ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 2, March – 2023 , Page No. : 85 – 95

Significance of Liver Function Tests and Elevated Lipid Profile in South Indian Diabetic Patients of Tertiary Care Center

[1]Akilandeswari Alagan Ramasamy, Study Design, Data Collection, Critical revision, Department of Medical Gastro enterology Government Kilpauk Medical College – Chennai - 600010

[2]S. Geetha, Approval, and Revision, Department of Medical Gastroenterology Government Kilpauk Medical College-Chennai- 600010

[3]J. Janifer Jasmine, Analysis, Manuscript preparation, Department of Medical Gastroenterology Government Kilpauk Medical College-Chennai- 600010

Corresponding Author: J. Janifer Jasmine, Analysis, Manuscript preparation, Department of Medical Gastro enterology Government Kilpauk Medical College – Chennai - 600010

Citation this Article: Akilandeswari Alagan Ramasamy, S. Geetha, Approval, J. Janifer Jasmine, "Significance of Liver Function Tests and Elevated Lipid Profile in South Indian Diabetic Patients of Tertiary Care Center", IJMSIR- March - 2023, Vol – 8, Issue - 2, P. No. 85 – 95.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Aims: To identify the significance of liver function tests and elevated lipid profile in south Indian diabetic patients.

Method: This study is an observational study conducted on 520 diabetic patients who visited the hospital for a checkup in June-2022-Dec-2022. The patients were observed and the data such as demographic details, fasting glucose, postprandial, HbA1C, Duration of DM, Weight (kgs), Height (cms), BMI, Aspartate trans aminase (AST), Alanine trans aminase (ALT), Alkaline phos phatase (ALP), Cholesterol, Triglycerides, High-Density Lipo protein (HDL), and ultrasound were observed, investigated, and the results were recorded. Gender-based impact of clinical data was also analyzed and tabulated.

Results: A total of 520 diabetic patients have selected for this study among them males were higher, 51-60 years was the highest age group present in this study. The highest numbers of patients are with 6-10 years of duration of diabetes and 44.4% of patients were obese. Among the elevation of liver function tests, 55.4% of patients showed elevation for AST, 54.6% of patients showed elevation for ALT, and 98.1% showed elevation for ALP.

Out of 520 diabetic patients, the abnormal levels of lipid markers were (CH-10.8%, TGL-22.3%, HDL-males-54.6%, females-30.2%). Fatty changes were found higher in the study subject by ultrasound.

Among the 520-study population 51-60 years of males (67.4%) were higher than females (32.6%) with statistical significance of (Chi-square - 24.7, p-value<0.01) and higher number of males (73.8%) patients were in 6-10 years of duration of diabetes than females. the higher number of males were obese than females.

All the markers of liver function test were elevated to males (AST-61.8%, ALT-65.1%, ALP-69.2%) than females (AST-38.2%, ALT-34.9%, ALP-30.8%) with statistical significance of (Chi-square - 21.05, p-value < 0.01). All the markers of lipid profile were elevated to males (CH-64.3%, TGL-83.6%, HDL-64.4%) than females (CH-35.7%, TGL-16.4%, HDL-35.6%) with statistical significance of (Chi-square - 19.08, p-value < 0.01).

The ultrasound done in the study patients showed a higher number of male patients had fatty changes (65.7%), and a higher number of female patients had fatty liver (56.7%) with statistical significance of (Chi-square - 30.02, p-value<0.01).

Conclusions: The results of this study clearly state that liver function tests and elevated lipid profile tests have a great significant impact on diabetic patients, as these tests can reveal certain unknown hidden factors such as liver diseases, fatty liver, fatty changes, high lipid, cardiovascular diseases, and early diagnosis leads to early treatment such as lipid-reducing interventions, or best care giver-and care taker communication or early prevention strategies, hence saving patients die due to these diseases, hence reducing mortality occur due to these diseases.

Keywords: Aspartate transaminase (AST), Alanine trans aminase (ALT), Alkaline phosphatase (ALP), Non-Alcoholic Fatty Liver Disease (NAFLD), Non-Alcoholic Stea to-Hepatitis (NASH).

Introduction

Diabetes mellitus is a global health issue leading to high morbidity and mortality of patients1. Liver dys function and lipid abnormality in an individual is typically classified as an elevated level of liver enzymes, total cholesterol, high level of trigly cerides, high-level LDL particles, and reduced level of HDL-C cholesterol.

As the liver plays a significant role in regulating glucose homeostasis and diabetes mellitus often reduces the HDL (good) cholesterol and increases the LDL (bad) cholesterol by increasing the lipolysis in the specialized cells called adipocytes leading to the increase of fatty acids, hence liver dysfunction and fatty liver have a high significance in diabetic patients.

Significance of Liver Dysfunction in Diabetic Patients

De Silva, N. M. G et al study describes that the liver function markers such as AST, ALT, and ALP are positively, and strongly, associated with diabetes mellitus, and increased levels of circulating AST, ALT, and ALP are indicating that chronic liver diseases in diabetic patients[2].

The Liver has a direct effect on type 2 diabetic patients, and NAFLD is one of the pathophysiological disorders that every diabetic patient face. Gastaldelli, A et al reported that NAFLD and diabetes are bidirectional physiological and metabolic disorder that affects 55% of diabetic patients, and Kanwal, F et al describes that NAFLD requires a concomitant holistic approach to treatment[3,4]. Chen, J et al found that the NR1C2 gene situated on the 6th chromosome is responsible for NAFLD[5].

Along with NAFLD, liver damage also occurs due to Non-Alcoholic Steatohepatitis (NASH). Franc que, S et al explain that NASH is a tissue-specific expression and involves pleiotropic functions that can induce a reduction of hepatic steatosis[6].

Yokote, K et al showed that glucose homeostasis, significantly ALT, and ALP were found higher in diabetic patients, but no significant change was found in fat content[7]. Gaeini, Z et al describe that liver disease is the biological marker and linkage to identify both liver dysfunction and diabetes[8].

© 2023 IJMSIR, All Rights Reserved

Shiba Baw, T et al found in their study, that there is a significant increase of AST and ALT found in diabetic patients[9]. Lu, J et al described that elevated ALT level was positively and significantly correlated with glucose level, especially in the fasting level[10].

Singh, A et al describe that in India, the elevated LFTs were found in 71.2% of diabetic patients, and this prevalence of LFT makes the importance of testing liver function tests in diabetic patients to detect fatty liver, NAFLD, NASH, and liver damage in the diabetic patients[11].

Teshome, G et al explained in their study, that the elevated LFTs or abnormal levels of LFTs are found in higher prevalence in diabetic patients than in non-diabetic individuals[12].

Hence glycemic index and liver function are highly interlinked, pathophysiological, and metabolic health issues and as diabetes is in the half of population of the globe, health care settings need to have significant, specific, and sensitive liver function tests to identify liver dysfunction in diabetic patients.

The above literature has made us

conduct this study to know the significance of liver function tests, live damage, and changes in diabetic patients.

Significance of Lipid Profile in Diabetic Patients

Van Laar, A. D et al reported that the risk factors of T2DM are imbalanced diet, obesity, stress, sedentary life, and increased fat leading to fatality due to high cholesterol [13]

Gudbjartsson, D. F et al also reported that there is an increase in the bottom 10% of lipids in diabetic patients increases the risk of cardiovascular diseases[14]. Ormazabal, V et al describes that non-alcoholic liver diseases such as fatty liver, and lipid disorders are significantly due to the high triglycerides, and total cholesterol, and an important risk factor in diabetic patients[15].

Markovic, R et al explain that higher lipids are found in elderly diabetic patients above the age of 65 years[16]. Oh, Y. S., et al found that high level of lipids mediates insulin resistance in diabetic patients[17]. Asghari, G., et al reported that pediatric lipid abnormalities will predict type 2 diabetes in adulthood, Wang, M., et al found that lipid abnormalities surely lead to an individual with increased blood sugar level (Diabetes)[18,19].

Feng, L., et al and Grundy, S. M et al conducted their studies to know the answer to the complex association of diabetes, dyslipidemia, and age [20,21]. Davison, G.W et al com mented in their study that the dys regulating meta bolism, dysregulating histone modification, dys regulation of DNA methylation and another risk of epigenetics are closely related and involved in the association of onset of diabetes mellitus in an in dividual[22].

With the above literature, it is very clear, the lipid profile in diabetic patients is an essential marker, and hence we conducted this study to find the significance of lipid profile in diabetic patients.

Ethical clearance

This study is conducted in the study subjects after approval of the ethical committee, and a consent form is received from each patient to collect their data for this study.

Inclusion criteria

- Diabetic patients
- Patients visited the hospital for liver dysfunction

Exclusion criteria

- Pregnant patients
- Children below 1 year
- Moribund patients

© 2023 IJMSIR, All Rights Reserved

Materials and methods

Methodology

Study Subjects:

The 520 diabetic patients who visited the hospital for checkups were selected based on inclusion and exclusion criteria from June-2022-Dec-2022 to conduct this study. The patients were observed and the clinical data were collected and recorded.

Data Collection

The 520 patient's demographic details, fasting glucose[23], postprandial[24], HbA1C[25], Duration of DM, Weight (kgs), Height (cms), BMI[26], Aspartate transaminase (AST)[27] (units/ liter), Alanine transaminase (ALT)[28] (units/ liter), Alkaline phosphatase[29] (ALP) (µg/ ml), Cholesterol[30] (mg/ dL), Triglycerides[31] (mg/ dL), High-Density Lipoprotein (HDL)[32] (mg/ dL), and Ultrasound[33] were observed, investigated, and the results were recorded.

Analysis

The 520-study patient's demographic, and clinical details were recorded, and the patients were categorized into 2 categories, based on gender the impact of clinical conditions are analyzed and the results were tabulated.

Statistical analysis of data

Statistical analysis was done using the statistical package SPSS version 21. The data were expressed as the frequency for descriptive variables, and the associations were expressed with a P value after the Chi-square test. The P value of <0.05 was considered statistically significant.

Results

A total of 520 diabetic patients were selected for this study after fulfilling the inclusion criteria and the basic characteristic of study patients tested for lipid profile were plotted in Table 1. Males were higher (n= 363, 69.8%), and females were (n=157, 30.2%).

Among the 520 diabetic patients ≤40 years of age were (n= 28, 5.4%), 41-50 years were (n=138, 26.5%), 51-60 years were (n=285, 54.8%), and >61 years of age groups were (n=69, 13.3%).

Table 1: Basic Characteristics of Lipid Profile in Diabetic Subjects

Variables	No (%)
Gender (n=520)	
Males	363 (69.8)
Females	157 (30.2)
Age Categories (in years)	
≤40 years	28 (5.4)
41-50 years	138 (26.5)
51-60 years	285 (54.8)
>61 years	69(13.3)
Duration of DM (in years)	
≤5	37 (7.1)
6-10	294 (56.5)
>11	189 (36.4)
BMI	
≥25	231 (44.4)
<24	289(55.6)
Liver Function test (Abnormal Value)	
Aspartate transaminase (AST) (units/liter) 8-45	288 (55.4)
Alanine transaminase (ALT) (units/ liter) 7-56	284 (54.6)
Alkaline phosphatase (ALP)(µg/ml) 30-40	510 (98.1)
Lipid Profile Tests (Abnormal Value)	
Cholesterol (mg/dL)>240	56(10.8)
Triglycerides (mg/dL)>200	116 (22.3)
High-Density Lipoprotein (HDL) (mg/dL)	
Males<40	284(54.6)
Females<50	157(30.2)
Ultrasound	
Cirrhosis	24 (4.6)
Fatty Liver	30 (5.8)
Fatty Change	239 (46.0)
Normal	227 (43.6)

© 2023 IJMSIR, All Rights Reserved

Among the 520 diabetic study patients, the duration of Diabetes Mellitus (DM) was ≤5 years in 37 (7.1%) patients, 6-10 years of DM were in 294 (56.5%) patients, and >11 years of DM was found in 189 (36.4%) patients. The height and weight of the diabetic patients were recorded to calculate the Body Mass Index (BMI). In this study diabetic patients with ≥25 BMI were 231 (44.4%) of patients, and <24 BMI were 289 (55.6%) (Table 1).

The lipid profile of this study's diabetic population was done and the results were recorded. Out of 77520 diabetic study patients, the elevated level of liver enzyme Aspartate transaminase (AST) was found in 288 (55.4%) patients, the elevated Alanine transaminase (ALT) was found in 284 (54.6%) of study patients, the elevated level of Serum amyloid P (SAP) was found in 510 (98.1%) of patients (Table 1).

High-level cholesterol (CH) was found in 56 (10.8%) of patients in this study, the elevated level of Triglycerides (TGL) was found in 116 (22.3%) of patients, and based on the lipid profile guidelines, the elevated level of High-Density Lipoprotein (HDL) was found in 284 (54.6%) males and females, the elevated HDL was found in 157 (30.2%) of diabetic patients (Table 1).

As the higher percentage of diabetic patients showed elevated liver enzymes, we also did an ultrasound in the 520 study patients to know the status of the liver, and we found Cirrhosis in 24 (4.6%) of patients, Fatty Liver in 30 (5.8%) of patients, Fatty Change also was found in 239 (46.0%) of patients, and the 227 (43.6%) diabetic study patient's ultrasound was normal (Table 1).

We wanted to check the impact of age and duration of diabetes in the diabetic study population based on gender, and the results were described in Table 2. Out of 520 diabetic patients tested for lipid profile, males were 363 and females were 157, out of 363 males the age was categorized into 4 categories, in which ≤40 years of males were 28 (100%), no females were found in ≤40 years of age group, in the age group of 41-50 years of total males and females were 138, among them 106 (76.8%) were males and 32 (23.2%) were females. In the age group of 51-60 years, both females and males were 285, among them males were 192 (67.4%), and females were 93 (32.6%), and in the last category of >61 years of age group, both males females were 69, among them males were 37 (53.6%), and females were 32 (46.4%) with statistical significance of (Chi-square - 24.7, p-value <0.01).

Table 2: Gender-Based Impact of Age and Duration of DM in Diabetic Patients Tested for Lipid Profile

Variables	Categories	Males (n=363) %	Females (n=157) %	Chi-square	P value
Age Categories (in years)	≤40 years (n=28)	28 (100.0)	0 (0.0)	24.7	<0.01*
	41-50 years (n=138)	106 (76.8)	32 (23.2)		
	51-60 years (n=285)	192 (67.4)	93 (32.6)		
	>61 years (n=69)	37 (53.6)	32 (46.4)		
Duration of DM (in years)	≤5 (n=37)	20 (54.1)	17 (45.9)	7.476	0.02381
	6-10(n=294)	217 (73.8)	77 (26.2)		
	>11(n=189)	126(66.7)	63 (33.3)		

* Statistically Significant

We also checked the impact of duration diabetes in the diabetic study population tested for lipid profile and the results are, among 520 study patients, ≤5 years of duration of diabetes was found in both males and females 37 patients, among them 20 (54.1%) patients were males and 17 (45.9%) of patients were females. The years of

© 2023 IJMSIR, All Rights Reserved

duration of diabetes which was 6-10years was found in 294 patients both males and females among them males were 217 (73.8%), and females were 77 (26.2%), and the years of duration of diabetes which was >11 years, both males and females were 189, among them males were 126 (66.7%), and females were 63 (33.3%) (Table 2).

We wanted to check whether a higher BMI has got a significant impact on the lipid profile of diabetic patients hence we did analyses based on genders with BMI and lipid profile as explained in Table 3. Out of 520 patients, with≥25 BMI were 231 patients, among them males 159 (68.8%) and females 72 (31.2%). In the study diabetic patients with <24 BMI 289 patients among them males 204 (70.6%), and females were 85 (29.4%).

Table 3: Gender-Based Impact of Age and Duration of DM in Diabetic Patients Tested for Lipid Profile

Variables	Categories	Males (n=363) %	Females (n=157) %	Chi-square	P value
BMI	≥25 (n=231)	159 (68.8)	72 (31.2)	0.1881	0.6645
	<24 (n=289)	204 (70.6)	85 (29.4)		
Liver Function Test (Abnormal Value)	AST (units/liter) (n=288)	178 (61.8)	110 (38.2)	21.05	**<0.01***
	ALT (units/liter) (n=284)	185 (65.1)	99 (34.9)		
	ALP (µg/ml) (n=510)	353 (69.2)	157 (30.8)		
Lipid Profile (Abnormal Value)	CH (mg/dL) (n=56)	36 (64.3)	20 (35.7)	19.08	**<0.01***
	TGL (mg/dL) (n=116)	97 (83.6)	19 (16.4)		
	HDL(n=441)	284 (64.4)	157 (35.6)		

* Statistically Significant

In the lipid profile, out of 520 study diabetic patients, elevated AST was found in 288 patients among them 178 (61.8%) were males and 110 (38.2%) were females. The elevated Alanine transaminase (ALT) was found in 284 patients among them 185 (65.1%) were males and 99 (34.9%) were females. In the study diabetic patients with elevated ALP were found in 510 patients among them 353 (69.2%) were males and 157 (30.8%) were females. The elevated cholesterol level was found in 56 patients among them 36 (64.3%) were males and 20 (35.7%) were females. We have also done triglycerides and elevated triglycerides were found in 116 patients among them 97 (83.6%) were males and 19 (16.4%) were females and elevated HDL was found in 441 patients among them 284 (64.4%) were males and 157 (35.6%) were females with the statistical significance of (Chi-square - 21.05, p-value - <0.01) (Table 3).

As the lipid profile variables showed significance in the study of diabetic patients we also performed an ultrasound in the study diabetic patients to know their liver status and the results were described in Table 4. From the ultrasound performed in the study of diabetic patients, we found that out of 520 patients, Cirrhosis was found in 24 patients among them 11 (45.8%) were males and 13 (54.2%) were female. The Fatty Liver was found in 30 patients among them 13 (43.3%) were males and 17 (56.7%) were females. In the ultrasound, Fatty Changes were the highest observed liver status and 239 patients had fatty changes among them 157 (65.7%) were males 82 (34.3%) were females. The ultrasound was normal in 227 patients among them 182 (80.2%) were males and 45

© 2023 IJMSIR, All Rights Reserved

(19.8%) were females with a statistical significance of (Chi-square – 30.02, p-value - <0.01) (Table 4).

Table 4: Gender-Based Impact of Age and Duration of DM in Diabetic Patients Tested for Lipid Profile

Ultrasound				
Categories	Males (n=363) %	Females (n=157) %	Chi-square	P value
Cirrhosis(n=24)	11 (45.8)	13 (54.2)	30.02	**<0.01***
Fatty Liver(n=30)	13 (43.3)	17 (56.7)		
Fatty Change (n=239)	157 (65.7)	82 (34.3)		
Normal (n=227)	182 (80.2)	45 (19.8)		

* Statistically Significant

Discussion

Diabetes mellitus is highly complicated with multiple organ complications, where liver dys function and high lipid profile makes diabetes even more complicated leading to high mortality due to its complication.

Huebschmann, A. G et al study shows that women are presumed to be presented with cardio-metabolic conserve with their sex hormones, maybe this advantage gives women protection over cardio vascular diseases due to high-risk conditions such as diabetes, liver dysfunction, high lipid profile, and our study also, we found that the males were higher than females with diabetes, liver dysfunction, and high-fat disorders[34].

Perdana, A et al reported that the majority of patients aged 46–55 years, in our study also, we found a higher number of patients were in the age group of 51-60 years[35]. de Jong, M et al study also described that the cut–off age was 60-65 years for their study in cardio vascular risk management in diabetic patients[36].

The prevalence of liver dysfunction in diabetic patients is high, and liver dysfunction leading to mortality is also high and study by Islam, S et al reported the prevalence of liver function tests (ALT-19%, AST-34.1%, ALP-36.8%), but did not report the gender prevalence, in our present study, we reported the prevalence of liver function tests as (ALT-54.6%, AST-55.4%, ALP-98.1%), and we also reported the gender prevalence of liver function tests in diabetic patients as (ALT-(males-61.8, females-38.2%), AST(males-65.1, females-34.9%), ALP-(males-69.2, females-30.8%)) with statistical significance of Chi-square-21.05, P value-0.01[37].

Noroozi Karima bad, M et al reported in their study, the AST was elevated to 2.97, ALT was elevated to 8.92, and ALP was elevated to 2.30, but they did not report in gender, in our present study, AST was elevated at 61.8% in males and females 38.2% in females, ALT was elevated to 65.1% in males, and in females, 34.9%, and ALP was elevated to 69.2% in male patients, and in the female patient, the raise was 30.8%[38].

Wan, J. Y et al study showed that their study, AST, and ALT did not show a significant elevation in diabetic patients, but ALP showed a significant elevation in their study patients, in our present study, we found ALP was elevated with 69.2% in male patients, and in the female patient, 30.8%[39].

Several studies reported the prevalence (overall) of abnormal LFTs, but the study by Ni, L et al reported that in their study, significant elevation of liver enzymes was found higher in males than in females, and our present study is compatible with their study[40].

Alzahrani, S. H et al described that for lipid profile, BMI, Glycated hemoglobin A1c (HbA1c), and smoking status are the major confounders in diabetic patients[11], we found higher elevated levels of lipid markers[41].

Cao, Y et al reported that there is a significant association between the increased level of non-HDL-C and the CVD risk in diabetic patients[42], and Brunner, F. J et al showed that in their study of 524 444 individuals, the strong

© 2023 IJMSIR, All Rights Reserved

association between the elevated level of non-HDL-C and cardiovascular diseases[43], in our present study we found CH-10.8, TGL-22.3, HDL-(males-54.6, females-30.2)

In diabetic patients, 44% increased occurrence of cardiovascular diseases is due to the increased levels of TG and decreased levels of HDL-C explained in Castañer, O. et al study, and our present study TG is showing 22.3 elevation in diabetic patients[44].

Gender-based prevalence of any disease is vital to treat any disease, Wright, A. K et al reported that lipid profile remains at a higher level in males than in females, our present study is compatible with their study and we report (CH-(males-64.3, females-35.7%), TGL - (males-83.6, females-16.4%), HDL-(males- 64.4, females-35.6%)) with statistical significance of Chi-square-19.08, P value-0.01[45].

Kumar, R et al explain in their study that the prevalence of cirrhosis is high in the diabetic population than in the non-diabetic, in our present study; we reported 4.65 elevated cirrhosis in diabetic patients[46]. Petroni, M. L et al reports that high BMI in children may later risk them for fatty liver-related liver failure and liver cancer, in our present study, we found 5.8% of fatty liver in diabetic patients, and 465 of fatty changes, we also reported the gender-based prevalence of (Cirrhosis-(males-45.8%, females-54.2%), Fatty liver- (males-43.3%, females-56. 7%, Fatty change- (males-80.2%, females-34. 3%) with statistical significance of Chi-square-30.02, P value-0.01[47].

Ference, B. A et al[48] reported that still, there is a debate that the causative factor for cardiovascular diseases in diabetic patients is high levels of triglycerides, and Taylor, R., et al[49] raises the question in their study, what is the unknown fact; whether liver dysfunction contributes to type 2 diabetes or insulin resistance induces liver enzymes and fat accumulation in the diabetic patients?

As above recently published studies still shows that the recent studies also show that there is an unknown fact hidden in liver dysfunction in diabetic patients, we found in our study, that highly elevated levels of liver function tests and has a great significant impact on diabetic patients, as these tests can reveal certain unknown hidden factors such as liver diseases, fatty liver, and fatty changes. The studies also show that there is a debate that diabetes induces elevated triglycerides or triglycerides induce diabetes, but we conclude in our present study that elevated levels of lipid markers are found in diabetic patients, hence testing lipid markers makes its signifi cance in diabetic patients, hence early diagnosis leads to early treatment such as lipid-reducing inter ventions, or best care giver-and care taker communication or early prevention strategies, saving patients die due to these diseases.

References

1. Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its com plications. Nature reviews endo crino logy, 14 (2), 88-98.

2. De Silva, N. M. G., Borges, M. C., Hingorani, A. D., Engmann, J., Shah, T., Zhang, X., & Lawlor, D. A. (2019). Liver function and risk of type 2 diabetes: bidirectional Mendelian randomization study. Diabetes, 68 (8), 1681-1691.

3. Gastaldelli, A., & Cusi, K. (2019). From NASH to diabetes and from diabetes to NASH: mechanisms and treatment options. JHEP Reports, 1(4), 312-328.

4. Kanwal, F., Shu brook, J. H., Younossi, Z., Nata Rajan, Y., Bugianesi, E., Rinella, M. E., & Cusi, K. (2021). Preparing for the NASH epidemic: a call to action. Metabolism, 122, 154822.

© 2023 IJMSIR, All Rights Reserved

5. Chen, J., Montagner, A., Tan, N. S., & Wahli, W. (2018). Insights into the Role of PPARβ/δ in NAFLD. International journal of molecular sciences, 19(7), 1893.

6. Francque, S., Szabo, G., Abdel Malek, M. F., Byrne, C. D., Cusi, K., Dufour, J. F., & Tacke, F. (2021). Nonalcoholic steatohepatitis: the role of peroxisome pro life rator-activated receptors. Nature reviews Gastro enterology & hepatology, 18(1), 24-39.

7. Yokote, K., Yamashita, S., Arai, H., Araki, E., Matsushita, M., Nojima, T., & Ishibashi, S. (2021). Effects of Pema fibrate on glucose metabolism markers and liver function tests in patients with hyper trigly ceridemia: a pooled analysis of six phase 2 and phase 3 randomized double-blind placebo-controlled clinical trials. Cardiovascular Diabetology, 20(1), 1-13.

8. Gaeini, Z., Bahadoran, Z., Mirmiran, P., & Azizi, F. (2020). The association between liver function tests and some metabolic outcomes: Tehran Lipid and Glucose Study. Hepatitis Monthly, 20(5).

9. Shiba Baw, T., Dessie, G., Molla, M. D., Zerihun, M. F., & Ayelign, B. (2019). Assessment of liver marker enzymes and its association with type 2 diabetes mellitus in Northwest Ethiopia. BMC research notes, 12, 1-5.

10. Lu, J., He, J., Li, M., Tang, X., Hu, R., Shi, L., & Bi, Y. (2019). Predictive value of fasting glucose, post load glucose, and hemoglobin A1c on risk of diabetes and complications in Chinese adults. Diabetes care, 42(8), 1539-1548.

11. Singh, A., Dalal, D., Malik, A. K., & Chaudhary, A. (2019). Deranged liver function tests in type 2 diabetes: a retro spective study. Int J Med Sci Publ Health, 4(3), 27-31.

12. Teshome, G., Amba chew, S., Fasil, A., & Abebe, M. (2019). Prevalence of liver function test abnormality and associated factors in type 2 diabetes mellitus: a com parative cross-sectional study. EJIFCC, 30(3), 303.

13. Van Laar, A. D., Grootaert, C., & Van Camp, J. (2021). Rare mono-and disaccharides as healthy alternative for traditional sugars and sweeteners? Critical Reviews in Food Science and Nutrition, 61(5), 713-741.

14. Gudbjartsson, D. F., Thorgeirsson, G., Sulem, P., Helgadottir, A., Gylfason, A., Saemundsdottir, J., & Stefansson, K. (2019). Lipoprotein (a) concentration and risks of cardiovascular disease and diabetes. Journal of the American College of Cardiology, 74(24), 2982-2994.

15. Ormazabal, V., Nair, S., Elfeky, O., Aguayo, C., Salomon, C., & Zuñiga, F. A. (2018). Association between insulin resistance and the development of cardio vascular disease. Cardiovascular diabetology, 17, 1-14.

16. Markovic, R., Grubel Nik, V., Vošner, H. B., Kokol, P., Završnik, M., Janša, K., & Marhl, M. (2022). Age-Related Changes in Lipid and Glucose Levels Associated with Drug Use and Mortality: An Observational Study. Journal of Personalized Medicine, 12(2), 280.

17. Oh, Y. S., Bae, G. D., Baek, D. J., Park, E. Y., & Jun, H. S. (2018). Fatty acid-induced lip toxicity in pancreatic beta-cells during development of type 2 diabetes. Frontiers in endocrinology, 9, 384.

18. Asghari, G., Hashem Inia, M., Heidari, A., Mirmiran, P., Guity, K., Shahrzad, M. K., & Hadaegh, F. (2021). Adolescent metabolic syndrome and its com ponents associations with incidence of type 2 diabetes in early adulthood: Tehran lipid and glucose study. Dia betology & Metabolic Syndrome, 13(1), 1-9.

19. Wang, M., Hou, X., Hu, W., Chen, L., & Chen, S. (2019). Serum lipid and lipoprotein levels of middle-aged and elderly Chinese men and women in Shandong Province. Lipids in Health and Disease, 18, 1-8.

20. Feng, L., Nian, S., Tong, Z., Zhu, Y., Li, Y., Zhang, C., & Yan, Z. (2020). Age-related trends in lipid levels: a large-scale cross-sectional study of the general Chinese population. BMJ open, 10(3), e034226.

© 2023 IJMSIR, All Rights Reserved

21. Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., & Yeboah, J. (2019). 2018. AHA/ ACC/ AACVPR/ AAPA/ ABC/ ACPM/ ADA/ AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation, 139(25), e1082-e1143.

22. Davison, G. W., Irwin, R. E., & Walsh, C. P. (2021). The meta bolic-epigenetic nexus in type 2 diabetes mellitus. Free Radical Biology and Medicine, 170, 194-206.

23. Care, D. (2018). Care in Diabetesd2018. Diabetes Care, 41(1), S137-S143.

24. Zilversmit, D. B. (1979). Atherogenesis: a post pran dial phenomenon. Circulation, 60(3), 473-485.

25. Jeppsson, J. O., Kobold, U., Barr, J., Finke, A., Hoelzel, W., Hoshino, T., & Wey Kamp, C. (2002). Ap proved IFCC reference method for the measurement of HbA1c in human blood. 78-89.

26. Obese, H. J. O. R. (1998). Body mass index (BMI). Obes Res, 6(2), 51S-209S.

27. Shrawder, E., & Martinez-Carrion, M. (1972). Evidence of phenylalanine transaminase activity in the iso enzymes of aspartate transaminase. Journal of Bio logical Chemistry, 247(8), 2486-2492.

28. Córdoba, J., O'Riordan, K., Dupuis, J., Borensztajn, J., & Blei, A. T. (1998). Diurnal variation of serum alanine transaminase activity in chronic liver disease. Hepatology, 28(6), 1724-1725.

29. Kaplan, M. M. (1972). Alkaline phos phatase. Gastro enterology, 62(3), 452-468.

30. Steinberg, D., Parthasarathy, S., Carew, T. E., Khoo, J. C., & Witztum, J. L. (1989). Beyond cholesterol. New England Journal of Medicine, 320(14), 915-924.

31. Brockerhoff, H. (1965). A stereospecific analysis of triglycerides. Journal of Lipid Research, 6(1), 10-15.

32. Gordon, D. J., Probst field, J. L., Garrison, R. J., Neat on, J. D., Castelli, W. P., Knoke, J. D., & Tyroler, H. A. (1989). High-density lipoprotein cholesterol and cardio vascular disease. Four prospective American studies. Circulation, 79(1), 8-15.

33. Newman, P. G., & Rozycki, G. S. (1998). The history of ultrasound. Surgical clinics of north America, 78 (2), 179-195.

34. Huebschmann, A. G., Huxley, R. R., Kohrt, W. M., Zeitler, P., Regensteiner, J. G., & Reusch, J. E. (2019). Sex differences in the burden of type 2 diabetes and cardio vascular risk across the life course. Diabeto logia, 62, 1761-1772.

35. Perdana, A., & Jafar, N. (2023). Effect of breadfruit leaf extract (Artocarpus altilis) on changes in SGPT and SGOT levels type 2 diabetes mellitus patients. Journal of Pharmaceutical Negative Results, 770-777.

36. de Jong, M., Vos, R. C., de Ritter, R., van der Kallen, C. J., Sep, S. J., Woodward, M., & Peters, S. A. (2019). Sex differences in cardiovascular risk manage ment for people with diabetes in primary care: a cross-sectional study. BJGP open, 3(2).

37. Islam, S., Rahman, S., Haque, T., Summon, A. H., Ahmed, A. M., & Ali, N. (2020). Prevalence of elevated liver enzymes and its association with type 2 diabetes: A cross-sectional study in Bangladeshi adults. Endo crinology, diabetes & metabolism, 3(2), e00116.

38. Noroozi Karim Abad, M., Khalili, P., Ayoobi, F., Esmaeili-Nadimi, A., & La Vecchia, C. (2022). Serum liver enzymes and diabetes from the Rafsanjani cohort study. BMC Endocrine Disorders, 22(1), 1-12.

39. Wan, J. Y., & Yang, L. Z. (2022). Liver Enzymes are associated with Hyperglycemia in Diabetes: A Three-

© 2023 IJMSIR, All Rights Reserved

Year Retro spective Study. Diabetes, Meta bolic Syn drome and Obesity: Targets and Therapy, 545-555.

40. Ni, L., Yu, D., Wu, T., & Jin, F. (2021). Gender-specific association between non-alcoholic fatty liver disease and type 2 diabetes mellitus among a middle-aged and elderly Chinese population: An observational study. Medicine, 100(6), e24743.

41. Alzahrani, S. H., Baig, M., Aashi, M. M., Al-Shaibi, F. K., Alqarni, D. A., & Bakhamees, W. H. (2019). Association between glycated hemoglobin (HbA1c) and the lipid profile in patients with type 2 diabetes mellitus at a tertiary care hospital: a retrospective study. Diabetes, metabolic syndrome and obesity: targets and therapy, 1639-1644.

42. Cao, Y., Yan, L., Guo, N., Yu, N., Wang, Y., Cao, X., & Lv, F. (2019). Non-high-density lipoprotein cholesterol and risk of cardiovascular disease in the general population and patients with type 2 diabetes: a systematic review and meta-analysis. Diabetes research and clinical practice, 147, 1-8.

43. Brunner, F. J., Waldeyer, C., Ojeda, F., Salomaa, V., Kee, F., Sans, S., & Koenig, W. (2019). Application of non-HDL cholesterol for population - based cardio vascular risk stratification: results from the Multinational Cardio vascular Risk Consortium. The Lancet, 394 (102 15), 2173-2183.

44. Castañer, O., Pinto, X., Subir Ana, I., Amor, A. J., Ros, E., Hernáez, Á., & Fitó, M. (2020). Remnant chole sterol, not LDL cholesterol, is associated with incident cardio vascular disease. Journal of the American College of Cardiology, 76(23), 2712-2724.

45. Wright, A. K., Kontopantelis, E., Emsley, R., Buchan, I., Mamas, M. A., Sattar, N., & Rutter, M. K. (2019). Cardio vascular risk and risk factor management in type 2 diabetes mellitus: a population-based cohort study assessing sex disparities. Circulation, 139(24), 2742 -2753.

46. Kumar, R. (2018). Hepato genous diabetes: an underestimated problem of liver cirrhosis. Indian journal of endocrinology and metabolism, 22(4), 552.

47. Petroni, M. L., Brodosi, L., Bugianesi, E., & Mar chesini, G. (2021). Management of non-alcoholic fatty liver disease. Bmj, 372.

48. Ference, B. A., Kastelein, J. J., Ray, K. K., Gins berg, H. N., Chapman, M. J., Packard, C. J., & Catapano, A. L. (2019). Association of triglyceride-lower ing LPL variants and LDL-C–lowering LDLR variants with risk of coronary heart disease. Jama, 321(4), 364-373.

49. Taylor, R., Al-Mrabeh, A., Zhyzhneuskaya, S., Peters, C., Barnes, A. C., Aribisala, B. S., & Lean, M. E. (2018). Remission of human type 2 diabetes requires decrease in liver and pancreas fat content but is dependent upon capacity for β cell recovery. Cell metabolism, 28(4), 547-556.

© 2023 IJMSIR, All Rights Reserved