C virus chronic infection. PLoS One 2011;6(8):1-10.

208. Peters L, Mocroft A, Soriano V, Rockstroh J, Rauch A, Karlsson A, et al. Hyaluronic acid levels predict risk of hepatic encephalopathy and liver-related death in HIV/viral hepatitis coinfected patients. PLoS One 2013; 8:5. 1-10.

209. Kelleher TB, Mehta SH, Bhaskar R, Sulkowski M, Astemborski J, Thomas DL, et al. Prediction of hepatic fibrosis in HIV/HCV co-infected patients using serum fibrosis markers: the SHASTA index. J Hepatol 2005; 43(1): 78–84.

210. Nunes D, Fleming C, Offner G, O'Brien M, Tumilty S, Fix O, et al. HIV infection does not affect the performance of noninvasive markers of fibrosis for the diagnosis of hepatitis C virus related liver disease. J Acquir Immune Defic Syndr 2005;40:538–44.

211. Croquet V, Vuillemin E, Ternisien C, Pilette C, Oberti F, Gallois Y, et al. Prothrombin index is an indirect marker of severe liver fibrosis. Eur J Gastroenterol Hepatol 2002;14(10):1133-41.

212. Coverdale SA, Samarasinghe DA, Lin R, Kench J, Byth K, Khan MH, et al. Changes in antipyrine clearance and platelet count, but not conventional liver tests, correlate with fibrotic change in chronic hepatitis C: value for predicting fibrotic progression. Am J Gastroenterol 2003; 98(6): 1384-90.

213. Friedman LS, Mantin P ,Munoz SJ. Laboratory methods for evaluation of the patients with liver disease. In: Zakim D, Boyer TD (eds). Hepatology: a textbook of liver disease, Ithedn. Philadelphia: Saunders; 2002. 661-708.

214. Frébourg T, Delpech B, Bercoff E, Senant J, Bertrand P, Deugnier Y, et al. Serum hyaluronate in liver diseases: study by enzymoimmunological assay. Hepatology 1986;63:392-5.

215. Pradat P, Alberti A, Poynard T, Esteban JI, Weiland O, Marcellin P, et al. Predictive value of ALT levels for histologic findings in chronic hepatitis C: a European collaborative study. Hepatology 2002;36(4 Pt 1):973-7.

216. Chen YP, Feng XR, Dai L, Zhang L, Hou JL. Non-invasive diagnostic screening of hepatic fibrosis in patients with chronic hepatitis B. Chin Med J Engl 2004; 1177: 1109-12.

الملخص العربي

إن فيروس الالتهاب الكبدي سي هو السبب الرئيسي لمرض الكبد المزمن ، حيث أن حوالي ١٧٠ مليون شخص حول العالم مصابون بشكل مزمن بفيروس الالتهاب الكبدي سي وتعد مصر هي أكثر الدول شيوعا في الإصابة بالفيروس حيث تصل معدلات الإصابة إلي ١٥-٢٠% من إجمالي السكان . يعد الالتهاب الكبدي المزمن سي أحد الأسباب الرئيسية لتليف الكبد، سرطان الكبد و أمراض الكبد ذات المرحلة المتقدمة و غالبا ما تكون العدوى بدون أعراض، ولكن العدوى المزمنة من الممكن أن تؤدي إلى تندب الكبد انتهاءا إلى تليف الكبد، الذي يكون واضحا بعد سنوات عديدة.

كان الانترفيرون مع أقراص الريبافيرين هو العلاج المعتمد من قبل إدارة الأغذية و العقاقير حتى وقت قريب مضي لعلاج فيروس سي. حديثا أدي ظهور فئة جديدة من العقاقير التي تعمل علي الفيروس بشكل مباشر إلي حدوث تطور ثوري في علاج الالتهاب الكبدي الفيروسي سي.

فيروس نقص المناعة البشرية هو عضو من عائلة الفيروسات الارتجاعية، يسبب متلازمة نقص المناعة المكتسب (الإيدز) في الإنسان. و تتميز هذه المتلازمة بفشل تقدمي في الجهاز المناعي مما يسمح بحدوث العدوى بالأمراض الانتهازية المهددة للحياة. ويعرف أن تزامن العدوى بفيروس التهاب الكبدي سي وفيروس نقص المناعة البشرية شائع الحدوث في الفئات الأكثر عرضة وذلك بسبب الطرق المشتركة لانتقال العدوى.

إن التقدم في علاج فيروس نقص المناعة المكتسبة أدي إلي أن تليف الكبد و أمراض الكبد المتقدمة أصبحت السبب الرئيسي للوفاة في المرضي المصابين بفيروس نقص المناعة البشرية.

كما انه من المعروف أن التقدم في مرض الكبد وصولا إلي مرحلة الفشل الكبدي المتقدم عادة ما يستغرق فترة زمنية تتراوح بين ٢٠- ٣٠ عاما في عدوي أحادية فيروس سي ولكن تزامن العدوى مع فيروس نقص المناعة البشرية يؤدي إلي تسارع هذا التقدم.

التليف الكبدي هو عملية التئام الجروح ردا على الإصابات الحادة أو المزمنة بالخلايا الكبدية حيث يؤدي الالتهاب الكبدي المزمن إلي تليف الكبد وحدوث خلل قد يكون خطيرا بوظائف الكبد.

تقليديا يعد التشخيص بواسطة العينة الكبدية هو المعيار الذهبي الذي يمكن من خلاله تقييم تطور التليف ولكنه إجراء اختراقي يحمل العديد من المضاعفات، وبالتالي فإن تحديد دلالات بديلة لتليف الكبد قد يكون مفيداً للحد من عدد عينات الكبد للمرضى المصابين بالالتهاب الكبدي.

حمض الهيالورونيك يتم تصنيعه فى الكبد عن طريق الخلايا الكبدية النجمية ويتم التخلص منه عن طريق الخلايا الغشائية الجيبية ويزداد حمض الهيالورونيك بالدم مباشرة مع تطور مرض الكبد المزمن

تهدف هذه الدراسة الي دراسة حمض الهيالورونيك في المصل كعلامة لتقييم درجة التليف و التنبؤ بأحداث خطيرة في المرضي المصابين بعدوي أحادية فيروس سي والعدوى المشتركة مع فيروس نقص المناعة البشرية ودراسة التغير في مستوي حمض الهياليورونيك في المصل قبل وبعد استخدام الانترفيرون في المرضي المصابين بفيروس سي.

وقد أجريت هذه الدراسة علي أربعة وثمانين مريضا تم تقسيمهم إلي ثلاث مجموعات رئيسية،المجموعة الأولي هي مجموعة العلاج بالانترفيرون وتنقسم إلي مجموعة ما قبل العلاج ومجموعة ما بعد العلاج. أما المجموعة الثانية هي مجموعة مرضي الالتهاب الكبدي سي المزمن وتنقسم إلي مجموعة المرضي الذين لديهم مرض كبدي متكافئ ومجموعة المرضي بمرض كبدي غير متكافئ أما المجموعة الثالثة فتشتمل علي مرضي فيروس سي المزمن المتزامن مع فيروس نقص المناعة البشرية وتنقسم الي مجموعة لديها مرض بالكبد و أخري ليس لديها أية أمراض بالكبد ومجموعة ثالثة من مرضي فيروس نقص المناعة البشرية كمجموعة حاكمة حيث تتكون كل مجموعة من ١٢ مريضا.

وقد خضع جميع المرضى لما يلى بعد اخذ موافقتهم المستنيرة:-

١. التاريخ المرضى الدقيق والفحص السريرى الشامل

٢. التحاليل المعملية وتشمل:
- تحاليل روتينية : صورة دم كاملة،سكر صائم،بولينا وكريا تنين بالدم
- وظائف الكبد والتي تشمل إنزيمات الكبد والزلال والبيليروبين والبروثرومبين والفوسفاتيز القاعدي
- دلالات فيروسية: الأجسام المضادة لفيروس سي ، الانتيجن السطحي لفيروس بي و الحمض النووي بالتفاعل التسلسلي لإنزيم بلمرة الحامض النووي لفيروس سي
- تشخيص فيروس نقص المناعة البشرية بواسطة الاليزا و ويسترن بلوت.
- المرضي الذين خضعوا لعلاج الانترفيرون تم إجراء الفحوص الآتية لهم : الهرمون المحفز للغدة الدرقية، ألفا فيتو بروتين ، الأجسام المضادة للبلهارسيا ،الأجسام النووية المضادة و فحص العينة الكبدية.

٣. فحص البطن بالموجات فوق الصوتية

٤. قياس مستوى حمض الهيالورونيك في المصل باستخدام فحص الإليزا.

و قد تم استبعاد المرضي الذين لديهم تليف كبدي نتيجة اية امراض اخري والمرضي المصابين بامراض شديدة و الذين يعانون من أمراض تؤثر علي مستوي حمض الهيالورونيك مثل إلتهاب المفاصل الروماتويدى وإلتهاب المفاصل و تصلب الشرايين العام المُترقي، الذئبة الحمامية العامة وتصلب الجلد والأمراض الخبيثة والإناث الحوامل.

وتم الحصول على النتائج وجدولتها وتحليلها إحصائياً:-

- حمض الهياليورونيك سجل اختلافا إحصائيا واضحا في كل المجموعات التي تم دراستها وتم تسجيل اعلي مستوي في مرضي فيروس سي الذين لديهم مرض كبدي غير متكافئ بمتوسط ١٤٨.٣٣نانو جرام/مل يليه مرضي فيروس سي المزمن المتزامن مع فيروس نقص المناعة البشري ولديهم مرض بالكبد بمتوسط ٥٨.٥٩ ثم مرضي الالتهاب الكبدي سي المزمن ولديهم مرض كبدي متكافئ بمتوسط ٤٨.٩٤ و مرضي فيروس سي قبل استخدام علاج الانترفيرون بمتوسط ٤٤.١٢.
- كان هناك تناسبا ايجابيا طرديا بين مستوي حمض الهياليورونيك ودرجة تليف الكبد التي كشف عنها بواسطة عينة الكبد في مجموعة العلاج بالانترفيرون.
- بمناظرة وظائف الكبد تلاحظ وجود تناسب طردي ولكن غير مؤثر بين حمض الهيالورونيك ومستوي الانين ترانسفيراز في كل المجموعات. أيضا وجد تناسبا طرديا بين حمض الهياليورونيك وكل من إنزيم الاسبرتات ترانسفيراز و البيليروبين الكلي و المباشر وعلي خلاف ذلك وجد تناسبا عكسيا قويا بين حمض الهيالورونيك وكلا من مستوي الالبيومين و نشاط البروثرومبين.
- بمناظرة نتائج فحص الموجات الصوتية تلاحظ وجود توافق بين هذه النتائج ونتائج فحص العينة الكبدية بالمجموعة الأولي ووجود تناسبا طرديا بينها وبين حمض الهيالورونيك في كل المجموعات الخاضعة للدراسة.

وبناءا علي النتائج السابقة يمكن استخلاص ان حمض الهيالورونيك يمكن ان يستخدم كعلامة غير اختراقية لدرجة التليف بالكبد يمكن الاعتماد عليه لاتخاذ القرارات المتعلقة بالعلاج و رصد الاستجابة له ، كما انه يوجد علاقة طردية بينه وبين شدة المرض في المرضي المصابين بفيروس سي المزمن ويمكنه التنبؤ بالأحداث الخطيرة بالكبد في عدوي فيروس سي المتزامن مع فيروس نقص المناعة البشرية.

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رسالة مقدمة

لقسم طب المناطق الحارة ـ كلية الطب ـ جامعة الإسكندرية
ضمن متطلبات درجة

الماجستير

فى

الماجستير فى طب المناطق الحارة

مقدمة من

سلوى محمد علي الحوفى

بكالوريوس الطب والجراحة ، ٢٠٠٥
كلية الطب، جامعة الإسكندرية

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