Aayushi, R and Umesh, K / J Health Sci Altern Med (2021) 3(2): 1-6
DOI: 10.14456/jhsam.2021.6

Journal of
Health Science and Alternative Medicine

Spacial Article Open Access

Concomitant Prevalence of Non-Communicable Diseases among NAFLD/NASH Patients: An Experience from a Tertiary Care Hospital in Delhi

Aayushi Rasogi[1*] and Umesh Kapil [2]

[1]*Department of Clinical Epidemiology, Institute of Liver & Biliary Sciences, New Delhi, India, 110070*

[2]*Department of Epidemiology and Clinical Research, Institute of Liver & Biliary Sciences, New Delhi, India, 110070*

Received August 26, 2021

Accepted August 26, 2021

Published August 30, 2021

***Corresponding author**:
Aayushi Rasogi, Department of Clinical Epidemiology, Institute of Liver & Biliary Sciences, New Delhi, India, 110070

E-mail: rastogiaayushi6@gmail.com

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH) is a multisystem disease and involves extra-hepatic organs and thus have strong association with components of metabolic dysfunction. Presence of single component of the metabolic dysfunction anticipates the appearance of additional metabolic components over time. With this objective, the present study aims at assessing the proportion of various metabolic components in NAFLD/NASH patients attending tertiary care hospital. **Methodology:** A record review was undertaken to extract the data of NAFLD/NASH patients who were presenting to outpatient clinics or/and inpatient wards in Department of Hepatology from August 2009 to March 2020. Medical records of NAFLD/NASH patients were extracted in pre-defined format. In case several visits of the patients were reported, the first visit was considered using unique hospital Identity number. The data was analyzed in STATA version 14. p-value of <0.05 was considered to be significant. **Results:** A total of 1398 patients were included in the final analysis. Mean age of patients was 54.4±11.9 years and 76% were males. The median ALT and AST was found to be 35 IU/l (IQR: 24 -56 IU/l) and 48 IU/l (IQR: 34–74 IU/l) respectively. The obesity (66.45%) and diabetes (51.86%) were found to be the most common non-communicable diseases associated with NAFLD/NASH patients. The odds of cirrhosis (LSM≥13) was 6.13 (95%CI: 4.43 – 8.48) times among diabetics as compared to odds of non-cirrhosis (LSM≥13) among non-diabetics (p <0.001). The univariate association with obesity and hypertension was also found to be significant. **Conclusion:** There is higher prevalence of non-communicable diseases among NAFLD/NASH patients.

Keywords: *Non-communicable diseases, NAFLD, Prevalence*

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disorders in western world [1, 2] and is emerging as the major cause of liver diseases in developing countries like India, with a prevalence ranging from 9% to 55% in general population [3, 4]. Prevalence of non-alcoholic steatohepatitis (NASH), a progressed form of NAFLD is estimated to be 1.5–6.45% in the general population whereas prevalence of NASH among biopsy confirmed NAFLD cases is 59.10% (95% CI: 47.55-69.73) [5, 6].

Earlier, NAFLD was considered to be a benign condition, however with advancements in imaging and medical technology, it has now being recognized as a disease with liver-related morbidities which can progress to cirrhosis, liver failures and hepatocellular carcinoma [7]. Over the years, it has been found that the clinical burden of NAFLD is not only restricted to liver-related morbidity and mortality, rather evidences suggest NAFLD to be a multisystem disease, involving extra-hepatic organs and several regulatory pathways. A meta-analysis of 86 studies with a sample size of 8,515,431 from 22 countries reported strong association of NAFLD with obesity (51.34%; 95% CI: 41.38-61.20), type 2 diabetes mellitus (T2DM) (22.51%; 95% CI: 17.92-27.89), hyperlipidemia (69.16%; 95% CI: 49.91-83.46%), hypertension (39.34%; 95% CI: 33.15-45.88), and metabolic syndrome (42.54%; 95% CI: 30.06-56.05)[1]. Thus, these evidences from clinical, experimental and epidemiological studies indicate strong association of NAFLD with components of metabolic dysfunction,

indeed NAFLD is considered to be the hepatic manifestation of metabolic dysfunction [8].

The pooled prevalence of NASH among T2DM patients was reported to be 37.3% (95% CI 24.7-50.0%) [9]. In addition to this, patients with NAFLD have higher risk of CVD-related mortality as compared to their counterparts in general population (15.5% versus 7.5%; P=0.04) [7]. Further, several studies have supported the concept that NAFLD and NASH anticipates the development of T2DM and metabolic syndrome [10, 11]. However, there is a continued scientific debate about the primacy of metabolic components over NAFLD or, conversely, NAFLD over the metabolic components [12].

Nevertheless, the presence of single metabolic conditions tends to aggregate in the individuals and the presence of each of the trait anticipates the appearance of additional metabolic components over time [13]. This aggregation of traits together result in progression of the disease to cirrhosis and development of hepatocellular carcinoma [14, 15]. Thus, it is important to study the clinical profile of NAFLD/NASH patients to understand the proportion of various metabolic conditions. With this objective, the present study aims at assessing the proportion of various metabolic components in NAFLD/NASH patients attending tertiary care hospital.

Methodology

Study design and setting

A record review was undertaken to extract the data of NAFLD/NASH patients who were presenting to outpatient clinics or/and inpatient wards in Department of Hepatology at the Institute of Liver and Biliary Sciences, New Delhi, from August 2009 to March 2020. ILBS is tertiary care hospital under Government of National Capital Territory of Delhi which provides specialized care in the field of liver and biliary diseases.

Study population

Inclusion criteria:

1. Age>18 years
2. Patients with NAFLD/NASH confirmed based on their histological and/or radiological features.
   Patients with cryptogenic fibrosis or cirrhosis in absence of significant alcohol consumption (>30gm/day in men and >20gm/day in women) [16] and absence of other liver related etiologies like viral hepatitis, liver-related autoimmune liver diseases, cholestatic or drug-induced liver injuries were also considered as NAFLD/NASH cases in the analysis [17].

Exclusion criteria:

1. Patients who were found to be positive for HBsAg and HBV-DNA.
2. Patients who were positive for Anti-HCV [18].

Operational definitions

Patients were considered to be diabetic as per the criteria defined by American Diabetes Association (fasting plasma glucose above 126mg/dl or oral glucose tolerance test above 200 mg/dl or HbA1C above 6.5%) [19], or those already on treatment with oral hypoglycemic or had mention of history of diabetes in his/her case report. Patients were considered to be hypertensive as per the definition provided by American Heart Association (systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg) or those are on antihypertensive medications or had mention of history of hypertension in his/her case report [20]. Obesity was defined as BMI above 24.99 kg/m^2 or had mention of overweight or obesity in their case report.

The medical records of NAFLD/NASH patients who visited outpatient clinics or/and inpatient wards in Department of Hepatology at the Institute of Liver and Biliary Sciences, New Delhi, from Aug 2009 to Mar 2020 were extracted in pre-defined format with necessary variables. In case several visits of the patients were reported, the first visit was considered and remaining visits were removed from the final list of analysis using unique hospital Identity (UHID) number. This was done to ensure inclusion of unique entries as well as presentation of case at his/her first time of visit to the hospital. Since it was a record review, all eligible NAFLD/NASH patients were included in the analysis.

The study conformed to the Declaration of Helsinki of 1975, as revised in 1983, and was undertaken with the permission of competent authority as well as Institutional Ethics Committee approval via letter F.37/(1)/9/ILBS/DOA/2020/20217/321 dated May 1, 2020. Since it was a record review, informed consent of patients was not required and to maintain the confidentiality of the patient, data was made anonymous by deleting the personal details such as name and address, henceforth using UHID as the unique number.

The data was analyzed in STATA version 14. Proportion, mean with standard deviation (SD) and median with inter quartile range (IQR) were used to provide descriptive statistics. A univariate analysis was performed using chi square where p value of <0.05 was considered to be significant. Odds ratio (OR) along was 95% Confidence intervals (CI) was provided to represent the association between cirrhotic status and other non-communicable diseases.

Results

A total of 89,448 records of NAFLD/NASH patients from Aug 2009 to Mar 2020 were found. Out of which, 82,794 records were found to be multiple entries of the same patients due to their several follow up visits to ILBS. A total of 1398 patients were included in the final analysis after exclusion of

multiple entries of same patients (82,794) and incomplete or missing data (5,256) as seen in Figure 1.

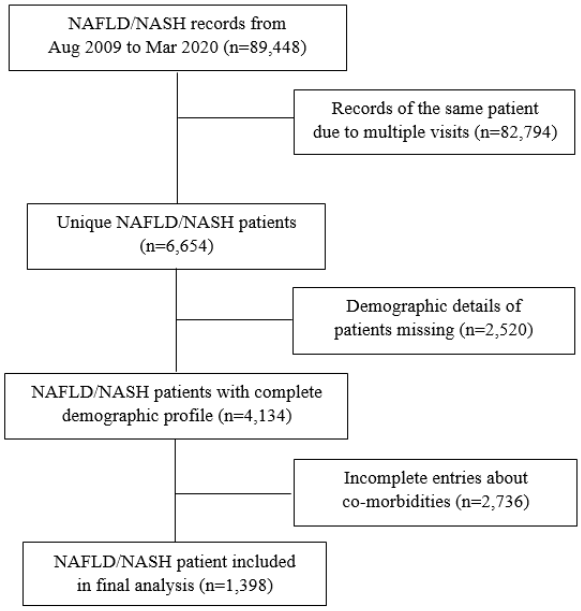

Figure 1 Flowchart of inclusion of NAFLD/NASH selection process followed for the impact assessment study

The mean age of participants was found to 54.4±11.9 years and 76% of the participant were males. The median ALT and AST was found to be 35 IU/l (IQR: 24-56 IU/l) and 48 IU/l (IQR: 34 – 74 IU/l) respectively. The mean BMI of the included NAFLD/NASH patients was found to be 26.24±3.89 kg/m2. The median value of Liver stiffness measurement (LSM) was found to be 20.6 kPa (IQR: 7.55 – 42.05 kPa) (Table 1).

Table 1. Clinical profile of patients having NAFLD/NASH (N =1398)

Characteristics	n (%)
Mean Age (SD)	54.4 (11.9)
Gender	
- Male	1,061 (75.89)
- Female	337 (24.11)
Mean BMI (kg/m^2)	26.24 (3.89)
BMI Category	
<18.5	38 (2.72)
18.5 – 24.9	444 (31.76)
24.9 – 29.9	713 (51.00)
>30	203 (15.52)
Median ALT (IQR), (n=1,172)	35 (24 -56)
Median AST (IQR), (n=1,176)	48 (34 – 74)
Median Liver stiffness measurement (IQR), (n =828)	20.6 (7.55 – 42.05)

History of diabetes was found to be among 51.86% of the participants whereas hypertension was found among 14.16% of the participants and more than two-third of the participants were obese as represented in table 2. The obesity (66.45%) and diabetes (51.86%) were found to be the most common non-communicable diseases associated with NAFLD/NASH patients. The coexistence of obesity among diabetic NAFLD/NASH patients was found to be 67.31% whereas the concomitant prevalence of obesity among hypertensive NAFLD/NASH patients was found to be 63.63%. The presence of diabetes among hypertensive NAFLD/NASH group was found to be 77.78% and 52.53% in obese NAFLD/NASH group as seen in figure 2. Approximately 15% were found to have no component of metabolic dysfunction, whereas at least one metabolic condition was present in 85% of the patients. The coexistence of all the three factors: obesity, diabetes and hypertension among NAFLD/NASH patients was found to be 6.87% (Table 2).

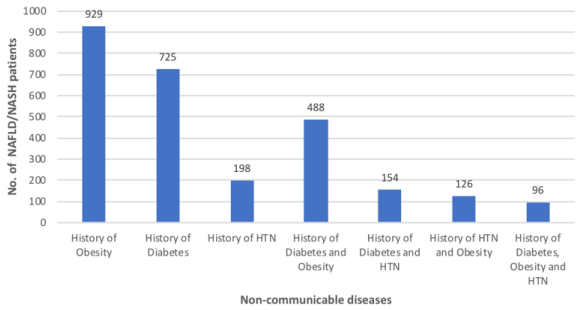

Figure 2 Co-existence of non-communicable diseases among NAFLD/NASH patients

Table 2. Concomitant existence of non-communicable diseases in NAFLD/NASH patients (N =1398)

Non-communicable disease	n (%)
Patients having:	
- No component of metabolic dysfunction	218 (15.59)
- One component of metabolic dysfunction	604 (43.20)
- Two components of metabolic dysfunction	480 (34.33)
- Three components of metabolic dysfunction	96 (6.87)
History of Diabetes	725 (51.86)
History of HTN	198 (14.16)
History of Obesity	929 (66.45)
History of Diabetes and Obesity	488 (34.91)
History of Diabetes and HTN	154 (11.02)
History of HTN and Obesity	126 (9.01)
History of Diabetes, Obesity and HTN	96 (6.87)

The odds of cirrhosis (LSM≥13) is 6.13 (95%CI: 4.43 – 8.48) times among diabetics as compared to odds of non-cirrhosis (LSM≥13) among non-diabetics (p <0.001). The univariate association with obesity and hypertension is also found to be significant as described in table 3.

Table 3 Association of non-communicable diseases on Liver stiffness measurement values (N=828)

Presence of non-communicable diseases	n (%)		Odds ratio (95% CI)	p-value
	Non-cirrhosis LSM <13; n=322	Cirrhosis (LSM≥13); n=506		
Obesity	206 (35.9)	368 (64.1)	1.50 (1.11 – 2.03)	0.008
Diabetes	66 (17.5)	310 (82.5)	6.13 (4.43 – 8.48)	<0.001
Hypertension	31 (26.1)	88 (73.9)	1.97 (1.27 – 3.06)	0.002

Discussion

NAFLD is a multi-system disease which is known to be the hepatic manifestation of metabolic dysfunction. Thus, NAFLD is associated with several non-communicable diseases such as diabetes, obesity and hypertension. Among 1328 NAFLD/NASH patients, at least one component of metabolic dysfunction was present in 96.1% and a small proportion of approximately 15.% didn't have any components of metabolic dysfunction. These findings are in line with a previous study undertaken in general population of blood donors from India [4].

Diabetes and obesity were found to be the most common non-communicable disease co-existing with NAFLD/NASH conditions in the present study. Although diabetes and obesity are well established risk factors of NAFLD, however, the actual pathological mechanism by which they induce NAFLD is unclear. It is uncertain whether obesity or diabetes induces NAFLD or whether there is an overlapping pathophysiological mechanism between them.

Majority of the NAFLD/NASH patients in the study were diabetics and consequently, have nearly six fold higher odds of having liver cirrhosis. The similar findings have been reported by a previous study where presence of diabetes increased the risk of NAFLD by three-folds. The underlying biological mechanism of the association is not fully illustrated, however, traces of liver inflammation, metabolic stress and insulin resistance can be figured between diabetes and NAFLD/NASH conditions. Further according to US-based population study NAFLD and diabetes were the first two common factors seen in patients suffering from hepatocellular carcinoma (HCC) [21]. In addition to this, presence of diabetes can independently increase the risk of developing HCC by two-to-three-folds indicating a strong role of diabetes in progression of NAFLD [22].

The odds of cirrhosis was also observed to be higher in those with obesity and having hypertension. It has been observed in several studies, prevalence of NAFLD increased with increasing BMI. The coexisting prevalence of obesity with NAFLD as observed from previous studies is found to be 72-90% [23]. Similar higher prevalence was observed in healthy individuals from India in an earlier study [24].

One of the limitations of our study is that information of various confounding factors such as socioeconomic, physical activity, diet which may have an influence on the high prevalence of metabolic risk factors and NAFLD in them were missing because the present study was a record review rather than a prospective data collection study. In addition to this, the study predominantly includes males and hence there could be an overestimation of the non-communicable diseases as males are more susceptible to such diseases. However the paucity of the female gender in our study could be the true reflection of the differential gender distribution among the NAFLD/NASH patients at our institute. Thus, the results of the present study can't be generalized to the whole country. Further the years of existence of the disease also effects the coexistence of non-communicable disease, however, since it was a record review information about the duration of the disease could not be extracted. Thus a prospective data collection study should be planned to overcome the limitations of the study and to estimate the true concomitant prevalence of non-communicable diseases among NAFLD/NASH patients.

Conclusion

There is higher prevalence of NAFLD with other non-communicable diseases such as obesity, diabetes and hypertension, indicating the expansion of a modern lifestyle epidemic in the population and thus would require necessary preventive strategies at various health system levels to control this lifestyle epidemic. As NAFLD is a multi-system disease, it requires a multi-disciplinary assessment which can initiate early treatment measures to decrease the diseases burden.

References

[1] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64:73–84. https://doi.org/10.1002/hep.28431.

[2] Bedogni G, Miglioli L, Masutti F, Tiribelli C, Marchesini G, Bellentani S. Prevalence of and risk factors for nonalcoholic fatty liver disease: The Dionysos nutrition and liver study. Hepatology 2005;42:44–52. https://doi.org/10.1002/hep.20734

[3] Das K, Das K, Mukherjee PS, Ghosh A, Ghosh S, Mridha AR, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. Hepatology 2010;51:1593–602. https://doi.org/10.1002/hep.23567.

[4] Duseja A, Najmy S, Sachdev S, Pal A, Sharma RR, Marwah N, et al. High prevalence of non‐alcoholic fatty liver disease among healthy male blood donors of urban India. JGH Open 2019;3:133‐9. https://doi.org/10.1002/jgh3.12117.

[5] Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol 2017;15:11–20. https://doi.org/10.1038/nrgastro.2017.109.

[6] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016;64:73–84. https://doi.org/10.1002/hep.28431.

[7] Adams LA, Lymp JF, St. Sauver J, Sanderson SO, Lindor KD, Feldstein A, et al. The Natural History of Nonalcoholic Fatty Liver Disease: A Population-Based Cohort Study. Gastroenterology 2005;129:113–21. https://doi.org/10.1053/j.gastro.2005.04.014.

[8] Marchesini G, Brizi M, Bianchi G, Tomassetti S, Bugianesi E, Lenzi M, et al. Nonalcoholic Fatty Liver Disease: A Feature of the Metabolic Syndrome. Diabetes 2001;50:1844–50. https://doi.org/10.2337/diabetes.50.8.1844.

[9] Younossi ZM, Golabi P, de Avila L, Paik JM, Srishord M, Fukui N, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. Journal of Hepatology 2019;71:793–801. https://doi.org/10.1016/j.jhep.2019.06.021.

[10] Cortez-Pinto H, Camilo ME, Baptista A, De Oliveira AG, De Moura MC. Non-alcoholic fatty liver: another feature of the metabolicsyndrome? Clinical Nutrition 1999;18:353–8. https://doi.org/10.1016/s0261-5614(99)80015-6.

[11] Anstee QM, Targher G, Day CP. Progression of NAFLD to diabetes mellitus, cardiovascular disease or cirrhosis. Nat Rev Gastroenterol Hepatol 2013;10:330–44. https://doi.org/10.1038/nrgastro.2013.41.

[12] Vanni E, Bugianesi E, Kotronen A, De Minicis S, Yki-Järvinen H, Svegliati-Baroni G. From the metabolic syndrome to NAFLD or vice versa? Digestive and Liver Disease 2010;42:320–30. https://doi.org/10.1016/j.dld.2010.01.016.

[13] Kawada T. Predictors of the Development of Metabolic Syndrome in Male Workers. Journal of Occupational & Environmental Medicine 2012;54:292–5. https://doi.org/10.1097/jom.0b013e3182492070.

[14] Palaniappan L, Carnethon MR, Wang Y, Hanley AJG, Fortmann SP, Haffner SM, et al. Predictors of the Incident Metabolic Syndrome in Adults: The Insulin Resistance Atherosclerosis Study. Diabetes Care 2004;27:788–93. https://doi.org/10.2337/diacare.27.3.788.

[15] Welzel TM, Graubard BI, Zeuzem S, El-Serag HB, Davila JA, McGlynn KA. Metabolic syndrome increases the risk of primary liver cancer in the United States: A study in the SEER-medicare database. Hepatology 2011;54:463–71. https://doi.org/10.1002/hep.24397.

[16] EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Journal of Hepatology 2016;64:1388–402. https://doi.org/10.1016/j.jhep.2015.11.004.

[17] Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2017;67:328–57. https://doi.org/10.1002/hep.29367.

[18] Krajden M, McNabb G, Petric M. The Laboratory Diagnosis of Hepatitis B Virus. Canadian Journal of Infectious Diseases and Medical Microbiology 2005;16:65–72. https://doi.org/10.1155/2005/450574.

[19] Association AD. Diagnosis and classification of diabetes mellitus. Diabetes Care [Internet]. 2006 Jan 1 [cited 2021 Jan 10];29(suppl 1):s43–8. https://care.diabetesjournals.org/content/29/suppl_1/s43.

[20] Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension 2020;75:1334–57. https://doi.org/10.1161/hypertensionaha.120.15026.

[21] Sanyal A, Poklepovic A, Moyneur E, Barghout V. Population-based risk factors and resource utilization for HCC: US perspective. Current Medical Research and Opinion 2010;26:2183–91. https://doi.org/10.1185/03007995.2010.506375.

[22] El-serag HB, Tran T, Everhart JE. Diabetes increases the risk of chronic liver disease and hepatocellular carcinoma. Gastroenterology 2004;126:460–8. https://doi.org/10.1053/j.gastro.2003.10.065.

[23] Ruhl CE, Everhart JE. Determinants of the association of overweight with elevated serum alanine aminotransferase activity in the United States. Gastroenterology 2003;124:71–9. https://doi.org/10.1053/gast.2003.50004.

[24] Duseja A, Najmy S, Sachdev S, Pal A, Sharma RR, Marwah N, et al. High prevalence of non‐alcoholic fatty liver disease among healthy male blood donors of urban India. JGH Open 2019;3:133‐9. https://doi.org/10.1002/jgh3.12117.