



RESEARCH ARTICLE

VARIATIONS IN FASTING BLOOD SUGAR AND GLYCOSYLATED HEMOGLOBIN LEVELS IN FATTY LIVER IN NORTH WEST PUNJABI POPULATION

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ABSTRACT

The present study was designed to investigate the variations in fasting blood sugar (FBS) and glycosylated haemoglobin (HbA1C) levels in fatty liver with or without alcohol intake. The main factors responsible for developing fatty liver were alcohol intake, type 2 diabetes mellitus, dyslipidemia and obesity. Fatty liver disease has been broadly classified into alcoholic fatty liver disease (AFLD) and non-alcoholic fatty liver disease (NAFLD). Extensive variations in FBS and HbA1C levels have been reported in fatty liver. It was observed that FBS and HbA1C levels were increased in NAFLD and AFLD patients as compared to the controls. It was observed that change in FBS and HbA1C levels in all the groups of NAFLD when compared to each other were not significant ($p > 0.0001$). All the subjects were evaluated for FBS and HbA1C.

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INTRODUCTION

The liver, a large complex organ, is well designed for its central role in carbohydrate, protein and fat metabolism. Accumulation of abnormal quantity of lipids in the liver, causes fatty liver. Previously, fatty liver was thought to be benign but it has recently become clear that fatty liver is a precursor of the more advanced liver disease, nonalcoholic steatohepatitis, a condition that may progress to cirrhosis in approximately 25% of patients¹. Fatty liver disease (hepatic steatosis) based on etio-pathogenesis was divided into two categories which is Alcoholic Fatty Liver Disease (AFLD) and Non Alcoholic Fatty Liver Disease (NAFLD)².

Extensive variations in FBS and HbA1C levels have been reported in Non-alcoholic Fatty Liver Disease (NAFLD) in different populations. There is no sufficient data available on the racial differences in the incidence of fatty liver disease and associated variations in FBS and HbA1c levels, so needs further studies.

In the past, excess alcohol consumption accounted for the majority of cases of fatty liver disease (FLD), but recently nonalcoholic causes of fatty liver disease have attracted considerable attention. Numerous studies have demonstrated that obesity, type 2 diabetes, dyslipidemia, hypertension, and insulin resistance are strongly associated with NAFLD. Non-

alcoholic fatty liver disease (NAFLD) is a clinicopathologic entity increasingly recognized as a major health burden in developed countries³. NAFLD is more frequent among people with diabetes and obesity, and it is almost universal among diabetic people who are morbidly obese⁴.

NAFLD encompasses a histological spectrum ranging from simple hepatic steatosis to nonalcoholic steatohepatitis (NASH), advanced fibrosis, and cirrhosis⁵.

The diagnosis of NAFLD was based on biochemical criteria and imaging (hepatic ultrasound). Characteristic ultrasonographic findings include a hyperechoic liver with or without hepatomegaly. Hamaguchi *et al* reported that ultrasonography has high sensitivity (91.7%) and specificity (100%) in detecting fatty liver⁶. Non alcoholic fatty liver disease is one of the most common cause of chronic liver disease⁷. Non alcoholic fatty liver is the object of significant scientific and clinical interest which is going to increase in the following years.

FBS and HbA1C levels in patients with Non-alcoholic Fatty Liver Disease were reported to be significantly higher than in control group which comprised of normal healthy individuals. It has been shown that excess deposition of fat in liver, usually termed non-alcoholic fatty liver disease, has strong cross-sectional associations with obesity, insulin resistance and type-2 diabetes mellitus⁸. Type-2 diabetes mellitus induced

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hyperglycemia enhances the pathogenicity of Non-alcoholic fatty liver diseases by increasing triglycerides, LDL-C and glucose formation⁹. The type-2 diabetic patients have more liver fat and more intra-abdominal fat than the non-diabetic subjects¹⁰. All the risk factors of fatty liver are common in North West Punjabi population, having a rich life style associated with fatty diet and chronic alcoholism. Hence it will be interesting to investigate the variations in FBS and HbA1C levels as predictors of developing fatty liver disease (AFLD and NAFLD) in North West Punjabi population.

The prevalence of NAFLD has increased over the last two decades and it affects approximately 30% of adults in the United States¹¹. Fatty liver disease has a benign clinical course, as long as inflammatory injury of the liver does not develop¹². Nonalcoholic Fatty Liver Disease (NAFLD) has become a global epidemic, and its prevalence is estimated to be 20–30% in general population of Western countries¹³. T2DM is commonly associated with dyslipidemia and hyperglycemia in NAFLD patients. Regardless of baseline insulin concentration, individuals with fatty liver had significantly ($p < 0.001$) more baseline clinical and metabolic abnormalities, including higher glucose and triglyceride concentration and lower high-density lipoprotein cholesterol concentration¹⁴.

Nonalcoholic fatty liver disease (NAFLD) frequently coexists with obesity, diabetes, and dyslipidemia¹⁵. The proportion of obesity and hyperlipidemia was higher in type 2 diabetes patients with fatty liver than without fatty liver¹⁶. Non alcoholic steatohepatitis (NASH) has been noted in 34% to 75% of patients with an increased plasma glucose concentration¹⁷. An autopsy study noted a trend toward a higher prevalence of NASH in patients with type 2 diabetes, whereas in contrast with type 2 diabetes, fatty liver is rare in subjects with type 1 diabetes mellitus¹⁸. So non alcoholic fatty liver disease (NAFLD) is rapidly becoming an important problem. If undiagnosed, this condition may progress silently and results into cirrhosis, portal hypertension, and liver-related death in early adulthood.

Aims And Objectives

1. To investigate variations in fasting blood sugar and glycosylated hemoglobin levels in alcoholic fatty liver disease in North West Punjabi Population.
2. To investigate variations in fasting blood sugar and glycosylated hemoglobin levels in non- alcoholic fatty liver disease associated with diabetes mellitus type 2, obesity and dyslipidemia in North West Punjabi Population.
3. To compare the levels of difference in fasting blood sugar and glycosylated hemoglobin levels in AFLD and NAFLD in the given population.

MATERIAL AND METHODS

The present study was undertaken in the department of biochemistry in collaboration with department of radiology, Govt. Medical College, Amritsar. It was a case control randomized prospective study. A total of 200 subjects were

included in the present study. These subjects were divided into 3 groups

- Group 1:** Hundred (n=100) age and sex matched healthy individuals were recruited as control from the general population.
- Group 2:** 50 NAFLD Patients. The subjects in this group were further stratified on the basis of risk factors of fatty liver such as diabetes mellitus type 2, dyslipidemia and obesity.
- Group 3:** 50 AFLD Patients. This group shall comprise of patients with only alcoholic fatty liver disease (AFLD).

The subjects suffering from other conditions that may alter the FBS were excluded from the study such as thyroid disorders, tuberculosis, coronary artery disease, malignancies, or subjects on hormone therapy and hypoglycemic drugs etc. The subjects included in the study were assessed for FBS and HbA1C. A comparison of FBS and HbA1C was done in patients of AFLD, NAFLD and normal healthy individuals.

Statistical analyses

The groups were individually compared by applying Students T test and ANOVA test was applied to calculate significance of difference in means of various parameters between the groups included under NAFLD patients. MS- office 2010 was used to perform the analysis.

RESULT

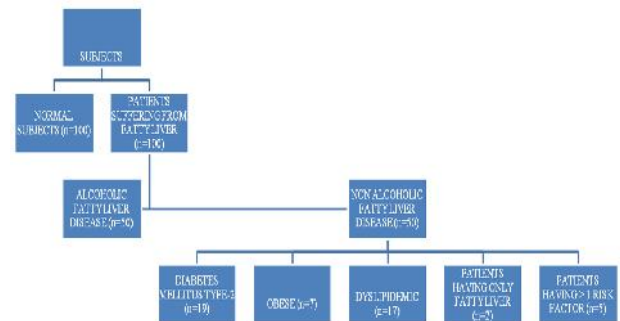


Figure 1 Classification Of Subjects (Normal Subjects And Fatty Liver Disease Patients)

Table 1 Variations In Fbs And Hba1c Levels In Patients Of Nafld, Afld And Normal Healthy Individuals

Group	N	FBS		HbA1c	
		Range	Mean ± SD (in mg%)	Range	Mean ± SD (in %)
Group-I (Normal subjects)	100	65-128	88.79±14.84	4.4-6.0	5.12±0.45
Group-II (NAFLD)	50	65-220	129.5±44.07	4.5-9.1	6.49±1.38
Group-III (AFLD)	50	65-288	104.84±41.12	4.5-10.5	5.74±1.27
T&P value	Gp I vs II	p<0.0001, HS	t= 8.3606	p<0.0001, HS	t= 9.0376
	Gp I vs III	p>0.0001, HS	t= 3.4847	p<0.0001, HS	t= 4.3749
	Gp II vs III	p>0.0001, HS	t= 2.8930	p>0.0001, HS	t= 2.8278

Table-1 shows comparison of FBS and HbA1c in normal individuals and patients suffering from NAFLD and AFLD. It was observed that FBS and HbA1c were increased in NAFLD and AFLD patients as compared to the controls. The difference in the levels of FBS and HbA1c in group I and group II were highly significant (HS) ($p < 0.0001$) with the levels of FBS and HbA1c increased in group II. The difference in the level of FBS was significant ($p > 0.0001$) and the difference in the level of HbA1c was also significant ($p < 0.0001$) in group I and group III with the levels of FBS and HbA1c increased in group III. The difference in the levels of FBS and HbA1c in group II and group III were also significant ($p > 0.0001$) with the levels of FBS and HbA1c decreased in group III.

Table 2 Distribution Of Subjects Having Non Alcoholic Fatty Liver Diseases (Nafld)

Subjects	No of subjects
DM Type-2	19
Obese	7
Dyslipidemic	17
Patients having only Fatty Liver	2
Patients having > 1 risk factor	5

Table 3 Variations In Fbs And Hba1c Levels In Nafld Patients

Group	N	FBS		HbA1c	
		Range	Mean ± SD (in mg%)	Range	Mean ± SD (in %)
DM type - 2	19	104-220	166.94±30.61	4.8-9.1	7.46±0.99
Obese	07	65-108	85.14±15.06	4.5-6.0	5.3±0.46
Dyslipidemic	17	68-178	103.29±33.28	4.6-8.5	5.59±1.04
Patients having only fatty liver	02	105-109	107±2.82	4.9-5.8	5.35±0.63
Patients with > 1 risk factor	05	122-178	157.8±23.76	6.1-8.5	7.76±0.96
ANOVA			F= 16.795, P= <0.0001 HS	F= 14.5713 P <0.0001 HS	

As shown in the Table 2, 19 subjects had DM Type-2, 7 were obese and 17 were dyslipidemic. Whereas, 2 subjects had only fatty liver without any associated risk factor while, 5 subjects had >1 risk factors.

Table - 3 shows comparison of FBS and HbA1c in patients suffering from NAFLD. Statistical analysis revealed highly significant ($p < 0.0001$) change in mean FBS and HbA1c levels when all the groups were compared together.

DISCUSSION

The liver plays a major role in metabolism, digestion, detoxification and elimination of substances from the body. The liver carries out a large number of critical functions, including manufacturing of essential proteins and metabolism of fats and carbohydrates. Fatty liver disease (steatosis) is a build-up of excess fat in the liver cells. In some cases, fatty liver disease damages the organ and leads to serious complications such as cirrhosis. Risk factors for fatty liver disease include overweight and obesity, diabetes, hyperlipidemia and alcohol consumption. Alcohol dehydrogenase and acetaldehyde dehydrogenase cause the reduction of nicotinamide adenine dinucleotide (NAD) to NADH (reduced form of NAD). The altered ratio of NAD/NADH promotes fatty liver through the inhibition of gluconeogenesis and fatty acid oxidation¹⁹.

In the present study, it was observed (Table 1) that FBS and HbA1c levels were increased in NAFLD and AFLD patients as compared to the controls. The mean FBS levels were found to be 88.79±14.84, 129.5±44.07 and 104.84±41.12 mg% in normal healthy individuals, NAFLD and AFLD patients. The mean HbA1c levels were found to be 5.12±0.45, 6.49±1.38 and 5.74±1.27 % in normal healthy individuals, NAFLD and AFLD patients. The difference in the levels of FBS and HbA1c in group I and group II were significant ($p < 0.0001$) with the levels of FBS and HbA1c increased in group II. The difference in the levels of FBS were significant ($p > 0.0001$) and the difference in the levels of HbA1c were also significant ($p < 0.0001$) in group I and group III with the levels of FBS and HbA1c increased in group III. The difference in the levels of FBS and HbA1c in group II and group III were also significant ($p > 0.0001$) with the levels of FBS and HbA1c decreased in group III.

The prevalence of newly diagnosed impaired fasting glucose was significantly higher in the participants with fatty liver than without fatty liver in both sexes²⁰.

Patients suffering from non alcoholic fatty liver (NAFLD) were further segregated into 5 groups according to the associated risk factors such as type-2 diabetes mellitus, obesity and dyslipidemia. In the present study, as shown in the (Table 2), 19 out of 50 non alcoholic fatty liver disease patients had DM Type-2, 7 out of 50 non alcoholic fatty liver disease patients were obese and 17 were dyslipidemic. Whereas, 2 subjects had only fatty liver without any associated risk factor while, 5 subjects had >1 risk factors.

In the present study, it was observed (Table 3) that mean FBS levels in patients of DFL was found to be 166.94±30.61 mg% whereas in patients of NAFLD associated with obesity it was 85.14±15.06 mg% and in dyslipidemic NAFLD patients it was 103.29±33.28 mg%. The mean FBS level in patients having only fatty liver was found to be 107±2.82 mg% whereas in patients of NAFLD with more than 1 risk factor it was 157.8±23.76 mg%. The mean HbA1c level in patients of DFL was found to be 7.46±0.99 %, whereas in patients of NAFLD associated with obesity it was 5.3±0.46 % and in dyslipidemic NAFLD patients it was 5.59±1.04 %. The mean HbA1c level in patients having only fatty liver was found to be 5.35±0.63 % whereas in patients of NAFLD with more than 1 risk factor it was 7.76±0.96 %. Statistical analysis revealed highly significant ($p < 0.0001$) change in mean FBS and HbA1c levels when all the groups were compared together. According to a study on Asian people, fatty liver was more prominent in men. However, in our study, the male-to-female ratio was almost equivalent. This might also represent the difference between the prevalence of fatty liver in the general population and that in type 2 diabetes mellitus patients. The prevalence of fatty liver varies from 10 to 20% in the general population²¹ and increases to 50-75% in subjects with type 2 diabetes mellitus²².

CONCLUSIONS

It was a case control randomized prospective study. Fatty liver was diagnosed in these patients by ultrasonographic examination. It was observed that FBS and HbA1c levels were

increased in NAFLD and AFLD patients as compared to the controls. The difference in the levels of FBS and HbA1c in group I and group II were significant ($p < 0.0001$) with the levels of FBS and HbA1c increased in group II. The difference in the level of FBS was significant ($p > 0.0001$) and the difference in the level of HbA1c was also significant ($p < 0.0001$) in group I and group III with the levels of FBS and HbA1c increased in group III. The difference in the levels of FBS and HbA1c in group II and group III were also significant ($p > 0.0001$) with the levels of FBS and HbA1c decreased in group III.

In NAFLD patients (n=50), 38 % patients had DM Type-2 (19 out of 50), 14 % patients had Obesity (7 out of 50), 34% patients had Dyslipidemia (17 out of 50), 4% patients (2 out of 50) had only fatty liver without any associated risk factor and 10% patients (5 out of 50) had >1 risk factor.

FBS and HbA1c levels were significantly increased in diabetic NAFLD patients as compared to the other groups included under NAFLD. The change in the mean FBS and HbA1c levels in all the groups of NAFLD when compared to each other were also significant.

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