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DIABETES MELLITUS;
DESCRIPTIVE STUDY ON DIABETES MELLITUS IN CHRONIC HEPATITIS C

Jeando Khan Daidano[1], Nazia Azam Yusfani[2], Bilqees Daidano[3]

1. MBBS, MD
Assistant Professor
Department of Medicine
PUMHS W Nawabshah.
2. MBBS, MSPH
Polio Eradication Officer
WHO Office Hyderabad.
3. 4th Year MBBS Student
PUMHS'W Nawabshah.

Correspondence Address:
Dr. Jeando Khan Daidano
Assistant Professor
Department of Medicine
PUMHS W Nawabshah.
jeandokhan@ymail.com

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ABSTRACT... Objectives: To determine the association of diabetes mellitus in chronic hepatitis C patients. **Study Design:** Descriptive Cross sectional study. **Period:** June 2016 to October 2017. **Setting:** Department of Medicine PMCH Nawabshah. **Material and Methods:** Total 107 patients were selected for this study. Informed consent was taken from all the patients, study was done using questionnaire. Statistical analysis was done by SPSS 15 version. **Results:** 107 patients were enrolled for this study 56 were males 51 were females. Age ranged 48 to 74 years, mean age was 52.65+_6.5. Patients selected after blood glucose level anti HCV positive and PCR positive. Diabetic Foot was present in 33 patients, renal failure noted in 2 patients. **Conclusion:** HCV infection is major problem in our country, incidence of diabetes in chronic hepatitis C patients increases the mortality. We can treat patients early with anti viral drugs for HCV infection and antidiabetic drugs for Diabetes Mellitus, with counseling morbidity and mortality can be reduced.

Key words: Diabetes Mellitus, Chronic Hepatitis C, Insulin Resistance, Steatosis.

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INTRODUCTION

World wide chronic hepatitis C is the main cause of CLD.[1] About 150 millions individuals are infected. Annual incidence estimated to be 1-3 cases/100000 peoples. Majority of the peoples are asymptomatic.[1] Patients with diabetes have increased risk of cirrhosis[2] and patients with history of acute and chronic liver disease develop diabetes mellitus. Use of hydrochlorothiazide, corticosteroid and due to hemochromatosis develop glucose intolerance. In chronic hepatitis C infection steatosis is common histological finding.[3] For progression of disease the role of steatosis pathogenic mechanism is still unknown. Association of diabetes mellitus with chronic hepatitis C is commonly noted now a days. Hepatotrophic virus causing diabetes mellitus, a large number of patients presenting with this disease. Glucose intolerance is noted in 80% of patients with history of cirrhosis. Out of these 10-20% have diabetes mellitus.[4] Physiologically liver plays a role in glucose utilization and release. The phenomenon is regulated by glucagon and insulin. Liver causes endogenous glucose utilization and production. Due to post receptor defect insulin resistance noted with glucose intolerance, resulting binding of insulin to target tissue is decreased, response of beta cells of pancreas is inadequate to secrete insulin due to the defect in insulin action.[5] Diabetes mellitus is associated with anti HCV positive patients. Higher rate of HCV infection 11.5% in 176 diabetic patients reported by simo et al. compared with 2.5% in 6172 patients study done by Chen et al.[6] Higher percentage of HCV found in type 2 diabetes patients as compared to HBsAg positive patients. Same ratio of HCV infection was found in Chinese patients.[6] Risk was increased in patients with history of tattooing, hemodialysis, intravenous drug abuse, blood transfusion, exposure to needles and abortion. Hepatitis C involve oxidative stress, lipid metabolism and mitochondrial function.[7] Increased risk of diabetes was associated with HCV infection in previous studies.[8] Glucose intolerance is more in HCV infection when compared with controls in liver disease.[9] In European peoples with diabetes mellitus, incidence of HCV infection is higher compared with general population.[9] Association of diabetes mellitus with HCV infection and in

nondiabetic patients patients certain genotypes are associated with extra hepatic presentation of the disease.[10]

MATERIAL AND METHODS

This study was carried out in the department of medicine PMCH Nawabshah, 107 patients were enrolled for this study, males were 56 and females were 51. Informed consent was taken, questionnaires was given to all the patients, detailed history was taken with general physical examination and systemic examination.

Inclusion Criteria

Anti HCV positive patients
Quantitative PCR positive
Diabetes mellitus

Exclusion Criteria

Anti HCV negative
HBsAg positive
Non diabetic

RESULTS

107 patients were enrolled for this study, both male and female were included, 56 were males and 51 were females. Age of the patients range 42-67 years mean age was 52.65+- 6.5. 85 were uneducated, 5 were with primary education, 6 middle, 7 were matric, 4 were intermediate. Occupation of the patients, 43 were farmers, 45 were house wife, 5 were unemployed, 10 had private job and 4 were in government job. 85 patients came from rural areas and 22 were from Arabian areas. On examination Jaundice was noted in 4 patients, 46 patients were in cirrhosis, heptomegaly noted in 23 patients, spleenomegaly in 54 patients, random blood sugar vary 211-438 mean 286.88+-55.12, fasting blood sugar from 128-184 mean140.29+-13. HbA1C range from 7-10 mean 8.24+-0.81. Bilirubin range 0.8-4.3 mean1.03+- 0.41. SGPT range 29-187 mean 47.36+-25. Viral load range 91238-3252634 mean1092673. PT range 12-15. Urea range 23-41. Creatinine range 0.8 -1.5. Renal failure was noted in two patients. Diabetic Foot was present in 33 patients. In statically analysis education noted primary by 1, inter by 2, matriculation by 3, intermediate by 4. Occupation 1 by farmers, 2 by housewife, 3 by unemployed, 4 by private job and 5 by Govt: service.

Variable		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	56	52.3	52.3	52.3
	2	51	47.7	47.7	100.0
Total		107	100.0	100.0	

Table-I. Sex

Variables	N	Minimum	Maximum	Mean	Std.Deviation
Age	107	42	67	52.65	6.517
Sex	107	1	2	1.48	0.502
Occupation	107	1	5	1.94	1.080
Education	107	1.00	5.00	1.5047	1.10209
Residence	107	1.00	2.00	1.2056	0.40605
RBS	107	211	438	286.88	55.120
FBS	107	128	184	140.29	13.203
HbA1C	107	7.00	10.00	8.2449	0.81776
Bilirubin	107	0.80	4.30	1.0336	0.41549
SGPT	107	29.00	187.00	47.3645	25.60159
V.Load	107	91238	3252634	1092673	515806.99905
PT	107	12.00	15.00	12.6729	0.71078
Urea	107	23.00	41.00	33.8411	5.05470
Creatinine	107	0.8	1.50	1.0178	0.17419
Valid N (Listwise)	107				

Table-II. Descriptive Statics

Variables	Sum of Squares	df	Mean Square	F	Significant
Age Between Groups	112.762	1	112.762	2.697	0.104
Within Groups	4389.444	105	41.804		
Total	4505.206	106			
Sex Between Groups	126	1	0.126	0.499	0.481
Within Groups	26.565	105	0.253		
Total	26.692	106			
Occupation Between Groups	83.644	1	83.644	219.456	0.000
Within Groups	40.020	105	0.381		
Total	123.664	106			
Education Between Groups	105.293	1	105.293	471.370	0.000
Within Groups	23.455	105	.0223		
Total	128.748	106			
RBS Between Groups	7861.833	1	7861.833	2.627	0.108
Within Groups	314183.6	105	9292.225		
Total	322045.4	106			
FBS Between Groups	163.004	1	163.004	0.935	0.336
Within Groups	18315.014	105	174.429		
Total	18478.019	106			
HbA1C Between Groups	0.706	1	0.706	1.057	0.306
Within Groups	70.178	105	0.668		
Total	70.885	106			
Bilirubin Between Groups	2.314	1	2.314	15.203	0.000
Within Groups	15.985	105	0.152		
Total	18.299	106			
SGPT Between Groups	9430.924	1	9430.924	16.492	0.000
Within Groups	60045.861	105	571.865		
Total	69476.785	106			
V. Load Between Groups	6.9E+010	1	6.946E+010	0.259	0.612
Within Groups	2.8E+013	105	2.679E+011		
Total	2.8E+013	106			
PT Between Groups	0.585	1	0.585	1.159	0.284
Within Groups	52.967	105	0.504		
Total	53.551	106			
Urea Between Groups	1244.955	1	1244.955	89.330	0.000
Within Groups	1463.344	105	13.937		
Total	2708.299	106			
Creatinine Between Groups	0.002	1	0.002	0.068	0.795
Within Groups	3.214	105	0.031		
Total	3.216	106			

Table-III. One way anova

Variables	Mean	N	Std. Deviation	Std. Error Mean
Pair Age	52.65	107	6.517	0.630
1 RBS	286.88	107	55.120	5.329
Pair Sex	1.48	107	0.502	0.49
2 Occupation	1.94	107	1.080	0.104
Pair FBS	140.29	107	13.203	1.276
3 HbA1C	8.2449	107	0.81776	0.07906
Pair Bilirubin	1.0336	107	0.41549	0.04017
4 SGPT	47.3645	107	25.60159	2.47500
Pair V. Load	1092673	107	515806.99905	49864.94
5 PT	12.6729	107	0.71078	0.06871
Pair Urea	33.8411	107	5.05470	0.48866
6 Creatinine	1.0178	107	0.17419	0.01684
Pair Education	1.5047	107	1.10209	0.10654
7 Residence	1.2056	107	0.40605	0.03925

Table-IV. Paired samples statistics

Variables	N	Correlation	Sig
Pair 1 Age-RBS	107	-0.139	0.153
Pair 2 Sex-Occupation	107	0.259	0.007
Pair 3 FBS-HbA1C	107	0.718	0.000
Pair 4 Bilirubin-SGPT	107	0.589	0.000
Pair 5 V.Load-PT	107	0.149	0.125
Pair 6 Urea-Creatinine	107	0.218	0.024
Pair 7Education-Residence	107	0.904	0.000

Table-V. Paired samples correlations

DISCUSSION

This study provide link between diabetes mellitus and HCV infection. In other cohort studies it was observed that diabetes mellitus was 21% in HCV infection as compared 12% in HBV infection. Elevated aminotransferases were observed in HCV infection. In USA HCV infection was more in diabetics than HBV with diabetics.[11] Pathogenesis still not well understood, that HCV infection causing diabetes mellitus. Beta cell dysfunction and insulin resistance are the factors causing glucose intolerance in chronic hepatitis C infection. HCV is independently involved in insulin resistance study done by Delgado-Borrego et al. HCV infected non diabetic insulin resistance is associated with fibrosis of liver early infection in non diabetic.[12] Diabetes mellitus is more in HCV infected liver transplant patients as compared to non HCV infected liver transplant patients.[13] There is increased incidence of type 2 diabetes mellitus among chronic hepatitis C patients compared to chronic hepatitis B patients, indicate chronic hepatitis C and diabetes are independent of cirrhosis.

Extra hepatic manifestation of HCV infection is in relationship of HCV infection and diabetes mellitus according to new epidemiological studies. Incidence of diabetes was more in HCV infected than non infected patients according to Mehta et al.[14] insulin resistance is associated with metabolic syndrome and HCV infection. Imbalance in the secretion of specific cytokines occurs due to insulin resistance, with obesity and adipose tissue inflammation. There are several mechanism of insulin resistance induced by HCV infection with impairment of insulin signaling pathway.[15] Insulin resistance associated with high viral load infected with HCV infection. It was observed that high hyperinsulinemia associated with increase in HCV RNA replication.[16] In HCV infection viral particles in the liver are thought to be organ of the development of insulin resistance, viral proteins interfere insulin signal pathway in liver cells or chronic infection in the liver cause insulin resistance indirectly by cytokines that cause insulin resistance in liver and systemically. The mechanism where the HCV infection induces phosphorylation of these proteins is not investigated. Insulin signaling cascade restricted at the level of PKB/AKtphosphorylation in chronic HCV infection in vitro and vivo in studies of liver biopsy.[17] Rhe HCV induced hepatic up regulation of protein phosphatase 2A by a mechanism. Insulin signal pathway by indirect interference of viral proteins by kawagnchi et al. who explained in vitro that HCV core protein induced up regulation of SOCS-3 inhibit the signal cascade of insulin receptor substrate 1 and 2. HCV core protein interfere insulin signaling cascade in vitro, by genotype specific mechanism described by pazienza et al.[18] In the early stage of disease HCV infection and insulin resistance are related. Due to hyperglycemia/hyperinsulinemia by insulin resistance in relation with fibrosis could be due to direct stimulation of stellate cells and extra cellular matrix is accumulated.[19] Steatosis and liver fibrosis by a mechanism related to the oxidative stress result due to fat accumulation within hepatocytes and secretion of inflammatory cytokines, activation of stellate cells. Insulin resistance impairs the response to anti viral drug treatment in a recent study.[20] Life expectancy is decreased in cirrhosis due to diabetes mellitus and early hepatic coma. Due diabetic autonomic neuropathy constipation develops ammonia level is raised resulting hepatic encephalopathy.[21] There is development of esophageal varices

due to insulin resistance in a recent study.[22] For the development of hepatoma diabetes is a risk factor. Response to anti viral treatment is decreased due to obesity and steatosis. Steatosis due to genotype 3 is not changed due to anti viral treatment of HCV infection.[23] Lower chance of SVR to patients with BMI more than 30 kg/m sq. weight loss associated with improvement in fibrosis and steatosis even mild of 3 months duration.[24] After anti viral treatment of chronic hepatitis C virus, insulin resistance is restored and glucose level become normal according to two studies.[25]

CONCLUSION

Chronic hepatitis C virus is main problem in our country, association of diabetes mellitus increases mortality is increased if untreated. Majority of the patients come late for treatment and with complications. Education about disease and treatment is necessary. With latest treatment of oral antiviral drugs to treat hepatitis C and treatment of diabetes mellitus morbidity and mortality can be reduced. Patients life style can be improved.

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What comes easy, won't last,
what lasts won't come easy.

– Unknown –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Jeando Khan Daidano	Concept, design, analysis, interpretation and manuscript drafting.	
2	Nazia Azam Yusfani	Manuscript revision, concept, data analysis and interpretation.	
3	Bilqees Daidano	History and data collection.	