Original Article

Prevalence of Non-alcoholic Fatty Liver Disease - A Population Based Study

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Abstract:

Background: Non alcoholic fatty liver disease (NAFLD) is defined as the accumulation of excess fat in the liver in the absence of significant alcohol consumption. NAFLD is a common cause of chronic liver disease. The overall prevalence of NAFLD in western countries varies from 15-40% and in Asian 9-40%. Its prevalence has not been determined in population based study in Bangladesh. The objectives of the study was to determine the prevalence and risk factors of NAFLD in adult rural population. **Methods:** This cross-sectional study was performed among adult population of two villages of Comilla district, Bangladesh from January to December 2015. Persons with alcohol consumption and other liver diseases were excluded. Individuals were undergone anthropometric, blood pressure measurements, thorough medical history and physical examinations. Laboratory measurements included were fasting blood sugar (FBS), fasting lipid profile, and liver function tests. NAFLD was diagnosed by transabdominal ultrasonography. Statistical analyses were performed using the SPSS software, version16.0 **Results:** Among 665 subjects, 213 were males (32%) and 452 were females (68%) with the mean age of 42.2 ± 15.04 years. NAFLD was diagnosed in 33% subjects. NAFLD were high in 41-60 age group (48.7%) and in female gender ($P = < 0.175$). Subjects with NAFLD had higher BMI ($P < 0.001$), higher prevalence of hypertension ($P < 0.001$), high FBS ($P < 0.001$), high cholesterol ($P = 0.026$), high triglyceride ($P < 0.001$) and high waist circumference ($P < 0.001$). Subjects with NAFLD had significantly higher prevalence of metabolic syndrome when compared to healthy subjects ($P < 0.001$). Conclusion: The prevalence of NAFLD in rural adult population of Bangladesh is 33% and is associated with female gender, obesity and features of metabolic syndrome.

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Introduction:

NAFLD is defined as the deposition of lipid, especially triglyceride, in hepatocytes exceeding 5% of total liver weight in the absence of other aetiologies of hepatic damage including hepatitis viruses, alcohol consumption and metabolic diseases[1]. The prevalence of the disease has increased dramatically during the previous decade probably because of both, the changes of life-style, eased physical activity and the increased detection rate[2]. The prevalence of NAFLD in the general population varies according to the type of diagnostic tools used. The overall prevalence of NAFLD in western countries varies from 15-40% and in Asian 9-40%[2-4]. Risk factors such as insulin resistance (IR), oxidative stress, diabetes, dyslipidemia, obesity and metabolic syndrome play an important role in the pathogenesis of this disease[5-8]. Metabolic syndrome and NAFLD shares similar prevalence pattern, pathogenesis, clinical features and outcome[9]. NAFLD is associated with greater overall mortality and independently predicts the risk of future Cardiovascular events[10]. The prevalence and associated risk factors of NAFLD may vary in different geographical region. Its prevalence has not been determined in population based study in Bangladesh.

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Objectives:

- General: The main aim of this population-based study was to determine the prevalence of NAFLD in Bangladeshi rural population.
- Specific:

1. To determine the age and sex prevalence of NAFLD among rural population
2. To identify the risk factors of NAFLD among rural population

Rationale:

Data on the prevalence of NAFLD in Bangladesh is limited. Most of the available studies are hospital based study. This study was designed to see the prevalence of NAFLD and its risk factor in rural population.

Methodology:

This cross-sectional study was performed in two villages of Comilla, Bangladesh during a 12-month period in randomly selected sample of adult general population. All inhabitants older than 18 years were invited to participate. Those who give Informed written consent to take part in this study, made an appointment with the study team for detailed history and physical examination and laboratory testing. Pregnant women or those who had delivered within past six months were excluded from the study. A team of two health assistants and two physicians performed interview, obtain medical histories and physical examinations. Standard questionnaires, designed by co-working of epidemiologists and hepatologists were used in this study. Initial investigation was transabdominal ultrasonograpy. If ultrasonograpy revealed fatty liver by using standard criteria , Intravenous blood samples was drawn from those subject to measure fasting blood sugar (FBS), triglyceride (TG), cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), serum transaminases (alanine aminotransferase), HBsAg and Anti HCV. Participants who reported current use of anti-hypertension or anti-diabetes medications were regarded as having hypertension or diabetes, respectively. NAFLD was diagnosed by means of upper abdominal ultrasonography (US) based on increased echogenicity of the hepatic parenchyma with an attenuation of the portal vein or diaphragm echogenicity. Transabdominal ultrasonography was performed using a Shimadzu ultrasound machine (Shimadzu Inc., Tokyo, Japan) with a 5-MHz to 7-MHz transducer probe (curvilinear). All the ultrasonogrphic evaluations was performed by one experienced radiologist. The US diagnostic patterns of fatty liver disease was followed. The severity of fatty liver was classified into three degrees: grade 1- mild fatty liver, visualization of the diaphragm and the intra hepatic vessel borders. Grade 2- moderate fatty liver, echogenicity is moderately increased, with slightly impaired visualization of the diaphragm or intra hepatic vessels. Grade 3- severe fatty liver, echogenicity is markedly increased with poor or no visualization of the diaphragm, the intra hepatic vessels, and posterior portion of the right lobe. NAFLD was diagnosed based on sonography and absence of heart disease, acute or chronic liver disease, acute or chronic kidney disease, any malignancy, alcohol consumption [more than 40 g (male) or 20 g (female) of alcohol per day for over five years], pregnancy, liver masses, abnormal copper metabolism or thyroid function test and history of any medication with adverse effects on the liver. Metabolic syndrome (MS) was diahnosed as a collection of cardiometabolic risk factors that includes obesity, insulin resistance, hypertension, and dyslipidemia. Hepatitis B surface antigen-positive and hepatitis C antibody-positive patients were excluded from the study. Statistical analyses were performed using the SPSS software, version 16.0. The prevalence of NAFLD were calculated as a proportion of diagnosed patients to included subjects. The chi-square test were used to compare the proportions between those with NAFLD and normal population. Independent t-test were used for comparing the parametric data between two categories. The results was expressed as mean ± SD and proportions as appropriate. A p-value less than 0.05 was considered statistically significant.

Results:

Among 665 subjects in this study 213 were male (32%) and 452 female (68%) with the mean age of 42.2 ± 15.04. The socio-demographic status of the participants is summarized in Table 1. Most of the participants (52.5%) were categorized as mid income while 316 (47.5%) patients where categorized as low income. 34% subjects were illiterate. Most were house wife (63.4%) and eats rice 3 times a day (54.5%) Table 2 summarizes the anthropometric and biochemistry characteristics of the study population.

NAFLD was diagnosed in 219 subjects by ultrasonography. 89 (44.6%) subjects had mild disease while severe and moderate fatty liver disease was found in 32 (14.9%) and 89 (40.5%) subjects respectively (Table 3). NAFLD were higher in 41-60 age group (48.7%) ($P < 0.102$) and more in female (40.7%) (Table 4 and 5).

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We compared the socio-demographic variables as well as anthropometric and biochemical measures between those with NAFLD and healthy subjects (Table 6). Subjects with NAFLD had higher BMI (P < 0.001). The prevalence of hypertension (P < 0.001), high FBS (P < 0.001), high cholesterol (P = 0.026), high triglyceride (P < 0.001) was also significantly higher in patients with NAFLD. Taking all these together, patients with NAFLD had significantly higher prevalence of metabolic syndrome when compared to healthy subjects (P < 0.001).

Table-I: Socio-demographic features of study population (n=665)

Variable	n	%
Age (in years)		
• 18 – 40	337	50.7
• 41 – 60	257	38.6
• > 60	71	10.7
• Mean ± SD	42.21 ± 15.04	
Gender		
• Male	213	32
• Female	452	68
Occupation		
• Farmer	18	2.8
• House wife	422	63.4
• Service	87	13.1
• Day labourer	43	6.5
• Business	39	5.9
• Stay abroad	6	0.8
• Student	31	4.6
• Others	20	3.0
Socioeconomic condition		
• Low	316	47.5
• Middle	349	52.5
Education		
• Illiterate	226	34.0
• Primary	222	33.4
• Secondary	132	19.9
• Higher secondary	41	6.2
• Graduation	44	6.6
Dietary history		
• Eating rice – 1 time a day	63	9.5
• Eating rice – 2 times a day	239	36.0
• Eating rice – 3 times a day	363	54.5
Life style		
• Walking <30 minutes per day	541	81.3
• Walking >30 minutes per day	124	18.7

Table-II: Anthropometric and biochemical characteristics of the study population

Variable	n	%
Blood pressure (mm of Hg)		
• High	289	43.5
• Normal	376	56.5
BMI (kg/m^2)		
• Underweight	66	10.0
• Normal	250	37.6
• Overweight	113	17.0
• Obese	236	35.4
Waist –hip ratio (Mean ± SD)		
○ Male	0.90 ± 0.08	
○ Female	0.90 ± 0.08	
○ High – > 0.9 in male	116	53.8
○ > 0.85 in female	331	73.3
Fasting blood glucose (mg/dl)		
• Normal	525	79.0
• IFG	56	8.4
• DM	84	12.6
AST (U/L)		
• Normal	655	98.6
• Elevated	10	1.4
ALT (U/L)		
• Normal	640	96.2
• Elevated	25	3.8
Total cholesterol (mg/dl)		
• Normal	556	83.6
• Elevated	109	16.4
HDL (mg/dl)		
• Normal	624	93.8
• Low	41	6.2
LDL (mg/dl)		
• Normal	556	85.1
• Elevated	99	14.9
Triglycerides (mg/dl)		
• Normal	455	68.4
• Elevated	210	31.6
TSH		
• Normal	630	94.7
• Low	35	5.3

Table-III: USG findings of study population

Variable	n	%
Size (mean ± SD)	**12.99 ± 1.61**	
NAFLD		
• Yes	219	33
• No	446	67
Grade of NAFLD		
• Grade -1	98	44.6
• Grade -2	89	40.5
• Grade -3	32	14.9
Gall stone		
• Yes	32	4.8
• No	633	95.2

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Table-IV: Age prevalence of NAFLD

	Total		Male		Female		P
Age group in years	**n**	**%**	**n**	**%**	**n**	**%**	
18 – 40	88	40.0	18	29.1	70	44.3	0.102
41 – 60	107	48.7	34	54.5	73	46.4	
> 60	24	11.3	10	16.4	14	9.3	
Total	219	100.0	62	100.0	157	100.0	

Table-V: Sex prevalence of NAFLD

	Total		Male		Female		P
Age group in years	**n**	**%**	**n**	**%**	**n**	**%**	
18 – 40	88	100.0	18	20.5	70	79.5	0.102
41 – 60	107	100.0	34	31.6	73	68.4	
> 60	24	100.0	10	40.9	14	59.1	
Total	219	100.0	62	28.2	157	71.8	

Table-VI: Risk factor analysis of Socio-demographic, Anthropometric and Biochemical characteristics between those with NAFLD and healthy subject

Variable	Healthy (n=446)	NAFLD (n=219)	P value
Age in year (mean ± SD)	**40.35 ± 15.69**	**45.11 ± 13.50**	**<0.001**
Sex			
• Male	140 (65.6)	73 (34.4)	<0.175
• Female	262 (59.3)	184 (40.7)	
Occupation			
• Farmer	14 (78.6)	4 (21.4)	<0.002
• House wife	250 (59.2)	172 (40.8)	
• Service	46 (53.0)	41 (47.0)	
• Day labourer	39 (90.9)	4 (9.1)	
• Business	23 (60.0)	16 (40.0)	
• Stay abroad	2 (25.0)	4 (75.0)	
• Student	24 (78.3)	7 (21.7)	
• Others	9(46.7)	11 (53.3)	
Socioeconomic condition			
• Low	230 (72.8)	86 (27.2)	<0.001
• Middle	177 (50.6)	172 (49.4)	
Education			
• Literate	153 (67.6)	73 (32.4)	<0.001
• Primary	132 (59.5)	90 (40.5)	
• Secondary	92 (70.0)	40 (30.0)	
• Higher secondary	16 (38.7)	25 (61.3)	
• Graduation	14 (33.3)	30 (66.6)	
Dietary history			
• Eating rice – 1 time a day	14 (22.9)	49 (77.1)	<0.001
• Eating rice – 2 times a day	142 (59.3)	97 (40.7)	
• Eating rice – 3 times a day	252 (69.3)	111 (30.7)	
Life style			
• Walking <30 min/day	344 (63.6)	197 (36.4)	<0.025
• Walking >30 min/ day	63 (51.1)	61 (48.9)	
Blood pressure			
• High	142 (49.1)	147 (50.9)	<0.001
• Normal	265 (70.4)	111 (29.6)	
BMI, kg/m^2 (mean ± SD)	22.28 ± 4.12	26.61 ± 5.53	<0.001
Waist –hip ratio	0.88 ± 0.07	0.93 ± 0.08	<0.001
Fasting blood glucose (mg/dl)			
• Normal	365 (69.5)	160 (30.5)	<0.001
• IFG	23 (40.5)	33 (59.5)	
• DM	21 (25.4)	63 (74.6)	
AST (U/L)			
• Normal	402 (61.3)	253 (38.7)	<0.078
• Elevated	3 (28.6)	7 (71.4)	
ALT (U/L)			
• Normal	398 (62.2)	242 (37.8)	<0.026
• Elevated	9 (36.8)	16 (63.2)	
Total cholesterol (mg/dl)			
• Normal	365 (65.6)	191 (34.4)	<0.001
• Elevated	43 (39.0)	66 (61.0)	
HDL (mg/dl)			
• Normal	389 (62.4)	235 (37.6)	<0.056
• Elevated	18 (45.2)	23 (54.8)	
LDL (mg/dl)			
• Normal	360 (63.6)	206 (36.4)	<0.046
• Elevated	51 (51.4)	48 (48.6)	
Triglycerides (mg/dl)			
• Normal	307 (67.6)	148 (32.4)	<0.001
• Elevated	100 (47.8)	110 (52.2)	
TSH			
• Normal	392 (62.3)	238 (37.7)	<0.211
• Elevated	17 (50.0)	18 (50.0)	

Discussion:

The natural history of NAFLD ranges from asymptomatic indolent to the end stage liver disease. The prevalence of ultrasonographically diagnosed NAFLD in industrialized countries ranges from 20% to 60%[11] with 21.8% in Japan and 24.3% in South Korea[12,13].

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Our study showed that approximately 33% of adults had NAFLD, which is much higher than other study.

Although the variations in the prevalence of the NAFLD can be attributable to genetic and environmental background, the differences in methodology and diagnostic criteria for NAFLD are another major problem. We included a randomly selected sample of adult general population. Ultrasonography was the basis of NAFLD diagnosis in our study. The prevalence of 33% ultrasonographically diagnosed NAFLD in this study was lower than Germany (40.0%)[14], but higher then Sri Lanka (32.6%)[15], USA (33%)[16] and Japan (21.8%)[12] , Italy (20%)[17], Taiwan (11.5%)[18], China (12.5% and17.2%) (4, 8), Philippines (12.2%)[19] and Brazil (2.3%). We found that NAFLD was associated high BMI, high waist circumference, hypertension, high FBS, high cholesterol and high triglyceride. These determinants of NAFLD are the metabolic and anthropometric features of metabolic syndrome[9]. Thus NAFLD is closely associated with metabolic syndrome in our region. Subjects with metabolic syndromes are at increased risk of developing diabetes mellitus and cardiovascular disease[10]. Thus, NAFLD could be considered as an additional feature of metabolic syndrome. In this study, the prevalence of NAFLD was higher in females than in males. This finding is different from several previous studies[20,21] because 68% of our study population is female and most of the male are lives in abroad.

We have noted some limitations to this study. First, the study population was slightly low and future studies with more participants are recommended. However, the precise cluster sampling used in this study resulted in a study population which is representative of the whole community in our region. Second, the measurements and the clinical examination were performed by several physicians and nurses which has resulted in inevitable inter observer variation affecting the reliability of the clinical findings and measurements. Third, ultrasonographic diagnosis of NAFLD is questionable. Currently using magnetic resonance imaging and liver biopsy are more acceptable for the diagnosis of NAFLD.

Conclusion:

The prevalence of NAFLD in adult rural population is 33%. NAFLD is associated with female sex, obesity, and other features of metabolic syndrome. As NAFLD has the possibility of progression toward end-stage liver disease and is associated with increased cardiovascular risk, appropriate action should be undertaken in our region for screening and control of this disease. Preventive strategies should also be pursued in our region.

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