Short Title:The prevalence of Risk Factors and Complications of Non -Alcoholic Fatty liver disease (NAFLD):A Review

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***The Prevalence of Risk Factors and Complications of Non – Alcoholic Fatty Liver Disease (NAFLD):A Review***

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| ***ABSTRACT***  Non alcoholic fatty liver disease(NAFLD) is currently most common cause of chronic liver diseases in developed countries because of the obesity epidemic.The disease increases liver related morbidity and mortality,and often increases the risk for other comorbidities,such as type 2 daibetes and cardiovascular disease.However cardiovascular disease is the common cause of death and only minority will develop fibrosis and liver related complications. The non alcoholic fatty liver disease(NAFLD) has a global prevalence of about 25%. Incidence is increasing with rising levels of obesity,type 2diabetes and metabolic syndrome,and NAFLD is predicted to become the leading cause of cirrhosis.The main risk factors involved in non alcoholic fatty liver disease are psoriasis,obesity,age,dementia,sarcopenia and cardiovascular diseases and the major leading complication of NAFLD is cirrhosis.  ***KEY WORDS***: cardiovascular diseases, obesity,psoriasis,dementia,sarcopenia.  Author for correspondence E mail:degamanasa2001@gmail.com,Tel:+919346414934 |

***INTRODUCTION***:

The epidemology of non alcoholic fatty liver disease (NAFLD) parallels that of obesity, which has steadily increasing throughout the world over the past 30 yrs .The natural history of NAFLD in some individuals, is considered as end stage liver disease. Thus, NAFLD is estimated to become the leading cause of liver related morbidity and mortality within 20 yrs and leading indication for liver transplantation in the next few years[1].A recent meta analysis estimated that the overall global prevalence of NAFLD is very high at 25.2%.According to analysis, the regional prevalence of NAFLD was reported to be highest in the middle east (31.7%)and south Africa (30.4%).Thus, NAFLD has been recognized as the most common chronic liver disease world wide. Compared with matched ,controlled populations without NAFLD and patients with NAFLD have increased risks of end stage liver disease, hepatocellular carcinoma ,and liver related mortality[2].NAFLD ranges from benign condition of non alcoholic fatty liver(NAFL)to non alcoholic to Steatohepatitis (NASH),which is considered to be severe end of the spectrum[3].Another recent analysis revealed that lean, non alcoholic ,non diabetic ,non smoking ethnic Asian Indians in comparison to matched Caucasians, Hispanics, black and eastern Asians had 2 to 3 fold increase in insulin resistance and 2 fold increase in hepatic triglyceride content. Recent concepts also suggests that the magnitude of adipose tissue dysfunction may have high metabolic impact than the severity of adiposity. Obesity is not only a major risk factor for NAFLD but also determines the severity of NAFLD[4].psoriasis is also considered a systemic diseases associated to comorbidities, as metabolic syndrome and NAFLD is seen in the hepatic manifestation of the metabolic syndrome. The possible association between psoriasis , obesity and metabolic syndrome, which are known risk factors for NAFLD and has been recently documented which is focusing in the crucial role of the adipose tissue in the development of the inflammatory background sharing the above entities[5].

***PREVALENCE OF RISK FACTORS OF NAFLD***

Lean: The prevalence of lean in NAFLD in general population found to be 10.2%,and among the NAFLD population the prevalence of the lean NAFLD was 19.2% with a broad countrywide variation. In an average around 40%of the non obese people have severe histological phenotype like that of obese people.Mortality rate is found to be higher and almost 40% of non obese people with NAFLD have NASH and almost 30% have significant fibrosis. In addition ,the management plan with group of patient have a distinct difference. For example :successful weight reduction strategy have higher potential benefits in non lean patients as compared to NAFLD patients with limited benefits. Based on the previous study and considering the differences in the underlying mechanisms of lean and non lean NAFLD ,we concluded that risk factors of NAFLD might differ between those groups and needs to be assessed. Therefore ,the aim of the study was to systematically evaluate the risk factors of lean NAFLD and to aid in management strategies for the prevention and control of NAFLD and related diseases[6].

Obesity: The prevalence of NAFLD in obese patients was estimated assuming that about 80% patients might develop NAFLD in American countries’ Mexico the prevalence of NAFLD in obese patients was estimated to be 26%.In general population the prevalence of NAFLD in obese patients was found to be 40-70% and 20-30% in normal population[7].In Bangladesh, the prevalence of NAFLD in obese patient was found to be 36.93%[8].

RISK OF CARDIO VASCULAR EVENTS :

Coronary heart disease: It has been noted that NAFLD patients have high risk of coronary artery disease as compared to the general population, relative risk :2.26;in 95%of children relative risk :1.04 -4.92 and consequently a high risk of mortality from cardio vascular disease relative risk in general population is 1.46 and in 95% of children relative risk is 1.31-1.64 .As per observance 219 cases of non fatal coronary heart disease ( MI,Revascularization procedures)and 212 cases of cardiovascular deaths were noted with high frequency in NAFLD patients[9].Study suggest that the presence of relationship between NAFLD and coronary artery disease.NAFLD is observed in 51% of patients with mild and insignificant coronary stenosis and the presence of NAFLD in 46.67%of patients with acute coronary syndrome.

Arrhythmias: NAFLD is associated with high risk of the incidence of arrhythmia, especially the atrial fibrillation or ventricular tachy arrhythmias observed in left ventricular diastolic dysfunction. Based on several analysis have suggested a possible role of NAFLD in development of cardiac rhythm impairment , a recent analysis involving two cross sectional and 3 cohort studies including a total of 238129 subjects found a higher risk of atrial fibrillation in NAFLD patients as compared to those with out those liver disease (relative risk -2.06 )in children relative risk 1.10-3.85. 12 cross sectional studies were conducted around the world among them six of 19 studies were conducted in Asia (Korea n=4,china n=2) nine in Europe(Germany n=2,finland n=1,Italy n=6)and four in USA.A total of 7012960 adult participants were included in meta analysis study in which 1083255 had NAFLD (15.45%) and 5929705 with no NAFLD.

Ischemic stroke:NAFLD was found in 42.7%of ischemic stroke patients and 22.7% of population from Iran .It has been estimated that the risk of ischemic stroke in NAFLD is 1.6 times greater than the in the general population[10].NAFLD is associated with increased risk of ischemic stroke ,a leading cause of mortality and long term disability world wide .In a study of 200 patients admitted with acute ischemic stroke ,NAFLD was present in 42.5%of patients [10].

Hypertension:Hypertension is diagnosed with prevalence of 50% of patients with NAFLD.According to study ,hypertension is highly associated with NAFLD, and the epidomological study shows an approximately 49.5%NAFLD prevalence in hypertension patients , which is higher prevalence in general population[11].A study in us , revealed that 1455 men and women aged between 39 to 79 yr old have been diagnosed NAFLD associated with hyperyension .A study in china revealed that among 4686 subjects 3177 men and 1509 women are associated risk of incident of NAFLD associated with hypertension[12].

Psoriasis:The studies shows that there is a possible link between psoriasis which is known as a risk factor for devolping NAFLD.And also known that the psoriatic patients after 40 yrs have a higher prevalence of NAFLD. The data shows that among 130 psoriatic patients ,nearly half 47%vs28%of controls affected by NAFLD which shows a strongly related to psoriasis according to the psoriasis Area Severiaty Index score.And a study shows that among 2292participants ,5.1% were affected with psoriasis and the prevalence of NAFLD shows that 46.2% in psoriatic patients that of 33.3%of patients without psoriasis[13].

Sarcopenia: The studies have suggested that there is an association between NAFLD and sarcopenia [14]. The sarcopenia may accelerate for the patient risk for developing NAFLD. The 40 % of patients with sarcopenia have the evidence of developing NAFLD [15].The study of population shows among 1278 (30.4%) had NAFLD and 29.5% had sarcopenia ,so this shows that the prevalence of NAFLD was significantly higher with sarcopenia. The sarcopenia in men have higher risk of NAFLD as compared to women[16].

Dementia: Dementia is a major risk factor associated with NAFLD.A study revealed that 16.0% of patients with NAFLD and 15.6% of patients without NAFLD were evaluated with dementia.So,the dementia is a major cause of mortality in western countries and effects millions world wide[17].

***Prevalence of complications of NAFLD:***

Chronic kidney disease: Chronic kidney disease has high prevalence of NAFLD. The meta analysis shows that patients with NAFLD has higher risk of incident CKD compared to patients without NAFLD.According to study in US, patients with NAFLD have increased risk of 41% of developing advanced stages of CKD compared to without NAFLD.In Italy, the studies revealed that NAFLD is highly associated with the risk of CKD,where the study is independent of age,BMI, sex.According to study in Korea, NAFLD is associated with increased risk of CKD with adjusted HR:1.22[2].In italy,NAFLD was independently associated with CKD 54.4% vs 24.4%[18].

Colorectal cancer(extra hepatic malignancies):Colorectal cancer is the most diagnosed malignancy and the leading cause of cancer related deaths. A recent observational studies shows that NAFLD was independently associated with increased prevalence and incidence of colorectal cancer. In china the studies shows that colorectal adenomas( odds ratio:4.89;95%CI,2.04-11.70) and also advanced colorectal neoplasms adjusted(OR,5.34;95%CI,1.92-14.84).In Austria ,the ultrasonography reveals that prevalence of colorectal lesions was 34%in the NAFLD group and 21.7% I controlled group. In Korea ,the ultrasonography reveals that NAFLD was independently associated with colorectal neoplasia(adjusted OR,1.10;95%CI,1.03-1.17)[2]

Liver Cirrhosis: Cirrhosis is a major public health problem which has high morbidity and mortality that is preventable and underestimated. The prevalence of NAFLD cirrhosis is 16.4%.In 2010 ,liver cirrhosis was the 23rd cause of death world wide with proportions attributable to HCV,HBV, and alcoholic consumption [19].Cirrhosis is the 13th most common cause of mortality world wide. Global cirrhosis deaths have been increased from 1.54% of death in 1980 to 1.95% in 2010,which caused more than one million deaths in each year. According recent studies by 2020,the number of individuals with NAFLD cirrhosis is been predicted to exceed than that of those compared with hepatitis B and C ,cirrhosis will become the leading indication for liver transplantation[20].

***Conclusion*:**

NAFLD is estimates to become the leading cause of liver related morbidity and mortality with in 20 yrs and leading indication for liver transplantation in next few years.NAFLD has been recognized as the most common chronic liver disease world wide.Despite new efforts to diagnose and contain the disease more research is needed to develop new strategies that will treat the disease and complications associated with it .More research should be done to help lean to effectively treat the complications and side effects of NAFLD.

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