

DIABETES MELLITUS;

Incidence of chronic hepatitis c patients

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ABSTRACT... Introduction: Hepatitis C virus (HCV) is a major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma (HCC). HCV infection and type 2 diabetes are two common disorders with a high impact on health worldwide. There is growing evidence to support the concept that HCV infection is a risk factor for developing type 2 Diabetes Mellitus. Both insulin resistance and diabetes can adversely affect the course of chronic hepatitis C, and lead to poor response to antiviral therapy and increased incidence of Hepatocellular carcinoma. **Objective:** The objective of the study was to assess the frequency of type 2 Diabetes mellitus in newly diagnosed chronic hepatitis C patients presenting in Allied hospital Medical unit II during six month period. **Design:** Cross sectional study. **Setting:** Medical unit-II, Allied Hospital, Faisalabad. **Period:** 01-08-2009 to 28-02-2010. **Material and methods:** All newly diagnosed patients of chronic hepatitis C on the basis of PCR for HCV-RNA were included in the study. Fasting and two hours postprandial blood sample were tested. Diabetes Mellitus was labeled as per slandered. **Results:** Out of 180 patients with CHC 19 (10.6%) were found to have Diabetes mellitus while 161 (89.4%) were non-diabetics. **Conclusions:** There is close association in the development of type 2 diabetes mellitus in patients with chronic hepatitis C.

Key words: Chronic hepatitis C, Type 2 Diabetes mellitus, insulin resistance.

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INTRODUCTION

Hepatitis B and C are global health care problems causing morbidity and mortality worldwide and spreading like an epidemic in developing countries like Pakistan, especially in rural areas^{1,2,3}. WHO estimated 1- 3% worldwide prevalence of HCV, and 3-4 million new cases arising each year⁴.

Blood and blood products transfusion and infected needles are two preventable modalities of spread of hepatitis C infection while sexual transmission remains controversial^{5,6}.

HCV is the cause of approximately 20% of cases of acute hepatitis, most often asymptomatic and rarely causes hepatic failure. The majority, up to 85% enter a chronic phase and out of these 20% will progress to cirrhosis and its complications after 20 years^{7,8,9,10,11,13}.

Chronic hepatitis C virus infection is present in 3 - 10 % of Pakistani population and genotype 3 is the most prevalent subtype¹². The rate of spontaneous

clearance of virus after it has persisted for at least six months is very low⁹.

Cirrhosis along with its complications like encephalopathy, ascites and portal hypertensive bleeding, is the 12th most common cause of death and the most common cause of non-malignancy related death among patients with diseases of the digestive tract^{14,15,16,17,18,19}.

Type 2 diabetes (T2D) and HCV infection are common conditions involving at least 170 and 130 million people respectively worldwide²⁰.

Like other complications of chronic hepatitis C including cirrhosis of liver and Hepatocellular carcinoma, there is growing evidence suggesting mutual link between chronic hepatitis C and increased risk of developing type 2 Diabetes mellitus and glucose abnormalities^{21,22}.

The risk factors associated with development of type 2

Diabetes mellitus in general population alone cannot account for the high prevalence of type 2 Diabetes mellitus in patients with chronic hepatitis C²³. Increased insulin resistance (IR) seems to be a specific feature of chronic hepatitis C²⁴. In chronic hepatitis C, insulin resistance and type 2 diabetes mellitus are more often seen than in healthy controls or chronic hepatitis B patients^{25,26}. Inflammatory cytokines, including TNF- α are an integral part of inflammation in chronic hepatitis C infection. It has recently been suggested that chronic sub-clinical inflammation is associated with insulin resistance, and precedes the development of type 2 DM²⁶.

In summary, hepatitis C promotes insulin resistance and insulin resistance induces interferon resistance, steatosis and fibrosis progression²⁷. Development of glucose abnormalities and type 2 Diabetes mellitus may lead to poor response to anti viral therapy and increased incidence of Hepatocellular carcinoma²⁸. T2D and IR are independent predictors of a more rapid progression of liver fibrosis and impaired response to antiviral treatment in chronic hepatitis C²⁹.

Diagnosing and treating insulin resistance in patients with chronic hepatitis C could not only avoid complications but also prevent disease progression and increased the sustained virological rate to treatment with pegylated interferon plus ribavirin³⁰.

Objective

To determine the frequency of type 2 Diabetes mellitus in newly diagnosed patients of chronic hepatitis in Faisalabad.

Operational definition

Fasting blood sugar level >110 mg/dl or >200mg/dl two hours after meal were labeled as having diabetes mellitus.

Patients both positive with Anti-HCV antibodies by ELISA and PCR for at least six months were labeled as

having chronic Hepatitis C disease.

MATERIAL AND METHOD

Study design

Cross sectional study

Study Setting

Medical unit II Allied Hospital Faisalabad.

Duration of study

Six months, from 01.08.2009 to 28.02.2010

Inclusion Criteria

Age >30 years, All patients with more than six months history of hepatitis C confirmed by enzyme linked immunosorbant assay (ELISA) and PCR for HCV- RNA qualitative test.

Exclusion Criteria

Patients with chronic hepatitis B, known diabetics or having family history of diabetes, HIV positive patients. Patients with clinical decompensated cirrhosis or cancer

Data collection procedure

All patients admitted in Allied hospital M unit II with hepatitis C on the basis of >6 months history of hepatitis C confirmed by enzyme linked immunosorbant assay (ELISA) and +ve PCR for HCV RNA. had been taken as having chronic hepatitis C. Informed written consent taken from patients after explaining procedure in detail. Fasting blood sugar level was taken early in the morning in sterilized syringes under aseptic measures. Random blood sugar was taken two hours after meals in sterilized syringes and sent for FBS RBS, SGPT and billirubin. Data of all patients was collected through Proforma.

RESULTS

In this study total 180 patients having chronic hepatitis C were included. Minimum age of the pt. was 34 and maximum 70 with a mean and STD of 53.40 and 8.64

	N	Minimum	Maximum	Mean	Std. Deviation
Age of the patients	180	34	70	53.40	8.64
Fasting blood glucose level	180	67	141	91.48	14.00
Random blood glucose level	180	123	310	161.29	35.10
Billirubin	180	.80	2.20	1.0906	.2150
SGPT of patients	180	22	56	33.53	5.18
Valid N (list wise)	180				

Table-I. Descriptive statistical analysis

		Frequency	Percent	Valid percent	Cumulative percent
Valid	Female	87	48.3%	48.3%	48.3%
	Male	93	51.7%	51.7%	100.0%
	Total	180	100.0	100.0	

Table-II. Sex distribution

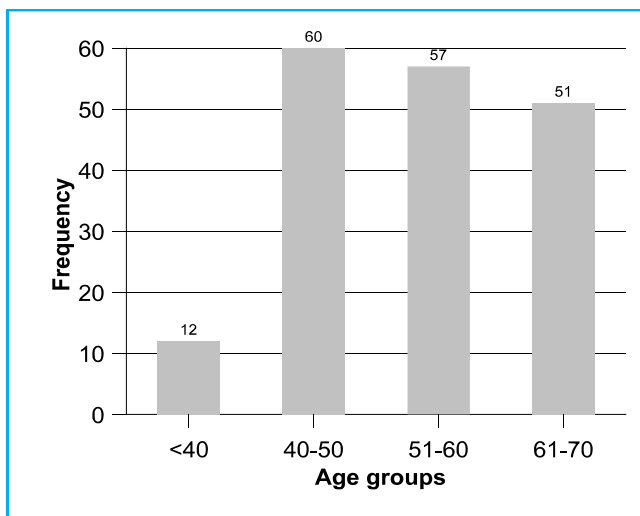


Fig-1. Age distribution of patients with CHC

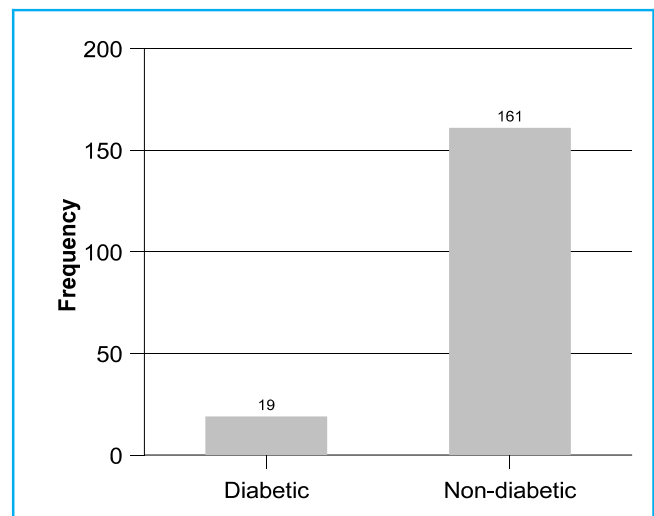


Fig-2. Diabetes mellitus in chronic HCV

respectively (table I) Out of total 180 patients, 93 (51.7%) were males and 87 (48.3%) were females (table II).

Among age distribution the study showed that out of total 180 patients 12 (6.7%) patients were having age

< 40 years. Majority of them were among 40-70 years of age groups. Sixty (33.3%) were having age from 40-50 years and 57 patients (31.7%) were having their ages between 51-60 years and remaining 51 patients (28.3%) were having ages between 61-70 years (Fig-1).

		Frequency	Percent	Valid percent	Cumulative percent
Valid	Diabetic	19	10.6%	10.6%	10.6%
	Non diabetic	161	89.4%	89.4%	100.0%
	Total	180	100.0	100.0	

Table-III. Association of chronic HCV with diabetes mellitus

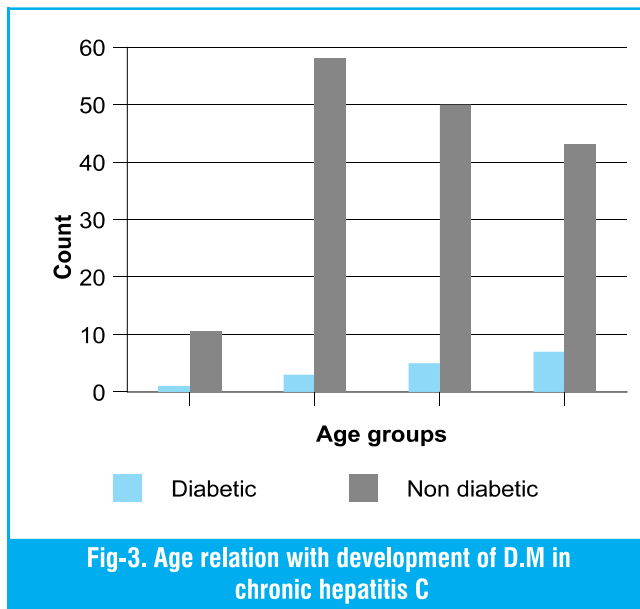


Fig-3. Age relation with development of D.M in chronic hepatitis C

The study showed, out of 180 patients with Chronic hepatitis C, 19 (10.6%) were found to have Diabetes mellitus while 161 (89.4%) were having no Diabetes mellitus on the basis of measured FBS, RBS levels falling in Diabetic range. (table III, Fig-2).

Out of 19 patients no one was having jaundice. Most patients presented with Diabetes Mellitus in pts. With CHC having age group 50-70. (Fig-3).

DISCUSSION

Hepatitis C and diabetes mellitus are global health care problems assuming epidemic. HCV infects approximately 170 million individuals worldwide and estimated to be responsible for approximately 250,000 to 350,000 deaths per year.

Chronic hepatitis C has recently been proposed as a

metabolic disease and insulin sensitivity as a predictive factor for liver fibrosis. There is well established relation between cirrhosis of liver and development of diabetes mellitus as its extra hepatic complication, Thyroid disorders being the next common endocrine association. Diabetes developed as a complication of cirrhosis is known as hepatogenous diabetes (HD). Around 30% to 60% of cirrhotic patients suffer from this metabolic disorder³¹. Allison et al.³² reported that cirrhotic patients with HCV more frequently have T2D than cirrhosis with other etiology.

This study was conducted to determine the frequency of type 2 D.M in patients having chronic hepatitis C. Out of 180 patients, 19 (10.6%) had Diabetes mellitus with somewhat male preponderance. Same was reported by Khokhar N³³ from Islamabad.

Qureshi F et al³⁴ reported threefold increase in the prevalence of D.M in the background of positive family history in chronic Hepatitis C. Claudia O Zein et al³⁵ reported 14.5% incidence against 7.8% in American population.

Alavian SM, et al³⁶ reported 18.3% prevalence of DM among HCV-infected patients from Iran. Suliman MI et al²² reported 19%, against 8%, incidence of DM in chronic hepatitis C patients in Bahawalpur.

Lecube et al,³⁷ reported three fold increase in glucose metabolism abnormalities even in pre-cirrhotic stage in patients with chronic hepatitis C independently of duration and stage of liver disease. Ryu JK et al³⁸

reported similar results in Korean patients. All these studies stands fairly close to my results.

As cross-sectional nature of these studies cannot establish whether D.M or chronic HCV occurred earlier, longitudinal studies are needed. We excluded both known diabetic patients and even the patients with strong family history of DM to prove the point. The Atherosclerosis Risk in Communities Study, from America showed de novo development of T2DM over 9 years of follow-up in high risk patients as defined by family history and BMI. In a Taiwanese study³⁹, over a follow-up of 7 years, 14.3% of anti-HCV-positive, 7.5% of HBsAg-positive, and 8.6% of seronegative individuals developed T2DM.

The high co-incidence of HCV and IR/T2Dm cannot be assigned to chance, some protein component of the virus directly or indirectly through cytokines, like TNF- α may be responsible. As abnormalities in glucose metabolism influences treatment outcome and disease progression, early detection and management of metabolic disorder is warranted.

Lifestyle modification and Insulin sensitizers are currently being evaluated in clinical trials.

Early screening of patients with chronic HCV infection for detection of diabetes and glucose metabolism disorders is recommended to improve patients' outcome and vice versa

CONCLUSIONS

HCV infection and type 2 diabetes are two common disorders with a high impact on health worldwide. The inference drawn from this study is that; a high frequency of type 2 Diabetes Mellitus among HCV-infected patients with chronic hepatitis has been observed, and supporting the concept that HCV infection is a risk factor for developing type 2 Diabetes.

Considering the disease burden and high economic cost of chronic hepatitis C treatment, early detection

of D.M will not only reduce the cost of treatment failure but will also help in identifying the patients who require early management of type 2 diabetes mellitus.

The control of glucose abnormalities in CHC not only improves response to anti viral therapy but also decrease incidence of hepatocellular carcinoma.

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