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Lipid and Glucose Profile in Non-alcoholic Fatty Liver Disease: A Hospital Based Study

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Abstract

Background: *Non-alcoholic fatty liver (NAFLD) is an important cause of chronic liver disease of worldwide distribution. Its prevalence is rapidly increasing in developing countries. In the Kingdom of Saudi Arabia, primary or secondary NAFLD is frequently encountered given that obesity and diabetes mellitus are prevalent.*
Objectives: *The current study assessed the frequency, clinical patterns, status of liver function and lipid profile in patients with NAFLD.*
Patients and Methods: *This observational cross sectional study enrolled patients attending Salman Bin Abdul Aziz University Hospital, Kharj between October, 2012 and December 2014. All patients were invited to complete a structured closed ended dichotomous questionnaire about risk factors of NAFLD. Physical examination, BMI, liver function tests, lipid profile, HOMA-IR, abdominal ultrasound were also performed in all patients. The NAFLD Liver Fat Score and presence of steatosis were used for predicting the NAFLD. The NAFLD fibrosis score was used for staging the NAFLD related fibrosis.*
Results: *Patients with NAFLD constituted 32% of total patients presenting to SAU university hospital. Viral hepatitis, drug-induced liver injury, autoimmune hepatitis, hemochromatosis, and Wilson's disease were excluded in these patients. NAFLD was greatly associated with 38% obese and 41% diabetic patients. Furthermore, 21% patients were also diagnosed with primary NAFLD. Various grades of steatosis were observed in ultrasound which is predominantly found in primary NAFLD. Additionally, patients with primary NAFLD have more elevated lipid profiles, HOMA-IR and liver enzymes. It's worth noting that the NAFLD fibrosis scores are way high in patients with primary NAFLD compared to secondary NAFLD.* ***Conclusion:*** *NAFLD is the most frequent chronic disease among patients attending liver clinic in Salman Bin Abdul Aziz University Hospital. Diabetes, obesity, and unexplained abnormal liver function tests are the striking features of the patients where NAFLD should be suspected. Consistent monitoring of the progression of NAFLD is an essential component for predicting fibrosis in these patients in due course of treatment.*

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases [1] in developed countries; about 20-50% of the total populations are suffering from this condition. [2] Diagnosis of this abnormal liver condition is chiefly based on the presence of hepatic steatosis, which can be assessed either by imaging or by histology and absence of secondary fat accumulation either due to alcohol consumption or due to genetic/ hereditary disorders[3]. The important risk factors associated with this disease are obesity, diabetes mellitus, and dyslipidemia. [4] NAFLD includes simple steatosis, steatohepatitis that may evolve in cirrhosis of 20-25% affected subjects [5.6].

NAFLD is characterized by the excessive accumulation of various lipids where hepatocytes are occupied by triglycerides [7]. Triglycerides constitute the majority of lipids stored in the livers of NAFLD patients where alterations of triglycerides mediated pathways have been demonstrated. [8] Steatosis develops when the rate of FA (fatty acid) input (uptake and synthesis with subsequent esterification to triglycerides) is greater than the rate of FA output (oxidation and secretion). Therefore, the amount of triglycerides present in hepatocytes represents a complex interaction among hepatic fatty acid uptake, derived from plasma free fatty acid (FFA) released from hydrolysis of adipose tissues, triglycerides, and FFA released from hydrolysis of circulating triglycerides, *de novo* fatty acid synthesis, fatty acid oxidation and fatty acid export. Therefore, triglycerides and FFAs play a critical role in steatosis. [9,10]

Obesity and diabetes mellitus represent one of the major public health problems in the Kingdom of Saudi Arabia. In a national survey, it was found that 30% Saudis are obese (body mass index ≥30 kg/m^2). [11] Since most NAFLD cases are associated with obesity, another study on the same population showed that the prevalence of NAFLD reaches up to 10%. [12]. Therefore, in the present study we have investigated the patterns of NAFLD and the lipid profile among Saudi patients.

PATIENTS AND METHODS

The study included patients with confirmed NAFLD (105 women and 127 men) with age range 29 to 55 years (mean ± SD, 41.88±7.64 in addition 26 healthy controls ranging in age from 29 to 55 years (mean ± SD, 40.56±9.13; 9 women, 17 men). The study was conducted between December, 2012 and September 2013 in Salman Bin Abdul Aziz University Hospital, Al Kharj, KSA. Prior to the enrolment in the study all patients were given informed consent form to read and understand the steps involved in the study also make aware of their role and responsibility in it. The study protocol conformed to the ethical guidelines of the 1975 declaration of Helsinki and was approved by the ethics committee of Salman Bin Abdul Aziz University Hospital.

Determination of eligibility was based on medical history, physical examination, standard tests and procedures performed during the screening visit. For the diagnoses of NAFLD, and to rule out other possible liver diseases, both the NAFLD group and the HC were evaluated by abdominal ultrasonography (US), clinical and laboratory findings. The time interval between US and the laboratory study was less than 1 week. Apart from vitamin B12, the other liver enzymes such as aspartate aminotransferase, alanine aminotransferase (ALT), and alkaline phosphatase, as well as the total cholesterol, triglycerides, serum lipoproteins, glucose, folic acid and hepatitis markers, were also evaluated. In addition, body mass index (calculated as weight in kilograms divided by the square of the height in meters) and the waist circumference (measured with a tape measure just above the umbilicus) were calculated.

Inclusion criteria for the NAFLD patients which were opted: (1) age ≥ 18 years, (2) bright liver on ultrasound imaging and elevated liver function tests for at least 6 months before enrollment and (3) patient's consent for liver biopsy. Age, gender, and body mass index (BMI)-matched individuals were recruited for control group.

BMI was calculated by the formula body weight (kg)/height^2 (in meter). Inclusion criteria for the controls were (1) age ≥ 18 years and (2) normal liver ultrasound imaging and normal liver function tests. Exclusion criteria for both NAFLD patients and controls were (1) ethanol consumption more than 20 g/day (2) liver cirrhosis, (3) other liver diseases (viral hepatitis, autoimmune hepatitis, primary sclerosing cholangitis, primary biliary cirrhosis and overlap syndromes, drug-induced liver disease, haemochromatosis, Wilson's disease, α1-antitrypsin deficiency), (4) type I diabetes mellitus, (5) pancreatitis, (6) uncontrolled hypothyroidism or hyperthyroidism, (7) adrenal insufficiency, (8) renal failure, (9) thrombotic disorders, (10) cancer, (11) pregnancy.

Serum aspartate transaminase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and glucose were measured within 1 h after blood was drawn, with standard methods using an automated analyzer (Olympus AU2700; Olympus, Hamburg, Germany). Low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald formula.

Blood glucose was measured by enzymatic photometric test which aimed at determining blood glucose after enzymatic oxidation by glucose oxidase. The colorimetric indicator is quinoneimine, which is generated from 4-aminoantipyrine and phenol, under the catalytic action of peroxidase (Trender's reaction).

HOMA-IR; homeostatic model is a method used to quantify insulin resistance and B-cell function.The approximate equation for IR used a fasting plasma sample and was derived by the use of insulin-glucose products divided by a constant.

$$\text{HOMA-IR} = \frac{\text{fasting glucose}\left(\text{mg}/\text{dl}\right) \text{x fasting insulin}\left(\text{uU}/\text{L}\right)}{405}$$

All patients had abdominal ultrasound examination.

RESULTS

The objectives of the present study were to investigate the clinical patterns and lipid profile in Saudi patients with NAFLD. This study was conducted on 126 patients with NAFLD. In addition to this, 26 control patients without NAFLD. No significant difference was observed between patients and control subjects in regards with their age and blood picture. However, the patients and control subjects differed in gender, BMI, comorbid conditions, liver functions and lipid profile. The patient's demographics are shown in Table 1**.**

Table 1: Demographics of patients and controls

Comparing the biochemical profile in patients with and without NAFLD should a significant different in cholesterol, triglycerides, ALST, AST and glucose levels. **(Table 2).**

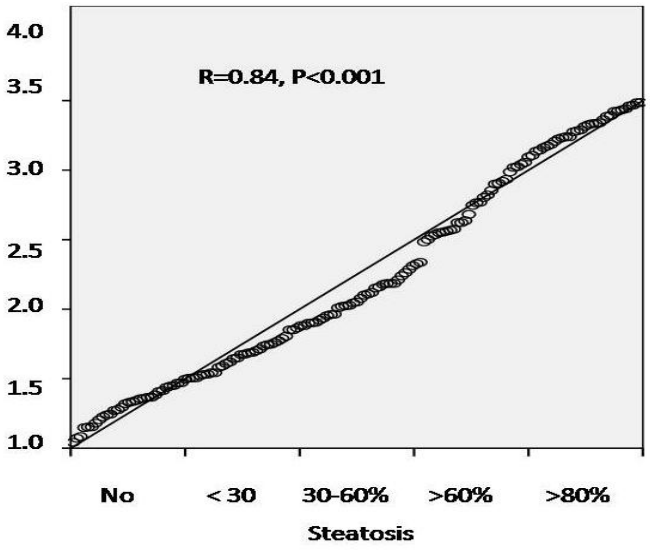
Table 2: Lipid profile, blood sugar and liver functions in patients and controls:

Parameter	**NAFLD Patients (n=126)**	**Control (n=26)**	**P value**
Cholesterol (mmol/L)	7.60±1.13	6.15±2.08	0.032*
Triglycerides (mmol/L)	3.16±1.16	2.00±0.88	0.02*
FBS *(80-110mg/dl)*	125.2±18.1	97.4±16.3	0.032*
HOMA IR <2 2-4 >4	 12% 53% 35%	 73% 23% 2%	
ALT (IU/L)	85.02±48.74	31.12±10.13	0.0001*
AST (IU/L)	77.47±49.97	29.04±13.16	0.0001*

A positive significant correlation was detected between triglyceride level and the degree of steatosis as shown in figure 1

Figure 1: Correlation between triglyceride levels and degree of steatosis detected by ultrasound.

Parameter	**NAFLD Patients (n=126)**	**Control (n=26)**	**P value**
Age	41.88±7.64	40.56±9.13	0.4048
Sex Male : female	 76:50	 17:9	 0.0387*
Body mass index	31.45±2.23	25.46±2.21	0.002*
Hemoglobin (gm/dl)	12.84±1.42	13.08±1.47	0.4147
Red blood cells	3.98±0.83	4.00±0.89	0.9014
White blood cells	8556.28±1970.03	8954.00±372.84	0.3283
Platelet	181.73±21.91	182.50±21.06	0.8652
Diabetes mellitus	64 (50.79)	4(15.3%)	0.021*



Analyzing the clinical and laboratory characteristics of patients showed that high BMI, blood sugar, cholesterol and triglycerides are important predictors of NAFLD.

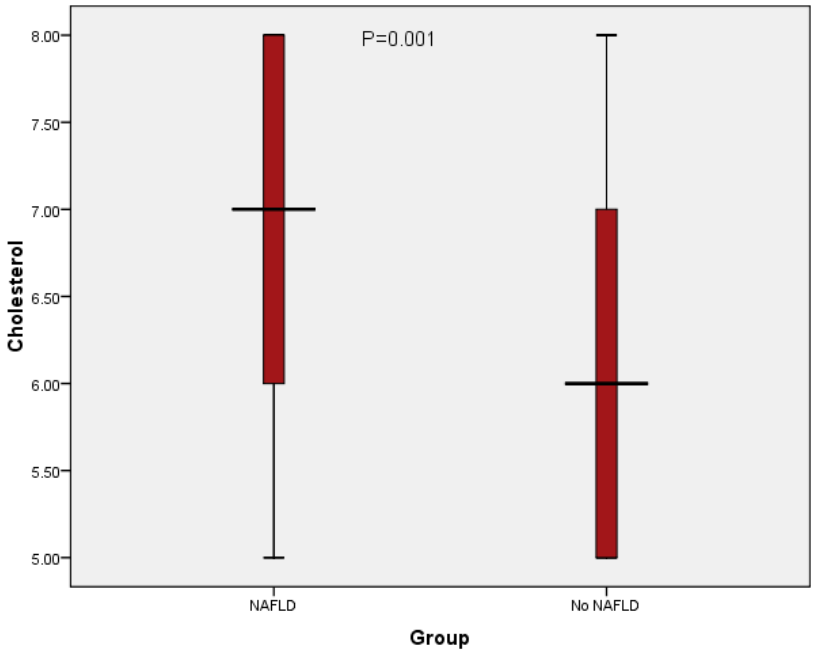
Table (3): Association of baseline predictors and sustained virologic response (SVR) in the 2 studied groups (after adjusting for baseline measurements)

Parameters	**Patient with NAFLD (Steatosis < 30%)**			**Patients with no NAFLD (Steatosis > 30%)**		
	OR	(95% CI)	*P*-value	OR	(95% CI)	*P*-value
Baseline Age [per decade, (older versus younger)]	0.69	(0.18, 2.59)	0.58	0.10	(0.01, 1.86)	0.12
Baseline BMI [per kg/m^2, higher versus lower]	0.99	(0.64, 1.53)	0.96	0.91	(0.50, 1.65)	0.75
Female	2.08	(0.013, 1.55)	0.027	0.05	(0.01, 1.77)	0. 3
Diabetes (present *versus* not present)	1.56	1.24–2.0	0.03	0.17	(0.09, 4.55)	0.4
Triglycerides (>3mmol vs <3mmo)	6.2	9.8–323.2	< 0.0001	3.1	11.3–273.2	0.05

Cholesterol (>6 mmol vs <6 mmol)	3.43	(0.03, 383.2)	< 0.0001	0.0371	(0.03, 6.7)	0. 031
HOMA IR >4	4.11	1.3-9.76	< 0.0001	0.314	(1.7-11.9)	0.026
Steatosis <30	4.8	0.9-17.4	0.002	5.2	1-21.4	0.004
Baseline ALT [per 10 U/L (higher versus lower)]	0.95	(0.79, 1.15)	0.62	0.12	(0.55, 1.21)	0.032

BMI, body mass index; ALT, alanine aminotransferase; HCV, hepatitis C virus; RVR, rapid virologic response; EVR, early virologic response; OR, odds ratio, CI, confidence interval. *

Figure 2: Cholesterol Level in NAFLD Patients and Control



*The cholesterol levels significantly differ between the two groups.

DISCUSSION

The characteristic features of NAFLD have not been adequately studies in Saudi Arabia. In the present study, we found that NAFLD was closely associated with obesity and diabetes mellitus. Diabetes and NAFLD often coexist, and there is evidence to suggest that diabetes can have a significant adverse effect on patients with NAFLD, leading to increased complications and premature mortality.[13] The liver plays a unique role in controlling carbohydrate metabolism by maintaining glucose concentration in a normal range, expressing a number of enzymes that are alternatively turned on or off depending on whether blood glucose levels are either rising or falling. In the post absorptive state 75% of total glucose disposal occurs in insulin- dependent tissues, approximately 50% in the brain and 25% in the splanchnic area including the liver. glucose utilization, which averages approximately 2mg/kg/min. Gluconeogenesis accounts for a substantial fraction (64%) of total glucose production even during the first 22 hours of a fast in humans. [14,15]

In Western countries, NAFLD is the most common liver disease and is a major cause for liver transplantation with a prevalence of 20-30%. In Asia-Pacific regions, the prevalence of NAFLD ranges from 5 to 30%.[16,17]. In KSA, AL-Hamoudi *et al*, 2012 reported that the NAFLD prevalence rates range of 7-10% among Saudis .[17]

In our study, we found that NAFLD was more frequent in males than females. Our findings are in agreement with the study Kopley *et al*, 2011[18]. We have observed abnormal values of serum ALT levels in all patients compared to controls with an independent association between higher ALT levels and high cholesterol and triglyceride levels as well as blood sugar levels. A correlation was established between triglyceride levels and fasting and post-prandial sugar values. Younossi *el al 2011* showed in community-based cross-sectional and case-controlled studies that ALT levels were independently related to blood sugar levels in patients with NAFLD.[19]

In conclusion in this study we have shown that there is a strong correlation between obesity, high glucose level and NAFLD. Additionally, NAFLD is the most frequent chronic disease among patients attending the liver clinic/ dept. of gastroenterology in the King Salman Bin Abdul Aziz University Hospital Al-Kherj Extreme caution should be taken while treating obese/diabetic patient for probable liver disease including fibrosis.

REFERENCES

[1] Angelico F, Del Ben M, Conti R, Francioso S, Feole K, Fiorello S, Cavallo MG. et al. Insulin resistance, the metabolic syndrome, and nonalcoholic fatty liver disease. J Clin Endocrinol Metab. 2004; 90:1578–1582.
[2] Al-hamoudi W, El-Sabbah M, Ali S, Altuwaijri M, Bedewi M, Adam M, Alhammad A, Sanai F, Alswat K, Abdo A. Epidemiological, clinical, and biochemical characteristics of Saudi patients with nonalcoholic fatty liver disease: a hospital-based study. Annals of Saudi Medicine. 2012 May-Jun; 32:288-92.
[3] Amarapurkar DN, Hashimoto E, Lesmana LA, Sollano JD, Chen PJ, Goh KL. How common is non-alcoholic fatty liver disease in the Asia-Pacific region and are there local differences?. Clinical Gastroenterology and Hepatology. 2007 Jun; 22(6):788-93.
[4] Barghouti, N.A. Younes, L.J. Halaseh, T.T. Said, S.M. Ghraiz. High frequency of low serum levels of vitamin B12 among patients attending Jordan University Hospital. Eastern Mediterranean Health Journal. 2009 Jul-Aug; 15(4):853-60.
[5] Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A. et al. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gatroenterology. 2006; 6:33.
[6] Bedogni G, Miglioli L, Masutti F, Castiglione A, Crocè LS, Tiribelli C. et al. Incidence and natural course of fatty liver in the general population: the Dionysos study. Hepatology. 2007; 46:1387–1391.
[7] Bellentani S, Scaglioni F, Marino M, Bedogni G.Epidemiology of non-alcoholic fatty liver disease. Digestive Diseases 2010; 28(1):155-61.
[8] Browning JD, Szczepaniak LS, Dobbins R, Nuremberg P, Horton JD, Cohen JC, Grundy SM, Hobbs HH. Prevalence of hepatic steatosis in an urban population in the United States: impact of ethnicity. Hepatology. 2004; 40:1387-95.

[9] Caldwell SH, Crespo DM. The spectrum expanded: cryptogenic cirrhosis and the natural history of non-alcoholic fatty liver disease. Journal of Hepatology. 2004;40:578–584
[10] Chen AR, Zhang HG, Wang ZP, et al. C-reactive protein, vitamin B12 and C677T polymorphism of N-5, 10-methylenetetrahydrofolate reductase gene are related to insulin resistance and risk factors for metabolic syndrome in Chinese population. Clin Invest Med. 2010; 33:290-297.
[11] Cylwik B, Czygier M, Daniluk M, et al. Vitamin B12 concentration in the blood of alcoholics. Pol Merkur Lekarski. 2010; 28:122-125.
[12] Ermens AA, Vlasveld LT, Lindemans J. Significance of elevated cobalamin (vitamin B12) levels in blood. Clin Biochem. 2003; 36:585-590.
[13] Farrell GC, Larter CZ. Nonalcoholic fatty liver disease: from steatosis to cirrhosis. Hepatology. 2006; 4:S99–S112.
[14] Fora MA, Mohammad MA. High frequency of suboptimal serum vitamin B12 level in adults in Jordan. SAUDI MEDICAL JOURNAL. 2005 Oct; 26(10):1591-5.
[15] Foster T, Anania FA, Li D, Katz R, Budoff M. The prevalence and clinical correlates of nonalcoholic fatty liver disease (NAFLD) in African Americans: the multiethnic study of atherosclerosis (MESA). Digestive Diseases and Sciences. 2013 Aug; 58:2392-8.
[16] Fragasso A, Mannarella C, Ciancio A, et al. Functional vitamin B12 deficiency in alcoholics: an intriguing finding in a retrospective study of megaloblastic anemic patients. Eur J Intern Med. 2010; 21:97-100.
[17] Gambino R, Cassader M, Pagano G. Meta-analysis: Natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Annals of Medicine 2011; 43(8):617-49.
[18] Hamaguchi M, Kojima T, Takeda N, et al. The metabolic syndrome as a predictor of non-alcoholic fatty liver disease. Ann Intern Med 2005; 143(10):722-8.
[19] Jacobs M, van Greevenbroek MM, van der Kallen CJ, et al. The association between the metabolic syndrome and alanine amino transferase is mediated by insulin resistance via related metabolic intermediates (the Cohort on Diabetes and Atherosclerosis Maastricht study). Metabolism. 2010.
[20] Kavimandan A, Sharma M, Verma AK, Das P, Mishra P, Sinha S, Mohan A, Sreenivas V, Datta Gupta S, Makharia GK. Prevalence of celiac disease in nutritional anemia at a tertiary care center.
[21] Kleiner DE, Brunt EM, Van NM, Behling C, Contos MJ, Cummings OW, .. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology. 2005; 41:1313–1321.
[22] Koplay M, Gulcan E, Ozkan F. Association between serum vitamin B12 levels and the degree of steatosis in patients with nonalcoholic fatty liver disease. Journal of Investigative Medicine. 2011 Oct; 59(7):1137-40.
[23] Lazo M, Hernaez R, Eberhardt MS, Bonekamp S, Kamel I, Guallar E, Koteish A, Brancati FL, Clark JM. Prevalence of nonalcoholic fatty liver disease in the United States: the Third National Health and Nutrition Examination Survey, 1988-1994. American Journal of Epidemiology. 2013 Jul 1; 178(1):38-45.
[24] Lee JY, Kim KM, Lee SG, Yu E, Lim YS, Lee HC, Chung YH, Lee YS, Suh DJ. Prevalence and risk factors of non-alcoholic fatty liver disease in potential living liver donors in Korea: a review of 589 consecutive liver biopsies in a single center. J Hepatol. 2007;47(2):239-44
[25] Leite NC, Salles GF, Araujo AL, Villela-Nogueira CA, Cardoso CR. Prevalence and associated factors of non-alcoholic fatty liver disease in patients with type-2 diabetes mellitus. Liver Int. 2009; 29:113–119.
[26] Neuschwander-Tetri BA. Hepatic lipotoxicity and the pathogenesis of nonalcoholic steatohepatitis: the central role of nontriglyceride fatty acid metabolites. Hepatology 2010; 52:774-788.
[27] Pflipsen MC, Oh RC, Saguil A, Seehusen DA, Seaquist D, Topolski R. The prevalence of vitamin B(12) deficiency in patients with type 2 diabetes: a cross-sectional study. The Journal of the American Board of Family Medicine. 2009 Sep-Oct; 22(5):528-34.
[28] Powell EE, Jonsson JR, Clouston AD. Dangerous liaisons: the metabolic syndrome and nonalcoholic fatty liver disease. Ann Intern Med. 2005;143:753–754
[29] Saverymuttu SH, Joseph AE, Maxwell JD. Ultrasound scanning in the detection of hepatic fibrosis and steatosis. Br Med J (Clin Res Ed) 1986; 292:13–15.
[30] Stabler SP, Allen RH. Vitamin B12 deficiency as a worldwide problem. Annual Review of Nutrition 2004; 24:299-326.
[31] Volkov I, Press Y, Rudoy I. Vitamin B12 could be a "master key" in the regulation of multiple pathological processes. J Nippon Med Sch. 2006;73:65-69
[32] Vuppalanchi R, Chalasani N. Nonalcoholic fatty liver disease and non-alcoholic steatohepatitis: selected practical issues in their management. Hepatology 2009;49:306-317
[33] Williams CD, Stenger J, Asike MI, Torres DM, Shaw J, Contreras M, Landt CL, Harrison SA. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. Gastroenterology 2011; 140:124-131.
[34] Younossi ZM, Stepanova M, Afendy M, Fang Y, Younossi Y, Mir H, Srishord M. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. Clinical Gastroenterology and Hepatology. 2011 Jun; 9(6):524-530.