

Dyslipidemias in Hepatitis C Virus Infection at Isra University Hospital Hyderabad

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ABSTRACT

Objective: To determine the incidence of dyslipidemias in hepatitis C virus infected patients presenting at Isra University Hospital Hyderabad.

Methodology: The descriptive study was conducted at the Department of Gastroenterology, Isra University Hospital and Hyderabad from June 2017 to December 2017. All the patients with Anti hepatitis C virus (HCV) positive for >6 months, aged between 18 years to 60 years of both gender were included in the study. Fasting blood samples were taken from these patients and sent to the Hospital diagnostic laboratory for lipid profile. The tests were collected on the reporting date. All the data was entered on the proforma by the researcher himself. Data was analyzed using SPSS software version 20.

Results: Total 80 patients were enrolled and the mean age of the patients was 46.52 ± 7.64 years. Male were found in the majority 48(60.0%). Out of all (13.2%) patients were obese. The mean of total serum cholesterol was 180.04 ± 13.12 mg/dl, mean of serum triglyceride was 130 ± 10.23 mg/dl, HDL mean was 30.23 ± 5.55 mg/dl, and mean of LDL was 125.42 ± 9.53 mg/dl. Dyslipidemia was 31(38.8%) out of all study subjects. Age >40 years and BMI >30 were significantly associated with dyslipidemia ($p=0.001$). However, no significant difference was found in dyslipidemia according to gender ($p=0.818$).

Conclusion: It is concluded that dyslipidemia was highly prevalent as 38.8% in HCV infected patients. Old age, smoking and BMI >30 were significantly associated with dyslipidemia. No significant impact of gender on dyslipidemia in HCV infected patients.

Keywords: Incidence, dyslipidemia, HCV.

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Introduction

Hepatitis C virus is a single stranded RNA virus (Hepacivirus) of the Flaviviridae family.¹ HCV infection causes liver fibrosis progression, cirrhosis of the liver, hepatic failure, and liver cancer including several systemic disorders.² Chronic hepatitis C is commonly associated with extra hepatic manifestations³, such as essential mixed cryoglobulinemia, porphyria cutanea tarda, type-II diabetes mellitus, sicca syndrome, lichen planus, thyroid disorders and peripheral neuropathy. One of these manifestations is dyslipidemias. Both high as well as low levels of lipids may be deleterious for health

as longstanding elevation of serum cholesterol can lead to atherosclerosis which can lead to progressive stenosis (narrowing) or even complete occlusion (blockage) of the involved arteries, pancreatitis is a known but rare cause of very high levels of triglycerides (>11.29 mmol/L [>1000 mg/dL]) in the general population and increased mortality, mainly due to depression, cancer, hemorrhagic stroke, aortic dissection and respiratory diseases are associated with low cholesterol.⁴ Experimental and clinical data suggest that LDL receptor (LDLR) is a co-receptor for HCV: (1) the levels of HCV RNA in primary hepatocytes correlate with LDLR mRNA expression and LDL uptake efficiency;⁵ (2) soluble LDLR can inhibit

HCV infectivity;⁵ (3) greater plasma LDL levels are associated with sustained virological response (SVR) after treatment with Peg-IFN plus RBV, likely due to competitive block of the HCV entry;⁶ (4) polymorphisms in LDLR, which are associated with plasma levels of LDL, have a synergistic impact on the likelihood of achieving SVR with Peg-IFN plus RBV in patients infected with viral genotypes 1 and 4^{6,7} as well as on viral kinetics after treatment⁸. Experiments with a monoclonal antibody against LDLR reveal that LDLR has a major role in post-entry phases of viral life cycle, probably increasing lipoprotein uptake, an essential factor for HCV replication.⁹ As the liver is the main determinant of serum lipoprotein synthesis and lipid metabolism, chronic liver diseases are often accompanied by impaired lipid metabolism.³ The relation between severity of liver disease and low levels of serum cholesterol, particularly low-density lipoprotein cholesterol (LDL-C) has previously been described. Lower total cholesterol and LDL-C levels were also described in hepatitis C virus (HCV)-infected patients. One of the proposed predictors of response to interferon in HCV infected patients are total serum cholesterol and LDL-C. Furthermore, it was determined that in comparison with patients chronically infected with hepatitis B, patients with chronic hepatitis C had lower total cholesterol levels.¹⁰ Binding of HCV to VLDL or LDL could facilitate its entry via the LDL receptor. A study from Brazil showed the male carriers of HCV have a significant fall in the HDL level (29%) and an increase in the VLDL level (27%) relative to the control group, and the lipid profile of female carriers of the same HCV genotype showed a similar fall in the HDL levels (27%) and rise in the LDL levels (26%), relative to the control group.¹¹ A study from the USA showed the prevalence of dyslipidemia was 70% in a cohort on aspects of lipid profile with chronic HCV infection. In this study those classified as dyslipidemia, low HDLc was the most common criteria of dyslipidemia (64%), followed by high TC (45%), high LDLC (43%), and high TG (32%).¹² Furthermore, this is also showed that during 24 week of treatment, 61% of participants who were not dyslipidemic at baseline became newly classified as dyslipidemic.¹² One European study found six hundred and twenty-eight (70.5%) out of 891 patients with hepatitis C had hyperlipidemia.¹³ According to American academy of rehabilitation 15% of patients with chronic hepatitis C had hyperlipidemia.¹⁴ Considering the clinical proof that HCV infection causes dyslipidemia and the results of International studies shows great variability in frequency of dyslipidemia in HCV infection. This study

has been conducted to assess dyslipidemia exists in HCV infection in our population.

Methodology

The descriptive study was conducted at the Department of Gastroenterology, Isra University Hospital and Hyderabad from June 2017 to December 2017. Non-Probability consecutive sampling was used. Total 80 patients were included by calculating sample size using WHO sample size calculator by taking proportion of 70%.

Inclusion criteria: Patients who are Anti HCV positive for > 6months, aged between 18 years to 60 years of both gender were included.

Exclusion criteria: Patients who are reactive for Anti-HbsAg and Anti-HDV on Elisa, cirrhosis of liver confirmed on ultrasound, diabetic patients, pregnant women, menopausal women, nephrotic Syndrome and Hypothyroidism were excluded.

This study was conducted after approval synopsis. Informed written consent was taken from the patients. All those cases were included in the study who is Anti-HCV positive on 2nd generation Elisa method. Then fasting blood samples of these patients were drawn and sent to a laboratory for total lipid profile in the pathological lab of IUH, Hyderabad. Patients were considered to have dyslipidemia when they had either all or any one altered out of the following as total cholesterol, HDL, LDL and triglycerides. Results of these tests were collected on reporting date and were entered on the proforma by the researcher himself.

Data was analyzed on computer using SPSS software version 20. Description statistics like frequency and percentage were compared for gender, smoking, obesity (BMI >30) and whether presence or absence of dyslipidemia. Mean \pm SD were calculated for age and BMI. Effect modifiers were specified like age, gender and smoking to see the effect of these on the outcome variable post stratification applying chi-square test with p value <0.05 as significant.

Results

Mean age of the patients was 46.52 \pm 7.64 years, with range of minimum 25 years and maximum 60 years. Males were found in majority 48(60.0%) as compare to females as 32(40.0%). After taking history of smoking, the 24(30.0%) patients were smokers, while 56(70.0%)

were nonsmokers. According to the body mass index, 11(13.2%) patients were presented with body mass index >30 , while most of the cases 79(86.8%) were noted with normal body mass index. (Table I)

Over all mean of total serum cholesterol was 180.04 ± 13.12 mg/dl, mean of serum triglyceride was 130 ± 10.23 mg/dl, HDL mean was found 30.23 ± 5.55 mg/dl, and mean of LDL was noted 125.42 ± 9.53 mg/dl. (Table II)

Table I: Descriptive statistics of the patients according to demographic variables (n=80)

Variables	Statistics
Age	Mean \pm SD 46.52 \pm 07.64 years
	Minimum 25 years
	Maximum 60 years
Gender	Males 48(60.0%)
	Females 32(40.0%)
History of smoking	Yes 24(30.0%)
	No 56(70.0%)
Body mass index (BMI)	>30 11(13.2%)
	<30 79(68.8%)

Table II: Patient's distribution according to Lipid profile (n=128)

LIPID PROFILE	Mean \pm SD
S-CHOLESTEROL	180.04 ± 13.12 mg/dl
S-TRIGLYCERIDES	130 ± 10.23 mg/dl
HDL-CHOLESTEROL	30.23 ± 5.55 mg/dl
LDL-CHOLESTEROL	125.42 ± 9.53 mg/dl

Overall dyslipidemia was found 31(38.8%) of the cases, while 49(61.2%) patients were found with normal lipid profile. Figure no 1.

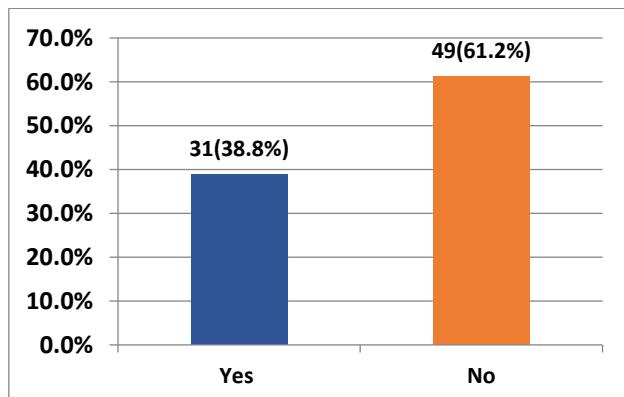


Figure no 1. Patients' distribution according to dyslipidemia (n=80)

Old age patients were found significantly associated with dyslipidemia as compare to youngers P-value 0.001. out of 7 patients of 18-30 years age group 6 were with normal lipid profile, out of 18 cases of 31-40 years, only 4 were noted with dyslipidemia, age group of 41-50 years

was most common containing 40 cases, and out of them 16 cases were noted with dyslipidemia, 15 cases were with age group of and out of them 10 were wonted with dyslipidemia. No significant difference was found in dyslipidemia according to gender p-value 0.818. (Table III)

Table III: Dyslipidemia according to age groups (n=80)

Variables	DYSLIPIDEMIA			P-value
	Yes	No	Total	
Age groups	18-30 years	01	06	0.001
	31-40 years	04	14	
	41-50 years	16	24	
	51-60 years	10	05	
Gender	Male	18	30	0.818
	Female	13	19	
History of smoking	Yes	16	08	0.001
	No	15	41	
BMI >30	Yes	08	03	
	No	23	46	0.001

Discussion

Hepatitis C infection is the most common cause of chronic liver disease throughout the world and affecting 3% of the population, and a high prevalence of it was also HCV infection reported in Pakistan.¹⁵ It is the commonest in males as in this study Males were 48(60.0%) and females were 32(40.0%) and mean age of patients was 46.52 \pm 7.64 years. Similarly, Hsu CS et al¹⁶ reported that males were in majority, and mean age of patients was 54.0 ± 11.6 years. However, Arain SQ et al¹⁵ reported that there 50% males and the mean age of patients was 34.16 ± 9.1 years. The difference in mean age and gender may due to sample size. On other hand, Almani MI et al¹⁷ reported that mean age of the patients was 39.9 ± 9.5 years. In the favor of this study MEHBOOB F et al¹⁸ conducted study on dyslipidemia in chronic liver disease and they found 102(63.75%) were male and females were 58(36.25%).

In this study, overall mean of total serum cholesterol was 180.04 ± 13.12 mg/dl, mean of serum triglyceride was 130 ± 10.23 mg/dl, HDL mean was 30.23 ± 5.55 mg/dl, and mean of LDL was 125.4 ± 9.53 mg/dl. On other hand Almani MI et al¹⁷ reported total cholesterol and triglycerides were 107 ± 30 mg/dl and 72.3 ± 23.5 mg/dl respectively, these findings of total cholesterol and triglyceride were lower according to this study. While Arain SQ et al¹⁵ found close results of lipid profile according to this study as mean total cholesterol was 159.7 ± 13.8 mg/dl, mean LDL 82.9 ± 12.1 mg/dl, mean HDL 30.3 ± 9.6 mg/dl and mean triglyceride as 114.0 ± 13

mg/dl in HCV infected patients. On other hand in a recent study of Aldabbagh L et al¹⁹ reported that the mean total cholesterol level was 174.8 ± 37.9 mg/dl, HDL-C 42.3 ± 9.5 mg/dl, LDL 106.3 ± 35 mg/dl and mean of triglycerides was 132.7 ± 34.2 mg/dl in HCV infected patients. The severity of hepatic disease lipid metabolism are profoundly disturbed, it may be disturbed in several ways.¹⁸ Dyslipidemia seen in CLD differs from other commonest causes of secondary dyslipidemia since circulatory lipoproteins are not seen in the abnormal rate but also have frequent abnormal composition, electrophoresis mobility and manifestation.¹⁸ It is reported that raises in the severity of hepatic disease has long been linked with progressively lower levels of lipids and a range of metabolic disorders.²⁰ Previous studies reported that lower levels of LDL-C, and TGs at the several stages of the chronic HCV infection.²⁰ In this study overall dyslipidemia was found 31(38.8%) in hepatitis infected patients. Vincent Wai et al²¹ reported that hypertriglyceridemia occurred in 31.4% of HCV-infected patients and 53.8% of non-infected patients ($P < 0.001$), and hypercholesterolemia occurred in 34.7% and 60.1%, respectively ($P < 0.001$).²¹

In this study, old age, smoker and obese patients were found significantly associated with dyslipidemia as compare to youngers P-value 0.001. However, no significant difference was found in dyslipidemia according to gender p-value 0.818. NO such studies have been found in the literature regarding association of old age, smoking and obesity with dyslipidemia in hepatitis C infected patients. HCV infection has been linked to dyslipidemia. According to several studies Hepatitis C infected patients have been found with markedly decreased in total cholesterol, LDL, HDL and triglyceride TG.^{18,20-22} However average of total cholesterol, LDL, HDL, and triglyceride TG were similar according to these studies.

Conclusion

It is concluded that the dyslipidemia was highly prevalent in HCV infected patients as 38.8%. Old age, smoking and BMI > 30 were significantly associated with dyslipidemia. However no significant impact of gender on dyslipidemia in HCV infected patients. It is big event behind morbidities in HCV infected patients. Lipid profile screening should be done with routine laboratory investigations mostly in old age, obese and smokers. This is a small sample size and single center study

SUGGESTIONS: Lipid profile screening should be done with routine laboratory investigations mostly in old age. Body weight should be controlled and smoking should be stopped to decrease prevent the early adverse outcome.

References

1. Ahmed I, Rahim K, Mahmood A, Saleha S. Molecular Biology of Hepatitis C Virus: An Overview. *Journal of Bio-Molecular Sciences*.JBMS. 2014;2(2):38-46.
2. Jukić LV, Kralj D. Extrahepatic Manifestations of Hepatitis C Virus Infection. Update on Hepatitis C. 2017:111.
3. Cacoub P, Comarmond C, Domont F, Savey L, Desbois AC, Saadoun D. Extrahepatic manifestations of chronic hepatitis C virus infection. Therapeutic advances in infectious disease. 2016;3(1):3-14.
4. Jacobs DR, Blackburn H, Higgins M, Reed D, Iso H, McMillan G, et al. "Report of the conference on low blood cholesterol: mortality associations". *Circulation*. 1992;86:1046-60.
5. Molina S, Castet V, Fournier WC, Pichard GL, Avner R, Harats D et al. The low-density lipoprotein receptor plays a role in the infection of primary human hepatocytes by hepatitis C virus. *J Hepatol*. 2007;46:411-19.
6. Pineda JA, Caruz A, Di Lello FA, Camacho A, Mesa P, Neukam K et al. Low-density lipoprotein receptor genotyping enhances the predictive value of IL28B genotype in HIV/hepatitis C virus-coinfected patients. *AIDS* 2011;25:1415-20.
7. Neukam K, Caruz A, Rivero JA, Barreiro P, Merino D, Real LM et al. Variations at multiple genes improve interleukin 28b genotype predictive capacity for response to therapy against hepatitis c genotype 1 or 4 infection. *AIDS* 2013;27(17):2715-24.
8. Rivero JA, Camacho A, Caruz A, Neukam K, Gonzalez R, Di Lello FA et al. LDLr genotype modifies the impact of IL28B on HCV viral kinetics after the first weeks of treatment with PEG-IFN/RBV in HIV/HCV patients. *AIDS* 2012;26:1009-15.
9. Albecka A, Belouzard S, Op de Beeck A, Descamps V, Goueslain L, Bertrand MJ et al. Role of low-density lipoprotein receptor in the hepatitis C virus life cycle. *Hepatol* 2012;55:998-1007.
10. Biró A, Horváth A, Varga L. Serum anti-cholesterol antibodies in chronic hepatitis-C patients during IFN-alpha-2b treatment. *Immunobiology* 2003;207:161-68.
11. Nogueira TC, Urbaczek CA, Falcóski ROT, Isabel FT, Graminha SAM. Evaluation of the lipid profile between individuals with hepatitis C. *Rev Cienc Farm Basica Apl* 2012;33(1):63-70.
12. Ramcharan D, Wahed AS, Conjeevaram HS, Evans RW, Wang T, Belle SH et al. Serum lipids and their associations with viral levels and liver disease severity in a treatment-naïve chronic hepatitis C type 1-infected cohort. *J Viral Hepatol*. 2011;18:144-52.
13. Murthy, Divakara G, Vu, Khoa, Venugopal, Suxhma. Prevalence and treatment of hyperlipidemia in patients with chronic hepatitis C infection. *Eur J Gastroenterol Hepatol*. 2009;21(8):902-07.

14. Moon J, Kallman J, Winter P, Srishord M, Fang Y, Gerber L et al. Disparities in Activity Level and Nutrition Between Patients With Chronic Hepatitis C and Blood Donors. *PMR*. 2012;4(4):436-41.
15. Arain SQ, Talpur FN, Channa NA, Khan R. Clinical evaluation and serum lipid profile between individuals with acute hepatitis C. *International Journal of Biochemistry Research & Review*. 2015;6(1):37.
16. Hsu CS, Liu CH, Liu CJ, Wang CC, Chen CL, Lai MY, Chen PJ, et al. Association of lipid profiles with hepatitis C viral load in chronic hepatitis C patients with genotype 1 or 2 infection. *American Journal of Gastroenterology*. 2009;104(3):598-604.
17. Almani MI. Correlation of Duration of Hepatitis C Infection with Triglycerides and Total Cholesterol. *Journal of Islamabad Medical & Dental College*. 2016;5(4):168-71.
18. Mehboob F, Ranjha FA, Masud S. Changes in Serum Lipid Profile Among Patients Suffering From Chronic Liver Disease. *Annals of King Edward Medical University*. 2007;13(3):209-.
19. Aldabbagh L, Hmood AR, Aldahalemi AK, Almuhan S, Almussawi AS. Dyslipidemia in patients with hepatitis C virus infection. *Annals of Tropical Medicine and Health*. 2020;23:23-941.
20. Badawi A, Di Giuseppe G, Arora P. Cardiovascular disease risk in patients with hepatitis C infection: Results from two general population health surveys in Canada and the United States (2007-2017). *PloS one*. 2018;13(12):e0208839.
21. Wong VW. Hepatitis C virus infection and diabetes: Not a straightforward relationship. *Journal of gastroenterology and hepatology*. 2012;27(11):1647-8.
22. Butt AA, Yan P, Simon TG, Chung RT, Abou-Samra AB, ERCHIVES Study Team. Changes in circulating lipids level over time after acquiring HCV infection: results from ERCHIVES. *BMC infectious diseases*. 2015;15(1):510.