ORIGINAL RESEARCH PAPER

General Medicine

OBSERVATION OF PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN PREDIABETICS

KEY WORDS: Pre-diabetics, Non alcoholic fatty liver disease

Dr. Rahul Anand Junior Resident, Department Of General Medicine, Patna Medical College & Hospital, Patna- 800004

Dr. Madan Pal Singh* Professor & Head Of Dept., Department Of General Medicine, Patna Medical College & Hospital, Patna- 800004 *Corresponding Author

ABSTRACT

INTRODUCTION: Non-Alcoholic fatty liver disease is the most common chronic liver disease in most parts of the world, specially industrialized countries. NAFLD is strongly associated with overweight/obesity and insulin resistance. The simultaneous occurrence of NAFLD and type 2 diabetes is common. Hence, there is a strong possibility that NAFLD may be more prevalent among prediabetics than general population.
AIM: To find out prevalence of Non-Alcoholic Fatty liver disease in prediabetics.
METHODS: In this cross-sectional study, 50 diagnosed cases of prediabetics were compared with 50 euglycemic people after random selection from OPD for NAFLD by using various biochemical parameters and ultrasonography.
RESULT: It was found that 40% of prediabetic population has NAFLD compared to only 16% in control population. The difference was significant (p=0.0135).
CONCLUSION: So we conclude that prediabetes is an independent risk factor for the development of NAFLD.

INTRODUCTION:

Pre-diabetes is the state that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of diabetes. It is comprised of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), depending on the test used to diagnose it. Some people have both IFG and IGT. IFG is a condition in which the blood sugar level measured in plasma is 100 to 125 mg/dL after an overnight fast. IGT is a condition in which the blood sugar level measured in plasma is 140 to 199 mg/dl 2-hour after oral glucose tolerance test (i.e. after 75 mg glucose load at 0-hr followed by plasma glucose estimation at 2-hr).

Nonalcoholic fatty liver disease (NAFLD) describes a range of conditions involving the liver that affect people who drink little or no alcohol. The mildest type is simple fatty liver (steatosis), an accumulation of fat within your liver that usually causes no liver damage. A potentially more serious type, nonalcoholic steatohepatitis (NASH), is associated with liver-damaging inflammation and, sometimes, the formation of fibrous tissue. In some cases, this can progress either to cirrhosis, which can produce progressive, irreversible liver scarring, or to liver cancer. So it encompasses spectrum of liver diseases ranging from simple steatosis to steatohep atitis, advanced fibrosis, and cirrhosis.

Association between the metabolic syndrome and NAFLD has been shown and many researchers consider NAFLD to be a manifestation of the metabolic syndrome. As prediabetes and NAFLD both are parts of metabolic syndrome association between these two are indicated in different researches. In Indian studies, fasting glucose level comes out to be an independent risk factor for development of NAFLD. Similarly, positive correlation with insulin resistance which is the pathophysiologic basis of IFG is indicated in western countries also. On the basis of the above discussion, there is a strong possibility that non-alcoholic fatty liver disease may be more prevalent among prediabetics than general population.

This is the basis of undertaking the present study designed to determine prevalence of NAFLD in prediabetes population from eastern India.

AIM

To determine the actual prevalence of non-alcoholic fatty liver disease in subjects with pre-diabetes

METHODS

STUDY POPULATION:
Subjects with prediabetes selected those attending Medicine OPD and those admitted in Medicine ward of Patna Medical College and Hospital. Both case and control population are matched according to age and sex distribution. They are also matched with respect to LDL-C, HDL-C and TG

STUDY PERIOD:
One and Half Year (March 2018 to August 2019)

SAMPLE SIZE:
50 subjects in prediabetic cohort and same no. of subjects as control cohort having normal fasting glucose (NFG) or normal glucose tolerance (NGT)

STUDY TECHNIQUE:
Cross sectional observational comparative study.

STUDY DESIGN: Prevalence study

STATISTICAL ANALYSIS:
Prevalence of NAFLD is determined by Fisher's exact test. Prevalence of NAFLD in relation to either IFG or IGT is determined by comparing means by independent t- test. The data for prevalence of NAFLD in pre-diabetic population will be analyzed with standard statistical software (SPSS version 19.0).

SAMPLE DESIGN:
CASE SELECTION:
A. INCLUSION CRITERIA:-

i. Age: 18-60 years
ii. Presence of prediabetes
iii. Non-alcoholic.
iv. Patients consenting to undergo radiological investig ation.

B. EXCLUSION CRITERIA:-

i. Age :< 18 years or >60 yrs.
ii. Acutely ill patients such as overt cardiac, renal, hepatic, respiratory failure or recent stroke.
iii. Alcoholic subjects. (Defined as history of alcohol intake > 40 gram/week)
iv. Past history of surgery

Jejuno-ileal bypass, Biliopancreatic bypass Gastropexy, Exte nsive loss of small intestines during surgery, *Post liver*

transplantation, Bariatric Surgery

V. HISTORY OF FOLLOWING DRUG INTAKE IN LAST 6 MONTHS:

Corticosteroids
Methotrexate
Glitazones
Amiodarone
Tamoxifen
ASA
Diltiazem
Didanosine
Nifedipine
Cocaine
Zidovudine, Stavudine
Statins
Intravenous tetracycline
Synthetic estrogens
Hypervitaminosis A

vi. History of starvation, rapid weight loss (>3kg in preceding 3 months), or total parental nutrition.
vii. Exposure to hydrocarbons, petrochemicals, or phosphorus.
viii. Infection with HBV, or HCV, or HIV.
ix. Recent pregnancy within 6 months.
x. Positive ANA titer.
xi. History of Reye's syndrome.
xii. History of familial lipid disorders, e.g., a -lipoprotein emia, hypoβ-lipoproteinemia.
xiii. Lipodystrophy syndrome.
xiv. Diabetic subjects
xv. Known liver disease (ALT >3 times normal/p-time >4 + of control).
xvi. BMI >35 & <17 and/or waist –hip ratio ≥1.0 (for males) & ≥0.85 (for females) is to be excluded.

CONTROL SELECTION:

A. INCLUSION CRITERIA:-

i. Age: 18-60 years.
ii. Normal fasting glucose or normal glucose tolerance.
iii. Non-alcoholic.
iv. Patients consenting to undergo radiological investi gation.

B. EXCLUSION CRITERIA: -

i. Age :< 18 years or >60 yrs.
ii. Alcoholic subjects. (Defined as history of alcohol intake > 40 gram/week).
iii. Past history of surgery:

Jejuno-ileal bypass,
Gastropexy,
Biliopancreatic bypass,
Extensive loss of small intestines during surgery,
Post liver transplantation,
Bariatric surgery

iv. History of following drug intake in last 6 months:

Corticosteroids
Methotrexate
Tamoxifen,
Diltiazem
Nifedipine
Synthetic estrogens
Zidovudine
Stavudine
Statins
Glitazones
Amiodarone
ASA
Intravenous tetracycline
Didanosine
Cocaine
Hypervitaminosis A

v. History of starvation, rapid weight loss (>3kg in preceding 3 months), or total parental nutrition.
vi. Exposure to hydrocarbons, petrochemicals, or phosphorus.
vii. Infection with HBV, or HCV, or HIV.
viii. Recent pregnancy within 6 months.
ix. Positive ANA titer.
x. History of Reye's syndrome.
xi. History of familial lipid disorders, e.g., aβ-lipoproteinemia, hypoβ-lipoproteinemia.
xii. Lipodystrophy syndrome.
xiii. Known liver disease (ALT >3 times normal/p-time >4 + of control).
xiv. BMI >35 & <17 and/or waist –hip ratio ≥1.0 (for males) & ≥0.85 (for females) is to be excluded.

STUDY PROTOCOL:

History & Clinical examination followed by Ultrasonography (USG) of upper abdomen

USG CRITERIA FOR DIAGNOSING HEPATIC STEATOSIS:

A. Hyper-echogenicity of liver parenchyma (defined as "hepatorenal echo contrast" based on evident ultraso nographic contrast between the hepatic and right renal parenchyma of the right intercostal sonogram in the midaxillary line).
B. Bright liver.
C. Variable liver volume increase.
D. Deep attenuation-attenuation of ultrasound in sub capsular strata, deep portion of the liver and impaired visualization of the diaphragm.
E. Difficult visualization of portal vein walls, gall bladder walls, & hepatic capsules.
F. Apparent dilatation of vessels (esp. supra-hepatic ones) & biliary duct.
G. False transonic aspect of right kidney parenchyma as opposed to that of the liver.
H. Vessel blurring- based on impaired visualization of the borders of the intrahepatic vessels and narrowing of their lumen.

RESULTS

The mean ± SD age of participants from prediabetic group was 44.1 ± 13.604 years as compared to 42.62 ± 12.843 of control group. Pre-diabetic group had 30(60 %) males while control group had 30 (60 %) males. Of 50 subjects with pre-diabetes, 20 (40%) had evidence of NAFLD on ultrasono graphy, while among 50 subjects from control group, 8 (16%) showed evidence of NAFLD on ultrasonography. This difference was statistically significant (p = 0.0135). The parameters and findings of the study are given in Table No. 1.

PREVALENCE OF NAFLD IN PREDIABETES

Fig No. 1 Parameters of The Study

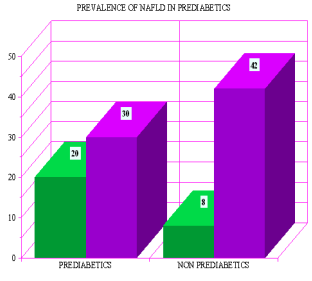

Table No. 1

Parameters	Cases (n=50)			Controls (n=50)			P value
Sex		No.	%		No.	%	1.000
	Male	30	60	Male	30	60	
	Female	20	40	Female	20	40	
	Mean	**SD**		**Mean**	**SD**		

Age	44.1	13.604		42.62	12.843		0.607
Fasting Blood Sugar	107.04	13.674		75.7	14.775		0.00
Oral Glucose Tolerance Test	150.42	25.598		118.66	12.836		0.00
LDL Cholesterol	124.1	44.281		121.94	39.855		0.528
HDL Cholesterol	48.32	18.61		47.0	17.213		0.684
Triglyceride	141.02	63.148		154.12	73.05		0.551
Non alcoholic fatty liver disease		**No.**	**%**		**No.**	**%**	0.0135
	Present	20	40	Present	8	16	
	Absent	30	60	Absent	42	84	

CONCLUSION

Given the high prevalence of prediabetes in population and propensity of NAFLD to progress to chronic liver disease which confer an important public health problem in future (see epidemiology of NAFLD), there is a paramount importance to detect actual percentage of population affected, so that timely intervention in the form of both preventive and therapeutic may be undertaken before this ticking bomb poses a mounting problem to our resource limited health care.

This is the basis of undertaking the present study designed to determine prevalence of NAFLD in prediabetes population from eastern India.

We found that prevalence of NAFLD amongst prediabetics was significantly higher than those without prediabetes.

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