JOURNAL OF DYNAMICS AND CONTROL

VOLUME 8 ISSUE 8

ULTRASOUND SCREENING FOR FATTY LIVER IN DIABETIC AND NON-DIABETIC PATIENTS

[#]Farzeen Zehra (B.S. Hons. RIT),

[$]Sidra Rasheed (B.S Hons. RIT),

[*]Syed Zaigham Ali Shah (B.Sc. Hons. MIT)

#Radiographer, Government College University, Faisalabad, Pakistan, $Radiographer, Canal View Diagnostic Centre (CVDC) Lahore, Pakistan, *Chief Radiology Technologist, Human Resource Development Centre (HRDC) Skardu, Pakistan

ULTRASOUND SCREENING FOR FATTY LIVER IN DIABETIC AND NON-DIABETIC PATIENTS

[1]Farzeen Zehra (B.S. Hons. RIT), [2]Sidra Rasheed (B.S Hons. RIT), [3]Syed Zaigham Ali Shah (B.Sc. Hons. MIT)

[1]Radiographer, Government College University, Faisalabad, Pakistan
Email: farzeen929276@gmail.com

[2]Radiographer, Canal View Diagnostic Centre (CVDC) Lahore, Pakistan
Email: srasheed59@gmail.com

[3]Chief Radiology Technologist, Human Resource Development Centre (HRDC) Skardu, Pakistan
Email: chieftech.radiology@hrdcskd.pk

ABSTRACT: *Introduction*: Fatty liver is a disease in which fat accumulates in hepatic cells. Non-alcoholic fatty liver disease develops when a person does not consume alcohol. The most frequent liver condition is NAFLD. Ultrasonography is a gold standard modality for the screening of fatty liver disease. The risk of diabetes mellitus increases in patients having fatty liver disease. *Objective:* To screen out the patients of diabetic and non-diabetic. *Material and Method:* It was a cross-sectional study. This study included patients with NAFLD and diabetes mellitus. From the Radiology department, ultrasonographic reports of patients having fatty liver disease were taken during the period of 7 months, from September 2020 to April 2021. This study included both sexes included. Based on grades of fatty land presence or absence of diabetes mellitus, patients were categorized into groups. *Results:* Out of 120 patients, 90 were diabetic and had fatty liver disease detected by ultrasonography. There was a risk of acquiring diabetes mellitus as the severity of a fatty liver increased. *Conclusion:* There was a linear relationship between non-alcoholic fatty liver (NAFLD) and diabetes mellitus (DM). It is suggested that patients with NAFLD should check their blood glucose levels routinely.

KEYWORDS: Fatty Infiltration, Non-alcoholic Fatty Liver Disease (NAFLD), Diabetes Mellitus (DM), Sonography, Non-insulin Dependent Diabetes Mellitus (NIDDM)

1. INTRODUCTION

The accumulation of fat in the hepatocyte is called fatty liver [1]. If a person is not consuming alcohol and the liver is fatty on ultrasound then it is called non-alcoholic fatty liver disease [2]. NAFLD has been linked to the progression of diabetic mellitus in previous research [3]. Metabolic problems associated with an inactive lifestyle have been linked to blood insulin resistance and type 2 diabetes mellitus. An inactive lifestyle is associated with increased adiposity and abnormalities in excess fat distribution, which can promote the growth of fatty liver disease and the advancement of fatty liver disease [4]. Some of the studies of NAFLD were centered on the levels of alanine transaminase (ALT) and others on clinical scoring schemes. Most of these investigations, though, were retrospective and relied on data from normal individuals' health inspections, and the determination of NAFLD was centred on ALT levels and, in some cases, clinical grading methods [5-8]. Real-time ultrasound scanning is regarded as a gold standard imaging modality for patients with presumed liver diseases. However, the liver may be impacted by a wide variety of disorders, two major forms are seen: focal and diffused diseased. Many studies have established the accuracy of ultrasound scanning in diagnosing a localized disease, such as extrahepatic biliary blockage or metastatic disease, and this is appreciated in clinical care [9-12]. Even though recognizably abnormal echo patterns have been linked to both steatosis and fibrosis in parenchymal liver disease [13]. The utility of scanning in diagnosis and treatment is debatable [12]. Obesity, alcoholism, diabetes, complete parenteral nutrition, protein deficiency, acute starvation, carbohydrate overload, chronic hepatitis C infection, and medication therapy are all symptoms of fatty liver or hepatic steatosis[14]. The amount of serum γ-glutamyltransferase (γ-GTP) was an independently associated significant predictor for non-insulin-dependent metabolic syndrome unit research (NIDDM) [15].

Because of its high accuracy, abdominal ultrasonography is consideredthe gold standard tech nique for diagnosing fatty liver disease [16]. Ultrasound images based on brightness levels are used for the diagnosis of fatty liver diseases [17]. Echogenicity is an increase in fatty liver. The ability to create an echo is called echogenicity i.e., the returning of signals in ultrasound can be used to conclude the brightness of an ultrasonographic image. Due to the lack of an accurate measurement of liver echogenicity, it is measured by comparing the echogenicity of other tissues [18, 19]. Fatty liver-induced pathophysiological changes, these changes can be evaluated by using ultrasound images, on the basis of attenuation of returning echo signals, echogenic liver-to-kidney contrast, and poor visualization of the portal vein and diaphragm [20, 21].

The morphology of the liver and its vasculature pattern are used to grade fatty liver. Diabetes mellitus is quite common in all age groups due to predisposing factors such as obesity and hepatic lipid metabolism impairment. It was discovered in research on obese people with diabetes that they all had non-alcoholic fatty liver disease and increased liver enzymes [22-24]. Fatty liver grading from grade 0 to grade III where 0 indicates normal size, echotexture, and the appearance of the liver. Grade I denote a mild condition, grade II denotes a moderate condition, and grade III denotes a severe condition [25-27].

Due to rapidly rising rates of obesity and type 2 diabetes in the Asian-Pacific area, fatty liver disease has become more frequent. Prevalence rates of 5-40 percent have been documented [28]. Fatty liver and metabolic problems such as insulin resistance and diabetes occur simultaneously, according to preliminary research [29, 30]. The fatty liver index has recently been linked to increased cardiovascular risk, insulin resistance, and intima-media thickness in matching investigations [31].

2. REVIEW OF LITERATURE

The most common type of liver problem is non-alcoholic fatty liver disease. Dilawar et al., 2007 suggested that Non-alcoholic fatty liver disease is most likely to occur in people with type 2 diabetes. They researched 100 T2DM patients of both sexes who had blood glucose levels of more than 140 mg/dl. Diffuse hyperechoic echo texture enhanced echo texture relative to kidneys, vascular blurring, and deep attenuation were used to identify fatty liver. 15 patients were prediabetic (BSR<179md/dl) and 85 were diabetic (BSR>180mg/dl), out of 100 patients. It is essential to increase the awareness among people regarding non-alcoholic diabetes mellitus. Non-alcoholic fatty liver disease seems to be more frequent in patients with type 2 diabetes (78%) than in those who are not diabetic (8%) [32].

Okomoto et al., in 2003 suggested that a fatty liver is an independent risk factor for diabetes mellitus was investigated over 10 years using ultrasound. A total of 840 people (such as 467 men and 373 women) were tracked for the duration of the study, which lasted ten years. No diagnosis of diabetes, a fasting blood glucose level of more than 110 mg/dl, and a serum hemoglobin A1C level of 6.4 percent or less were all considered non-diabetic. All of the tests were performed after 12 hours of fasting. Abdominal ultrasonography was done by a technician. Although a basic study 10 years later indicated a relationship between fatty liver and hyperglycemia, a multivariable logistic regression assessment refuted this finding. In such a multiple logistic regression study, fasting plasma glucose levels at the beginning and age were revealed to be substantially related to diabetes. Fatty liver is not an independent risk factor for diabetes throughout this 10-year follow-up study. Increased fasting plasma glucose values were a cause of diabetes even when they were within the normal range [33].

Kasturiratne et al., 2013 reported that non-alcoholic fatty liver is linked to diabetes mellitus and impaired fasting glycaemic. To determine the connection between NAFLD and the incidence of diabetes mellitus in the Sri Lankan urban population, a community-based study was conducted. In 2007, contributors of the Ragama Health group were tested for NAFLD using well-established ultrasonography standards. Those who did not have diabetes at the beginning of the research were monitored for three years. Diabetes mellitus prevalence rates were compared between people with and without NAFLD at the start of the study. In 2007, 2984 individuals were examined, 926 of them had NAFLD and 676 of them had diabetes. In 2007, 2276 individuals were declared diabetes-free, and in 2010, 1914 individuals were assessed again. After three years, 104 of the 528 individuals with NAFLD and 138 of the 1314 individuals without NAFLD acquired diabetes mellitus for the first time. Individuals with and without NAFLD had diabetes mellitus rates of 64.2 and 34 per 1000 person-years of follow-up, respectively. NAFLD is associated with a greater risk of diabetes mellitus in people who have it identified by ultrasonography. NAFLD management, like lifestyle modifications, may assist in avoiding the current diabetes epidemic [29].

Preceding studies of Ferraioli and Monteiro in 2019 indicate that the primary cause of liver diseases is non-alcoholic fatty liver disease. According to a detailed analysis, diabetes mellitus and cardiovascular risk are linked to the amount of fat accumulated in the liver. Assessable ultrasound is a method of calculating backscatter coefficients, attenuation coefficients, and sound wave speeds based on the analysis of radiofrequency echoes detected by an ultrasound device. The controlled attenuation parameter (CAP) processes the attenuation of the ultrasound beam. Even though there is overlap between sequential grades of liver steatosis, CAP is reliable in grading fatty infiltration, and scores are unaffected by liver fibrosis. Some ultrasound makers have already developed software for quantifying the attenuation of an ultrasound beam. According to earlier findings, proprietary technologies that include ultrasound devices are more accurate than CAP for grading fatty liver. Another method for assessing fatty liver is based on sound speed computation, and the initial results appear to be more compromising [34].

The link between the liver's high-amplitude echoes and widespread fatty infiltration is now well known. Foster et al., in 1980 provided their findings on the accuracy with which ultrasonography may detect a fatty liver. The liver ultrasound images were studied to see whether there were any histologically normal livers or livers with fatty infiltration. A brightly reflective echo pattern had been seen in only 2 out of 40 patients with normal liver biopsies, but with fatty infiltration 12 out of 20 patients showed this pattern. 9 out of 10 patients had a brightly reflective echo pattern with moderate or severe fatty infiltration [35].

Sun and Kim 2011 suggested, that even though fatty and diabetes mellitus are known to be linked, the link between the two in the progression of T2DM remains unknown. They assessed the 5-year chance of getting type 2 diabetes in people who had fatty liver and were categorized by insulin sensitivity using quartiles of fasting insulin concentrations. This study looked at the clinical and biochemical data of 11091 Koreans who underwent a medical examination which included fasting insulin levels and abdominal ultrasonography. Fatty liver affected 27% of the population at the start of the research. Almost half of the individuals with fatty liver (47%) had baseline insulin values in the highest quartiles, compared to just 17% of those without fatty liver. Irrespective of baseline insulin concentration, those with fatty liver had considerably higher glucose and triglyceride levels, as well as lower high-density lipoprotein cholesterol levels. Moreover, irrespective of baseline insulin concentration, people with fatty liver had a markedly higher risk of developing T2DM than people without fatty liver. Although its association with insulin resistance, ultrasound-detected fatty liver leads to an increased risk of T2DM by itself [36].

3. MATERIALS AND METHODS

3.1 Study Design

It was a cross-sectional study.

3.2 Setting

Data was collected from the Department of Radiology Aga Khan Health Services and District Head Quarter Gilgit.

3.3 Study Duration

This study was conducted over a period of 7 months, from September 2020 to April 2021.

3.4 Sampling Technique

It was a convenient sampling technique.

3.5 Sample Size

This study included 120 patients with fatty liver from grades 0 to III.

3.6 Inclusion Criteria

Patients of both sexes are included in this study.

This study includes patients greater than 35 years of age because insulin resistance (T2DM) is a risk factor for non-alcoholic fatty liver disease.

This study included 120 patients with a random glucose level above 140mg/dl diagnosed is type 2 diabetes mellitus.

3.7 Exclusion Criteria

The patients who were taking alcohol and medicines that cause fatty liver disease in pregnant women were excluded from the study.

Patients with high blood pressure were excluded from studies.

3.8 Scanning Technique

Patients with abdominal pain or a feeling of fullness in the upper right side of the abdomen came to the department of radiology for abdominal ultrasonography. For the association of fatty liver with diabetes mellitus, we include all the patients with or without diabetes mellitus. To avoid any machine artifacts, all of the patients were scanned by a brilliant radiologist utilizing their ultrasound machines, namely the Toshiba Apolio 300 CV Colour Doppler and the Xario 100 Canon.

In this study, we have taken parameters on the bases of ultrasound findings such as grades of fatty liver (0 to III), parenchymal texture, liver to kidney contrast, and echogenicity of the portal vein. The grading of fatty liver is done on the basis of echogenicity or echotexture of the liver, echogenicity of the portal vein, and liver to kidney contrast. Grade 0 indicates that the echogenicity of the liver is normal and well-defined visualization of the portal vein. Grade I indicate there is a slight and diffuse increase of liver echogenicity with a normal conception of the diaphragm and the portal vein. Grade II indicates that the echogenicity of the liver is moderately increased and the visualization of the portal vein and diaphragm is slightly impaired. Grade III indicates echogenicity of the liver is markedly increased and the visualization of the portal vein and diaphragm is poor.

This study aims to correlate non-alcoholic fatty liver with diabetes mellitus.

4. RESULTS

This study included 120 patients of both sexes, 58 patients were male and 62 patients were female, which is given in Table 4.1. The mean value of collected data is 59.56667. Age distribution in different groups is given in Table 4.2. There were 10% patients of age in between 31 to 40 years, 20.83% of patients between 41 to 50 years, 25% patients of age in between 51 to 60 years, 20% patients of age in between 61 to 70 years, 15.83% patients of age in between

71 to 80 years and 8.3% patients of age in between 81 to 90 years. It is shown that the highest frequency of age was between 51 to 60 years.

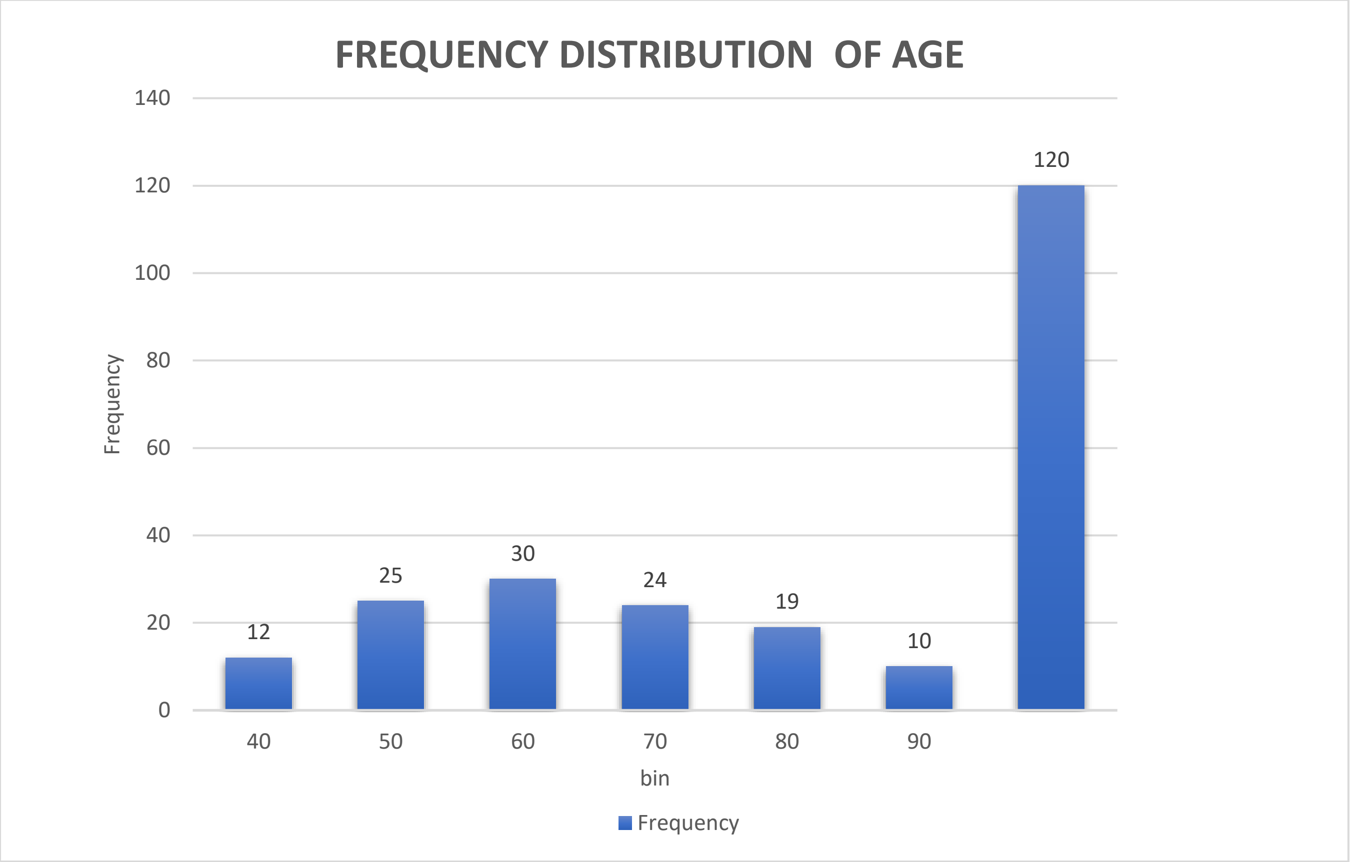
Table 4.1: Ratio of Male: Female

Count Male and Female	
Male	58
Female	62
TOTAL	**120**

Table 4.2: Age Distribution Frequency

Age Limit	***Frequency***	***Relative Freq.***	**Percentage Freq.**
31-40 Yrs.	12	0.1000	10.00%
41-50 Yrs.	25	0.2083	20.83%
51-60 Yrs.	30	0.2500	25.00%
61-70 Yrs.	24	0.2000	20.00%
71-80 Yrs.	19	0.1583	15.83%
81-90 Yrs.	10	0.0833	8.33%
Total	**120**	**1.0000**	**100.00%**

Graph 4.1: Age Frequency Distribution Graph

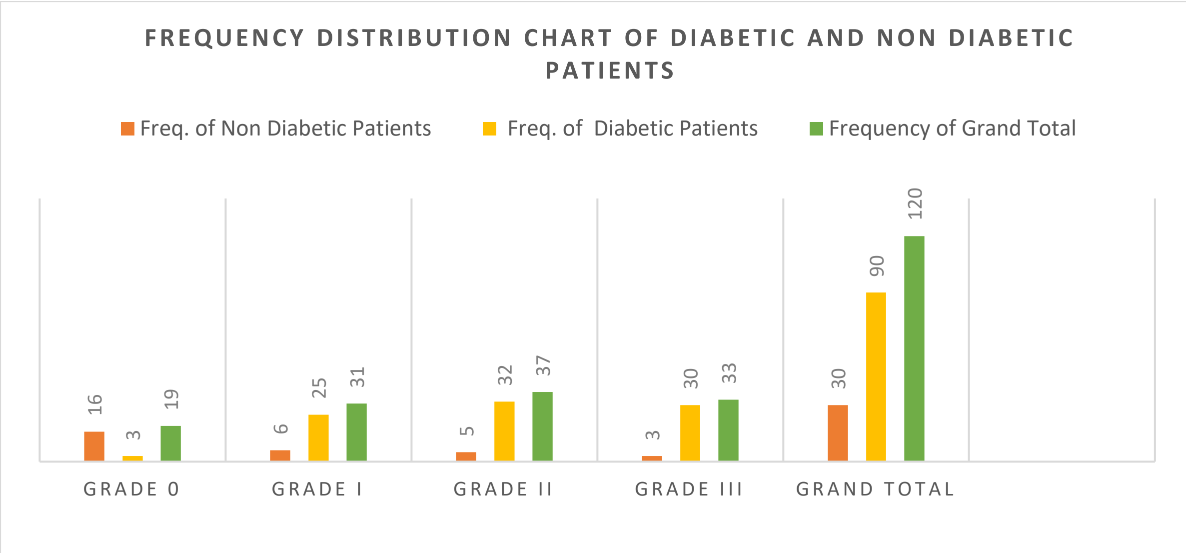


In this study, 120 patients with fatty liver disease were divided into the grading of fatty liver with the help of ultrasound findings and a history of diabetes. There were 19 patients with grade 0 fatty liver, out of which 16 (53.33%) patients had normal blood glucose levels, i.e., negative diabetes, and only 3 (3.33%) patients had mildly increased blood glucose, i.e., positive diabetes (Table. 4.3). There were 31 patients with grade I fatty liver out of which 6 (20%) patients had no history of diabetes and 25 (27.78%) patients had type 2 diabetes mellitus. There were 37 patients with grade II fatty liver out of which 5 (16.67%) patients had no diabetic history and 32 (35.56%) patients had type 2 diabetes mellitus. 33 patients of grade III fatty liver out of which 3 (10%) had no diabetic history and 30 (33.33%) patients had type 2 diabetes mellitus.

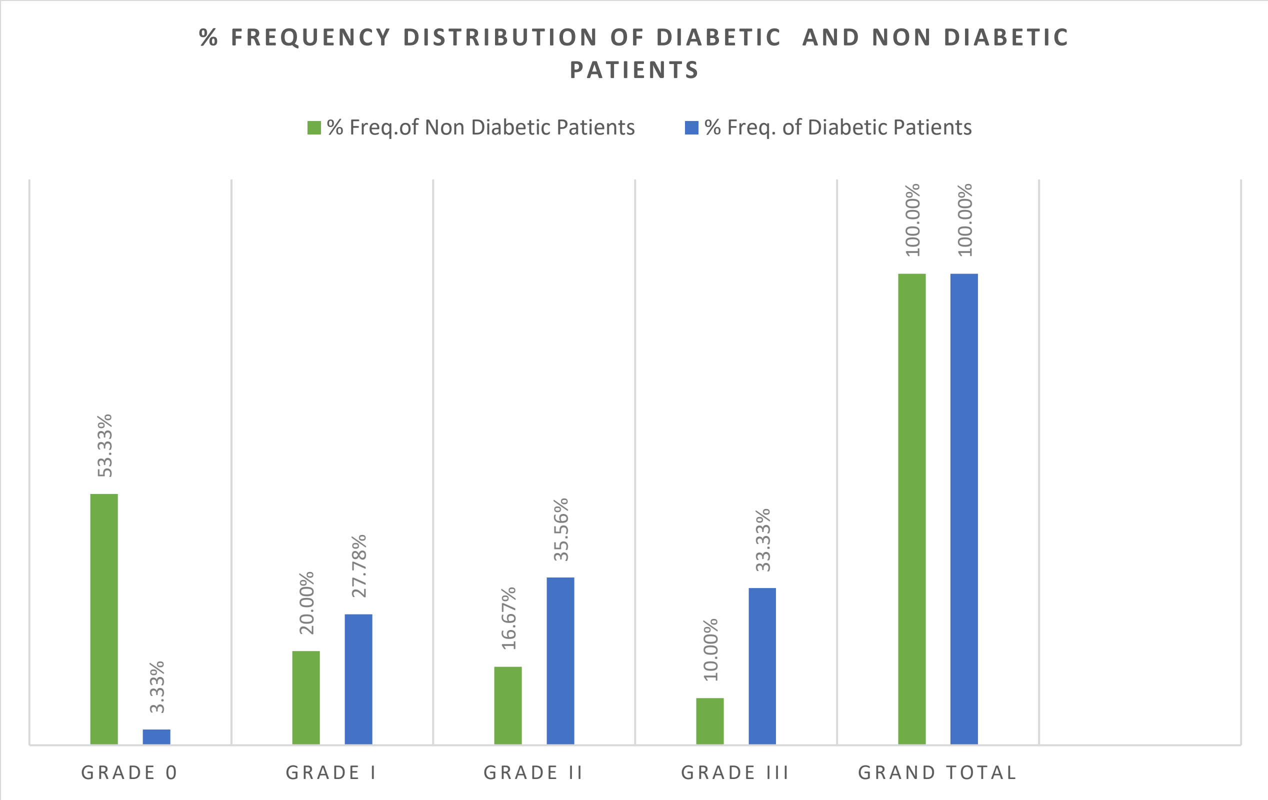
Table 4.3: Frequency Table of Diabetic and Non-Diabetic Patients

Grades Of Fatty Liver	Freq. of Non-Diabetic Patients	% Freq. of Non-Diabetic Patients	Freq. of Diabetic Patients	% Freq. of Diabetic Patients	Frequency of Grand Total	% Frequency of Grand Total
Grade 0	16	53.33%	3	3.33%	19	15.83%
Grade I	6	20.00%	25	27.78%	31	25.83%
Grade II	5	16.67%	32	35.56%	37	30.83%
Grade III	3	10.00%	30	33.33%	33	27.50%
Grand Total	**30**	**100.00%**	**90**	**100.00%**	**120**	**100.00%**

Graph 4.2: Frequency Distribution of Diabetic and Non-Diabetic Patients



Graph 4.3: % Frequency Distribution of Diabetic and Non-Diabetic Patients



Linear association was seen in table 4.3 and graphs 4.2, and 4.3 that there were 3.33% patients with diabetes mellitus in grade 0, 27.78% patients with diabetes mellitus in grade I, 35.56% patients with diabetes mellitus in grade II, and 33.33% patients of diabetes mellitus in grade III. These results show that there was a risk of diabetes mellitus as the grading of the liver increased.

On ultrasound findings of grades of fatty liver disease that there were changes in the Liver Parenchymal texture (Tables 4.4 and 4.4), liver-to-kidney contrast (Table 4.5), and the echogenicity of the portal vein (Table 4.6) as the grades of the fatty liver increased. In this study 19 patients with grade 0 fatty liver, there were normal liver parenchymal texture, liver to kidney contrast, and the echogenicity of portal vein as were shown in the normal liver. In 31 patients with the grade, I fatty liver had slight and diffuse liver parenchymal texture, liver to kidney contrast was hyperechoic and echogenic portal vein. 37 patients with grade II fatty liver had increased liver parenchymal texture, hyperechoic liver to kidney contrast, and decreased portal vein echogenicity. 33 patients with grade III fatty liver had markedly increased liver parenchymal texture, poor liver-to-kidney contrast, and the portal vein is invisible i.e., absence of portal vein echogenicity as shown in Tables 4.4, 4.5, and 4.6.

 ISSN:1672-6553

Table 4.4: Frequency Distribution Table of Liver Parenchymal Changes

Fatty Liver Grade0/ I/II/III	Liver Parenchymal Changes				
	Increased	Markedly Increased	Normal	Slight and Diffuse	Frequency
Grade 0	0	0	19	0	19
Grade I	0	0	0	31	31
Grade II	37	0	0	0	37
Grade III	0	33	0	0	33
Grand Total	37	33	19	31	120

Graph 4.4: Frequency Distribution Graph of Liver Parenchymal Changes

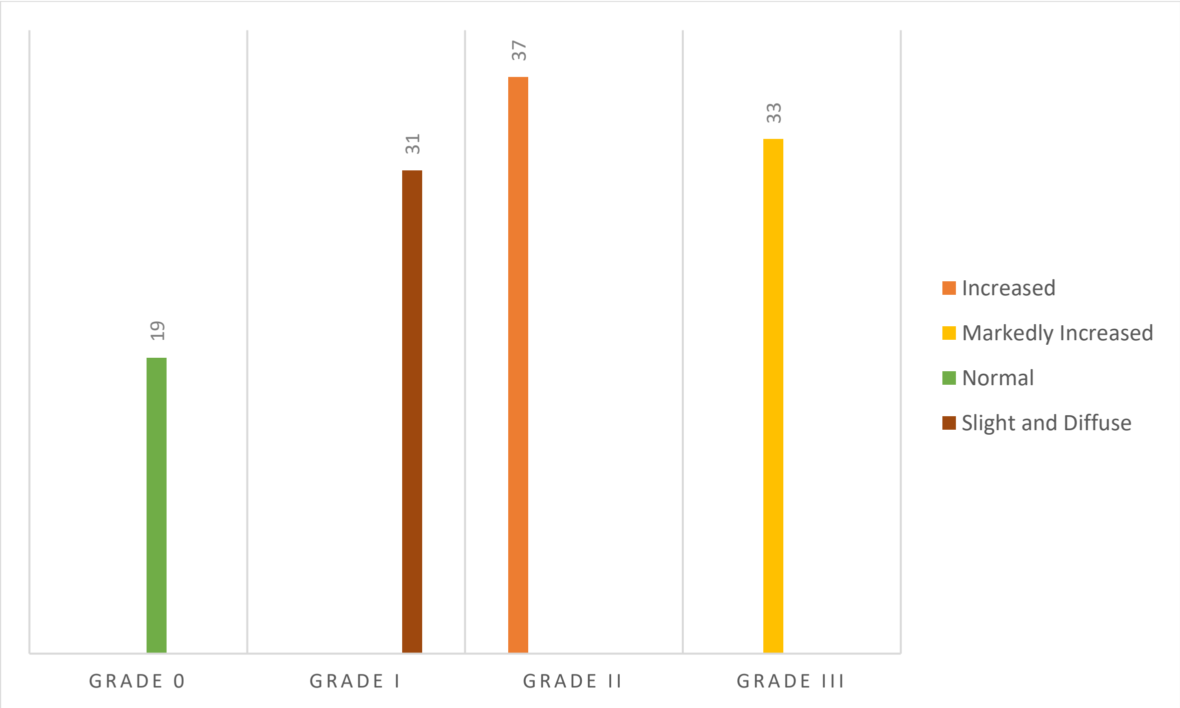


Table 4.5: Frequency Distribution Table of Liver to Kidney Contrast Changes

Fatty Liver Grade0/ I/II/III	LIVER to Kidney Contrast			
	Hyperechoic	Normal	poor	Grand Total
Grade 0	0	19	0	19
Grade I	31	0	0	31
Grade II	37	0	0	37
Grade III	0	0	33	33
Grand Total	**68**	**19**	**33**	**120**

Graph 4.5: Frequency Distribution Chart of Liver To Kidney Contrast Changes

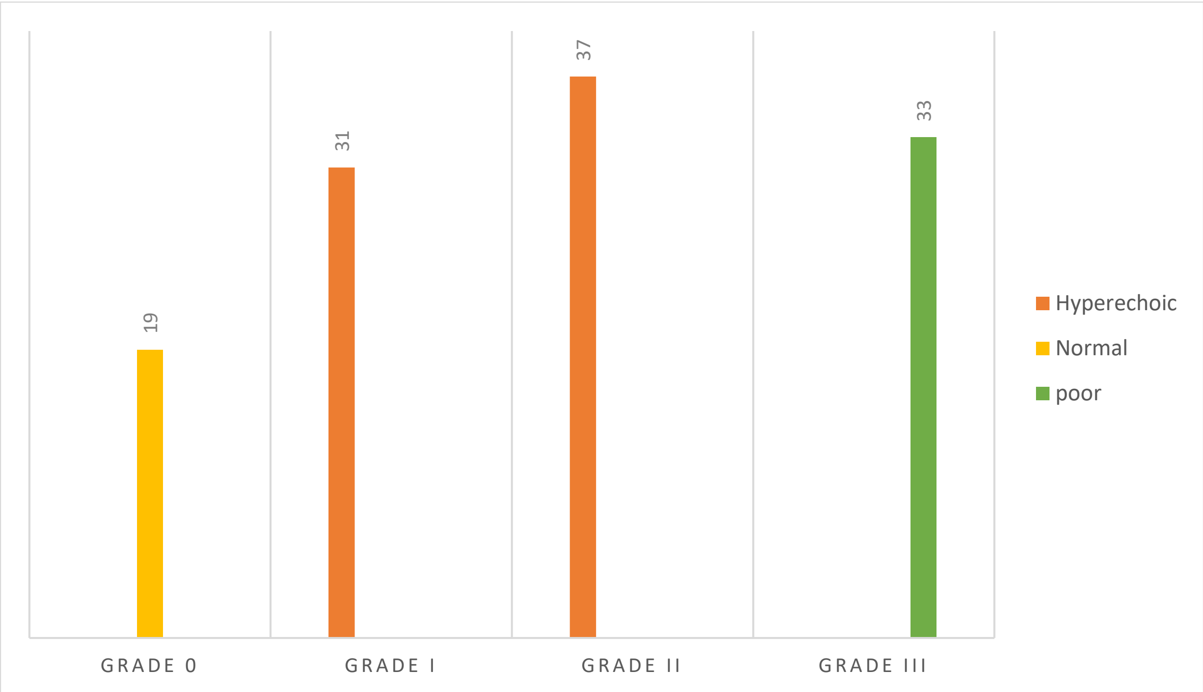
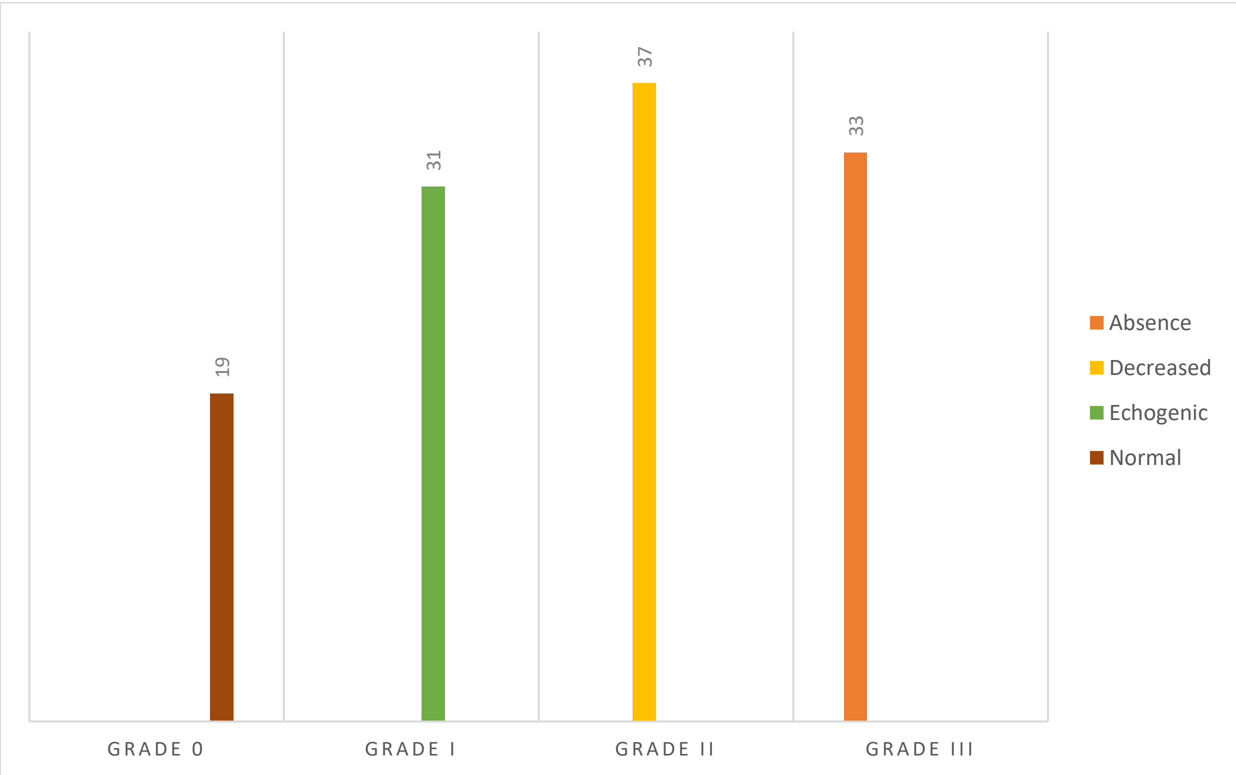


Table 4.6: Frequency Distribution Table of Changes in Portal Vein Echogenicity

Fatty Liver Grade0/ I/II/III	**Portal Vein Echogenicity**				
	Absence	**Decreased**	**Echogenic**	**Normal**	**Grand Total**
Grade 0	0	0	0	19	19
Grade I	0	0	31	0	31
Grade II	0	37	0	0	37
Grade III	33	0	0	0	33
Grand Total	**33**	**37**	**31**	**19**	**120**

Graph 4.6: Frequency Distribution Chart of Changes in Portal Vein Echogenicity



5. DISCUSSION

This study suggested that there was a link between non-alcoholic fatty liver disease and diabetes mellitus. In this study, 75% of patients were diabetic with non-alcoholic fatty liver disease. According to previous research, 50 percent to 70 percent of individuals with fatty liver identified by ultrasonography had type-II diabetes mellitus, and a link between fatty liver and diabetes mellitus is familiar [37]. Because there was a significant rise in random blood sugar levels as the severity of fatty liver increased, it was statistically shown that there was a clear association between fatty liver and diabetes mellitus. Therefore, this makes known that the incidence of diabetes mellitus is more when the severity of fat accumulation in the liver increases [38]. NAFLD is common in diseases characterized by insulin resistance, including type 2 diabetes, obesity, dyslipidemia, and metabolic syndrome [39]. The incidence of fatty liver in type 2 diabetes mellitus was 75 percent in this study, which corresponds to 60.8 percent in Luxmi, Sattar, and Ara's investigations [40]. Many studies confirmed previously that non-alcoholic fatty liver disease patients are more susceptible to diabetes mellitus. In addition, Targher et al., 2007 reported that blood glucose level seems to be high as the grades of fatty liver increase, which is correlated with the conducted studies [41]. According to a recent study, ultrasonic scanning performed as part of routine clinical capability was 87 percent sensitive and 89 percent specific in detecting fatty liver or liver fibrosis that had been detected by histology [42]. For patients with non-alcoholic fatty liver disease, abdominal ultrasound has been used mainly in clinical procedures and protocols because it is a safe and very cheap method. And its major necessity is a high degree of specificity and sensitivity. The values of sensitivity and specificity of ultrasound in non-obese patients range from 83% to 94%, and 84% to 100% respectively [42, 43]. Kasturiratne et al., 2013 found a three-year probability of diabetes mellitus in an urban adult Sri Lankan population, which was associated with the occurrence of NAFLD at baseline. NAFLD had a significantly greater risk of developing diabetes mellitus when evaluated ultrasonically; a person with NAFLD was 1.6 times more likely than a person without NAFLD to acquire diabetes mellitus [29].

6. CONCLUSION

According to the findings, there was a clear connection between fatty liver and diabetes mellitus. This was statistically proved that 75 % patients of with fatty liver disease had diabetes mellitus. Ultrasonography was used to screen the fatty liver disease. Ultrasonography is the gold standard imaging modality to rule out fatty liver diseases. According to screening and obtaining the patient's medical history, the risk of diabetes mellitus increased considerably as the grade of the fatty liver increased.

7. RECOMMENDATION

Different studies should be conducted on this topic using ultrasound as a gold standard modality because of its specificity and sensitivity in detecting fatty liver diseases. These studies should be conducted on a large scale, including a massive number of patients and along with their diabetic history. The results of the research will aid in determining the risk of diabetes in individuals with non-alcoholic fatty liver disease. Patients with non-alcoholic fatty liver disease should monitor their blood glucose levels regularly to decrease this risk.

REFERENCES

1. Podolsky D. Infiltrative, genetic, and metabolic diseases affecting the liver. HARRISONS PRINCIPLES OF INTERNAL MEDICINE. 2005;16(2):1869.
2. Angulo P. Nonalcoholic fatty liver disease. New England Journal of Medicine. 2002;346(16):1221-31.
3. Yki-Järvinen H. Liver fat in the pathogenesis of insulin resistance and type 2 diabetes. Digestive diseases. 2010;28(1):203-9.
4. Rector RS, Thyfault JP, Wei Y, Ibdah JA. Non-alcoholic fatty liver disease and the metabolic syndrome: an update. World journal of gastroenterology: WJG. 2008;14(2):185.
5. Adams LA, Waters OR, Knuiman MW, Elliott RR, Olynyk JK. NAFLD as a risk factor for the development of diabetes and the metabolic syndrome: an eleven-year follow-up study. Official journal of the American College of Gastroenterology| ACG. 2009;104(4):861-7.
6. Yamada T, Fukatsu M, Suzuki S, Wada T, Yoshida T, Joh T. Fatty liver predicts impaired fasting glucose and type 2 diabetes mellitus in Japanese undergoing a health checkup. Journal of gastroenterology and hepatology. 2010;25(2):352-6.
7. Kim CH, Park JY, Lee KU, Kim JH, Kim HK. Fatty liver is an independent risk factor for the development of Type 2 diabetes in Korean adults. Diabetic Medicine. 2008;25(4):476-81.
8. Balkau B, Lange C, Fumeron F, Bonnet F. Nine-year incident diabetes is predicted by fatty liver indices: the French DESIR study. BMC gastroenterology. 2010;10(1):1-9.
9. Wheeler P, Theodossi A, Pickford R, Laws J, Knill-Jones R, Williams R. Non-invasive techniques in the diagnosis of jaundice--ultrasound and computer. Gut. 1979;20(3):196-9.
10. Taylor K, Rosenfield A. Grey-scale ultrasonography in the differential diagnosis of jaundice. Archives of Surgery. 1977;112(7):820-5.
11. Lawson TL. Hepatic abscess: ultrasound as an aid to diagnosis. The American journal of digestive diseases. 1977;22(1):33-7.
12. Theodossi A, Spiegelhalter D, Portmann B, Eddleston A, Williams R. The value of clinical, biochemical, ultrasound and liver biopsy data in assessing patients with liver disease. Liver. 1983;3(5):315-26.
13. Joseph A, Dewbury K, McGuire P. Ultrasound in the detection of chronic liver disease (the "bright liver"). The British journal of radiology. 1979;52(615):184-8.
14. Clark JM, Brancati FL, Diehl AM. Nonalcoholic fatty liver disease. Gastroenterology. 2002;122(6):1649-57.
15. Perry IJ, Wannamethee SG, Shaper AG. Prospective study of serum γ-glutamyltransferase and risk of NIDDM. Diabetes Care. 1998;21(5):732-7.
16. Joy D, Thava VR, Scott BB. Diagnosis of fatty liver disease: is biopsy necessary? European journal of gastroenterology & hepatology. 2003;15(5):539-43.
17. İçer S, Coşkun A, İkizceli T. Quantitative grading using grey relational analysis on ultrasonographic images of a fatty liver. Journal of medical systems. 2012;36(4):2521-8.

18. Sissons G. Clinical Diagnostic Ultrasound (2nd edn). Ed. by GM Baxter, PLP Allan and P Morley, pp. xi+ 687, 1999 (Blackwell Science, Oxford, UK),£ 195.00 ISBN 0 632 03744. British Institute of Radiology; 2001.
19. Seçil M. Temel ultrasonografi ve Doppler. Meta Basım Matbaacılık. 2008.
20. Sasso M, Miette V, Sandrin L, editors. Novel controlled attenuation parameter for the evaluation of fatty liver disease. 2009 IEEE International Ultrasonics Symposium; 2009: IEEE.
21. Jeong J-W, Lee S, Lee JW, Yoo D-S, Kim S, editors. Computer-assisted sonographic analysis of the hepatorenal and textural features for the diagnosis of the fatty liver. 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference; 2006: IEEE.
22. Namikawa C, Shu-Ping Z, Vyselaar JR, Nozaki Y, Nemoto Y, Ono M, et al. Polymorphisms of microsomal triglyceride transfer protein gene and manganese superoxide dismutase gene in non-alcoholic steatohepatitis. Journal of hepatology. 2004;40(5):781-6.
23. Jou J, Choi SS, Diehl AM, editors. Mechanisms of disease progression in nonalcoholic fatty liver disease. Seminars in liver disease; 2008: © Thieme Medical Publishers.
24. Vuppalanchi R, Chalasani N. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis: Selected practical issues in their evaluation and management. Hepatology. 2009;49(1):306-17.
25. Lee SS, Park SH, Kim HJ, Kim SY, Kim M-Y, Kim DY, et al. Non-invasive assessment of hepatic steatosis: prospective comparison of the accuracy of imaging examinations. Journal of hepatology. 2010;52(4):579-85.
26. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterology. 2002;123(3):745-50.
27. van Werven JR, Marsman HA, Nederveen AJ, Smits NJ, ten Kate FJ, van Gulik TM, et al. Assessment of hepatic steatosis in patients undergoing liver resection: comparison of US, CT, T1-weighted dual-echo MR imaging, and point-resolved 1H MR spectroscopy. Radiology. 2010;256(1):159-68.
28. Amarapurkar DN, Hashimoto E, Lesmana LA, Sollano JD, Chen PJ, Goh KL, et al. How common is non-alcoholic fatty liver disease in the Asia–Pacific region and are there local differences? Journal of gastroenterology and hepatology. 2007;22(6):788-93.
29. Kasturiratne A, Weerasinghe S, Dassanayake AS, Rajindrajith S, de Silva AP, Kato N, et al. Influence of non-alcoholic fatty liver disease on the development of diabetes mellitus. Journal of gastroenterology and hepatology. 2013;28(1):142-7.
30. Grønbæk H, Thomsen KL, Rungby J, Schmitz O, Vilstrup H. Role of nonalcoholic fatty liver disease in the development of insulin resistance and diabetes. Expert review of gastroenterology & hepatology. 2008;2(5):705-11.
31. Gastaldelli A, Kozakova M, Højlund K, Flyvbjerg A, Favuzzi A, Mitrakou A, et al. Fatty liver is associated with insulin resistance, risk of coronary heart disease, and early atherosclerosis in a large European population. Hepatology. 2009;49(5):1537-44.
32. Dilawar M, Andrabi WI, Rauf MA, Tahir DS, Yousaf A, Aleem S, et al. Suspect and Screen by Ultrasound for Non-Alcoholic Fatty Liver Disease in Pre-Diabetic and Patients with Type 2 Diabetes Mellitus. PAKISTAN JOURNAL OF MEDICAL & HEALTH SCIENCES. 2017;11(1):157-9.
33. Okamoto M, Takeda Y, Yoda Y, Kobayashi K, Fujino MA, Yamagata Z. The association of fatty liver and diabetes risk. Journal of epidemiology. 2003;13(1):15-21.
34. Ferraioli G, Monteiro LBS. Ultrasound-based techniques for the diagnosis of liver steatosis. World journal of gastroenterology. 2019;25(40):6053.
35. Foster K, Dewbury K, Griffith A, Wright R. The accuracy of ultrasound in the detection of fatty infiltration of the liver. The British journal of radiology. 1980;53(629):440-2.
36. Sung K-C, Kim SH. Interrelationship between fatty liver and insulin resistance in the development of type 2 diabetes. The Journal of Clinical Endocrinology & Metabolism. 2011;96(4):1093-7.
37. Angulo P, Keach JC, Batts KP, Lindor KD. Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. Hepatology. 1999;30(6):1356-62.

38. Haukeland JW, Damås JK, Konopski Z, Løberg EM, Haaland T, Goverud I, et al. Systemic inflammation in nonalcoholic fatty liver disease is characterized by elevated levels of CCL2. Journal of hepatology. 2006;44(6):1167-74.
39. Neuschwander-Tetri BA. Nonalcoholic steatohepatitis and the metabolic syndrome. The American journal of the medical sciences. 2005;330(6):326-35.
40. Luxmi S, Sattar RA, Ara J. Association of non-alcoholic fatty liver with type 2 diabetes mellitus. Jlumhs. 2008;9:188-93.
41. Targher G, Bertolini L, Padovani R, Rodella S, Tessari R, Zenari L, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. Diabetes care. 2007;30(5):1212-8.
42. Saverymuttu S, Joseph A, Maxwell J. Ultrasound scanning in the detection of hepatic fibrosis and steatosis. Br Med J (Clin Res Ed). 1986;292(6512):13-5.
43. Yajima Y, OHTA K, NARUI T, ABE R, SUZUKI H, OHTSUKI M. Ultrasonographical diagnosis of fatty liver: significance of the liver-kidney contrast. The Tohoku journal of experimental medicine. 1983;139(1):43-50.