Effects of hepatitis B and C infections on lipid profile and complement 3 , 4 in patients in AL- Najaf governorate.

تأثير الأصابة بالتهاب الكبد الفايروسي نوع (C,B)على صورة الدهون والمتممة (4,3) في مرضى محافظة النجف الأشرف .

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Abstract

The study was conducted 30 out patients infected by viral hepatitis type C , 30 infected with viral hepatitis type B and 20 control people to determine the effect of infection with viral hepatitis C and B on levels of complement 3 and complement 4, TG, HDL, LDL and VLDL in patients infected with viral hepatitis C and B compared with healthy group. Who have visited Al-Sadder medical city and Al-Hakeem Hospital in Al- Najaf governorate during the period from March 2014 till January 2015. The results showed significant decrease (P< 0.01) in levels of C3 and C4. also decrease in levels of HDL , VLDL and triglyceride in patients in both HBV& HCV in compared to control group ,but increased LDL concentration in patients compared to control group and the increase in patients with type B more than type C.

Key Word: viral hepatitis, complement 3, complement 4.

الخلاصة

صممت الدراسة الحالية لتحديد تأثير الإصابة بالتهاب الكبد الفيروسي نوع (C ,B) على مستوى المتم (3 , 4) لدى المصابين بالتهاب الكبد الفايروسي الوافدين الى مدينة الصدر الطبية ومستشفى الحكيم العام في محافظة النجف الاشرف مقارنة بالنسب الطبيعية وتضمنت الدراسة 60 مريضاً , 30 مريضاً مصاباً بالتهاب الكبد الفيروسي من نوع C و 30 مريضاً مصاباً بالتهاب الكبد الفيروسي من نوع B أذ تم جمع عينات الدم من شهر آذار 2014 ولغاية شهر كانون الثاني 2015. حيث سجلت النتائج نقصاً معنوياً(P<0.01)في مستوى كل من المتممة (4,3) لدى الأشخاص المصابين مقارنة بمجموعة السيطرة . كذلك سجلت النتائج انخفاض معنوي (P< 0.01) في مستوى كل من (HDL.VLDL.TG) لدى المصابين بكلا النوعين (HBV,HCV) مقارنة بالأشخاص الأصحاء في حين سجلت الدراسة زيادة معنوية في مستوى LDL وان مقدار هذه الزيادة لدى المصابين بال تهاب الكبد الفايروسي نوع B اعلي من الأشخاص المصابين بالتهاب الكبد الفايروسي نوع C.

Introduction

Hepatitis means inflammation of the liver. There are many reasons for the liver to be inflamed by viral, toxic, metabolic, pharmacologic, or immune- mediated attack on the liver [1]. Viral hepatitis is a major global health problem all over the world [2, 3]. The infection with chronic hepatitis B (HBV) and C (HCV) viruses, and alcoholic and non-alcoholic fatty liver disease are the major etiologies. [4]

Acute infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) can result in chronic hepatitis if the infection persists for more than six months. The rate of spontaneous clearance varies according to the virus, the age of the patient at onset of infection and other factors.[5]

Hepatitis B virus (HBV) infection is a worldwide problem, two bilions people have been infected with hepatitis B virus (HBV), 360 million have chronic infection, and 600,000 die each year from HBV-related liver disease or hepatocellular carcinoma (HCC) · Hepatitis B virus (HBV) belongs to the Hepadnavirida family, Humans are the only known natural host. HBV

enters the liver via the bloodstream, and replication occurs only in liver tissue [6]. HBV can be transmitted vertically from mother to children or horizontally through sexual or household contact or by unsafe injections, but chronic infections acquired during infancy or childhood account for a disproportionately large share of worldwide morbidity and mortality.[7]

HCV is a single-stranded, positive-sense RNA virus in the *flaviviraidae* family.[2] HCV is spread primarily via human blood by unscreened blood transfusions, inadequately sterilized needles, syringes etc.[9] Among intravenous drug users in developed countries 20-40% are being infected with HCV during their first year of intravenous drug abuse and after five years more than 90% are infected. Spreading of HCV by sexual contacts may occur but are less frequent. Casual contact or coughing provides no risks of HCV spreading neither are food or water infectious. There is also a low risk (5%) for mother-to-infant transmission of HCV observed globally.[10]

HCV has different prevalence in different parts of the world. In the main parts of Africa, Europe, Southeast Asia and America the prevalence is below 2.5%. In the Western Pacific the prevalence varies between 2.5-4.9% and in the countries of Middle East the HCV infected represent 1% to more than 12% of the population.[11] There are distinct local variations with extreme high prevalence for example in Cameroon, Republic of the Congo, Central African Re public, Equatorial Guinea and Mongolia, all with more than 10% of the population infected.[12] The highest known prevalence is in Egypt with 24% of the population infected. The exceptionally high amount of infected in Egypt is due to a national paranteral antischistosomal therapy (PAT) campaign, in which inadequate sterilization of injection equipment was common[.5] During an acute HCV infection only 20-30% of the infected persons develop symptoms[.4] On the other hand only about 20% of the infected can see a spontaneous clearance. The remaining 80% of the infected develop a chronic infection, 10-20% of these 80% develop cirrhosis and 1-5% with a chronic infection develops liver cancer within 20-30 years.[11] WHO estimated in October 2000 that 170 million people worldwide are chronically infected with HCV. This number equals 3% of the population in the world![9]

The complement (C) system is a set of biochemical pathways that removes pathogen components from an organism as part of the innate and acquired immunity programs. Activation of the complement system triggers a wide range of cellular responses ranging from apoptosis (cell death) to opsonization (antigen/antibody binding) [13]. It has been widely recognized that the complement system plays a critical role in the pathogenesis of a variety of chronic human diseases, including autoimmune diseases, atherosclerosis, the vascular complications of diabetes, complement-mediated hemolytic anemia, and infertility in both males and females [14,15] so that The aim of this study is to study of effect infection by viral hepatitis B and C virus on complement (C3,C4) level and (HDL,LDL,VLDL and TG).

Specimens

Samples were collected in the period from August 2014 until February 2015 , 30 samples were collected from patients and 20 healthy who attended AL-Sadder Teaching Hospital and AL-Zahra Hospital in AL-Najaf governorate, blood samples were drawn by vein-puncture into specimen tubes and remains for 30 minutes at room temperature. After that the samples were centrifuged 3000 rpm for 5 minutes (Backman /counter, Germany**)** to separate the serum, the samples were kept in deep freeze at -20C^{o} till used for the determination of complement 3(C3) , C4 and lipid profile test.

Method

Measured complement 3 and complement 4 by used(EASY RID MULTIPLATE) are plates for determination in radial immunodiffusion of human plasma proteins in serum and plasma. It made by Liofilchem s.r.lare in 4 configurations

procedure

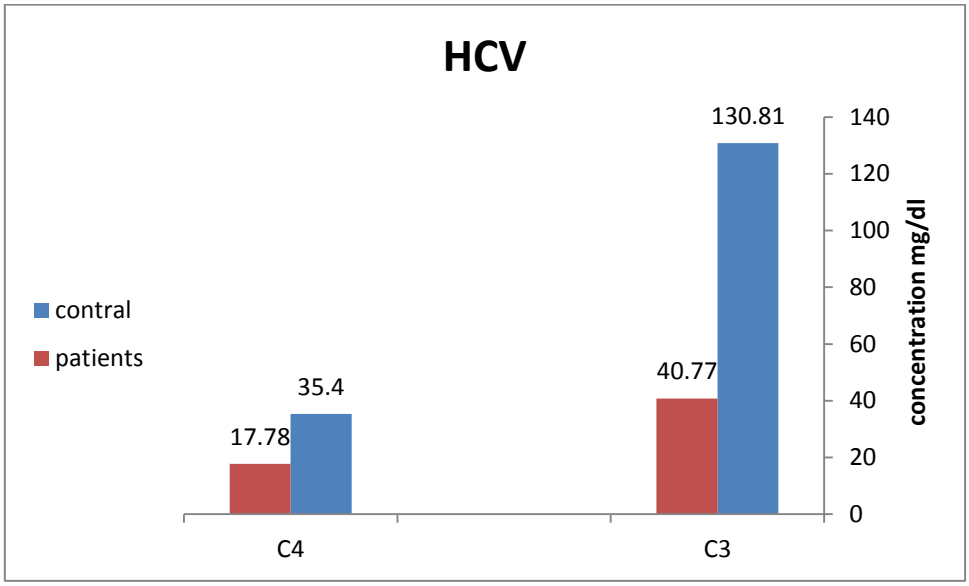
1- Remove easy rid multiplate from the envelope, open the plate and leave it for about 5 at room temperature so that any condensed water in the wells can evaporate.
2- fill the well with 5 µl of sample.
3- After the samples have diffused into the gel for about 20º, close the plate with the lid and leave to stand ,overturned ,in the envelope , at room temperature for 48 hours.
4- After 48 h , measure the precipitin rings diameters using a suitable measuring device (mm).The proteins concentration foe the precipitin ring diameters can be read using the attached tables.

Statistical analysis

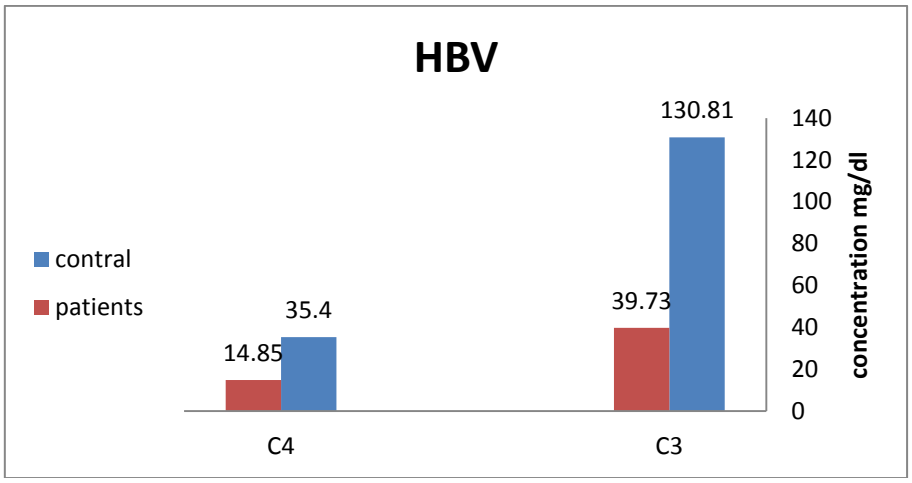
Data were analyzed using the data are expressed as the mean ± standard error (SE). The comparison between the patients and healthy groups were analyzed by one-way ANOVA. A p-value < 0.01 was considered significant.

Result

The present study recorded significant ($p < 0.01$) decrease in the concentration of the complement 3 and 4 in infected with HBC where as concentration of the complement C3 was (40.77 mg /dl ±.991) compared to healthy (130.81 mg /dl ± 0.891) where as the complementary 4(17.78 mg /dl ± 0.960) compared to healthy people (35.4mg / dl ± 0.769) as shown in Figure(1). The study also showed significant($p < 0.01$) decrease in the concentration of C3 and C4 in infected with viral hepatitis B ,where the concentration C3 was (39.73 mg / dl ±0.897) compared to the control group (130.81 mg / dl ± 0.891). The C4 concentration was (14.84 mg / dl ± 0.763) in patients compared to the control group (35.4 mg / dl ± 0.769) as shown in Figure(2).

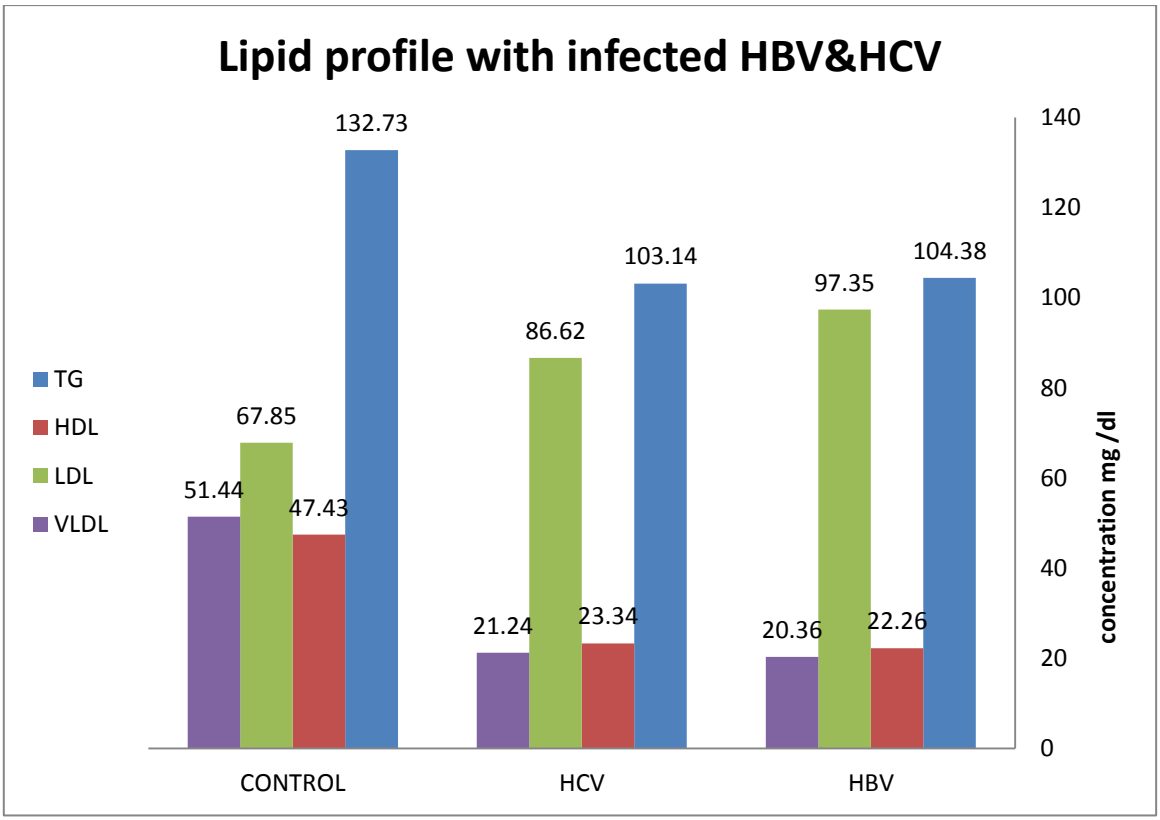


Figure(1) C3 andC4 concentration of viral hepatitis C patients and control group.
*Significant difference between control group and patients ($P < 0.01$)



Figure(2) C3 andC4 concentration of viral hepatitis B patients and control group.
*Significant difference between control group and patients (P < 0.01)

The study also showed significant decrease in the concentration of HDL, LDL ,VLDL and TG in patients with viral hepatitis B and C($p < 0.01$),where the concentration HDL was(22.26 mg / dl ± 4.657),(23.34 mg / dl ± 4.673) respectively compared to the control group (47.43mg / dl ± 4.873) .while the LDL concentration was (97.35mg / dl ± 6.694) ,(86.62 mg /dl ±5.567) respectively in patients compared to the control group (67.85 mg / dl ± 3.589) .whilst VLDL concentration was (20.36 mg /dl ± 5.437) , (21.24 mg /dl ±5.598) respectively compared to the control group (51.44± 4.986) and TG concentration was (104.38 ± 6.574) ,(103.14 mg /dl ±5.972) respectively compared to the control group (132.73±5.682) as shown in Figure(3).



Figure(3) Lipid profile concentration of viral hepatitis B ,C patients and control group.
*Significant difference between control group and patients (P < 0.01)

Discussion

The complement system consists of about 30 soluble and membrane bound proteins and activated by three distinct pathways either on pathogen surface or in plasma. Activation of these pathways depends on different molecules for their initiation , all three activation pathways converges the level of C3 to form the C5 converters such as the C4b,C2a,C3b. C3b and C4b bound to immune complex potentiate antibody response and enhance immunologic [16].small complement fragment C3a,C4a act on specific receptors to produce local inflammatory responses[17]. C3 and C4 of human complement plays a central role in innate immune function as its activation is required to trigger classical as well as alternative complement pathways .

In viral hepatitis the mechanisms responsible for HBV and HCV persistence and disease pathogenesis remain poorly understood and interaction of hepatitis viruses and the host immune system is likely involved [18]Although the complement has been shown to contribute to the protection of host from virus infection [19,20]

In this study , we have observed that sera from patients infected with hepatitis C and B virus displayed significatly lower C3 and C4 level than sera from healthy individuals ($p < 0.01$). previous studied reported decreased C3 and C4 serum levels in patients with hepatitis C [21,22,23].

As in our study (24) found that serum complement C4 level was low in patients with CHC. Reduction in C3 and C4 concentrations in these patients may reflect complement consumption or reduced production due to a decline in the number of functioning hepatocytes. This hypothesis is supported by the simultaneous decrease in the concentrations of C4 and albumin, which are produced in the liver. Since the liver is the major site of synthesis of most of the complement components, the low serum complement level has been proposed to be induced by the defective synthesis of the components [25,26].These results indicate that patients with hepatic disease have severe complement depletion that is probably multifactorial in origin. This impairment in complement function may be returned to two mechanisms: afailure to synthesis a certain number of components and regulatory proteins of complement and an increased consumption due to activation of the complement system. The increase consumption theory was supported by several reports [27,28].

The low level of (HDL.VLDL and TG) in patients infected with viral C and B came in line with the findings of the [29] and the high level of LDL because the inverse relationship between the level and the rest of the lipid . From results of present study concluded that there is a significant decrease in C3 and C4 also significant decrease in level of HDL,VLDL and TG in infected with viral hepatitis C and B in compared to the control group but significant increased in level LDL, The increase in patients with type B more than type C.

References

1- Ansreolo.T.E,Binjamin.I.J,Griggs.R.C.*et al*.Andreoli and carpenter s Cecil essentials of medicine. in : Kochar R, Sheikh M.A, Fallon B.M.(2010)."Acute and chronic Hepatitis". China: Saunders ; p.466.
2- Center of the disease control. 2011. (CBC/ministry of health /Baghdad – Iraq) .
3- Sorrell MF, Belongia EA, Costa J, et al.National Institutes of Health Consensus(. 2009) "Development Conference Statement: management of hepatitis B". Ann Intern Med; 150: 104-110.
4- Lazarevich NL (2000). Molecular mechanisms of alpha-fetoprotein gene expression. Biochemistry (Mosc). 65:117–133
5- Khan MH Farrell GC,Byth Weltman MD George J.*et al* (2000)"Which patients with hepatitis Cdevelop liver complications Hepatology";31:513-20.
6- Colin W. S, Edgar P. S, Lyn F, Anthony E. F , Beth P. B. (2006).Hepatitis B Virus Infection: Epidemiologyand Vaccination. Epidemiologic Reviews.;28(1):112-125.
7- Niederhauser c. Reducing the risk of hepatitis B virus transfusion- transmitted infection(2011). Journal of Blood Medicine.; 2: 91-102.

8- Candotti D, Allain J.P.(2009).Transfusion-Transmitted hepatitis B virus infection. Journal of Hepatology; 51(4): 798-809.
9- World Health Org anization, http://www.who.int, (accessed May 2004), Fact Sheet N° 164, October 2000
10- Szabo, E.; Lotz, G.; Paska, C.; Kiss, A.; Schaff, Z., 2003, Viral hepatitis: new data on hepatitis C infection, Pathol Oncol Res *9*, 215-221.
11- Anonymous, Global surveillance and control of hepatitis C. Report of a WHO Consultation organized in collaboration with the Viral Hepatitis Prevention Board1999, Antwerp, Belgium, Journal of viral hepatitis, *6*, 35-47.
12- Bartenschlager, R.; Lohmann, V **(**2000) Replication of the hepatitis C virus, Baillieres Clin Gastroenterol, *14*, 241-254.
13- Holt DS, Botto M, Bygrave AE, Hanna SM, Walport MJ, Morgan BP(2001). Targeted deletion of the CD59 gene causes spontaneous intravascular hemolysis and hemoglobinuria. Blood.;98:442-449. 6.
14- Qin X, Dobarro M, Bedford SJ, et al.(2005).Further characterization of reproductive abnormalities in mCd59b knockout mice: a potential new function of mCd59 in male reproduction. J Immunol.;175:6294-6302.
15- Acosta J, Qin X, Halperin J. (2004) "Complement and complement regulatory proteins as potential molecular targets for vascular diseases". Curr Pharm Des.;10:203-2
16- Walport MJ.(2001) "Complement. Second of two parts". N.Engl J Med.;344:1140-1144.
17- Steinberg JB, Kapelanski DP, Olson JD, Weiler JM. (1993) "Cytokine and complement levels in patients undergoing cardiopulmonarybypass"J Thorac Cardiovasc Surg.;106:1008-1016. 18- Rehermann B, Nascimbeni M. (2005) "Immunology of hepatitis B virus and hepatitis C virus infection". Nat Rev Immunol.;5:215-229.
19- Speth C, Stoiber H, Dierich MP. (2003)."Complement in different stages of HIV infection and pathogenesis". Int Arch Allergy Immunol.;130:247-257.
20- Mehlhop E, Diamond MS. .(2006)." Protective immune responses againstWest Nile virus are primed by distinct complement activation pathways". J Exp Med;203:1371-1381.
21- Kittlesen DJ, Chianese-Bullock KA, Yao ZQ, Braciale TJ, Hahn YS(.2000). "Interaction between complement receptor gC1qR and hepatitis Cvirus core protein inhibits T-lymphocyte proliferation". J. Clin. Invest. 106:1239–1249.
22- Krawczynski K, et al. (1992). "Hepatitis C virus antigen in hepatocytes Immune morphologic detection and identification". Gastroenterology 103:622– 629.
23-Budhaditya Mazumdar, Hangeun Kim, Keith Meyer, Sandip K. Bose,Adri an M. Di Bisceglie,Ratna B. Ray,and Ranjit Ray·(2011). "Hepatitis C Virus Proteins Inhibit C3 Complement Production |Journal of Virology p. 2221–2228
24- Dumestre-Perard C, Ponard D, Drouet C, et al. (2002).Comple- ment C4 monitoring in the follow-up chronic hepatitis C treatment. Clin Exp Immunol; 127: 131-6.
25- Fox, R.A., F.J. Dudley and S. Sherlock, "The serum concentration of the third component of complement b1C/b1A in liver disease". Gut., 12: 574-578
26- Kourilsky, O., C. Leroy and A.P. Peltier, (1973)." Complement and liver cell
27-Inai,S.,H.Kitamura,T.Fujita,J.Kojima and.K.Nagaki,(1976)."Differences between plasma & serum complement in patients with chronic liver disease".Clin. Exp.Immunol.,25(3):403-9.
28-Kitamura, H., K. Nagaki, K. Inoshita, K. Iida and S. Inai, (1977). " The cold activation of the classica complement pathway: The cause of the differences between plasma and serum complement in liver cirrhosis. Clin. Exp. Immunol., 27(1): 34-7.
29- Zainal Israa G., Safa A.A. and Wajeehkk Obead.(2013)"Biochemical parameters in relation to serum alpha fetoprotein and leptin levels in Iraqi patients with chronic liver disease. international journal of life science and pharma Research ISSN 2250-0480.Vol.3/Issu