Original Research Article

Understand the risk factors associated with non alcoholic fatty liver disease and changes in biochemical parameters in the patients: a prospective study

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ABSTRACT

Background: The true prevalence of both NAFLD and NASH are elusive but estimates based on imaging and autopsy studies suggest that about 20-30% of the adults in United States and western countries have excess fat accumulation in the liver. About 10% of these, strictly speaking about 2-3% of the adult population fulfils the criteria of NASH. True prevalence of NAFLD in Indian patients is not known. So, this study was planned to look for current trend of NAFLD in Indian patients.

Methods: This prospective observational study was conducted in the Department of Medicine on 65 patients with ultra-sonography finding of fatty liver disease with no history of alcohol, in one year study duration.

Results: It is observed that maximum patients are of middle age from age 31-60 years comprising 76% of patients. Out of total patients, 34% and 66% were males and females respectively. Out of 65 patients, 45(69%) had obesity and maximum number of the patients had waist hip ratio and neck circumference more than the cut off value. Out of 65 patients, 19(29%) had hypercholesterolemia and 42(65%) had hyper-triglyceridemia. Out of 65 patients, 32(49%) had higher alanine transaminase (ALT) level and 17(29%) patients had higher AST level. Out of 65 patients, 29(45%) had the homeostasis model assessment of insulin resistance (HOMA-IR) less than cut off value (less than 2.25) and remaining 36(55%) were having HOMA-IR more than 2.25. The sensitivity for the cut off value for HOMA-IR is 72.7% and specificity is 49.1%.

Conclusions: Obesity, neck circumference, and waist hip ratio are higher than its cut off value for both sex, insulin resistance evaluated through HOMA- IR directly relates to the causation of NAFLD but at some extents higher triglyceride levels are also associated but the values of ALT and AST levels did not give any clue in these cases of NAFLD.

Keywords: Alanine transaminase, Cholesterol, Homeostasis model assessment of insulin resistance, Non alcoholic fatty liver disease, Non alcoholic steatohepatitis, Triglyceride

INTRODUCTION

Fatty liver disease in absence of alcohol abuse is now emerging as a major health burden in the world. It represents the hepatic manifestation of the metabolic syndrome, a variably defined aggregate of disorders related to obesity, insulin resistance, diabetes mellitus type 2, hypertension, and hyperlipidemia.[1]

Non alcoholic fatty liver disease (NAFLD) is defined by excessive fat accumulation in the form of triglycerides (steatosis) in liver (>5% of hepatocytes histologically).[2]

A subgroup of the patients have liver cell injury and inflammation in addition to excessive fat (steatohepatitis),that condition is designated as Non Alcoholic Steato-Hepatitis (NASH).

The definition of the NAFLD requires (a) there is evidence of hepatic steatosis, either by imaging or by histology and (b) there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption, use of steatogenic drugs or hereditary disorders.[3] NAFLD is histologically further categorised into NAFL and NASH.

The true prevalence of both NAFLD and NASH are elusive but according to the American association of the study of the liver disease(AASLD) single topic conference held on 20 September 2002 ,estimates based on imaging and autopsy studies suggest that about 20-30% of the adults in united states and western countries have excess fat accumulation in the liver.[4]

About 10% of these, strictly speaking about 2-3% of the adult population fulfils the criteria of NASH. True prevalence of NAFLD in Indian patients is not known. So, this study was planned to look for current trend of NAFLD and associated risk factors, and their role in NAFLD patients in India.

METHODS

This prospective observational study was conducted in the Department of Medicine on 65 patients with ultra-sonographic finding of fatty liver disease with no history of alcohol, from February 2015 to September 2015.

Total 65 patients with ultrasonographic finding of fatty liver disease were selected either on OPD basis or on IPD basis of Department of Medicine, MY Hospital, Indore, MP, India.

Total 65 patients with non-alcoholic fatty liver disease presenting to the Department of Medicine, M.G.M. Medical College & MY Hospital, and Indore, M.P., during the study period, willing to provide their voluntary written informed consent were included in the study. The convenient sampling technique was used.

Inclusion criteria

- All cases of fatty liver disease assessed on imaging.
- Patients of either gender.
- All cases of NAFLD with ongoing alcohol consumption of not taking >21 drinks/week (10 gm/drinks) in males and >14 drinks/week in females for over two years.
- Patients and/or his/her legally acceptable representative willing to provide written voluntary informed consent for participation in the present study.

Exclusion criteria

- Those having history of alcohol abuse more than baseline.
- Those on steatogenic drugs for more than six month.
- Those who cannot be followed during the study period.
- Prisoners and orphans.
- Patients and/or his/her legally acceptable representative not willing to provide written voluntary informed consent for participation in the present study.

After identifying the suitable candidate for the study, patient and/or his/her legally acceptable were explained in detail about the study, its risks/benefits, costs involved, about the study procedures etc. in detail. After getting their verbal approval for participation, a voluntary written informed consent was obtained from patient and/or his/her legally acceptable representative.

After obtaining the consent, the patients having fatty liver disease, but no history of alcohol consumption were asked to undergo following blood investigations viz. RBS, serum cholesterol, serum triglycerides, fasting insulin level, AST, ALT, and then their anthropometric measurements like head circumference, neck circumference, arm circumference, height, weight, waist to hip ratio were measured and recorded. After that he was asked to come for follow up.

Following outcome were measured- RBS, serum cholesterol, serum triglycerides, fasting insulin level, AST, ALT, and then their anthropometric measurements like head circumference, neck circumference, arm circumference, height, weight, and waist to hip ratio were also performed.

Statistical analysis

Statistical analysis was done by the statistician and accordingly the appropriate tests like Mann Whitney 'U' test and Spearman's rho coefficient correlation test were applied. For analysis, statistical software SPSS latest Version 20.0 was used. A p value of <0.05 was considered as statistically significant. In the final report, the data has been represented in the form of tables and graphs.

RESULTS

In our study the total 65 patients with ultra-sonography finding of fatty liver disease without the history of alcohol intake were selected either on OPD basis or on IPD basis of Department of medicine, MY Hospital, Indore, MP, India. The patients were evaluated and asked for various anthropometric measurements, imaging and laboratory investigations were performed. All the parameters were recorded in standard format. Our findings are as follows:

Table 1 shows, total 65 patients were included. In this study most of the patients were of the age group 41-50 years i.e. 33% of total patients and minimum numbers of patient were of the age group 71-80 years with 2% of total patients. With this table it is observed that maximum patients are of middle age from age 31-60 years comprising 76% of patients.

Table 1: Distribution of cases according to age group.

S. No.	Age group	No. cases	Percentage
1	20-30	6	9%
2	31-40	16	25%
3	41-50	21	33%
4	51-60	12	18%
5	61-70	8	12%
6	71-80	2	3%
Total		65	100%

As shown in Table 2, maximum patients i.e. 45 patients are obese constituting 69% of total cases.

Table 2: Distribution of subject according to BMI.

BMI	No. of cases	Percentage
<18.5(underweight)	0	0%
18.5 -22.9 (Normal range)	5	8%
23-24.9(overweight)	15	23%
25-29.9(Obese - I)	23	35%
>30 (Obese - II)	22	34%

Table 3 shows, that in both categories of gender maximum number of the patients had waist hip ratio more than the cut off value. 21(95%) male patients had

Waist Hip Ratio (WHR) more than 90 cm and all female patients had WHR more than 80 cm.

Table 3: Distribution of subject according to Waist Hip Ratio (WHR).

Gender	WHR	No. of cases	Percentage
Male	≤90	1	5%
	≥90	21	95%
Female	≤80	0	0%
	≥80	43	100%

Table 4: Distribution of subject according to neck circumference.

Gender	Neck circumference	No. of cases	Percentage
Male	>35.5 cm	14	64%
	<35.5 cm	8	36%
Female	≥32 cm	42	98%
	< 32 cm	1	2%

Table 4 shows, both categories of gender had maximum number of patients with neck circumference more than the cut off value. 64% males had neck circumference more than 35.5cm and 98% females had neck circumference more than 32cm.

As shown in Table 5, out of 65 patients, 19 patients had hypercholesterolemia i.e. 29% patients had elevated cholesterol levels and remaining 46 patients i.e. 71% were having normal cholesterol level. 42 patients had higher Triglyceride levels i.e. 65% patients had elevated Triglyceride levels and remaining 23 patients i.e. 35% were having normal Triglyceride levels.

Table 5: Distribution of subject according to serum cholesterol and triglyceride levels.

Cholesterol	Case (n)	Percentage	Triglycerides	Cases (n)	Percentage
<200mg/dl	46	71%	≤150mg/dl	23	35%
>200mg/dl	19	29%	≥150mg/dl	42	65%

Table 6: Distribution of subject according to ALT, AST, and HOMA-IR.

ALT (U/L)	Cases (n)	%	AST (U/L)	Cases (n)	%	HOMA-IR	Cases (n)	%
<36	33	51%	<43	48	74%	<2.25	29	45%
>36	32	49%	>43	17	26%	>2.25	36	55%

As shown in Table 6, out of 65 patients, 32 patients had higher ALT level i.e. 49% patients had elevated ALT level and remaining 33 patients i.e. 51% were having normal ALT level. Only 17 patients had higher AST level i.e. 29% patients had elevated AST level and remaining

48 patients i.e. 74% were having normal AST level. 29 patients had the HOMA-IR value less than the cut off value i.e. 45% patients had HOMA-IR less than 2.25 and remaining 36 patients i.e. 55% were having HOMA-IR

more than 2.25. The sensitivity for the cut off value for HOMA-IR is 72.7% and specificity is 49.1%.

DISCUSSION

Total 65 patients with ultra-sonography finding of fatty liver disease without the history of alcohol intake were selected either on OPD basis or on IPD basis of Department of medicine, MY Hospital, Indore, MP, India. The patients were evaluated and asked for various anthropometric measurements, imaging and laboratory investigations were performed.

In this study total 65 patients were included. Most of the patients were of the age group 41-50 years i.e. 33% followed by 31-40 years i.e. 25% and from age group 51-60 years 18% of total patients and minimum number of patients were of the age group 71-80 years with 2% of total patients. So, with this we concluded that maximum patients are of middle age from age 31-60 years comprising 76% of patients. in our study maximum patients (66%) were females and 34% patients were males of total patients. As per study done by Bellentani S et al, prevalence of NAFLD is higher in males and increases with increasing age, with a male-to-female ratio of 2:1.[5]

As per the study done by Hingorio et al, and Roli Agrawal et al, the maximum number of the patients were obese, had neck circumference and waist hip ratio above their cut off value both in males and females.[6,7]

It was found that 45 patients i.e. 69% were obese and maximum number of the patients i.e. 95% males and 100% females had their waist hip ratio above the cut off value and 64% males and 98% females had neck circumference more than the cut off value.

Eung Ju Kim et al, did a study according to them high cholesterol and triglyceride levels are associated with NAFLD and atherosclerosis.[8] Out of 65 patients, only 19 patients had hypercholesterolemia i.e. 29% patients had elevated cholesterol levels and remaining 46 patients i.e. 71% were having normal cholesterol level and 42 patients had higher triglyceride level i.e. 65% patients had elevated Triglyceride levels and remaining 23 patients i.e. 35% were having normal Triglyceride levels that means in our study higher triglyceride levels is more associated with NAFLD then cholesterol levels.

As per Siddharth Verma et al, study that there is no optimal ALT level to predict NASH and advanced fibrosis.[9] Metabolic risk factors should be evaluated to select patients for a liver biopsy to confirm NASH and advanced fibrosis. In our study too out of 65 patients, 32 patients had higher ALT levels i.e. 49% patients had elevated ALT levels and remaining 33 patients i.e. 51% were having normal ALT levels.

Similarly, AST levels in our study also signifies that maximum patients had the normal AST levels in NAFLD i.e. out of 65 patients only 17% patients had higher AST levels i.e. 29% patients had elevated AST levels and remaining 48 patients i.e. 74 % were having normal AST levels.

Li YL et al, conducted a study to investigate the serum leptin and adiponectin levels in NAFLD patients, and their relationship with insulin resistance and concluded increased serum leptin levels and decreased serum adiponectin levels in NAFLD patients independently associated with HOMA-IR but in our study we found that out of 65 patients, 29 patients had the HOMA-IR value less than the cut off value i.e. 45% patients had HOMA-IR less than 2.25 and remaining 36 patients i.e. 55% were having HOMA-IR more then 2.25 for which the sensitivity for the cut off value for HOMA-IR is 72.7% and specificity is 49.1%.[10]

CONCLUSION

Obesity, neck circumference, and waist hip ratio are higher than its cut off value for both genders, insulin resistance evaluated through HOMA-IR directly relates to the causation of NAFLD but at some extents higher triglyceride levels are also associated but the values of ALT and AST levels did not give any clue in these cases of NAFLD.

ACKNOWLEDGEMENTS

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