Molecular basic D-dimer in chronic hepatitis and liver cirrhosis

by Indranila Kustarini Samsuria

Submission date: 19-Mar-2021 03:40PM (UTC-0700)
Submission ID: 1537389609
File name: ular_basic_D-dimer_in_chronic_hepatitis_and_liver_cirrhosis.docx (375.54K)
Word count: 3031
Character count: 16862

Molecular basic D-dimer in chronic hepatitis and liver cirrhosis

Indranila KS, Purwanto AP, Imam BW, Herniah AW, Edward KL

Department of ciinical pathology medical faculty Diponegoro University/ Dr. Kariadi Hospital Semarang

Abstract

Introduction: Chronic Hepatitis and iiver cirrhosis is a chronic liver disease resuiting in hepatic dysfunction as hemostasis. Chronic hepatitis causes liver cirhhosis complicationsm as hiperfibrinolisis event marked bt an increase in D dimer in the incidence molecular basic of blending D-dimer in chronic hepatitis and cirrhosis examined and, analyzed the differences. The research objective is to distinguish the levels of D-dimer in chronic hepatitis and cirrhosis.

Methods: A cross sectional study in 16 patients with chrobic hepatitis and cirrhosis in hospital dr. Kariadi in periode March-May 2014. Level of D-dimer used the latex enhance turbidimetric assay. Data analysis using mann whitney test for D-dimer in chronic hepatitis and cirrhosis

Results: The median D-dimer in chronic hepatitis are 190±82.30 μg/L and in the cirrhosis atre 4860±57μg/L. *the* results of different test levels of D-dimer significantly betwen chronic hepatitis and cirrhosis with p=0.00

Conclusions: there is a signiflcant difference in the levels of D-dimer in cnronuic neparrns and cirrhosis

Keywords : Hepatitis, cirrhosis, bleeding, hemostasis.

Background. Heart disease is a disease of the liver due to various causes within a period of 6 months.These diseases include chronic hepatitis and cirrhosis. This disease has a mortality and morbidity were significantly increased in developing countries mainly caused by hepatitis B and C initial of chronic hepatitis stage is usually asymptomatic.

Hepatitis can *be* cured, inactivated hepatitis can develop into chrrironic hepatitis. Inflammation of the liver in hepatitis make liver damage and destruction of liver cells are characterized by biomarker liver function tests. Hepatitis B is an infection of hepatitis B virus (HVB}, can be acute or chronic. Chronic hepatitis B infection can be detected by the presence of HBsAg positive for more than 6 months.

Infection with hepatitis C virus (HCV) can be acute or chronic, with symptoms are asymptomatic, so people do not feel sick. Hepatitis C is than chronis if anti-HCV or HCV- RNA was detected positive for more

direction to the development of heart failure.

Liver *cirrhosis* is a *chronic* disease which is a chronic eoo--'St~ iilW!t *iir:1c?fJc.* Gnhosis hepatis anatomically according to Sherlock is a fibrosis that extencis to the formation of nodules in all parts of

Presented in the 14th Asian Society for clinical pathology and laboratory medicine congress (2016) Taipei, Taiwan March 25-27, 2016

the liver, and fibrosis not onty in one tobe. Cirrhosis is a chronic liver disease in which the damage occurred continuously, and nodular regeneration occurs, as well as the proliferation of connective tissue **to prevent diffuse** parenchvmal **necrosis or in the onset of inflammation Any chronic condition occursin**
the liver can lead to cirrhosis of the liver. approximately 80-90 percent of heart disease suffer from the
damage before clinical symptoms of liver failure appeared.

Liver disease increased disease in the hole of the European Union, the researchers report in the journal of Hepatology. WHO (world health organization) found that 170,000 deaths each year are caused by **cirrhosis** hapatis. **The main causes of** liver **disease are excessive** alcohol ccnsumotion. viral **infections** and obesity. infection with hepatitis Band C according to Elzouki et al (2013) experienced by people aged 21 29 years and males more than females.

Cirrhosis and chronic liver disease is a common cause of death in the United States in 2002, some 27 257 deaths (9.5 per 100,000 population) dominated by men. In Asia, cases of hepatitis occurred about 9.98 **million cases to about 585 800 deaths in 2011.** lndcnesia **is in** ranks third .in **,ru-U-ie.D.t.~ wjth** hepatitis **in the** world, after India and China, whose estimated number of 30 million people Indonesia, including areas with high endemicity and in the high prevalence of more than 8%, according to WHO criteria. A total of
10 391 sera were examined and found positive HBsAg prevalence of 9.4% in 2007. Bandung is an area that have a moderate prevalence of hepatitis B virus, which is 4-5%. Number of people living in Bandung

100,000 people with HBsAg.

WHO estimates there are 54,000 deaths and 955,000 disabiiity COrn'~\'r.'fs ¶'.·tiit.?,"b :rmff:, lrifo associated with acute hepatitis C virus infection. HVC infection becomes chronic infection , 3-4 million people have

HVC infections each year. 170 million people are chronically infected and develop into chronic liver diseases, cirrhosis and liver cancer. While 350,000 people die every year because of this HVC.

Liver is an important organ in the primary and secondary hemostasis. Liver damage associated with coagulation disorder that worsens as the heart damage. Liver failure on chronic liver disease resulting in an increase fibrinolysis. Hiperfibrinolysis in cirrhosis of the liver is indicated by elevated levels of tissue plasrnlnogen **activator** {tPA) **and** plasrninogen **activator** inhibitcr-J **j.PAJ-J,\..a~..d.rler.re.asEd** levels **of** plasminogen, antiplasmin, and factor XIII. tPA levels increase due to increased acquisition by the endothelium due to reduced clearance of the liver. PAI-1 levels increased, but not as high levels of tPA.This situation resulted in an increasing degradation products of fibrinogen and D-dimer.

D-dimer plasma level is an accurate sign of fibrinolysis activity, which indicates the activity of plasm in and thrombin. D-dimer test is also used to determine the diagnosis Disseminated intravascular coagulation (DIC) in chronic liver disease, especially patients with liver cirrhosis. Anticipated increase in fibrinolvsis (hiperflbrinolvsis] resulting **in fatal bleeding** incidents .

The theory above is in accordance with the results of Islamuddin (2011) found elevated levels of D-dimer associated with the occurrence of bieeding esophagus in psien *heraticc,~rdi'0':5",i.* *[Ni'aiwnjaya* et ai {20B} writes that peningkatana fibrinolytic activity becomes an important factor responsible for the tendency
of bleeding in liver disease.

Presented in the 14'h Asian Society for clinical pathology and laboratory medicine congress (2016)

0- dimer become an important parameter to assess the status of fibnnorvsrs in chronic liver disease, U (2011) wrote that the 0-dimer can be used as effective indicators at different degrees of liver disease. Pan et al (2006} wrote that the levels of D-dlmer in hepatic cirrhosis in a significant rise higher than the chronic hepatitis.

Measurement of levels of D-dimer mostly performed on patients cirrhosis of the liver, and still little is done in patients with chronic hepatitis. D-dimer difference to both diseases are not much discussed in most studies. The usefulness of D-dimer examination theoretically been known chronic liver disease, geed to see the risk of bleeding and DIC. This studv v.:H! measure the difference cf D-dfmer in patients with chronic hepatitis and cirrhosis of the liver, so it can be differences in the levels of D-dimer in both these circumstances.

The research question : is there a difference between the levels of 0-dimer chronic hepatitis with cirrhosis of the liver? The aim of the research objectives are: to analyze the differences between the levels of D-dimer chronic hepatitis and cirrhosis of the liver.

D-dimer levels are parameters that have been widely studied in hepatic cirrhosis, among others, to look at the incidence of bieeding and assessmem of disease progression. VVt'i','/m:::~-'Umfe:'i :!'i'l~hronic hepatitis is still hard to find in previous studies that the research needs to be done about it.

Our studies interested in conducting research on the D-dimer in chrome nepanns compared to cirrhosis of the liver. Chronic hepatitis taken on this research that chronic liver inflammation caused by infection with hepatitis Band C, which is different from the research that has been done had dedicated chronic hepatitis due to hepatitis B virus infection. Cirrhosis of the liver is taken from this research is that only patients suffering liver failure with a history of viral infections hepatitis B and C.

Hepatitis

Chronic hepatitis is a liver disease histologically patterned as necrosis, inflammation and fibrosis of hapatorit in various weight levels, light for more than 6 months. The most common cause of chronic hepatitis is viral infection. Hepatitis virus infection plays a role in heart most is the hepatitis virus B (HVB) and C (HCV). Chronic persistent hepatitis have histopathologic features are localized inflammatory infiltrrasi, and the border area between cells portal. Chronic lobular hepatitis have histopathologic virus features are accompanied by portal inflammatory focal necrosis and inflammation in the liver lobuler that resembles acute hepatitis improved. chronic active hepatitis have histopathologic there is erosion in periportal hepatocytes by inflammatory cells (necrosis metal piece or interface hepatitis), usually accompanied periportal connective tissue that extends into the heart lobuler.As seen in table 1.

Table 1. Classification of chronic hepatitis

classification	contemporary classification	
	levels (activity)	stage (fibrosis)
chronic persistent hepatitis;	minimal or mild	no or mild

Chronic lobular hepatitis	mild or moderate	light
chronic active hepatitis	mild, moderate, severe	mild, moderate, severe

D-dimer

D-dimer is formed through crosslinking of factorXIII and fibrin monomer hydrolysis by plasmin and is a marker for eariy diagnosis of thrombosis, as well as an indicator of abnormal coagulation and fibrinolysis. D-dimer concentration will increasewith impaired hepatic function.

In the process of abnormal clot formation, *a* fibrin clot formed at the last stage of the coagulation process. Fibrin generated by the activity of thrombin that breaks fibrinogen into fibrin monomers. Fibrinogen is a glycoprotein with a formula Aα, Bβ, γ. Consists of three pairs of polypeptide chains are not identical and mutually plait namely 2 cahin Aa, 2 B~, and 2y. Fibrinogen molecule is bound dimeric by disulfide bond at the terminal end. Couplechain Aa and B~chains have fibrinopolipeptida a small one, at the terminal called fibrinopolipeptidaA and B.

Process of change fibrinogen into fibrin consists of three phases: Enzymatic, polymerization and stabilization. At the stage of enzymatic,2 molecuies of fibrinopeptideA and 2 molecules of fibrinopeptide B are broken down and fibrinogen is converted by thrombin into fibrin monomer soluble. followed by the release of fibrinopeptide B into contact with monomer units with more powerful and forming clots unstable. The next stage is the stabilization, in which the addition of thrombin, factor XIII A and calcium ion {Ca 2+) to form unsoluble stable fibrin. Thrombin causesthe activation factor XIII which acted as transamidase. Factor XIIIa causescross-linked of fibrin monomer which adjacent to form stable covalent bonds (fibrin Mesh). *Chains* a and y plays *a* role in the, fnr.m;rtjn.o. cf. a stante fibrin unsoluble. the flow of cross-linked fibrin formation can be seen in Fig.1

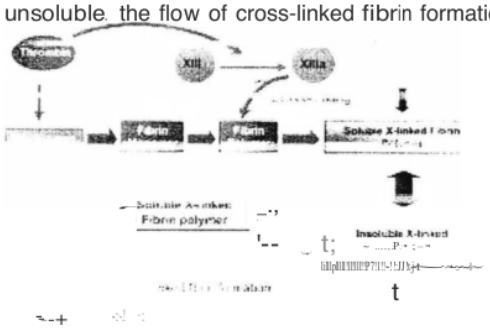

Figure 1. D- Dimer Formation by Soheir, et al

Plasminogen is normally present in the plasma will be absorbed by fibrin. When in fibrin, plasminogen is converted by tissue plasminogen activator {tPA) into plasmin derived from tPA-plasminogen complex -

fibrin. Plasm in *is* fibrinolvtic enzyme *is* the *main* function breaks down tibrinogen and fibrin which produce a variety of products degeneration fibrinogen (fibrin degradation products). If plasmin lyse fibrin unsoluble, *it* will increase the amount of soluble fibrin degradation products. Fibrir degradation product (FDP) that is produced in the form of fragments X, Y, D, and E. Two fragments D and one fragmen E of the fragment binds strongly affecting the D-dimer. The dynamics of the formation of D-

Figure 2. schematic d- dimer by Soheir et al

D-dimer examination principle is to use monoclonal antibodies that recognize epitopes on the 0-dirner fragment. There are several methods of inspection are enzyme linked immunosorbent assay (ELISAj, latex agglutination (LA) and whole blood agglutination (WBA).

Latex agglutination method used in this studv using the antibody coated an latex particles. Agglutination macroscopically visible if the, e is an increase in D-dimer in plasma. This method is less sensitive to the screening, the test is not expensive but easy to do, but in some studies indicate that this methoc! has less sensitivity to mendeteksiu D-dimer in pulmonary embolism and acute venous thrombosis. the rr.ethod has a sensitivity in the range of 80-100% and a negative predictive value of 90% depending quantitative 0-dimer. for example latex enhanced turbidimetric test. The principle of this method is the formation of covalent bonds plystyrene particles on a monoclonal antibody against cross-linkage region daru D-dimer. Cross-linkage has a structure of stereometrik. Agglutination reaction that occurs detected using turbidimetry. This method results comparable to conventional ELISA.

Methods study: The design of this research is descriptive analytic cross sectional approach. the scope of the research was conducted in a poly medicine and inpatient ward dr. Kariadi Semarang and examination of serum levels of D-dimer in Laboratory Installation RS. dr.. Kariadi. Research time of examination of samples up to the presentation of the results is in March and May 2014. The disciplines studied are clinical pathology and subpart hepatologY and hematologiPopulation research targets are patients who come to the clinic in internal medicine dr. Kariadi Semarang. Population is affordabie chronic and patients with liver disease, cirrhosis of the liver with a history of chronic hepatitis who come to the clinic medicine and hospitalization in internal medicine hospital dr. Kariadi Semarang. The subject research is conducted done by purposive sampling to meet the inclusion and exclusion criteria. A **cross sectional study in 16 patients** with chrobic **hepatits and cirrhosis in hospital** dr. Kariadi . **Level of 0**-dimer used the latex enhance turbidimetric assay. Data analysis using Mann Whitney test for D-dimer in chronic hepatitis and cirrhosis.

Inclusion criteria were patients aged Z 21 years, not using drugs that cause coagulation disorders such as aspirin, heparin or warfarin. Not using contraception, not pregnant, and without a history of malignancy **cf the** liver **or ether organs. \tVithout a** histcrv **of** corcnarv heart **disease er beirg** exncsed **to the** disease, with no history of stroke or being exposed to the disease, do not have an infection, do not experience joint disease, no history of autoimmune disease or being exposed to the disease. willing to participate in research. Exclusion criteria: lipemik sample and hemolysis.

Materials and research reagents composed of D-dirner reagents innovance, D- dimer reagents accelerator, and D-dimer innovance reconstitution medium. Examination of the workings of D-dimer: 1) there is no special preparation for the examination of D-dimer. Principle probes D-dimer is a polystyrene [illegible] covalent bonds on a monoclonal antibody against cross-linkage of D-dimer. 2) The specimen used is blood plasma with the anticoagulant sodium citras 32% .3) Put all the reagents, standards of work, and spesimen.4) Blood homogenized, centrifuged at 3000 rpm for 5 minutte .5) Supernatant was taken and stored temperature <- 20° C is stable until 2 months , while at room temperature can be stable till 8 hours. 6) The levels of 0-dimer is checked using the tools and reagents from coagulometer Sysmex CA-1500 with latexz Enhance turbidimetric test method. 7) D-dimer normal value of 0-500 μg / L.

Data coiieci:ed induded interviews, physicai examinations and *laborato.,y te.sh £:o.Vected* data is done by editing, coding, and entered into a computer programme. Data D- dimer in chronic hepatitis and cirrhosis Mann Whitney test and significance declared at p <0.05. Across the studies that met the inclusion and exclusion criteria, requested approval of informed consent. Permit research done by asking ethical clearance from the ethics committee of health research Diponegoro University School of Medicine / dr. Kariadi Semarang No. 070 / EC / FK-RSDK / 2014

Results:

Research conducted on 32 patients consisted of 16 patients with chronic hepatitis and 16 patients with cirrhosis of the liver. the control patients in hospitals and hospitalization. patient characteristics are shown in Table 2.

Table 2. patient characteristics

patient characteristics	variable	
	chronic hepatitis	cirrhosis Hepatis
~~age (year)~~		
median± SE	40,50±3,30	51,50±2,29
min-max value	22-67	35-62

Presented in the 14th Asian Society for clinical pathology and laboratory medicine congress (2016)

tong suffered from hepatitis (month),		
min-max value	7-252	108-168

long-suffering liver cirrhosiu (months)		
min-max value		3-72

The median D-dimer in chronic hepatitis are **190±82 30 p g/L and in the cirrhosis** atre **4860±57** *μ*g/L. the results of different test leveis of D-dimer significantly between chronic hepatitis and cirrhosis with p=0.00

Conclusions there is a significant difference in the levels of D-dimer in chronuic hepatitis and cirrhosis Pre

Reference:

Ricardo R, Rui TM, Miguel S. Classification and staging of chronic liver disease from multimodal data. iEEE Trans Biomed Eng. 2012;60(5):1336-44

Park W, Keefe EB> Diagnosis and treatment of chronic hepatitis B. Minervagastroenterol Dietol. 2004;50:289-303

Margit A. Diagnosis and treatment of chronic hepatitis C and its potential role in the pathogenesis of hepatocelluiar carcinoma. Budapest : Semmeiweis uUniversity 2001;

Islamudin. Hubungan peningkatan kadar 0-dimer dengan perdarahan varises edofagus pada sirohsis hati stadium dekompensata. Padang Universitas Andalas; 2011:pI-60.

elZouki AN, Smeo MN, Sammud M, Elahmer O, Daw Mm, Furarah A et al. Prevalence of hepatitis Band C virus infections and their related risk factors in Libya : a national seroepidemiological srvey. Eastern Mediteranean Health J 2013; 19(7):589-99.

Joel JH, Michaei B. Cirrhosis and chronic iiver failure. Part I diagnosis and evaiuation. Am Fam Physician 2006;74(5):756-62.

Dhanujaya Y, Usha A, Anand CV. Study of piasma D-dimer levels in various stages of liver disease. J Liver 2013;2(2):1-3

Li XF. The clinical significance of plasma fibrin degradation products and D-dimer in patients with type B hepatitis and liver cirrhosis. Int. J of laboratory medicine 2011;08:I-4.

Pan YH, Huang X, Zhang F. Clinical significance of the determinations of piasma fibrinogen and D-dimer to hepatitis B. J of chinese microcirculation 2006;05:I-4.

Soheir SA, Nigel SK, Charles SG. D-dimer antigen : current concepts and future prospect. Blood J 200;113(13):2878-87.

Molecular basic D-dimer in chronic hepatitis and liver cirrhosis

ORIGINALITY REPORT

6%	4%	3%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.ascpalm.org Internet Source	1%
2	Submitted to iGroup Student Paper	1%
3	Edward Kurnia Setiawan Limijadi, Lisyani Budi Suromo, Imam Budiwiyono. "Prothrombine and activated partial thromboplastin time are prolonged in hepatic cirrhosis", Universa Medicina, 2016 Publication	1%
4	univmed.org Internet Source	1%
5	phdold.sote.hu Internet Source	1%
6	eprints.soas.ac.uk Internet Source	<1%
7	"Hepatobiliary Diseases", Springer Nature, 1992 Publication	<1%
	www.apbmt.org	

8	Internet Source	<1%
9	www.hbmhealthcare.com Internet Source	<1%
10	www.mdpi.com Internet Source	<1%
11	"The 21st Conference of the Asian Pacific Association for the Study of the Liver", Hepatology International, 2011 Publication	<1%
12	Shiv K. Sarin, R.C. Guptan, Varsha Thakur, Shailaja Malhotra, Veena Malhotra, Kakoli Banerjee, Pramod Khandekar. "Efficacy of low-dose alpha interferon therapy in HBV-related chronic liver disease in Asian Indians: a randomized controlled trial", Journal of Hepatology, 1996 Publication	<1%
13	www.medicinenet.com Internet Source	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		

Molecular basic D-dimer in chronic hepatitis and liver cirrhosis

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8

PAGE 9

PAGE 10