Diabetes Mellitus, Liver Dysfunction in Diabetes Mellitus, Non-Alcoholic Fatty Liver Disease

Karthikeya T M[1], Dr. N N Anand[2], Dr. Divya Sriramulu[3]

[1] *Assistant Professor, General Medicine, Sree Balaji Medical College and Hospital, Chennai, India.*
Email: tmkarthikeya@gmail.com, ORCID: 0009-0006-2827-8129

[2] *Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, India.*
Email: drnaganand1971@gmail.com, ORCID: 0000-0001-7816-5110

[3] *Senior Resident, General Medicine, Sree Balaji Medical College & Hospital, Chennai, India.*
Email: divyasriram21@gmail.com, ORCID: 0009-0000-8874-4052

KEYWORDS	ABSTRACT
Metabolic Dysfunction, Diabetes Mellitus (DM), Hyperglycemia, Fibrosis, Hepatocellular Carcinoma, Endocrine	*Purpose:* The main purpose of the study is to derive the prevalence of hepatic derangement based on higher chances of fatty liver within the patients suffering from type 2 diabetes mellitus. *Methods:* A primary quantitative study is conducted based on 100 patients attending Sree Balaji Medical College and Hospital from February 2023 to December 2023 and suffering from type 2 diabetes mellitus. The main sample elements are considered to remain from the age range of 30 to 60 years and belong to both genders. *Results:* Most people found with a comorbidity disease of fatty liver as a side effect of diabetes mellitus type 2 are suffering from diabetes for almost 6.58 years, and they show a higher range of triglyceride and cholesterol values. *Conclusion:* A balanced diet with different nutrients present within their food items like Carbohydrates, and proteins can be helpful for them to maintain their health along with higher density of exercise.

1. Introduction

Diabetes Mellitus (DM) is one of the Global problems with an "escalating incidence" in mostly developed and industrial countries. The elementary concern regarding this disease is the DM-associated complications within the human body that can affect multiple organs and seize the internal system of the body. DM causes liver functionalities including "abnormal glycogen deposition", "non-alcoholic fatty liver", "fibrosis", and "hepatocellular carcinoma." Besides this excessive deposition of fat within the liver affects the capacity of insulin and leads the body toward different types of "metabolic disfunction." The issue of fatty liver and "hyperglycemia" destroy the "hepatocytes" within the body and influence the "morbidity and mortality" among most diabetes patients. Various mechanisms of DM are responsible for inducing damage to the liver through the formation of fatty liver. Different types of factors cause liver damage among Diabetes patients and, "insulin resistance" is the primary factor of "hyperglycemia" and "compensatory hyperinsulinemia."

The terms "Diabetes" and "mellitus" are derived from the Greek word "Diabetes" meaning "a passer through a Siphon" and "mellitus" means sweet. This name is suggested by the Greek people as they think that due to Diabetes, more amount of Urine is produced, attracting bees and flies[1]. The traditional process of investigating diabetes within the body was to check the attraction of bees to the urine of a person. Within the medieval culture, doctors used to check urine themselves as described within the "Gothic belief" system. The role of the Pancreas in diabetes was discovered by Mering and Minkowski in the year 1889[2]. They examined the process within the pancreas of dogs and viewed that after removing the pancreas from dogs, they experienced all the symptoms of diabetes and died within a short span. Later in 1910. Sir Albert exposed that diabetes lacked a chemical compound that was named "insulin." After some years, the "endocrine" role of "pancreas" within the metabolism system was discovered.

Sir Harold Percival in 1935 discovered type 1 and type 11 diabetes with the examination of the first clinical patient in 1922. The proneness of diabetes has been increasing among people within the last

two decades and around 30 million people were affected in 1985 and 382 million people in 2013[3]. Studies show that based on the results of "International Diabetes Federation projects", around 592 million people will be affected with diabetes in 2035. The historic discovery of "Insulin" by "Branting and Best" in 1921, solved the issues related to the treatment of diabetes and the "metabolic defects" within the body. Despite this explanation of the treatment, various effective diseases such as "Cellulitis Carbuncle", "pneumonia" and "tuberculosis" lead to a high mortality rate of people[4]. Modern "antibiotics" reduce the problems and the effects of diabetes within the body. Diabetes affects the "microvascular" organs and creates various complications within the human body.

The higher rate of "glucose circulating" within the blood flow causes diabetes and the level of blood glucose in blood differs for various reasons. Type 1 diabetes occurs due to issues in the "immune system" which results in the ineffective system of the human body for fighting "infection", and attacks and demolishes the "beta cells" of the pancreas that produce insulin in the human body[5]. Most researchers think that diabetes 1 is caused due to "genetic factors" and "environment-related factors" including viruses that instigate the disease. Type 11 diabetes happens due to lifestyle and gene-related problems. Being overweight causes "insulin resistance" and the extra fat within the body influences the resistance within the heart and blood vessels[6]. The body needs more quantity of insulin to keep the entrance of glucose within the body and at the initial level, the pancreas makes the supply of extra insulin but over time, this organ fails to submit those and the glucose level rises.
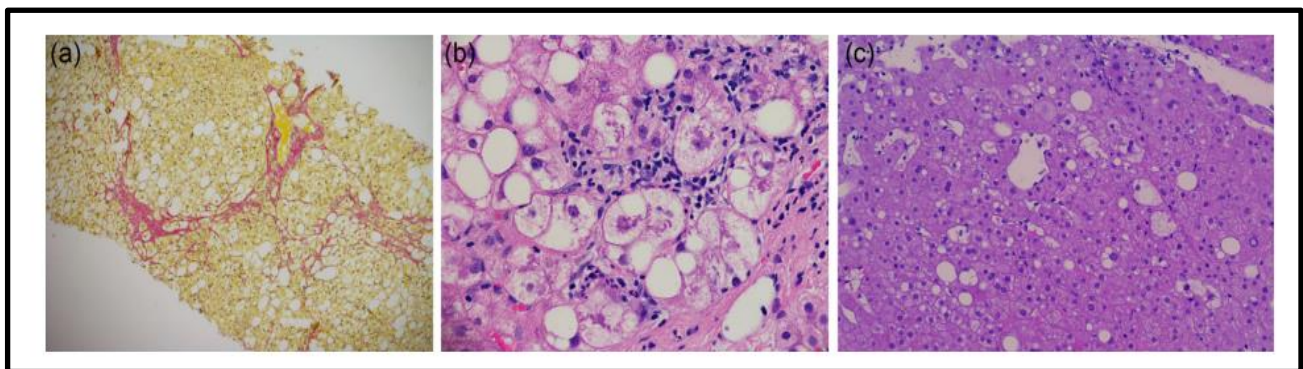

Figure 1: Different structures of non-alcoholic Fatty lever[7]

Apart from that, diabetes is caused by "Genetic mutations" and these issues are usually carried through the family members. In most cases, these gene mutations influence diabetes by making the pancreas less able to produce insulin. "Cystic fibrosis" is another important cause that causes Mucus to produce scars in the pancreas to provide the proper amount of insulin[7]. Various hormonal diseases create diabetes within the human body. Non-alcoholic fatty liver (NAFLD) presents an "accumulation" of "triglycerides" with "hepatocytes" with the formation of "intracellular lipid droplets." The dysfunction of metabolism is directly associated with fatty liver disease, causing the "systematic defusion of metabolism"[8]. "Liver Fibrosis" is another important effect of type 11 DM and the advanced levels of "Cirrhosis" and "fibrosis" increase the level of HCC. The medical intervention of those patients with "NAFLD-HCC" causes metabolic dysfunction among patients.

This study deals with the following objectives.

- To generate the prevalent hepatic derangements suffered by persons bearing Type 2 Diabetes Mellitus
- To develop Correlations between the outcomes of liver function tests with the Ultrasonographic proofs of fatty liver occurrence within the patients of Type 2 Diabetes Mellitus

2. Materials and Methods

The study has focused on conducting a ***primary quantitative*** analysis of the collected sets of information based on the answers given by the research respondents. The researcher obtained the respondents by randomly sampling the patients showing different symptoms that can be considered as the symptoms of Diabetes Mellitus Type 2. The population of the patients consisted of a variegated one bearing different types of patients based on their demographic criteria like age, gender, and other factors. Despite randomly selecting the research participants as the elements of the sample, the researcher has focused on following two specific inclusion criteria regarding the choice-making of sample elements[9]. The two criteria followed by the researcher include the patients diagnosed to be suffering from Type 2 Diabetes Mellitus and belonging to the age group of 30 to 60. However, the gender of the patients was not considered an important criterion while choosing the sample elements, and the researcher chose patients belonging to both genders in the study.

The researcher used 100 participants both male and female patients from February 2023 to December 2023 of Sree Balaji Medical College and Hospital. Various exclusion criteria were there for choosing the patients such as the consumption of alcohol and experience of hepatitis of patients. Additionally, the amount of taking "hepatoxic drugs" such as "Methotrexate", "Amiodarone", and "Glucocorticoids" of patients affects the diabetes among patients. Among the participants, the surgery of their abdominal parts was checked as this was another important part of making them samples for the study. Real chronic disease and the failure of kidneys in heart disease patients are elementary issues in the human body that instigate diabetes issues among patients. Informed consent from all the participants was taken for engaging them in the survey related to DM, dysfunction of the liver, and non-alcoholic fatty liver[10]. All the 100 patients that were selected for the survey, were under surveillance for at least 24 hours to investigate the symptoms and changes within the hospital.

This study is a "cross-sectional" study and the "random selection" were used for choosing the participants of the study using the "random number charts." The detailed disease history was checked of the patients as per the regulation of the "annexure" along with the collection of blood samples of them for the detailed study. Comparing the information associated with patients and the analysis of that information were taken for the detailed study design as per the "Chi-square" test and the "t-test" of students. Based on the embedded proforma of those patients, the basic information related to the name, age, sex of the patients, occupation and marital status were taken for the primary investigation and the basic information[11]. Various columns were present within that proforma such as the "polyuria", "polydipsia", "polyphagia" and the loss percentage of body weight, vision-related issues, and the "peripheral neuropathy." The history of hypertension, "tuberculosis", and "Jaundice" were there to check the effect of that disease on patients.

The personal history of patients associated with appetite timing, dietary plans, sleeping criteria and "bowl and bladder" affect the diabetes of patients. Besides this, smoking habits and the intake of alcohol within the body affect diabetes. Some lab tests were there for the patients to check the diabetes rate such as the "blood pressure rate", "respiratory rate", "height-weight measurement" and the temperature of patients were the important criteria for the selected patients for the survey[12]. The USG of the abdominal part of the patients were taken to investigate properly about type 11 DM within patients. The blood levels of patients were checked and the anti-HCV was investigated for measuring the diabetes level among the patients.

3. Results and analysis

As previously mentioned in this study, 100 patients were selected for this study mainly to understand the correlation between diabetes mellitus and non-alcoholic fatty liver disease, two of the most crucial variables of this study. Considering the purpose of this study a clinical survey has been constructed in which descriptive statistics of the collected data have been analysed by understandable data

represented in the ongoing research. Through understanding the distribution of the patient's data, the interrelation between the selected variables can be understood.

Distribution of Age

Table 1: Mean distribution of age among the selected subjects

Group	N	Mean	Std. Deviation	t
Patients diagnosed with fatty liver	60	52.83	6.648	1.583
Patients diagnosed without fatty liver	40	54.33	6.435	p = 0.115 ns

The difference between mean and SD values can be considered one of the most crucial factors associated with the summarisation of the collected information along with representing ideas regarding the distribution of the collected data in the dataset. Considering the findings from this section the mean value of the age of patients diagnosed with fatty liver has been reported as 52.83 against a SD value of 6.648. These particular findings indicate an uneven distribution of the ages of the patients with fatty liver in the dataset. On the other hand, the mean value of ages of the patients without fatty liver has been accounted as 54.33 with an SD value of 6.435. This is also identified as an indicator of uneven distribution of data in the dataset.
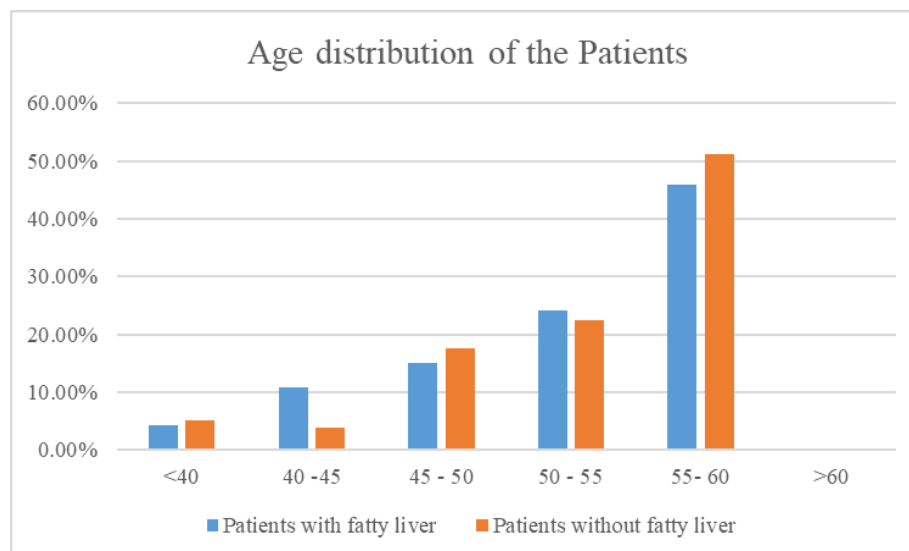

Figure 2: Graphical representation of age distribution among the patients

The above figure represents the distribution of the ages among the samples used in this study. Considering the findings from this section, it can be considered that most of the samples belong to the 55-60 years age group which represents 45.8% of overall participants as patients with fatty liver. On the other hand, 51.2% of participants in the 55-60 years group have been identified without fatty liver. This particular aspect can also be considered to provide evidence regarding age as an effective contributing factor associated with exposure to fatty liver.

Distribution of Diabetes mellitus among a selected group

Table 2: Mean value of diabetes mellitus among a selected group

Group	N	Mean	Std. Deviation	t
Patients diagnosed with fatty liver	60	6.58	3.693	2.461
Patients diagnosed without fatty liver	40	8.36	6.551	p = 0.015 sig

The result from the descriptive statistics from this section indicates a mean value of 6.58 with an SD value of 3.693 in the group of patients with fatty liver. Considering this finding, it can be considered that the distribution of diabetes mellitus in this group is clustered in this situation. On the other hand, in the group of patients without fatty liver, the mean value has been reported as 8.36 with an SD value of 6.551 which is considerably higher than the group of patients with fatty liver. Therefore, it can also

be considered that there is a significant correlation between fatty liver and diabetes mellitus.

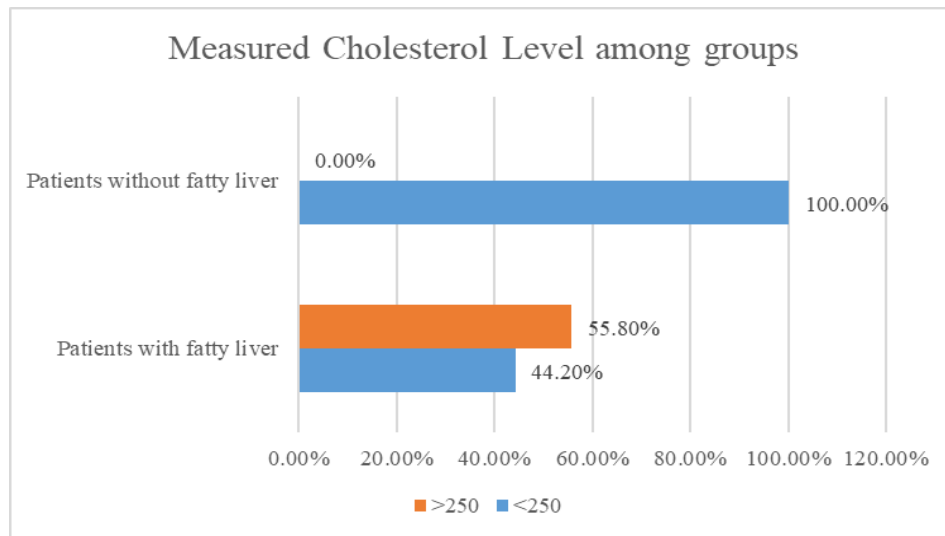*Distribution of cholesterol levels in the selected groups*

Figure 3: Measured cholesterol level among the subjects by groups

Cholesterol level has been undertaken as an indicator of liver dysfunction and in terms of understanding the coherence between the fatty liver and liver dysfunction. Originating from the findings of this section, it has been reported that 55.8% of patients with fatty liver have cholesterol levels higher than 250 mg/dl whereas, 0% of patients associated with the fatty liver group identified with cholesterol levels higher than 250 mg/dl. This can be considered as critical evidence regarding the role of fatty liver in liver dysfunctioning of the patients.

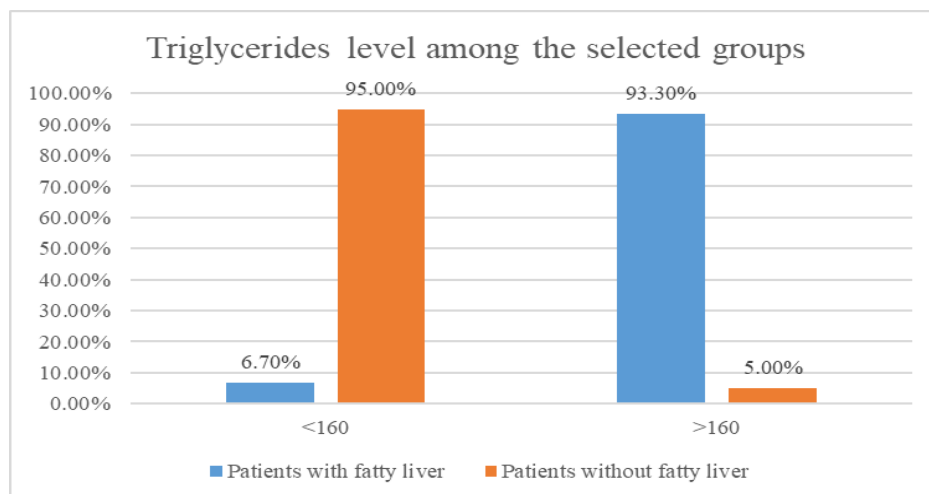*Triglyceride distribution level among the groups*

Figure 4: Level of Triglycerides among the patients by group

The level of triglycerides can also be considered as an indicator of liver dysfunction which has been used in this study to accumulate the prevalence of the indicator in identifying fatty liver. The findings from this section indicate that 93.30% of patients with fatty liver have a higher level of triglycerides than the normal which is 160 mg/dl. On the other hand, only 5% of patients without fatty liver have been reported to have triglyceride levels higher than 160 mg/dl. This indicates that by identifying the level of triglycerides among the patients the severity of fatty liver can be predicted.

Mean distribution of Sugar level in each group

Table 3: Distribution of sugar levels among each group

	Group	N	Mean	Std. Deviation	t
FBS	Patients diagnosed with fatty liver	60	193.30	98.899	0.310
	Patients diagnosed without fatty liver	40	198.89	124.067	p = 0.757 ns
PPBS	Patients diagnosed with fatty liver	60	262.82	102.597	0.010
	Patients diagnosed without fatty liver	40	262.64	99.423	p = 0.992 ns
HbA1C	Patients diagnosed with fatty liver	60	9.69	1.948	0.289
	Patients diagnosed without fatty liver	40	9.55	2.248 p = 0.773 ns	p=0.773 ns

Given that every participant had Type 2 diabetes, the individuals' blood sugar levels were nearly the same in the groups with and without fatty livers. FBS was 193.3 mg/dl in the group with fatty liver and 198.89 mg/dl in the group without fatty liver. Similarly, PPBS readings were almost 262 mg/dl in both groups. Even yet, the groups with fatty liver and those without had HbA1C levels of 9.69 and 9.55, respectively. It was determined that there was no discernible difference between these mean values. The findings of this section critically reflect the higher distribution of the sugar level indicator among the group of patients with fatty liver. Therefore, from the findings of this section, it can be considered that there is a significant correlation between diabetes mellitus with liver dysfunctioning and fatty liver syndrome among the patients.

4. Discussion

Critical analysis of the generated sets of information based on the 24 hours-based evaluation of the conditional movement of the patients, the aforementioned results are found. Among the total number of 100 patients, the mean value regarding age is found as 52.83 which includes the standard deviation value of 6.648. Now the number of people bearing no issues regarding fatty liver is found to be 54.33 which defines the difference between the two values to be minimal. Hence, the criticism cannot be done based on the prevalence of fatty liver among the patients belonging to the age group between 50 and 60. However, depending on the evaluation of each patient individually, the highest number of patients suffering from the issue of fatty liver belongs to the age group of 55 and 60, and the number of the total patients suffering from fatty liver is found to be 55 that is almost 45.18% of the total number of patients. However, clarity is absent regarding the reason behind these people suffering from fatty liver whether their issue is diabetes type 2 or anything else.

The most drastic demographic factor that has been seen as an important signifier of the issue regarding fatty liver among patients is their gender. The results showed that the patients belonging to the male gender category and suffering from fatty liver are found to be 80, which is almost 66.70% of the total number of patients. There remain various factors that can be considered as the main criteria behind the prevalence of fatty liver among male patients than the female ones including Hormonal differences, lifestyle procurement, composition of body, hereditary factors and various comorbidities[13]. Among these factors, the most important two variables are hormonal differences and comorbidities. The most significant somatotrophic hormone present in female patients is Oestrogen which provides protective effects against the accumulation of fat in the liver, the most vulnerable organ present within the gastrovascular cavity. Moreover, men are found to be more vulnerable to diseases like diabetes mellitus type 2 and hypertension, and their vulnerabilities make them unstable against reciprocating fatty liver disease.

The main reason behind the female patients bearing the age group more than 50 found to be suffering from fatty liver is menopause. Menopause leads to the cessation of oestrogen secretion in the female body which makes them vulnerable to the disease of fatty liver[14]. From the data that are found by analysing the health conditions of these patients, it is found that the patients bearing diseases like fatty liver and suffering from diabetes mellitus type 2 are almost 6.58 years old. Astonishingly, the patients

bearing diabetes mellitus type 2 but not suffering from fatty liver are found to be under medication for diabetes mellitus for almost 8.36 years. The main reason that is derived by the researcher to be the main reason behind people suffering from diabetes mellitus type 2 for more time but not suffering from fatty liver is that their diseases were diagnosed at an early stage, and the ones bearing fatty liver as a side effect of the diabetes mellitus 2 mainly have their hereditary tendency of higher chances of occurrence of fatty liver within the body.

There remain different reasons including the most vital one as the natural insulin resistance present within them that leads to increment of accumulation of fat in the liver. The main reason behind the phenomenon is that the regulation of fat storage inside the gastrovascular cavity is conducted by insulin. The low effectiveness of insulin generally leads to the excessive storage of fat within the body of the patient which mostly creates an overweight tendency within them[15]. The obesity present in Type 2 Diabetes Mellitus patients leads them to suffer from issues with the visceral fat storage within their bodies that contributes to the deposition of fat storage in the liver. Among these patients suffering from fatty liver disease as a side effect of diabetes type 2 mellitus are found to be suffering from higher comorbidity like the presence of triglycerides within their blood[16]. Among the patients present within the sample bearing fatty liver as a side effect of diabetes mellitus type 2 is found to bear the average value of their blood triglyceride as 229.4 mg/dl which is higher than the normal range of triglyceride that varies from 120 to 150 mg/dl in an average.

On the other hand, the mean value of the LDL cholesterol, the harmful cholesterol to be found among these patients suffering from diseases like fatty liver as a comorbidity created due to Diabetes type 2 Mellitus is found to be 161.47 mg/dl which is highly significant. On the other hand, HDL cholesterol, commonly known as the "good cholesterol" is found among patients with fatty liver in comparatively fewer amounts, bearing a ratio of 36.06 mg/dl, which denotes a higher statistical significance with a p-value less than 0.0001. The main reason behind the occurrence of such problems is obesity due to the inherited insulin-based fat storage regulation-related discrepancies.

5. Conclusion

The main reason behind the fatty liver occurrence in patients suffering from diseases like diabetes mellitus type 2 is that type 2 diabetes creates an issue like insulin resistance, along with the impairment of the ability of the liver regarding regulations of fat metabolism. Insulin resistance provides more conversion of the excess carbohydrates into the higher lipid storage in the gastrovascular cavities. Fatty liver diseases create an overweight issue within the patients that generates coexistence of the diseases with various metabolic syndromes that include conditions like hypertension and dyslipidemia. The chronic inflammation of the disease worsens the condition of fatty liver patients which leads them in higher consume excessive foods and procure unhealthy diets. The severity of liver diseases increases over time which ultimately leads to diseases like cirrhosis of the liver along with steatohepatitis that develop complications regarding the management of diabetes and overall health management of the patients. Various treatment processes are present regarding the dietary modifications and management of weight that include balanced diet conduction, along with dietary elements consisting of foods bearing low carbohydrate value, and management of weight. The weight loss of the body of an individual significantly improves the health of the liver and the management of diabetes, and regular exercise for at least 2 and a half hours is needed for the betterment of health for these patients.

Reference

[1] Mantovani A, Petracca G, Beatrice G, Tilg H, Byrne CD, Targher G. Non-alcoholic fatty liver disease and risk of incident diabetes mellitus: an updated meta-analysis of 501 022 adult individuals. Gut. 2021;70(5):962-9.

[2] Muthiah M, Ng CH, Chan KE, Fu CE, Lim WH, Tan DJ, Nah B, Kong G, Xiao J, Yong JN, Tan B. Type 2 diabetes mellitus

in metabolic-associated fatty liver disease vs. type 2 diabetes mellitus non-alcoholic fatty liver disease: a longitudinal cohort analysis. Annals of Hepatology. 2023;28(1):100762.

[3] Lee CH, Lui DT, Lam KS. Non-alcoholic fatty liver disease and type 2 diabetes: An update. Journal of Diabetes Investigation. 2022;(6):930-40.

[4] Lee BW, Lee YH, Park CY, Rhee EJ, Lee WY, Kim NH, Choi KM, Park KG, Choi YK, Cha BS, Lee DH. Non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus: a position statement of the Fatty Liver Research Group of the Korean Diabetes Association. Diabetes & metabolism journal. 2020;44(3):382-401.

[5] Binet Q, Loumaye A, Preumont V, Thissen JP, Hermans MP, Lanthier N. Non-invasive screening, staging and management of metabolic dysfunction-associated fatty liver disease (MAFLD) in type 2 diabetes mellitus patients: what do we know so far. Acta Gastroenterol Belg. 2022;85(2).

[6] López-Pastor AR, Infante-Menéndez J, Escribano Ó, Gómez-Hernández A. miRNA dysregulation in the development of non-alcoholic fatty liver disease and the related disorders type 2 diabetes mellitus and cardiovascular disease. Frontiers in Medicine. 2020;7:527059.

[7] Paternostro R, Trauner M. Current treatment of non-alcoholic fatty liver disease. Journal of Internal Medicine. 2022;292(2):190-204.

[8] Kumar R, Saha P, Kumar Y, Sahana S, Dubey A, Prakash O. A review on diabetes mellitus: type1 & Type2. World Journal of Pharmacy and Pharmaceutical Sciences. 2020;9(10):838-50.

[9] Zhang XX, Kong J, Yun K. Prevalence of diabetic nephropathy among patients with type 2 diabetes mellitus in China: A meta-analysis of observational studies. Journal of diabetes research. 2020;2020(1):2315607.

[10] Belete R, Ataro Z, Abdu A, Sheleme M. Global prevalence of metabolic syndrome among patients with type I diabetes mellitus: a systematic review and meta-analysis. Diabetology & metabolic syndrome. 2021;13:1-3.

[11] Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, Khare S, Srivastava A. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):535-45.

[12] Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia–a systematic review, meta-analysis, and meta-regression. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(4):395-403.

[13] Han H, Cao Y, Feng C, Zheng Y, Dhana K, Zhu S, Shang C, Yuan C, Zong G. Association of a healthy lifestyle with all-cause and cause-specific mortality among individuals with type 2 diabetes: a prospective study in UK Biobank. Diabetes care. 2022;45(2):319-29.

[14] Kyrou I, Tsigos C, Mavrogianni C, Cardon G, Van Stappen V, Latomme J, Kivelä J, Wikström K, Tsochev K, Nanasi A, Semanova C. Sociodemographic and lifestyle-related risk factors for identifying vulnerable groups for type 2 diabetes: a narrative review with emphasis on data from Europe. BMC endocrine disorders. 2020;20:1-3.

[15] Zhang Y, Pan XF, Chen J, Xia L, Cao A, Zhang Y, Wang J, Li H, Yang K, Guo K, He M. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. Diabetologia. 2020;63(1):21-33.

[16] Caturano A, D'Angelo M, Mormone A, Russo V, Mollica MP, Salvatore T, Galiero R, Rinaldi L, Vetrano E, Marfella R, Monda M. Oxidative stress in type 2 diabetes: impacts from pathogenesis to lifestyle modifications. Current Issues in Molecular Biology. 2023 ;45(8):6651-66.