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FREQUENCY OF TYPE-2 DIABETES MELLITUS AMONG HEPATITIS C POSITIVE PATIENTS

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ABSTRACT:

INTRODUCTION: *Hepatitis C Virus (HCV) infection is a frequent cause of acute and chronic hepatitis and leads to the development of Cirrhosis and Hepatocellular Carcinoma (HCC). It is estimated that about 150-200 million people have been in contact with HCV world wide, and approximately 85% are chronically infected.*
The spectrum of severity of HCV varies widely and progression towards cirrhotic stage and development of Type-2 Diabetes Mellitus (T2DM). It depends on several, mostly host-related co-factors such as: age, sex, level of alcohol consumption, Over weight (BMI), Immune status (Tissue necrosis factor alpha [TNF-alpha]), Genotype (1-b, 2-b, 3-a/b), Positive family history of diabetes, liver or kidney transplantation, hepatic steatosis /fibrosis, insulin resistance (IR) and co-infections.
Both HCV infection and T2DM are chronic conditions with significant morbidity and mortality. T2DM is approaching epidemic proportions worldwide and by the year 2025, more than 300 million peoples will have been diagnosed with T2DM.
MATERIAL & METHODS: *In this prospective and observational study 206 cases of HCV positive on Elisa method were inducted. All cases were segregated into different states of liver disorders and were screened for Blood Sugar level, for one year i.e.; 1st November 2008 to 31st October 2009 at Medical Wards at Liaquat University Hospital (LUH) Jamshoro/Hyderabad, so as to observe the frequency of T2DM among HCV positive patients.*
RESULTS: *Among 206 cases of HCV positive, male were 133 (64.56%) and female were 73 (35.43%). In our study, we found a strong association between HCV & T2DM and out of 206 HCV infected cases, 24 (11.65%) were found to be diabetic (T2DM). In these males were 18 (75%) and females were 06 (25%). Out of 130 cases of Chronic Hepatitis, T2DM was found in 11 (8.46%), from 60 cases of Liver Cirrhosis, T2DM was found in 08 (13.33%), from 07 cases of HCC, T2DM was found in 01 (14.28%) and from 09 cases of Obesity, T2DM was seen in 04 (26.66%). In 24 cases of T2DM with HCV positive, Genotype 3a was found among 20 (83.33%) and Genotype 1b was found in 04 (16.66%) respectively.*
CONCLUSION: *In our study we found the strong association of T2DM with HCV infection, which not only affects the course of liver disease but also affects to the treatment course as well. Therefore, it is necessary to screen and control earlier for presence of T2DM that will provide a dual benefit to the sufferer i.e. disease course will not be affected and the treatment response rather will be better.*

KEY WORDS: Type-2 Diabetes Mellitus, Hepatitis C Virus, Chronic Hepatitis, Liver Cirrhosis, HCC, Obesity.

INTRODUCTION:

Hepatitis C Virus (HCV) infection is a frequent cause of acute and chronic hepatitis and leads to the development of Cirrhosis and Hepatocellular Carcinoma (HCC). It is estimated that about 150-200 million people have been in contact with HCV world wide, and approximately 85% are chronically infected [1,2]. Globally, the seroprevalence of HCV varies as in Pakistan it is 6% in 10 million people [3,4], in USA (1.8%) and in Japan (1.5-2.3%) [5].

The spectrum of severity of HCV varies widely and progression towards cirrhotic stage and development of Type-2 Diabetes Mellitus (T2DM). The latter seems to depend on several, mostly host-related co-factors such as: age, sex, level of alcohol consumption, Over weight (BMI), Immune status (Tissue Necrosis Factor Alpha [TNF-alpha]), High HCV load [6], Genotype (1-b, 2-b, 3-a/b), Positive family H/O Diabetes, Liver/Kidney

transplantation, hepatic steatosis / fibrosis, Insulin Resistance (IR) and co-infections [7-11]. One of these co-factors is T2DM, that has been recognized to modify the course of HCV even at the stage of IR, a condition that precedes the development of T2DM [7,8]. This aspect is important, because IR seems not only to accelerate the course of chronic hepatitis C but also to influence the response to anti-viral therapy [9,10].

Moreover, antecedent HCV infection markedly increases the risk of T2DM in susceptible subjects. Recent research revealed several molecules including TNF-Alpha, Suppressor of cytokine signaling 1 & 3 Proteins, Insulin - Receptor Substrates 1 & 2 and other adipokines, are potentially involved in the development of IR [11]. Even non diabetic HCV patients have IR and specific defects in the Insulin Signaling Pathway [12]. Activation of TNF-Alpha has a pivotal role in the inflammatory process of chronic HCV & TNF-Alpha levels co-relate with degree of inflammation and by same mechanism/pathway produces IR [13,14]. Both HCV infection and T2DM are chronic conditions with significant morbidity and mortality. T2DM is approaching epidemic proportions world wide and by the year 2025, more than 300 million peoples will have been diagnosed with T2DM [15,16]. Therefore, regular screening for T2DM should be started earlier than the suggested age of 45 or more in all HCV infected patients [17].

MATERIAL AND METHODS:

In this prospective and observational study 206 cases of HCV positive on Elisa method were inducted. All cases were segregated into different states of liver disorders and were screened for Blood Sugar level, for one year i.e. 1st November 2008 to 31st October 2009 at Medical Wards at Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro/Hyderabad, Sindh, Pakistan so as to observe the frequency of T2DM among HCV positive patients.

All the entitled patients were thoroughly examined and details were recorded in a proforma & were subjected to the following important investigations.

1. Complete Blood Count (Sysmex Poch 100 I Japan).
2. Urine DR
3. HCV Antibodies on Eliza (International Immuno-Diagnostics Foster City, USA).
4. Fasting/Random Blood Sugar.
5. LFTs
6. U/S Abdomen
7. Genotyping .
8. Liver Biopsy (If required).

TABLE (I).

SEX RATIO AMONG HCV POSITIVE T2DM PATIENTS.

Total number of patients	= 206
Male	= 133 (64.56%)
Female	= 73 (35.43%)
M:F Ratio	= 1.8:1

TABLE (II).

BREAKUP OF HCV POSITIVE PATIENTS.

Total number of patients	= 206
Chronic Hepatitis	= 130 (63.10%)
Liver Cirrhosis	= 60 (29.12%)
HCC	= 07 (3.36%)
Obesity	= 09 (4.36%)

TABLE (III).

FREQUENCY OF T2DM AMONG HCV POSITIVE PATIENTS ACCORDING TO LIVER DISORDERS & OBESITY.

Chronic Hepatitis	[n=130]	= 11 (8.46%)
Liver Cirrhosis	[n=60]	= 08 (13.33%)
HCC	[n= 07]	= 01 (14.28%)
Obesity	[n=09]	= 04 (26.66%)

Over all mean frequency of T2DM in HCV +ve Patients = 24 (11. 65%).

TABLE (IV)

BREAKUP OF SEX RATIO AMONG HCV +VE PATIENTS.

Liver Disorder/Obesity	No: Patients	Males	Females
Chronic Hepatitis	= [130]	80 (61.53%)	50 (38.46%)
Liver Cirrhosis	= [60]	40 (66.66%)	20 (33.33%)
HCC	= [07]	06 (85.71%)	01 (14.28%)
Obesity	= [09]	07 (77.77%)	02 (22.22%)

TABLE (V).

BREAKUP OF SEX RATIO AMONG HCV +VE T2DM PATIENTS.

Liver Disorder/Obesity	No: Patients	Male	Female
Chronic Hepatitis	= [11]	08 (72.72%)	03 (27.27%)
Liver Cirrhosis	= [08]	06 75%)	02 (25%)
HCC	= [01]	01 (100%)	0 (0%)
Obesity	= [04]	03 (75%)	

M: F Sex Ratio = 3:1

INCLUSION CRITERIA:
All the cases were included suffering from HCV infection or T2DM with HCV Positive.

EXCLUSION CRITERIA:
All the cases with HCV Negative or already suffering from T2DM without HCV infection were excluded.

RESULTS:
In our study we selected 206 cases of HCV Positive on Eliza, among these males were 133 (64.56%) & females were 73 (35.43%) with 1.8:1 M: F ratio. Table (I).

Among 206 patients, Chronic Hepatitis patients were 130 (63.10%), Liver Cirrhotic patients were 60 (29.12%), patients with Hepatocellular Carcinoma (HCC) were 07 (3.36%) and patients with Obesity were 09 (4.36%). Table (II).

In patients with chronic hepatitis T2DM was found in 11 (8.46%), in liver cirrhosis T2DM was found in 08 (13.33%), in HCC, T2DM was found in 01 (14.28%) and in obesity T2DM was found among 04 (26.66%) respectively.

In our study we found the frequency of T2DM among HCV positive patients as 11.65%. Table (II).

In chronic hepatitis males were 80 (61.53%) & females were 50 (38.46%), in liver cirrhosis males were 40 (66.66%) & females were 20 (33.33%), in HCC males were 06 (85.71%) and the number of females was 01 (14.28%); in obesity males were 07 (77.77%) and females were 02 (22.22%). Table (III).

While in T2DM patients with chronic hepatitis males were 08 (72.72%) & females were 03 (27.27 %), in liver cirrhosis, males were 06 (75%) & females were 02 (25%), in HCC patients, males was 01 (100 %) & none of the female found to have T2DM and among obese diabetic patients, males were 03 (75%) & females was 01 (25%). Here M:F ratio was 3:1. Table (V).

In chronic hepatitis the patients were between 30-50 years of age, in liver cirrhosis patients were between 50-60 years, in HCC patients were between 40-50 years and in obesity patients were between 60-70 years of age respectively. Table (VI).

Out of 24 cases of T2DM, Genotype -1b was found in 04 (16.66%) and genotype-3a was found in 20 (83.33%) cases respectively. Table (VII).

TABLE (VI).

AGE BIFERCATION AMONG HCV +VE & T2DM PATIENTS.

Liver Disorder/Obesity	Age in Years.
Chronic Hepatitis	30-50
Liver Cirrhosis	50-60
HCC	40-50
Obesity	60-70

TABLE (VII).

FREQUENCY OF GENOTYPE AMONG T2DM PATIENTS.

Genotype	No: Patients.
3a	20 (83.33%)
1b	04 (16.66%)

DISCUSSION:
Among 206 cases of HCV positive, males were 133 (64.56%) and females were 73 (35.43%). In our study, we found a strong association between HCV & T2DM and out of 206 HCV infected cases, 24 (11.65%) were found to be diabetic (T2DM). In these males were 18 (75%) and females were 06 (25%). Out of 130 cases of Chronic Hepatitis, T2DM was found in 11 (8.46%), from 60 cases of Liver Cirrhosis, T2DM was found in 08 (13.33%), from 07 cases of HCC, T2DM was found in 01 (14.28%) and from 09 cases of Obesity, T2DM was seen in 04 (26.66%). In 24 cases of T2DM with HCV positive, Genotype 3a was found among 20 (83.33%) and Genotype 1b was found in 04 (16.66%) respectively.

Our results match with many studies conducted either in Pakistan or abroad, in various aspects.

Lecube etal [18], in their study found 4.9-33% prevalence of T2DM in chronic Hepatitis patients and that of Liver Cirrhosis was found in 19.6-50%. Both figures are higher than our study.

Wang CS etal [19], in their community-based study also found a strong association between T2DM and HCV infection in advanced age group (35-49 years). The results of this study nearly match to our study results in same features.

In Third National Health & Nutrition Examination Survey (NHNES-III), showed that in age 40 years or more with HCV infection, have more than three times chances to have T2DM as compared to non-HCV infected T2DM (Adjusted OR 3.77) [20]. Our results never match in some parameters.

Suliman MI etal [21], at Bahawalpur Hospital found 19% T2DM among chronic HCV cases. Again the results are higher than our results.

Khokhar N [22], in their study among 411 cases of HCV positive in which males were 244 (55.07%) & females were 199 (44.92%). Here Chronic Hepatitis cases were 71 (17.27%) and Liver Cirrhotic cases were 32 (7.78%). Out of 71 cases of chronic hepatitis 60 (84.5%) were found to be suffering from T2DM and out of 32 cases of liver cirrhosis 10 (31.25%) cases were suffering from T2DM. Over all they found the prevalence of T2DM 18.28%, while in our study it was 11.65%. The dominant Genotype in their study, was 3. In our study we also found type 3 genotype.

Kaabia N etal [23], in their study of 1269 patients of diabetes found the dominant genotype 1b whereas we found type 3a dominant genotype, though genotype 1b was 16.66% in our study.

White DL etal [24], analyzed 34 eligible retrospective and prospective studies. In retrospective study the adjusted OR = 1.68, 95% CI, 1.15-2.20 and in retrospective study they found the OR = 1.67 95%, CI, 1.28-2.06, showing a significant risk of T2DM among HCV infected group as compared to non-HCV infected control group respectively. Our study also proves the close relationship between HCV & T2DM.

Hussain RR etal [25], in their study among 700 patients, they found HCV positive with T2DM in 118 (16.85%), very nearer to our result as 11.65% respectively.

Zein NN etal [26], in their study in 64 patients of HCV, before transplantation found T2DM in 16 (25%) cases. Monto A etal [27], in 297 patients found HCV positive in 280 (94.3%), T2DM among 23 (7.7%) and Genotype 3a was found. In our study we also found Genotype 3a in high percentage.

In another study Mason AL etal, [28] in 1117 Chronic HCV patients in their retrospective analytic study 21% of T2DM and the Genotype was 2a in 29% of HCV positive patients with T2DM. While we found T2DM

in 11.65% with 3a Genotype predominantly.

CONCLUSION:

In our study we found the strong association of T2DM with HCV infection, which not only affects the course of liver disease but also affects to the treatment course as well. Therefore, it is necessary to screen and control earlier for presence of T2DM that will provide a dual benefit to the sufferer i.e.; disease course will not be affected and the treatment response rather will be better.

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