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The Liver Associated Diseases in patient with Diabetes Mellitus from Islamabad Region

[a*]Farah Shaikh, [b]Awais Qarni, [c]Kashaf Fatima, [d]Shifa Aziz

[a]*Department of Allied Health Sciences, Bashir Institute of Health Sciences, Bara Kuhu, Islamabad, Pakistan*
[b]*Nayab Laboratories Islamabad, Pakistan*
[c]*Department of Medical Laboratory Technology, University of Lahore, Pakistan*
[d]*Institute of Allied health sciences (IAHS), Wah Medical College, NUMS, Armed Forces Post graduate medical Institute (AFPGMI), Islamabad, Pakistan*

*CORRESPONDENCE
Farah Shaikh
Department of Allied Health Sciences, Bashir Institute of Health Sciences Islamabad

E-mail:
farah.ksa97@gmail.com

ABSTRACT

Background: Type 2 Diabetes is a risk factor for progression of many liver associated diseases such as NAFLD, Hepatitis B and C, HCC, Liver Cirrhosis, Acute kidney diseases, glomerulonephritis and obesity. We examined prevalence of advanced liver disease in people of type 2 Diabetes and analyzed the changes in liver, renal and lipid profile as a screening tool. **Methods:** A Hospital based cross-sectional study was performed and data was collected from hematology, chemistry and clinical Pathology department of Umar diabetic foundation and The diabetic center. In this descriptive study, LFTs, RFTs, Lipid profile and Micro albumin were measured in the diabetic patients. **Results**: A total of 60 patients from different regions of Islamabad were tested during this time. Amongst 51 patients were Diabetic, 4 were prediabetic and 5 patients were completely normal with no associated disease. Out of those 51 diabetic patients, 26 were male and 25 were female. Furthermore, 30 out of 51 patients were diagnosed with Non-Alcoholic Fatty liver Disease, which was the highest percentage amongst other associated diseases of our report. Other than this, these diabetic patients also presented with high ratio of acute kidney infections and Obesity. **Conclusion**: Type 2 diabetes is associated with a large number of liver disorders including fatty liver, cirrhosis, hepatocellular carcinoma, and acute liver failure. In addition, there is an unexplained association with HCV. Moreover, blood parameters such as liver enzymes, RFTs and sometimes lipid profile is also disturbed. Comprehensive strategies need to be developed to incorporate screening, prevention and treatment of type 2 diabetes at a community level.

Keywords: Type 2 diabetes, HCC (Hepatocellular carcinoma), NAFLD (Nonalcoholic fatty Liver disease), Obesity.

INTRODUCTION

Diabetes is basically a Greek word means frequent urination. The word diabetes is actually short form of 'diabetes mellitus' and the word "mellitus" means sweet urination. This actually indicates one of the major symptoms of Diabetes. In 17th century diabetes was known as "Pissing evil" [1]. Diabetes has 3 major types i.e. Type I diabetes, Type II Diabetes and Gestational diabetes. In these types, type I and type II have more importance as 98% of people are affected with these two types. Both of these types are directly associated with liver problem. Major sign and symptoms include frequent urination, frequent thirst, frequent weight lost and have numb and tingling hands and feet [2]. Type I diabetes was once known as 'Juvenile diabetes'. In Type I, body stops the production of insulin. This is basically due to an autoimmune response. Genetic factor or may be some other unknown cause may be due to any virus such as hepatitis C viruses. Although insulin and glucagon are two major contraction hormones that

balances your blood and body sugar level. That's why insulin production is key for an active sugar maintenance. If the production of insulin stops body will not be able to stop the production of Glucose causing blood sugar increase which can cause other serious health complication such as nerve damage, kidney damage etc. Type 1 diabetes can strike at any age, although there are two distinct peaks, youngsters aged 4 to 7 years old experience the first peak, while children aged 10 to 14 years old experience the second. These types of diabetic patient are insulin dependent [3]. Type II diabetes is basically known as adult-onset diabetes. It is more common in adults of both male and female. In type II, your body doesn't use insulin well and can't keep blood sugar at normal levels [4]. Due to this increase of sugar in blood, other type of complication especially liver problem occurs frequently. On the other hand, liver disease was considered to be an important cause of death in T2DM, where in one prospective cohort study, cirrhosis accounted for 12.5% of all death causes. Virtually the entire spectrum of liver disease is seen in patients with type 2 diabetes [5]. This includes abnormal liver enzymes, non-alcoholic fatty liver disease (NAFLD), cirrhosis, hepatocellular carcinoma, and acute liver failure. In about 80% of cirrhotic individuals, insulin resistance can be seen, and 20-63 percent of these patients will acquire diabetes (hematogenous diabetes). The prevalence is mostly determined by diagnostic criteria, cause, and the length of time since cirrhosis was diagnosed.

Liver is an important organ of the body which at a time do both metabolism and filtration. Glucose metabolism and energy balance are the two major activities in human body and both of them are perform by liver. Liver has special enzymes that control the whole function of liver. These enzymes include ALT (Alanine transaminase), ALP (Alkaline Phosphatase) which break the protein for cell energy, AST (Aspartate transaminase) which is important in amino acid metabolism and GGT (Gamma-glutamyl transferase) metabolize drugs and other toxins and helps in transport [6]. These enzymes are basically proteins and works in optimum conditions. Slight injury or any type of disease related to liver for example hepatitis B or C disturbs the normal value of enzymes which is the main indication of liver dysfunction. Liver diseases such as abnormal liver enzymes, NAFLD, or Hepatocellular carcinoma all are associated with both of major types of diabetes. Liver cells produce different enzymes and hormones that are essential for body normal function. Any slight change in the condition leads to serious type of complication. Insulin resistance have been noticed in a significant proportion of patient with cirrhosis ranging between 35% and 80% [7]. Studies have shown that an increased risk of hepatocellular carcinoma in patient with diabetes and increased incidence of diabetes in hepatocellular carcinoma patient. In addition to this, obesity is one of the major causes of diabetes.

The literature related to liver diseases in diabetic patients. Different methods, principles and results are also discussed. In the year 2007, Keith G Tolmanet et.al, performed a study in the population of US, where they observed that the patients with T2DM have a significance of liver diseases and cirrhosis was the cause of 12.5 % death in diabetic patients. They also look into the management in patients with diabetes and liver diseases and concluded that either the presence of diabetes causes liver diseases or the presence of liver diseases causes diabetes [8].Simona Moscatiello.et al, in 2006 studied the ominous association of diabetes mellitus and liver diseases, they are linked together that persistent diabetes mellitus can lead to cirrhosis in future, therefore extensive monitoring of NAFLD and analysis of insulin signaling in HCV patient should be done by using molecular biology test, biochemical test, clinical studies, histological studies and diagnosis of clinical markers to prevent and treat diabetes mellitus and liver disease [9].In 2010, Ramon Arturo Kobashi Margain et al performed a retrospective study in population of Mexico on 129 patients with liver diseases, as 61 patients suffered from cirrhosis, 44 (34.1%) from Hepatitis C, 28 from HCC and 30 patients were diagnosed with T2DM out of which 18 were males and 12 were females and most of the T2DM patients had cirrhosis (21 out of 61 -34.4%). Therefore they suggested that T2DM was most prevalent in patients with liver diseases [10].In the year 2015 Evan J. Raff et al. performed a study on 480 patients with diabetes and came up with the results that D.M is the main cause in increasing the risk of cirrhosis and HCC in patients suffering with ALD and NAFLD [11].Chen et.al performed a meta-analysis in the year 2015 in which they included 21 cohort studies with 24 reports in their analysis, the study showed that patients with Hepatitis C and cirrhosis with the presence of D.M had a higher risk of developing HCC than patients without D.M, therefore they should go through an active monitoring of HCC presence annually [12].A study was performed in the year 2019 by Aziz ul Hasan Aamir et al in the demographic population of Pakistan, in which they conducted HbA1c test on 18,856 eligible people from which 10.91% were pre-diabetic and 16.98% were suffering from T2DM and its prevalence was highest in age 51-60 years. from which they concluded that the prevalence of T2DM is more than thought in Pakistan and is greater in older age patients [13].In the year 2016, Sohaib Akhtar et al conducted a cross sectional analysis of 1650 individual, in patients with age between 20-80 years by using cluster random sampling technique and came up with the results that the prevalence of diabetes were 11.1% and prediabetes was 16.0% and T2DM was 11.0% in females and 11.2% in males patients and therefore T2DM has become a main health issue in population of District Dir lower [14].In the year 2016 Sultan Ayub Meo et.al, conducted a study to check the

prevalence of T2DM in Pakistan. In this study they observed and calculated the prevalence of T2DM of each province separately, as the prevalence of T2DM in Sindh province was 16.2% in males and 11.70% females and in Punjab it was 12.14% in males and 9.83% in females, in Baluchistan 13.3% in males and 8.95 in females, in KPK (Khyber Pakhtunkhwa) it was 9.2% in males and 11.60% females and the current prevalence of T2DM in Pakistan was 11.77%, as it was 11.20% in males and 9.19% in females ,as in rural areas it was 10.34% and in urban areas it was 14.81% , therefore they concluded that T2DM in Pakistan is higher in males than females and found more in urban areas than rural areas [16].

MATERIALS AND METHODS

This is a Laboratory based cross-sectional study, which was performed in local population of Islamabad. The data was collected from haematology, chemistry, and clinical pathology department of "The Diabetes Centre" and "Umar Diabetic Foundation". The study was performed at haematology, chemistry, and clinical department of "The Diabetes Centre'' and "Umar diabetic foundation." Permission had taken from the committee of both The Diabetes Centre and UDF. All samples were processed under the supervision of senior laboratory personnel. Samples from the patients were collected after taking proper consent from the patients. Data collected includes patients' age, gender, lab ID, Urine RE, LFT`s, RFT's, Lipid profiles and Hb1Ac findings of all patients.

Consecutive sampling technique was used for data collection. Three types of blood and fluid samples i.e. whole blood, blood serum, and urine samples were taken from patient directly. A total of 60 patients were included in this study which included diabetic patients with altered LFTs, Patients diagnosed with diabetes, and Diabetic patients with symptoms related to liver disease. However, non-diabetic or patients with normal blood sugar levels were not included in this study.

After collecting samples certain tests were performed which include HbA1c was performed on I-Chroma (Kit based test on the whole blood sample), Levels of liver enzymes such as ALT, AST and ALP were monitored in serum samples. These are Kinetic based test and were performed on Micro lab 300 which is based on principle of Spectrophotometer, and Urine R/E was performed on strip-based method and Combur 10 was used for this. RFT's such as urea, uric acid, creatinine, and micro albumins were monitored in serum samples and was performed on Micro lab 300. Lipid profile includes cholesterol, triglycerides, LDL and HDL were monitored in serum samples and was performed on Micro lab 300.

RESULTS

In our study, 60 patients were selected for the diagnosis of diabetes. Among those selected patients 5(8.3%) of them were non-diabetic while 4(6.7%) patients were diagnosed with Pre-Diabetes and 51(85%) were confirmed with diabetes as shown in figure1

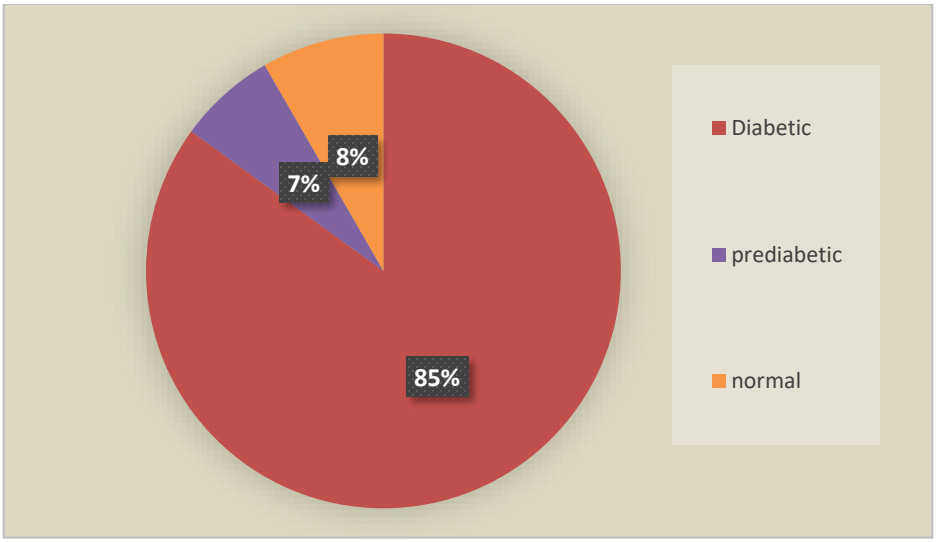

Figure 1. Pie chart showing the distribution of sample size between normal, diabetic and pre diabetic patients

Out of those 51 diabetic patients, 26 were male (50.98%)and 25were female (49.02%) as shown in figure 2

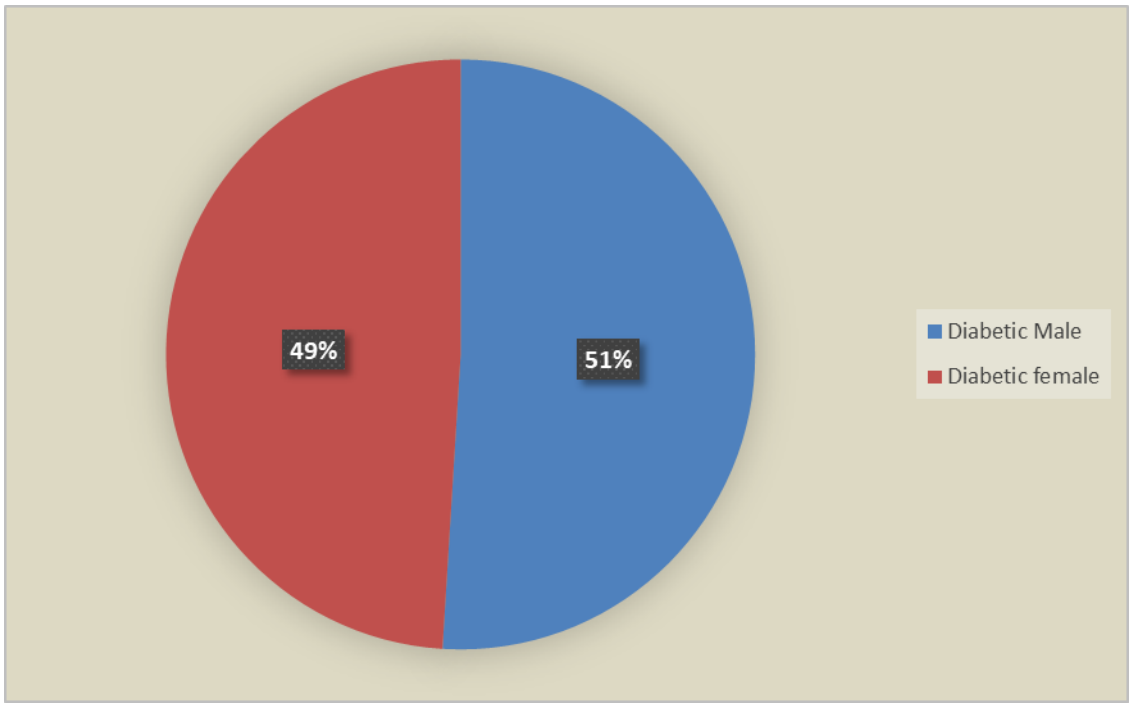

Figure 2. Pie chart showing the percentage of male and female diabetic patients

The overall average age of these diabetic patients is 54 years. Further analysis of the study shows that 14 patients suffering from the diabetes were having normal functioning of the liver (27.45%) while 34 patients were suffering from diabetes were having abnormalities of liver functioning (66.6%) and the other 3 diabetic patients were having both abnormal liver and abnormal renal functioning (5.88%) as shown in histogram figure 3.

Figure 2. Graphical representation of diagnosed samples of Plasmodium species.

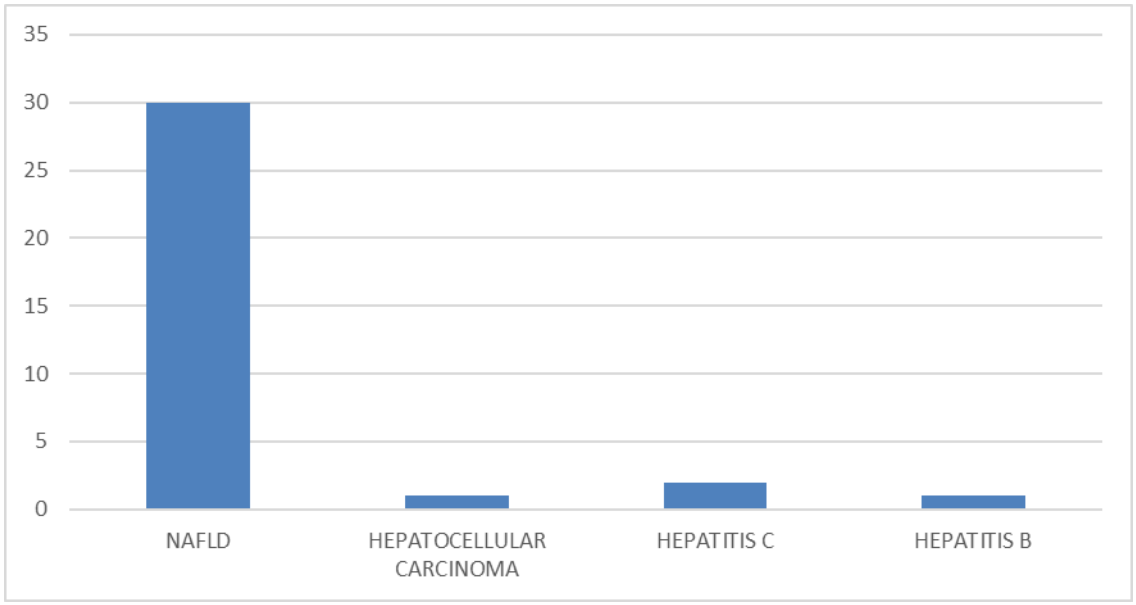

Figure 3. Histogram showing those diabetic patients that are confirmed with liver associated diseases

In our research report 22(43.13%) out of 51 diabetic patients had high glucose level in their urine examination moreover, 30 patients were having NAFLD (58.8%). 2 patients had hepatitis C (3.9%) and 1 patient was having hepatitis B (1.96%).1 patient was

having Hepatocellular carcinoma. (1.96%) In our research report, no patients were found with Cirrhosis and acute liver failure.

Patient with type2 diabetes seem more likely to develop major complication. Likewise, in our study 8 patient presented with obesity (13.3%), 6 patients had kidney failure (10%) and 1 patient was diagnosed with Glomerulonephritis (1.6%) and 1 with pancreatitis (1.6%) as shown in figure 4.

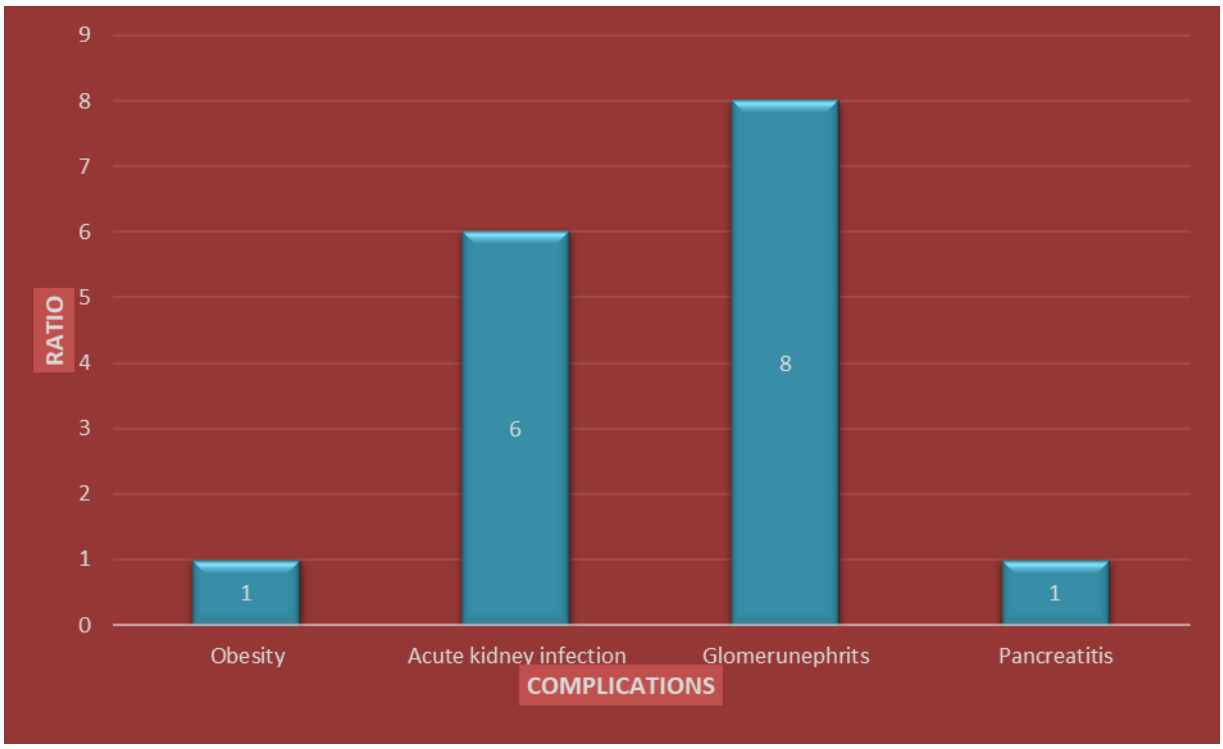

Figure 4. Histogram showing major complications in diabetic patients.

DISCUSSION

According to already performed studies, it has been observed that there is some significance of occurrence of liver diseases and abnormal liver enzymes in diabetic patients. In this section, we will see how our report's result correlate with the available literature review.

A study conducted by Sultan Ayub Meo et al in 2016 in observed the prevalence of T2DM in Pakistan during their research study was 11.77%.As in our research study we observed the percentage of diabetic patients 85%, pre-diabetic 6.7% and normal patient with no diabetic condition were 8.3%. This high percentage is observed because only the diabetic center was targeted for collecting data.

A study conducted by Aziz ul Hassan Aamir et al in 2019 depicted the mean age observed as 51-60 years in Pakistan during their research. Similarly, in our study we concluded that our mean age was 54 years which would fall into the author's observed age group. Thus, our study correlate with the study performed nationwide.

In 2016, a study conducted by Sultan Ayub Meo et al observed that the prevalence of T2DM in Pakistan was greater in males than females as in males it was 11.20% and in females it was 9.19% however in our study the prevalence of diabetes also showed significant evidence with this study as males were 50.98% and females were 49.02%. The results are in accordance with the available literature.

A study conducted by Ramon Arturo Kobashi Margain et al in 2010 observed 47.2% cirrhosis,34.10% hepatitis C and 21.07% HCC in diabetic patient but in our research study we had 58.82% NAFLD,3.92% hepatitis C,1.96% hepatitis B,1.96% HCC and no patient with cirrhosis and Acute liver failure in diabetic patient. Thus, our study does not correlate with the study performed internationally may be due to small size of our report. However, a large-scale study can help us in determining the exact

parameters. A study conducted by author Jamal Zafar et al in 2011 observed that impaired fasting glucose (IFG) and diabetes mellitus in patients had combined prevalence of 20.55% in males and 18.09% in females and this was due to the risk factor such as obesity, family history, hypertension and increasing age. However, in our study the percentage of diabetes was 85% with the risk factor such as kidney diseases 10%, obesity 13.33%, Glomerulonephritis and pancreatitis 1.6% each. Since our study only targeted patients from diabetic centers so we did not have a detailed data in regards of prevalence of these diseases in diabetic patients among the local population.

CONCLUSION

Diabetes can cause many problems in the patient's body such as obesity, retinopathy, CVD, Renal function disease, numbness in legs and abnormal liver diseases due to abnormal liver enzymes and many more conditions. Letting the liver function diseases undiagnosed, leads to devastating health complications. Therefore, this study was conducted to evaluate the evidence of liver diseases in patients with diabetes. From our study, amongst the 51 diabetic patients, 33 had abnormal liver functioning, 30 were diagnosed with NAFLD and 2 with Hepatitis C, 1 each with HCC and Hepatitis B respectively. This study also observed 3 diabetic patients with abnormal liver and renal functioning at the same time and 14 diabetic patients with normal liver functioning and 16 patients with complications like acute/chronic kidney diseases, pancreatitis, obesity, and Glomerulonephritis. Lipid profile, LFT, RFT, Urine R/E for glucose level, HbA1c and serum micro albumin were also studied for these patients. By analyzing these tests values we concluded that the liver enzymes are mainly disturbed in diabetic patients and if left untreated could lead to severe liver damage. Other research studies also showed the significance of liver associated diseases in diabetic patients. In our study NAFLD was one of the common cases among diabetic patients. It should be kept in mind that prolong or chronic NAFLD can lead to HCC and liver cirrhosis over the time. Therefore, monitoring of diabetes and liver enzymes should be done bi-annually in patients to overcome this issue because if left ignored, can be fatal for diabetic patients due to undiagnosed liver diseases.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

S Usman, H Rafiq, S Khan, H Zubaid collected and interpreted the secondary data from hospital. MS Nazar prepared the draft and made changes according to checklist for the cross-sectional study. U Ayub revised the final draft of manuscript. .

AVAILABILITY OF DATA AND MATERIALS

N/A

CONSENT FOR PUBLICATION

N/A

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