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Research Article

INCIDENCE OF HEPATIC DYSFUNCTION IN PATIENTS WITH DIABETES MELLITUS ADMITTED IN DARBHANGA MEDICAL COLLEGE AND HOSPITAL

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ABSTRACT

Objective: The objective of the study was to find out the difference in the severity of the disease, pattern of liver injury, and clinical and biochemical profile in patients with liver dysfunction with and without diabetes mellitus (DM) and metabolic syndrome.

Methods: It was an observational study, the study conducted in the Department of General Medicine, Darbhanga Medical College and Hospital. Fifty consecutive patients with liver dysfunction along with diabetes and 50 consecutive patients with liver dysfunction without diabetes who satisfied the following inclusion criteria and did not have any of the exclusion criteria were selected for the study during the study period from January 2020 to December 2021.

Results: The mean age in patients with and without D.M. was 52.54 years and 52.58 years, respectively, with no significant difference between the two groups (p=0.283). The causes of liver dysfunction were as follows: Alcohol in 40 patients (24 without D.M. and 16 with D.M.), cryptogenic in 41 (14 without D.M. and 27 with D.M.), hepatitis C virus in eight (three without D.M. and five with D.M.), and hepatitis B virus in 12 (nine in without D.M. and two in with D.M.). The D.M. group had a considerably higher frequency of patients with cryptogenic cirrhosis (p=0.007). Diabetic individuals exhibited a significantly higher frequency of anemia, hypoalbuminemia, and hypercreatininemia than non-diabetic patients, according to laboratory testing. The majority of the patients of both groups showed mild ascites (88% without D.M. vs. 82% with D.M.). It shows diabetic patients had significantly higher MELD and higher Child-Pugh scores (p=0.001 and 0.004, respectively).

Conclusion: D.M. is found all over the world, and there is a growing body of evidence associating it with cirrhosis. As a result, both are likely to rise in value. Coexisting diabetes appears to be linked to more severe liver injury and consequences preceding cirrhosis, as well as greater mortality once cirrhosis has developed.

Keywords: Diabetes mellitus, Non-alcoholic fatty liver disease, Cirrhosis, Ascites.

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INTRODUCTION

Diabetes mellitus (DM) is a major global public health issue that is increasing in incidence and prevalence, especially in the developing countries [1]. Concerns about this chronic disease center on major DM-related consequences that might damage several essential organ systems, resulting in more severe and irreversible pathological disorders, including nephropathy, retinopathy, vasculopathy, neuropathy, cardiovascular disease, and hepatopathy [2].

D.M. has been linked to a variety of liver disorders, including abnormal glycogen deposition, non-alcoholic fatty liver disease (NAFLD), fibrosis, cirrhosis, hepatocellular carcinomas (H.C.C.s), abnormal increased hepatic enzymes, acute liver illness, and viral hepatitis, according to several studies [3,4]. Furthermore, an excess of fat in the liver can exacerbate insulin resistance and lead to serious metabolic dysfunction.

Hepatocytes can be destroyed by a fatty liver and high blood sugar, leading to increased morbidity and death in diabetic patients. [3] However, to increase awareness of the full process involved, this issue requires further research and explanation from multiple angles. As a result, the many D.M. mechanisms that cause liver injury through the production of a fatty liver are investigated.

In diabetic patients, several important mechanisms have been identified as causing liver damage. Insulin resistance, which is the most common cause of hyperglycemia and compensatory hyperinsulinemia, is the most common reason [5-7]**.** The liver, as a collection of insulin-sensitive tissues, is one of the first organs to be affected by hyperglycemia-induced oxidative stress, which can result in liver tissue injury [7-9]. This is followed by a disruption in protein, carbohydrate, and lipid metabolism, which results in increased oxidative stress and, as a result, the inflammatory cascade is triggered [6,8,9]. Both oxidative stress and inflammatory reactions play a role in exacerbating D.M.'s clinical condition [10].

D.M. can induce an overabundance of fat cells in the liver, leading in a fatty liver and, as a result, NAFLD. As a result, 2–3% of NAFLD patients develop hepatic inflammation, necrosis, and fibrosis, all of which are signs of nonalcoholic steatohepatitis (NASH) [2,10]. Cirrhosis develops in injured or fibrotic livers, which leads to the formation of H.C.Cs and, finally, liver failure [10-12].

METHODS

Type of study
This was an observational study.

Place of study
The study was conducted at the Department of Medicine, Darbhanga Medical College, Hospital, Bihar.

Period of study
The study duration was 1 year.

Selection of study subjects
Fifty consecutive patients with liver dysfunction along with diabetes and 50 consecutive patients with liver dysfunction without diabetes who satisfied the following inclusion criteria and did not have any of the exclusion criteria were selected for the study.

Sample size
One hundred patients with liver dysfunction; 50 patients with diabetes and 50 without diabetes.

Inclusion criteria
- Consecutive patients with clinical and biochemical features consistent with liver dysfunction as below:
  - Acute-onset illness with discrete symptoms (anorexia, nausea, fever, malaise, vomiting, etc.)
  - Jaundice (bilirubin >2 mg/dl) or elevated liver enzymes (aminotransferases >2 × upper limit of normal).
- Age above 18 years
- Patients with chronic liver disease (C.L.D) of HBV and HCV etiology
- Treatment naïve
- History of significant alcohol intake is defined as alcohol use of more than 40 g per week.

Exclusion criteria
The following criteria were excluded from the study:
- H.I.V. seropositivity
- Any malignant disease, including hematological malignancies
- Patients on immunosuppression
- Comorbidities – hypothyroidism, autoimmune diseases, etc.

Methodology
The present study was conducted after obtaining clearance and approval from the Institutional Ethics Committee Darbhanga Medical College and Hospital, Bihar; written informed consent was taken from the patients. This study was conducted in the department of medicine, and it was an observational study. The study was conducted for a period of 2 years. Demographic data were collected under the following headings: Age, sex, anthropometric and vital parameters, and duration of hepatic dysfunction and diabetes. Fifty consecutive patients with liver dysfunction along with diabetes and 50 consecutive patients with liver dysfunction without diabetes who satisfied the following inclusion criteria and did not have any of the exclusion criteria were selected for the study. The American Diabetes Association's criteria were used to define diabetes diagnosis.

Statistical analysis
Data were double-checked for accuracy and completeness before being coded and entered into version 19.0 of the Statistical Package for the Social Sciences for analysis. Frequency tables, cross-tabulations, and figures are used to present the findings. Categorical data were shown as a frequency chart with percentages. The mean and SD of continuous data with a normal distribution are shown. Student's t, Chi-square, and Mann–Whitney tests were used to compare groups. A statistically significant difference was defined as one with a $p<0.05$.

RESULTS

A total one hundred patients with hepatic dysfunction were included in the study, 50 out of them were presented with DM and the remaining 50 were presented without D.M. The mean age in patients with and without D.M. was 52.54 years and 52.58 years, respectively, with no significant difference between the two groups (p=0.283).

The sex distribution of study subjects in both with and without D.M. patients is presented in Table 2. Among patients without D.M., majority (58%) were male, and in patients with D.M., majority were female (56%). Above analysis, both the groups were comparable in terms of gender distribution (p=0.161).

The causes of liver dysfunction were as follows: Alcohol in 40 patients (24 without D.M. and 16 with D.M.), cryptogenic in 41 (14 without D.M. and 27 with D.M.), hepatitis C virus in eight (three without D.M. and five with D.M.), and hepatitis B virus in 12 (nine in without D.M. and two in with D.M.). In the D.M., the percentage of patients with cryptogenic cirrhosis was much higher group (p=0.007). Data regarding the etiology are presented in Table 3.

The duration of hepatic dysfunction among patients with and without D.M. is manifested in Table 4. The mean duration was 4.84 years and 6.96 years without and with the D.M. group. Above analysis, both the groups were comparable in terms of duration of liver dysfunction (p=0.133).

Table 5 shows the comparison of mean levels of different biochemical variables between the two groups. Diabetic individuals exhibited a significantly higher frequency of anemia, hypoalbuminemia, and hypercreatininemia than non-diabetic patients, according to laboratory testing.

Incidence of ascites in patients with and without D.M. is mentioned in Table 6. The majority of the patients of both groups showed mild ascites (88% without D.M. vs. 82% with D.M.). Above analysis, we found that the incidence of ascites was comparable in both groups (p=0.400).

Incidence and grade of encephalopathy were higher in patients with D.M. compared to those without D.M.; however, the difference was not significant (p=0.375). Data are shown in Table 7.

A comparison of the mean Child-Pugh score and MELD score between the two groups is presented in Table 8. It shows that diabetic patients had significantly higher MELD and higher Child-Pugh scores (p=0.001 and 0.004, respectively).

Patients with D.M. had cumulative survival significantly lower than patients without D.M. (p=0.013). At the end of the follow-up, two patients without D.M. and 10 patients with D.M. died. Data are presented in Table 9.

DISCUSSION

DM, a metabolic condition defined by blood sugar and insulin dysregulation [13], has an estimated global prevalence of about 9%, and by 2030, 300–400 million individuals will likely be affected globally [14] causing considerable economic and social burdens [14]. C.L.D has been neglected as yet another diabetes sequel, in contrast to other chronic consequences of D.M., due to the greater profiles of alternate pathogenic causes. However, D.M. is now recognized as a well-established cause in many patients with cirrhosis, a serious public health crisis of worldwide proportions endangering the general

Table 1: Age Distribution among two groups

Age group	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
18–30 years	2	4.0	1	2.0	0.283
31–40 years	5	10.0	2	4.0	
41–50 years	12	24.0	15	30.0	
51–60 years	21	42.0	23	46.0	
>60 years	10	20.0	9	18.0	
Total	50	100.0	50	100.0	
Mean age	52.58±10.35		52.54±9.14		

DM: Diabetes mellitus

Table 2: Sex distribution

Sex	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
Male	29	58.0	22	44.0	Chi-square-1.960
Female	21	42.0	28	56.0	p-value-0.161
Total	50	100.0	50	100.0	

DM: Diabetes mellitus

Table 3: Etiology

Etiology	Without D.M. (n=50)		WithD.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
Alcohol	24	48.0	16	32.0	0.076
Cryptogenic	14	28.0	27	54.0	0.007
HCV	3	6.0	5	10.0	0.356
HBV	9	18.0	2	4.0	0.027

Table 4: Duration of hepatic dysfunction

Duration	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
<5 years	28	56.0	18	36.0	Chi-square – 4.027
5–10 years	15	30.0	22	44.0	p-value – 0.133
>10 years	7	14.0	10	20.0	
Total	50	100.0	50	100.0	
Mean duration	4.84±3.75		6.96±3.81		

Table 5: Comparison of different biochemical variables

Biochemical variables	Without D.M. (n=50)	With D.M. (n=50)	p-value
	Mean±SD	Mean±SD	
FBG (mg/dl)	89.9±8.79	141.84±15.45	0.01
Hemoglobin (g/dl)	12.28±1.33	9.11±0.85	0.013
IN	1.48±0.13	1.47±0.14	0.447
Serum creatinine (mg/dl)	1.43±0.43	1.94±0.99	<0.0001
Serum albumin (g/dl)	2.78±0.49	2.17±0.39	<0.0001
ALT (IU/L)	96.9±30.26	100.26±30.38	0.414
AST (IU/L)	64.4±19.67	80.72±18.08	0.303
Serum total bilirubin (mg/dl)	3.82±1.83	4.206±1.69	0.852
Serum sodium (mEq/L)	137.78±4.45	136.00±6.006	0.026

Table 6: Incidence of ascites

Ascites	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
Mild	44	88.0	41	82.0	Chi-square – 0.705
Severe	6	12.0	9	18.0	p-value – 0.400
Total	50	100.0	50	100.0	

population and imposing substantial financial burdens [13], the etiology of which was long termed "cryptogenic" [15]. Cirrhosis-related mortality is indeed on the rise. Cirrhosis certainly contributes to dysglycemia through a variety of pathways, whereas D.M. predisposes individuals to significant liver disease [16].

DM can change the morphology and physiology of the liver, and it can be triggered by hepatic disorders [17]. Hepatomegaly is the most prevalent clinical manifestation, and most patients have normal or modestly abnormal transaminases and bilirubin. Since hepatic involvement in type 2 diabetes patients can range from clinically asymptomatic steatosis to NAFLD, NASH, cirrhosis, or even hepatocellular cancer, it is important to know what to look for. Cirrhosis was the fourth greatest cause of death, accounting for 4.4% of all fatalities caused by diabetes [18]. It is crucial to have the necessary biochemical markers and tests to detect and diagnose liver impairment early in this condition [18].

A liver biopsy is the gold standard diagnostic test, however due to its invasive nature, it is not suitable as a screening test. Only when there is a doubt regarding the diagnosis is it used [19]. It is also within most patients' financial means. The study employed biochemical markers such AST/ALT, alkaline phosphatase, and total bilirubin to see if they could detect hepatic involvement in D.M.

Table 7: Incidence of encephalopathy

Encephalopathy	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
Nil	45	90.0	40	80.0	Chi-square – 1.960
Grades I–II	4	8.0	8	16.0	p-value – 0.375
Grades III–IV	1	2.0	2	4.0	
Total	50	100.0	50	100.0	

Table 8: Comparison of mean Child-Pugh score and MELD score

Variables	Without D.M. (n=50)	With D.M. (n=50)	p-value
	Mean±SD	Mean±SD	
Child-Pugh score	9.14±1.52	10.12±1.53	0.004
MELD score	19.78±3.61	22.52±5.99	0.001

Table 9: Mortality

Mortality	Without D.M. (n=50)		With D.M. (n=50)		p-value
	Frequency	Percentage	Frequency	Percentage	
Survived	48	96.0	40	90.0	Chi-square – 6.060
Dead	2	4.0	10	10.0	p-value – 0.013

As a result, the purpose of this study was to find out how much hepatic involvement people with type 2 diabetes have, as well as the link between hepatic dysfunction and diabetes duration and metabolic syndrome.

The study was conducted at Darbhanga Medical College and Hospital's Department of Medicine. The present study included 100 patients with liver dysfunction, 50 with DM and 50 without DM who presented to the department of medicine. Despite the fact that metabolic syndrome is known to produce fatty liver, NASH, cirrhosis, and H.C.C.s [20], it has been hypothesized that D.M. is a risk factor for C.L.D on its own. According to a study conducted in an open population of 438,000 patients with type 2 diabetes and 2,059,000 controls, diabetic subjects had a 2-fold higher risk of developing serious liver disease than non-diabetic subjects after adjusting for obesity, dyslipidemia, and arterial hypertension [16]. Patients with C.L.D caused by HCV, alcohol, or hemochromatosis, on the other hand, had a higher rate of insulin resistance, glucose intolerance, and D.M. This was more common in patients with hepatitis B virus-related C.L.D, autoimmune, or cholestasis than in patients with hepatitis C virus-related C.L.D, autoimmunity, or cholestasis [21].

The results of this study back up the findings of two prospective comparative studies that found D.M. increased the mortality of people with liver cirrhosis [22].

One of these researchers found that diabetes patients had a 51% 5-year mortality rate compared to 0% for non-diabetic patients [22]. In another study, diabetic patients had a 3-and 5-year death rate of 23.8% and 43.4%, respectively, compared to 5.3% and 5.3% in non-diabetic patients [23]. The reasons for death in these investigations, like in ours, were liver problems. This could be because D.M. hastens the evolution of fibrosis and the emergence of hepatocellular cancer [24].

In certain investigations, the D.M. has been established as an independent predictor of death [22]. A new study of 75 patients with liver cirrhosis and refractory ascites found a 52% 1-year survival rate. Advanced age, liver cancer, and D.M. were all independent predictors of mortality on admission, but not the Child-Pugh score [25]. D.M., cryptogenic etiology of cirrhosis, blood creatinine >1.5 mg/dL, Child-Pugh score Class C, and MELD were all found to be substantially linked to death in our study.

Patients with DM appear to have a higher chance of developing a number of liver diseases, and patients with both liver disease and diabetes have a higher risk of developing severe liver disease, cirrhosis, liver failure, and H.C.C.s. The implications for clinical management are clear. The recognition of diabetes as a significant risk factor for liver injury may aid in the diagnosis and treatment of C.L.D.

CONCLUSION

- D.M. is found all over the world, and there is a wealth of research tying it to cirrhosis. As a result, both are likely to rise in value. Coexisting diabetes appears to be linked to more severe liver injury before cirrhosis develops, as well as more severe consequences and death once cirrhosis have developed.
- There is evidence that the metabolic abnormalities associated with diabetes lead to liver injury, however, the connection of cirrhosis with hepatogenous diabetes complicates this relationship.
- When compared to non-diabetic patients, patients with D.M. had significantly higher cryptogenic etiology, anemia, renal impairment, hypoalbuminemia, C.P. score, MELD score, and B.M.I.
- More research of this type should be undertaken in undeveloped countries to gain a better understanding of the liver's role in D.M. and to find the best management strategy for these patients.

CONFLICTS OF INTEREST/AUTHORS' CONTRIBUTION

SS and PKS were involved in the supervision of the analysis and made significant contributions to the writing and editing of the manuscript.

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