

CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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HOW TO CITE THIS ARTICLE:

Shrawan Kumar, BD Mangal, Ishan Parasher, Manish Kumar Singh, NN Sharma, Pranjal Pankaj. "Cardiovascular risk factors in patients with non alcoholic fatty liver disease". Journal of Evolution of Medical and Dental Sciences 2013; Vol2, Issue 34, August 26; Page: 6584-6593.

ABSTRACT: INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD), comprising a spectrum of condition ranging from pure steatosis to steatohepatitis and cirrhosis. Increasing the recognition of the importance of NAFLD and its strong relationship with metabolic syndrome has stimulated interest in the possible role of NAFLD in the development of cardiovascular disease. **AIMS AND OBJECTIVE:** To study the relationship between 1.Cardiovascular diseases and diabetic patients having non-alcoholic fatty liver.2.Cardiovascular diseases in obese and hypertensive patients having non-alcoholic fatty liver. **MATERIALS AND METHODS:** The study was conducted on 50 diagnosed patients of NAFLD, with objective to identifying the association of various cardiovascular risk factor associated with it.The study was design to study the association or co-relation between NAFLD to various cardiovascular risk factor, diagnosed by standard laboratory, imaging and by physical measurement. We used the standard value of p and chi square for establishing statistically significant association between multiple variables in our study. **RESULTS:** In our study out of 50 patients, 30 male and 20 female patients, 05 males and 03 females in group A, 20 males and 13 females in group B and 05 male and 04 female patients in group C, the p value (≤ 0.05) and chi square value (=15). 50 patients of NAFLD were randomized into two groups, group A (NAFLD with obesity, p value 0.0048, chi value of 10.667) and group B (NAFLD without obesity p = (NA) and chi square value = (NA). Patients of NAFLD were randomized into two groups, group A (NAFLD with diabetes, p value 0.0002 and chi value of 16.8) and group B (NAFLD without diabetes, p value = (NA) and chi square value =NA).Patients of NAFLD were randomized into two groups, group A (NAFLD with Hypertension p value 0.0009 and chi value of 14) and group B (NAFLD without Hypertension disease p value is (NA) and chi square value is (NA). **CONCLUSION:** We hereby conclude from the present study that NAFLD is not only the disease of liver; rather it has statistically high significant association with cardiovascular disease (ischemic heart disease), obesity, diabetes, older age group, male sex, metabolic syndrome etc.

KEYWORDS: NAFLD, FATTY LIVER, CARDIOVASCULAR RISK FACTORS

INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD), comprising a spectrum of condition ranging from pure steatosis to steatohepatitis and cirrhosis. Increasing the recognition of the importance of NAFLD and its strong relationship with metabolic syndrome has stimulated interest in the possible role of NAFLD in the development of cardiovascular disease. The possible molecular mediator linking NAFLD and CVD include the release of pro-atherogenic factors from the liver (C-reactive protein, fibrinogen, plasminogen activator inhibitor-1 and other inflammatory cytokines) as well as contribution of NAFLD per se to whole-body insulin resistance and atherogenic dyslipidemia in turn favoring CVD progression. The clinical impact of NAFLD on CVD risk deserves particular attention in view of implication for screening and surveillance strategies in the growing number of

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patients with NAFLD. Liver is the central for the production of classical biomarkers of inflammation and endothelial dysfunction, the secretion of which partly depends on the factor that are unregulated in the presence of insulin resistance and metabolic syndrome: IL-6 and TNF are the major stimuli responsible for increase hepatic production of C-reactive protein(CRP), fibrinogen and other acute phase protein. The fibrinogen and CRP levels, which are known CVD risk factor, are increased in NAFLD patient.

AIMS AND OBJECTIVE:

1. To study the relationship, if any, between cardiovascular diseases in diabetic patients having non-alcoholic fatty liver.
2. To study the relationship, if any, between cardiovascular diseases in obese and hypertensive patients having non-alcoholic fatty liver.

MATERIAL AND METHODS: The study was conducted on 50 diagnosed patients of non alcoholic fatty liver disease, with objective to identifying the association of various cardiovascular (ischemic heart disease) risk factor associated with it, like diabetes, hypertension, obesity, dyslipidemia etc. The study was design to study the association or co-relation between non alcoholic fatty liver disease to various cardiovascular risk factor, diagnosed by standard laboratory, imaging and by physical measurement. We used the standard value of p and chi square for establishing statistically significant association between multiple variables in our study.

Inclusion criteria:

- Adult above 30 years of age.

Exclusion criteria:

- Person not willing to take participation.
- Adult with increased alcohol intake.
- Patients having any congenital heart disease.
- Patients on the treatment of diabetics.
- Patients on hypolipidemic drugs.
- Smokers.

Defining criteria for the diabetes, hypertension, obesity (BMI), waist circumference and metabolic syndrome.

1. Obesity diagnosis and classification:

BMI is calculated by dividing the subject's mass by the square of his or her height, typically expressed either in metric or US "customary" units.

BMI < 18.5 → normal weight,

BMI = 25.0-29.9 → overweight,

BMI = 30.0-34.9 → Class I obesity,

BMI = 35.0-39.9 → Class II obesity,

BMI ≥ 40.0 → Class III obesity.

2. Criteria for defining diabetes: (WHO criteria)

Fasting plasma glucose level ≥ 7.0 mmol/l (126 mg/dl).

- Plasma glucose ≥ 11.1 mmol/l (200mg/dl) two hours after a 75g oral glucose load as in a glucose tolerance test.
- Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/l (200 mg/dl)
- Glycated haemoglobin (HbA1C) $\geq 6.5\%$

3. Dyslipidemia:

- Triglycerides level 150 mg/dl (1.7mmol/l) or greater.
- HDL-Cholesterol < 40 mg/dl (< 1.04 mmol/l) in men and < 50 mg/dl (< 1.29 mmol/l) in women.

4. Central obesity (measured by BMI):

- Waist circumference > 102 cm (40 inches) in men
- Waist circumference > 88 cm (35 inches) in women
- Central obesity is defined as waist circumference but can be assumed if BMI > 30 kg/m² with ethnicity specific values.

5. Metabolic syndrome:

- WHO criteria (1988).
- Insulin resistance.
- Abdominal obesity (waist-to-hip ratio > 0.9 in men or 0.85 in women, or BMI > 30 kg/m²).
- Triglycerides 150 mg/dl (1.7 mmol/l) or greater, and/or HDL-Cholesterol < 40 mg/dl (1.04 mmol/l) in men and < 50 mg/dl (< 1.29 mmol/l) in women.
- Blood pressure $\geq 140/90$ mm Hg.

RESULTS AND OBSERVATION: The study was conducted on 50 diagnosed patients of non alcoholic fatty liver disease, with objective to identifying the association of various cardiovascular (ischemic heart disease) risk factor associated with it, like diabetes, hypertension, obesity, dyslipidemia etc.

The patient was divided in to three age groups,

Group A \rightarrow 30-49 years

Group B \rightarrow 50-69 years

Group C \rightarrow 70-90 years

TABLE - 1. Distribution of age and sex in non alcoholic fatty liver disease

Age group in years	No. of NAFLD	Male	Percentage	Female	Percentage
30-49	08	05	62%	03	37%
50-69	33	20	60%	13	39%
70-90	09	04	44%	05	55%
Total	50	29	58%	21	42%

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P VALUE	= 0.001
CHI VALUE	= 22.31

This test shows very significant association of non alcoholic fatty liver disease with male sex.

TABLE - 2. Association of ischemic heart disease with diabetes in NAFLD

Age group in Years	NAFLD	Patient of ischemic heart disease with diabetes mellitus			
		YES		NO	
30-49	08	02	25%	06	75%
50-69	33	07	21%	26	87%
70-90	09	06	66%	09	50%
TOTAL	50	15		35	

CHI SQUARE VALUE	= 2.8
P VALUE	≤ 0.25

Test is statistically non significant.

TABLE - 3. Relationship between cardiovascular (ischemic) diseases with hypertensive in NAFLD

Age group in years	NAFLD	Ischemic heart disease with hypertension (Group A)		Ischemic heart disease without hypertension (Group B)		Z Value	P Value
30-49	08	02	25%	06	75%	0.08	≥ 0.05
50-69	33	06	18%	27	81%	1.3	≤ 0.05
70-90	09	04	44%	05	55%	1.42	≤ 0.05
Total	50	12		38			

On applying FISHER Z TEST of proportional analysis, **GROUP "A"** of age between 50-69 and 70-90 has significant association with NAFLD.

TABLE - 4. Showing association of ischemic heart disease with hypertension and obesity in non alcoholic fatty liver disease

AGE GROUP	NAFLD	IHD WITH HYPERTENSION	IHD WITH OBESITY
30-49	08	02	03
50-69	33	06	04
70-90	09	04	05
TOTAL	50	12	12
P VALUE		NA	
CHI VALUE		NA	

The test result is not significant due to small sample size.

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TABLE - 5. Cardio-vascular disease (ischemic heart disease): association with or without metabolic syndrome in non alcoholic fatty liver disease.

	NAFLD	IHD WITH MEABOLIC SYNDROME (GROUP A)		IHD WIYHOUT METABOLIC SYNDROME (GROUP B)	
CARDIO VASCULAR DISEASE (ISCHEMIC HEART DISEASE)	30-49	02	25%	04	26%
	50-69	02	25%	08	53%
	70-90	04	50%	03	20%
	50	08		15	

	P VALUE	CHI SQUARE	RESULT
GROUP A	NA	NA	NON SIGNIFICANT
GROUP B	0.2466 (< 0.25)	2.8	75% SIGNIFICANT AT P ≤ 0.25

The test result shows **GROUP A** is not significant and **GROUP B** is significant at **P VALUE < 0.25** which is statistically significant for small sample size.

TABLE - 6. Association of obesity in patients of non alcoholic fatty liver disease.

	AGE GROUP	GROUP A (OBESE)		GROUP B (NON OBESE)	
NON ALCOHOLIC FATTY LIVER DISEASE	30-49	05	18%	03	13%
	50-69	17	62%	16	69%
	70-90	05	18%	04	17%
	50	27		23	

The test result shows significant association of obesity with non alcoholic fatty liver disease.

TABLE - 7. Association of diabetes with non alcoholic fatty liver disease

	AGE GROUP	DIABETIC (GROUP A)		NON DIABETIC (GROUP B)	
NON ALCOHOLIC FATTY LIVER	30-49	02	25%	06	75%
	50-69	20	60%	13	39%
	70-90	08	88%	00	00%
	50	30		19	

	P VALUE	CHI SQUARE VALUE	RESULT
GROUP A	0.0002	16.8	SIGNIFICANT
GROUP B	NA	NA	NONSIGNIFICANT

Test result shows significant association of diabetes with non alcoholic fatty liver disease.

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TABLE – 8. Association of cardiovascular disease (ischemic heart disease) with non alcoholic fatty liver disease.

	AGE GROUP	WITH CARDIOVASCULAR DISEASE (GROUP A)		WITHOUT CARDIOVASCULAR DISEASE (GROUP B)	
NON ALCOHOLIC FATTY LIVER DISEASE	30-49	05	62%	13	37%
	50-69	10	30%	13	39%
	70-90	07	77%	02	22%
		22		28	

	P VALUE	CHI VALUE	RESULT
GROUP A	0.36799(>0.05)	02	NONSIGNIFICANT
GROUP B	NA	NA	NONSIGNIFICANT

	TEST P VALUE	TEST CHI SQUARE VALUE	RESULT
GROUP A	0.79	2.5	NONSIGNIFICANT
GROUP B	0.1738	3.5	NONSIGNIFICANT

Test result shows that there is no relation of obesity with ischemic heart in non alcoholic fatty liver disease.

TABLE – 9. Association of hypertension with non alcoholic fatty liver disease.

	AGE GROUP	HYPERTENSIVE (GROUP A)		NON HYPER TENSIVE (GROUP B)	
NAFLD	30-49	03	11%	05	21%
	50-69	18	66%	15	65%
	70-90	06	22%	03	13%
		27		23	

	P VALUE	CHI SQUARE VALUE	RESULT
GROUP A	0.0009	14	SIGNIFICANT
GROUP B	NA	NA	NONSIGNIFICANT

Test result shows there is significant association of hypertension with non alcoholic fatty liver disease.

TABLE – 10. Association of metabolic syndrome with non alcoholic fatty liver disease.

	Age group	GROUP A (METABOLIC SYNDROME)		GROUP B (NON METABOLIC SYNDROME)	
NAFLD	30-49	02	11%	06	27%
	50-69	11	61%	12	54%
	70-90	05	27%	04	18%
		18		22	

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GROUPS	P VALUE	CHI SQUARE TEST	RESULT
GROUP A	0.0302	07	SIGNIFICANT
GROUP B	NA	NA	NONSIGNIFICANT

The test result shows metabolic syndrome has significant association with non alcoholic fatty liver disease. $p < 0.25$ may be significant for small sample size.

TABLE - 11. Comparison of association of diabetes and metabolic syndrome in non alcoholic fatty liver disease.

AGE GROUP	DIABETES	METABOLIC SYNDROME	NAFLD
30-49	37% 03	25% 02	08
50-69	60% 20	33% 11	33
70-90	100% 09	55% 05	09
	64% 32	36% 18	50

The above result shows that diabetes has greater association with non alcoholic fatty liver disease than metabolic syndrome has.

DISCUSSION: The study was concluded on 50 diagnosed patient of non alcoholic fatty liver disease mainly by USG. Patient was divided into three group according to age, group a (30-49), group b (50-69) and group c (70-90). The study was design to study the association or co-relation between non alcoholic fatty liver disease to various cardiovascular risk factor, diagnosed by standard laboratory, imaging and by physical measurement. We used the standard value of p and chi square for establishing statistically significant association between multiple variables in our study.

Distribution of age and sex in non alcoholic fatty liver disease: In our study on 50 patients, divided into three groups, group a, group b and group c; there were a total of 30 male and 20 female patients, 05 males and 03 females in group a, 20 males and 13 females in group b and 05 male and 04 female patients in group c. the p value (≤ 0.05) and chi square value ($=15$) of the study signify the statistically significant association of male sex with NAFLD.

Association of cardiovascular disease (ischemic heart disease) with diabetes in non alcoholic fatty liver disease: In this study on 50 NAFLD patients, 15 patients (30%) were found to have both ischemic heart disease and diabetes. The chi square value ($=2.8$), and p value (< 0.25) of the test indicate no statistically significant association but p value (< 0.25) indicate 75% significant association which become significant in small sample size. Similar results were found with study of Targhar G, Bertolini L et al (2007)

Association of obesity in non alcoholic fatty liver disease: In this study 50 patient of non alcoholic fatty liver disease were randomized into two groups, group A (NAFLD with obesity) and group B (NAFLD without obesity). Further these were divided into three age groups. On analysis group A has p value 0.0048 and chi value of 10.667, group B has p value = (NA) and chi square value = (NA). On comparative study between group A and B, group A has statistically significant association and similar results were also observed by study of Agarwal AK et al (2011).

Association of diabetes in non alcoholic fatty liver disease: In this study 50 patients of non alcoholic fatty liver disease were randomized into two groups, group A (NAFLD with diabetes) and group B (NAFLD without diabetes). These further divided into three age groups. On analysis

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group A has p value 0.0002 and chi value of 16.8, group B has p value = (NA) and chi square value = (NA). On comparative study between group A and B, group A is statistically significant, similar results were also observed by Mantovani A et al (2012) in their study.

Association of hypertension with non alcoholic fatty liver disease: In this study, 50 patients of non alcoholic fatty liver disease were randomized into two groups, group A (NAFLD with Hypertension) and group B (NAFLD without Hypertension disease). These further divided into three age groups. On analysis, group A has p value 0.0009 and chi value of 14. While in group B, the p value is (NA) and chi square value is (NA) and similar results were also found with study of Catena C et al (2012).

Association of metabolic syndrome with non alcoholic fatty liver disease: In this study, 50 patients of non alcoholic fatty liver disease were randomized into two groups, group A (NAFLD with metabolic syndrome) and group B (NAFLD without metabolic syndrome). These further divided into three age groups. On analysis, group A has p value 0.0302 and chi square value is 07, while in group B, the p value is (NA) and chi square value is (NA). This was supported by Liu CJ (2012).

Comparison of association of diabetes and metabolic syndrome in non alcoholic fatty liver disease: In this study, 50 NAFLD patients were randomized into two groups; Group A (NAFLD patients with diabetes mellitus) and Group B (NAFLD patients with metabolic syndrome). Comparative study was done to find the association between them. Test suggests that diabetes has a greater association with non alcoholic fatty liver disease than does metabolic syndrome have. Association of diabetic with non alcoholic fatty liver disease increases as age advances. Similar results were also observed by Paloma AV et al (2009).

CONCLUSION: We hereby conclude from the present study that **NAFLD** is not only the disease of liver; rather it has statistically high significant association with cardiovascular disease (ischemic heart disease), obesity, diabetes, older age group, male sex, metabolic syndrome etc. So every patient suspected or diagnosed to have non alcoholic fatty liver disease should be investigated for above mentioned disorder for comprehensive management.

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Date of Submission: 11/08/2013.

Date of Peer Review: 12/08/2013.

Date of Acceptance: 22/08/2013.

Date of Publishing: 26/08/2013