Clinico-Epidemiology, Risk Factors and Biochemistry of Nonalcoholic Fatty Liver Disease in Medicine OPD of A Tertiary Hospital

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Abstract

Background: Non Alcoholic Fatty Liver Disease (NAFLD) is one of the major causes of end stage liver disease worldwide and increasing in Bangladesh day by day. The study was conducted in Medicine Outpatient Department (OPD) of Chittagong Medical College Hospital to observe the clinic-epidemiology, risk factor and biochemical changes in patients with sonographyically proven NAFLD.

Materials and methods: This was a prospective observational study.Patients presented with ultrasonography having NAFLD were enrolled and case record form were filled up after examination and investigations. Data were analyzed by SPSS 25. For statistical significance students t Tests (Continuous variables) and chi square tests (Categorical variables) were done where appropriate.

Results: Total patients were 110, 71.8% were male, mean age were 40.1±9.5 years, 92.7% were obese though other risk factors were present with variable frequencies. 72.7% were symptomatic whether abdominal discomfort was highest of clinical symptoms that they had (58.2%). Triglyceride was more than 150 mg/dl in 81.8% cases and there was hyper transaminasemia in 80% cases.

Conclusions: This was a small study and there was no histopathologically proven cases but was to do an screening in OPD. Further study would be required to conclude as hypertriglyceridemia and abdominal obesity are the risk factors in NAFLD cases.

Key words: Life style; Non Alcoholic Fatty Liver Disease (NAFLD); Risk factor.

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Introduction

NAFLD is one of the leading causes of chronic liver disease. As the sedentary lifestyle and increasing adherence to western style food consumption is common in modern days NAFLD is becoming more prevalent in the world. NAFLD encompasses a group of conditions where there is an accumulation of excess fat in the liver without significant alcohol use. It includes a range of disorders from isolated Non Alcoholic Fatty Liver (NAFL) without inflammation and Non Alcoholic Steato Hepatitis (NASH) with inflammation, which in turn can eventually lead to fibrosis and cirrhosis.[1] It is defined by presence of steatosis in 5% of hepatocytes or more in the absence of other causes of fatty liver. The metabolic syndrome is the major known risk factor for NAFLD. Dietary contributors such as high fructose intake appear to increase the risk of disease. Genetic associations have also been identified.[2] According to recent estimates, NAFLD affects as many as one billion individuals throughout the world. Similarly, in the USA, NAFLD affects nearly 80-100 million individuals, making it the number 1 etiology of CLD.[3] Nearly 25% of patients with NAFL progress to NASH, however, the true prevalence of biopsy-proven NASH is difficult to determine, as the majority of NAFL patients do not undergo biopsy. Although the prevalence of NAFLD is increasing throughout the world, there appears to be a significant geographical variation. Overall global prevalence of NAFLD is reported to be 25.2%, according to a recent meta-analysis, with the highest rates being in the Middle East (32%) and South America (31%) and the lowest in Africa (14%).[4] NAFLD prevalence was 71.18%, 62.8% and 40.77% among diabetic, hypertensive, and individuals with family history of liver disease, respectively. Respondents with high BMI (Overweight and obesity) have a higher prevalence of NAFLD. In Bangladesh the overall prevalence of NAFLD is 33.86%. Female living in rural areas and middle age adults (45-54years) diabetic,

hypertensive and individuals with increased body mass index are at increased risk of developing NAFLD. High-income individuals had more than 1.5 times higher prevalence of NAFLD than low-income individuals.[5,6] The prevalence of NASH in the general population is estimated to be in the range of 1.5% and 6.45%.[2] However, the true prevalence of NASH is difficult to ascertain, primarily because of inaccuracies of diagnostic modalities used.[4]

It is unequivocal that T2DM, obesity and related metabolic syndrome (Hyperlipidemia, increased waist circumference, hypertension) play a major role in the pathogenesis of NAFLD. According to a large systematic review, involving 222,816 diabetic patients from 25 countries, the NAFLD prevalence in T2DM patients is as high as 61.1%.[7] Similarly, the prevalence of NASH and advanced fibrosis ($F3) in biopsied diabetic patients was reported as 64% and 10.4% respectively.[7,8] NAFLD prevalence increases with increasing body mass index and it is estimated that 95% of morbidly obese patients undergoing weight-loss surgery have NAFLD.[8-10] Among the non-modifiable risk factors, age, sex and ethnicity are implicated in the pathogenesis of NAFLD.[11] According to population studies, NAFLD is more common in males and prevalence increases with age. NAFLD also causes substantial economic impact due to health care dollar spending. The 10-year burden of NAFLD is estimated to reach more than 1 trillion dollars in the USA alone. In Europe, the 10-year burden is expected to reach 334 billion euros.[12]

Several methods (Both proprietary and nonproprietary) have been suggested for minimally invasive quantification of hepatic fat and inflammation and for NASH diagnosis and assessment-including imaging and biomarker panels. However, no widely accepted reliable methods other than liver biopsy are yet available for non- or minimally invasive differentiation and risk estimation of simple steatosis and NASH in routine practice. Moreover, a major barrier for identification of subjects eligible for pharmacological intervention and enrolment in clinical trials is represented by the lack of non- or minimally invasive means of targeting those subjects undergoing liver biopsy that are likely to meet the histopathological criteria for NASH with fibrosis.

It is not possible to accurately differentiate NAFLD from NASH and NASH of different severity and consequently, to select the ideal candidate for experimental trials by using one single marker. Presently, as strategies of treatment for NASH patients at risk of progression are implemented, biomarkers are essential for screening and identification of treatment responses. Noninvasive imaging techniques such as MRI are evolving at increasing pace, and MRI-PDFF currently provides early diagnosis and prognostic information on NAFLD but it is not largely available. Serum biomarkers for fibrosis diagnosis in NASH perform better in excluding advanced fibrosis and cirrhosis rather than accurately diagnosing fibrosis stages. Procollagen C3 levels permit to discriminate between patients with or without histological diagnosis of NASH and a relatively linear relationship with the grade of NASH. Imaging methodologies and, in particular, MRE are accurate although limited by costs and duration of the exams. Emerging OMICS markers may be promising in the early identification of patients at risk of progressing to advanced fibrosis. However, their accuracy is limited by their challenging methodological implementation.[9]

Besides coronary artery disease, several other cardiovascular complications are reported in NAFLD patients, such as premature atherosclerosis to left ventricular dysfunction and hypertrophy, aortic sclerosis, congestive heart failure, and cardiac arrhythmias (atrial fibrillation and prolonged QTc). Based on the recent meta-analysis including 34000 patients, presence of NAFLD is associated with 65% increase in fatal and nonfatal cardiovascular events at medial 7-year follow-up period.[1] Alterations in lipid and lipoprotein metabolism are major contributing factors linking NAFLD to CVD. Moreover, many promising NASH therapies in development also improve dyslipidemia in clinical trials. Given the current lack of approved pharmacological therapies for NASH, a clear understanding of the underlying factors that drive elevated CVD risk in NAFLD will be critical for the effective care and management of this growing patient population.[10]

As the health related burden of NAFLD is high considering its prevalence, risk associations and complications and lack of accurate non or minimally invasive tolls for diagnosis, there is constant need of research in this area. Few studies are available in our country to non-invasively diagnose

NAFLD and its cardiovascular risks assessment. Ultrasound fails to identify the mild form of liver steatosis, up to 50-80% of patients with NAFLD may have normal liver enzymes and the gold standard liver biopsy suffers considerable sampling error.[5] There is considerable lack of consensus for best performing biomarker in diagnosing and follow up of NAFLD, sophisticated imaging techniques are expensive and time consuming too. Novel therapeutic agents are also under active research.[9]

Materials and methods

This descriptive, observational study was conducted in Medicine Outpatient Department of Chittagong Medical College Hospital during March 2015 to August 2015. The study protocol was approved by the ethics review board (Memo no. CMC/PG/2015/22; Date:3/2/2015).

We included the patients from OPD who came to us with an ultrasonographic diagnosis of Non Alcoholic Fatty Liver Disease (NAFLD) after getting consent. Clinical data were taken with interview and clinical examination of the patients. Necessary investigations were asked for. Data were recorded in predesigned Case Record Form (CRF). Data were analyzed with SPSS 25. Categorical variables were summarized as frequencies and percentages. Continuous data were expressed as mean (± Standard deviation). For statistical significance students t Tests (Continuous variables) and chi square tests (Categorical variables) were done where appropriate.

Results

In our study total sample size was 110 (n=110), mean age was 40.1±9.5 years with a male predominance (71.8% vs 28.2%). Service holder (25.5%) businessman (24.1%) and housewives (24.1%) were frequent in occupations, 70% of the patients lived as tenant.We got ultrasonographical Grade 1 (78.1%) and Grade 2 (24.9%) NAFLD though no grade related variation in socio-demography.

Table I : Demographic characteristics stratified NAFLD grading

	Total (n=110)	Grade1 NAFLD (n=86)	Grade 2 NAFLD (n=24)	p value
Age, mean±SD	40.1±9.5	40.3±10.2	39.6±6.6	0.733
Sex				
Male	79 (71.8)	63 (57.3)	16 (14.5)	0.526
Female	31 (28.2)	23 (20.9)	8 (7.27)	

Among the risk factors central obesity was present among 92%(n=102) cases, obesity was present among 87.3%(n=96), 83.6% (n=92) cases had metabolic syndrome. Other risk factors present among the patients were diabetes (29.1%) hypertension (35.5%) Ischaemic Heart Disease (IHD) (30%) smoking (27.3%) sedentary life style (45.5%). No significant differences between grade 1 and grade 2 regarding risk factor.

Table II : Risk factors of respondences

	Total (n=110)	Grade1 NAFLD (n=86)	Grade 2 NAFLD (n=24)	p value
DM	32 (29.1)	26 (23.6.1)	7 (6.3)	0.993
Hypertension	39 (35.5)	27 (24.5)	12 (10.9)	0.092
IHD	33 (30.0)	27 (31.4)	6 (5.4)	0.545
Smoking	30 (27.3)	25 (22.7)	5 (4.5)	0.423
Sedentary	50 (45.5)	40 (36.3)	10 (41.7)	0.673
Overweight/Obesity	96 (87.3)	75 (68.1)	21 (24.5)	0.954
Central obesity	102 (92.7)	79 (71.8)	23 (20.9)	0.683
Metabolic syndrome	92 (83.6)	70 (63.6)	22 (20)	0.229

Among the patients 72.7% (n=80) were symptomatic, rest were asymptomatic. Among symptomatic patients 58.8% (n= 64) were presented with abdominal discomfort, rest symptoms were fatigue (36.5%, n=40) dyspepsia (32.7%, n=36) malaise (11.8%, n=13).

Table III : Clinical features of respondences

	Total (n=110)	Grade1 NAFLD (n=86)	Grade 2 NAFLD (n=24)	p value
Symptomatic	80 (72.7)	63 (57.27)	17 (15.45)	0.814
Fatigue	40 (36.4)	30 (27.27)	10 (9.09)	0.541
Malaise	13 (11.8)	12 (10.9)	1 (0.9)	0.189
Abdominal discomfort	64 (58.2)	51 (46.3)	13 (11.8)	0.652
Dyspepsia	36 (32.7)	26 (23.6)	10 (9.09)	0.291
Palpable liver	25 (22.7)	9 (0.9)	16 (14.5)	<0.001

In laboratory parameter, among the patients hypertriglyceridemia were common 81.8% (90%), in 80%(n=88) patient serum alanine transaminase were more than 40 mg/IU, in 83.6% cases total cholesterol were more than 200 mg/dl.

Table IV : Laboratory parameters of patients

	Total (n=110)	Grade1 NAFLD (n=86)	Grade 2 NAFLD (n=24)	p value
RBS, ≥110 mg/dl	96 (87.3)	72 (65.4)	24 (21.8)	0.034
Cholesterol, ≥200 mg/dl	92 (83.6)	72 (65.4)	20 (18.1)	1.0
LDL, ≥130 mg/dl	33 (30.0)	24 (21.8)	9 (8.1)	0.396
Low HDL	102 (92.7)	80 (72.7)	22 (20)	0.802
TG, ≥150 mg/dl	90 (81.8)	71 (64.5)	19 (17.2)	0.703
ALT, >40 IU	88 (80.0)	66 (60)	22 (20)	0.165

Firm, non-tender, regular surface.

Discussion

NAFLD is a rising problem of the country and becoming the major cause of liver cirrhosis. In our study mean age of the patients was 40.1±9.5 years showing which is a little bit lower than Yinf -Chin Lin et al but higher than (30.91%) in Alam S et al.[13,4] 3rd and 4th decade of life are the most vulnerable age for developing the risk factors of NAFLD.

There is a male preponderance in maximum studies. In our study 71.8% were male. Service holder (25.5%), businessman (24.1%) and housewives (24.1%) were frequent in occupations revealing the association of sedentary life style with NAFLD.

In our study among the risk factors central obesity (Waist hip ratio >0.9 for men, >0.85 for women)was present among 92% (n=102) cases, obesity (BMI>25 kg/m2) was present among 87.3% (n=96), 83.6% (n=92) cases had metabolic syndrome. Other risk factors present in the patients were diabetes (29.1%), hypertension (35.5%), Ischaemic Heart Disease (IHD) (30%) smoking (27.3), sedentary life style (45.5%). No significant differences between Grade 1 and grade 2 regarding risk factor. These findings are similar to Zarean et al.[14] In their study they showed that type 2 DM increase the risk 1.35 times then nondiabetic, obesity, low physical workload increase the risk of NAFLD. In Alam S et al showed hypertension, DM, higher income, family history as risk factor.[4] Diabetes and hypertriglyceridemia were predominant risk factor showed by Yinf -Chin Lin et all.[13] In multiple studies it was shown that components of metabolic syndrome were associated with development of NAFLD. Obesity, specially truncal obesity along with hypertension, DM and hyperlipidemia are the recognized risk factors and need to be modified for prevention and treatment of NAFLD.

In Grade 1 NAFLD maximum cases were asymptomatic. 72% of our patient were symptomatic among them 58.8% had abdominal discomfort and 36.6 % had fatigue, dyspepsia. Many studies showed fatigue and abdominal right upper quadrant pain were the main symptoms in symptomatic cases. This is a silent killer.[14-17]

Among blood biochemistry ALT was elevated mildly in our study as well as others.[18]

Limitations

This study was carried out based on ultrasonographic diagnosis of NAFLD and there was no histopathological confirmation. The sample was collected from outpatient department for which cases with severity were not included in the study.

Conclusion

This is not a large study nor a complete study conclude about NAFLD. Despite of its limitation it demonstrate the picture of nonalcoholic fatty liver disease in our setting. It may act as a precursor of a large,complete study to get the risk factors, clinical and biochemical picture of NAFLD. In short we can say male of $3r^d$ -$4t^h$ decade with obesity and metabolic syndrome are more prone to develop NAFLD.

Recommendation

Larger study should be done for better prediction of risk factors of NAFLD.

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Contribution of authors

RAMEU: Design, conception, acquisition of data, data analysis, drafting and final approval.

MJI: Conception, acquisition of data, drafting & final approval.

SD: Acquisition of data, interpritation of data, data analysis & final approval.

AC: Acquisition of data, data analysis & final approval.

SRC: Acquisition of data, drafting, critical revision & final approval.

MMK: Manuscript drafting, interpritation of data & final approval.

MMH: Data analysis, interpritation data, critical revision & final approval.

Disclosure

All the authors declared no competing interest.

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