

Comparison of Clinical, Biochemical, and Histopathologic Profiles between NAFLD in Asian-Indians and United States Adults

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ABSTRACT

Background and aims: Nonalcoholic fatty liver disease (NAFLD) is very common in both Asian and Western countries. Geographic variation leads to differences in epidemiological and demographic characters of NAFLD patients. Studies conducted upon different ethnic groups in the United States (US) show a higher prevalence of NAFLD in Hispanics and African-Americans. There is however, a paucity of studies involving Asians. It has been observed that Asian-Indian NAFLD patients have unique characteristics compared to their counterparts in the West. This study is the first attempt at comparing the characteristics of Asian-Indian and US NAFLD patients.

Materials and methods: A retrospective analysis of clinical, biochemical, and histological data was performed for 633 Asian-Indian NAFLD patients and 451 US NAFLD patients. Clinical parameters [age, gender, body mass index (BMI), diabetes, hypertension, etc.], biochemical tests (liver function tests, lipid profile, and fasting blood sugar), hepatic ultrasound and hepatic histology were compared between the two cohorts.

Results: Eighty-two percent of US NAFLD patients were more than 40 years of age compared to 51.3% of Asian-Indian patients ($p < 0.01$). US (male 56.3%) and Asian-Indian (male 81.7%) ($p < 0.01$) patients differed from each other as regards gender prevalence. Rates of obesity were greater in the US patients compared to Asian-Indians ($BMI 32.6 \pm 5.3 \text{ kg/m}^2$ vs $26.2 \pm 3.4 \text{ kg/m}^2$). There was a higher prevalence of both diabetes and hypertension (diabetes 42.1% vs 33%, and hypertension 56.8% vs 29.7%, $p \leq 0.01$) in US patients. ALT levels were also significantly higher in US NAFLD patients compared to Asian-Indians ($ALT 82.78 \pm 71.30$ vs 53.66 ± 37 , $p \leq 0.01$). A higher proportion of US patients were found to have the more advanced liver disease at the time of diagnosis compared to Asian-Indians (Stage 3 fibrosis 10.42% vs 0%, and Stage 4 fibrosis 2.66% vs 0%, $p < 0.01$).

Conclusion: Asian-Indian and US NAFLD patients differ significantly on several parameters. Further studies need to be carried out to understand the mechanistic basis of these differences better.

Keywords: Epidemiology, Ethnicity, Ethnology, NAFLD, Nonalcoholic fatty liver disease, Nonalcoholic steatohepatitis.

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INTRODUCTION

Nonalcoholic fatty liver disease is a common liver disorder in both Asian and Western countries. With the epidemic of metabolic syndrome (MS) spiraling upwards, there has been a heightened awareness and early recognition of asymptomatic patients with raised transaminases and NAFLD has become a common cause of referrals to hepatology clinics.¹ Traditionally NAFLD was considered relatively benign; however, it has now been clearly shown to progress to cirrhosis, liver failure, and hepatocellular carcinoma.

The prevalence of NAFLD has been found to be 15–46% in the West^{2–4} and 8–40% in Asian countries.^{5–9} The prevalence of NAFLD varies with different geographical locations but even in the same location, some races are more prone to develop NAFLD and nonalcoholic steatohepatitis (NASH). Weston et al.¹⁰ looked at the prevalence of NAFLD in different ethnic groups of patients in the USA who had been newly diagnosed as having chronic liver disease (CLD). In this study, they found that Hispanics had disproportionately higher representation in the NAFLD group compared to the base population while Caucasians and African-Americans had lower representation. Another study from Italy found that in spite of having a lower BMI, Asian-Indians had the highest levels of fasting serum insulin and insulin resistance (IR) estimated by homeostasis model assessment for IR (HOMA-IR) compared to Eastern Asians,

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Caucasians, African-Americans, and Hispanics.¹¹ Asian-Indians also had higher hepatic triglyceride (TG) content in comparison with Caucasians. This inter-ethnic difference in the prevalence of NAFLD and NASH is believed to be related not only to different lifestyles but also to a strong genetic predisposition.

The pathophysiology of NAFLD has also not been completely understood yet. It is evident that multiple factors are at play - lifestyle, diet, environmental factors, genes, bile acids, gut microbiota - and these could significantly vary across ethnicities and populations. Madan et al.¹² in their study concluded that North-Indian NAFLD patients have mild histological disease at presentation. Another study from coastal Eastern India showed that Indian subjects with NAFLD were younger, had lower BMI, lower prevalence of diabetes mellitus and MS, but similar necro-inflammatory activity score and fibrosis compared to patients in the West.¹³

This study is the first attempt at comparing the characteristics of Asian-Indian and US NAFLD patients.

MATERIALS AND METHODS

Study Design

It was a retrospective study comparing clinical, biochemical, and histopathologic profiles of NAFLD between Asian-Indian patients and patients from the US. The study was approved by the ethics committees of both centers.

Patients

Data of NAFLD patients were collected from the data bank of the Department of Gastroenterology, SCB Medical College, Cuttack, India, and the Division of Gastroenterology and Hepatology, Brooke Army Medical Center, Fort Sam Houston, Texas, US. The study cohort included 633 Asian-Indian NAFLD patients and 451 US NAFLD patients.

Methods

Comparisons between the study cohorts included clinical (age, sex, BMI, diabetes, hypertension, etc.), biochemical tests (liver function tests, lipid profile, and fasting blood sugar), hepatic ultrasound and hepatic histology. Statistical analysis was performed using SPSS 17.0 software. The results were expressed as median (range) for continuous variables and as frequencies (proportions) for categorical variables. Independent sample *t* test and Chi-square test were used to compare the variables. A “*p*” value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of Asian-Indian NAFLD patients in the study cohort was 42.3 ± 10.1 years (range 17–80 years) whereas the mean age of US NAFLD patients was 49.7 ± 10.6 (range 20–75 years). The majority of US NAFLD patients (82.3%) were more than 40 years of age compared to half (51.3%) of Asian-Indian patients ($\chi^2 = 109.551$, $p \leq 0.01$) (Fig. 1). There was a difference in gender prevalence in the US (male 56.3%) and Asian-Indian (male 81.7%) ($\chi^2 = 82.442$, $p \leq 0.01$ value) patients. When a cutoff BMI ≥ 30 kg/m² was defined as obesity, 71.2% of US NAFLD patients turned out to be obese whereas only 11.2% of Asian-Indian were obese but if obesity as per Asian standard (BMI ≥ 25 kg/m²) was considered, 63.7% of Asian-Indians were found to be obese. US patients had higher rates of

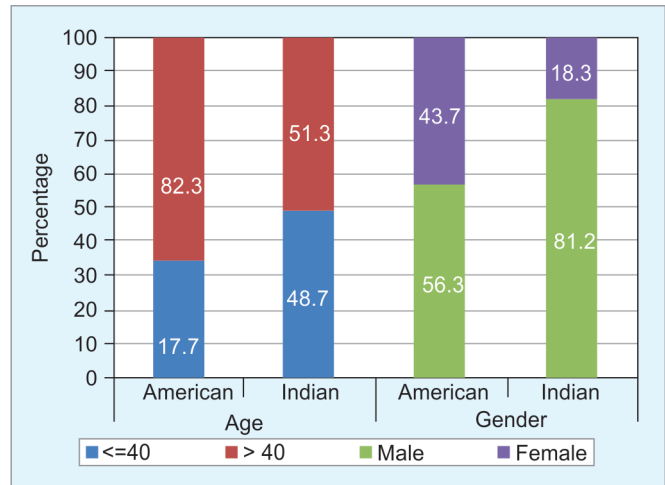


Fig. 1: Age and sex distribution of NAFLD population by country

Table 1: Distribution of NAFLD patients as per BMI

Standard of classification	BMI class	American		Indian		χ^2 test "p"
		Number	%	Number	%	
American Standard	Normal	21	4.7	230	36.3	0.000
	Over-weight	109	24.2	332	52.4	
	Obese	321	71.2	71	11.2	
	Total	451	100	633	100	
BMI range (Asian)	Normal	9	2	99	15.6	0.000
	Over-weight	12	2.7	131	20.7	
	Obese	430	95.3	403	63.7	
	Total	451	100	633	100	
American Standard for American Cases	Normal	21	4.7	99	15.6	0.000
	Over-weight	109	24.2	131	20.7	
	Obese	321	71.2	403	63.7	
	Total	451	100	633	100	

obesity as compared to Asian-Indian patients. (BMI 32.6 ± 5.3 kg/m² vs 26.2 ± 3.4 kg/m²) (Table 1).

With regard to comorbid conditions, US patients had a higher prevalence of both diabetes and hypertension (diabetes 42.1% vs 33%, and hypertension 56.8% vs 29.7%, $p \leq 0.01$). More than three-fourths of US NAFLD patients had elevated transaminases compared to half of the Asian-Indian patients. US NAFLD patients also had significantly higher ALT levels compared to Asian-Indians (ALT 82.78 ± 71.30 vs 53.66 ± 37, $p < 0.01$). Though a higher percentage of US NAFLD patients had dyslipidemia, Asian-Indian NAFLD patients had higher mean TG levels compared to US NAFLD patients. The histological comparison showed that a greater proportion of US patients had the more advanced liver disease at the time of diagnosis compared to Asian-Indians (Stage 3 fibrosis 10.42% vs 0%, and Stage 4 fibrosis 2.66% vs 0%, $p < 0.01$) (Fig. 2).

DISCUSSION

Worldwide, the overall prevalence of NAFLD ranges from 6.3 to 33% with a median of 20% in the general population. The

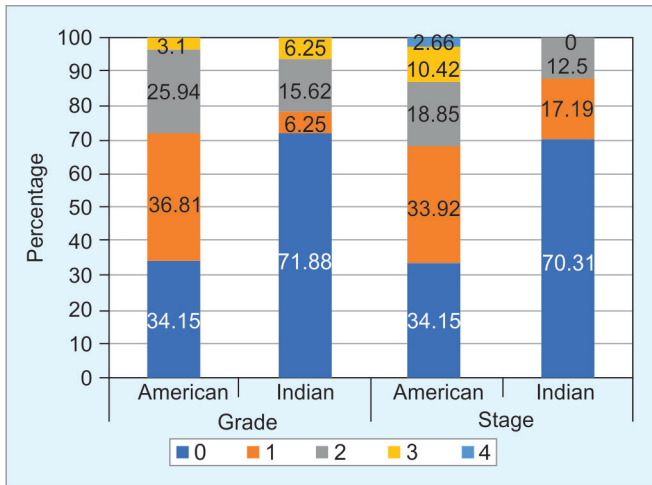


Fig. 2: Histological comparison of NAFLD patients

prevalence also varies with variations in age, gender, geographic location, and ethnicity.¹⁴ Studies conducted earlier have pointed out key differences between the phenotypes of NAFLD cohorts in Northern India and those from the West.¹² These differences are not surprising, considering the fact that the body fat distribution and risk of adverse cardiovascular events with a similar proportion of body fat differs between Asian-Indians and their Western counterparts. This has even prompted the lowering of BMI and waist-hip ratio (WHR) cutoffs for defining overweight and obesity among Asians.^{15,16}

This study is the first attempt at comparing the characteristics of Asian-Indian and US NAFLD patients. This study demonstrates that Asian-Indian NAFLD patients were younger and had been detected a decade earlier compared to the US NAFLD patients. This may be due to sedentary lifestyle, westernization of dietary habits, and abnormal body fat distribution of Asian-Indians. Indians have a higher percentage of body fat and an adverse pattern of body fat distribution including abdominal adiposity even within BMI ranges considered normal for Caucasians.¹⁷ In contrast to earlier Western studies which show a higher prevalence of NAFLD among females, this study showed a higher male prevalence both in US and Asian-Indian NAFLD patients.

Though the mean BMI of Asian-Indian NAFLD patients was less than that of the US NAFLD patients, an almost similar percentage of Asian-Indian and US NAFLD patients were found to be obese, if the cutoffs for BMI were considered as per Asian standards. It could possibly be attributed to the fact that Indian patients have a similar body fat percentage as Caucasians even at lower BMI levels. Similar to the study by Duseja et al.,¹⁸ the prevalence of diabetes and hypertension were found to be less in Asian-Indian patients in comparison to US NAFLD patients. Misra et al.¹⁹ reported that because of body composition and genetic predisposition, Asian-Indians more commonly have atherogenic dyslipidemia (i.e., a combination of hypertriglyceridemia, low level of HDL cholesterol, and high level of LDL cholesterol). In our study, we similarly found that Asian-Indian NAFLD patients have higher mean TG and lower HDL cholesterol in comparison with US NAFLD patients.

The histological comparison showed that a greater proportion of US patients had the more advanced liver disease at the time of diagnosis compared to Asian-Indians (Stage 3 fibrosis

10.42% vs 0%, and Stage 4 fibrosis 2.66% vs 0%, $p \leq 0.01$). Similar histological findings among NASH patients have been reported in other studies from India.^{12,19}

This study shows that Asian-Indian NAFLD patients are younger, have lower BMI, lower transaminases, and have milder histology compared to US NAFLD patients. There have been attempts to homogenize NAFLD without taking into account the significant differences across population groups worldwide. This study clearly shows that significant differences between Asian-Indian and US NAFLD patients exist. Further studies are required to better delineate these differences and understand mechanistically why these differences exist. This would help us in comprehending the pathophysiological details of the entity and help develop preventive and therapeutic strategies to curb the pandemic of NAFLD.

REFERENCES

- Adams LA, Sanderson S, Lindor KD, et al. The histological course of nonalcoholic fatty liver disease: a longitudinal study of 103 patients with sequential liver biopsies. *J Hepatol* 2005;42(1):132–138. DOI: 10.1016/j.jhep.2004.09.012.
- Farrell GC, Larter CZ. Nonalcoholic fatty liver disease: from steatosis to cirrhosis. *Hepatology* 2006;43:S99–S112. DOI: 10.1002/hep.20973.
- Bedogni G, Miglioli L, Masutti F, et al. Prevalence of and risk factors for nonalcoholic fatty liver disease: the Dionysos nutrition and liver study. *Hepatology* 2005;42(1):44–52. DOI: 10.1002/hep.20734.
- Williams CD, Stengel J, Asike MI, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology* 2011;140(1):124–131. DOI: 10.1053/j.gastro.2010.09.038.
- Singh SP, Nayak S, Swain M, et al. Prevalence of nonalcoholic fatty liver disease in coastal eastern India: a preliminary ultrasonographic survey. *Trop Gastroenterol* 2004;25(2):76–79. PMID: 15471321.
- Singh SP, Agrawal O, Meher C. Nonalcoholic fatty liver disease (NAFLD) in Orissa. *Orissa Physician J* 2005;1:8–15.
- Das K, Das K, Mukherjee PS, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. *Hepatology* 2010;51(5):1593–1602. DOI: 10.1002/hep.23567.
- Mohan V, Farooq S, Deepa M, et al. Prevalence of non-alcoholic fatty liver disease in urban south Indians in relation to different grades of glucose intolerance and metabolic syndrome. *Diabetes Res Clin Pract* 2009;84(1):84–91. DOI: 10.1016/j.diabres.2008.11.039.
- Amarapurkar D, Kamani P, Patel N, et al. Prevalence of non-alcoholic fatty liver disease: population based study. *Ann Hepatol* 2007;6(3):161–163. PMID: 17786142.
- Weston SR, Leyden W, Murphy R, et al. Racial and ethnic distribution of nonalcoholic fatty liver in persons with newly diagnosed chronic liver disease. *Hepatology* 2005;41(2):372–379. DOI: 10.1002/hep.20554.
- Petersen KF, Dufour S, Feng J, et al. Increased prevalence of insulin resistance and nonalcoholic fatty liver disease in Asian-Indian men. *Proc Natl Acad Sci USA* 2006;103(48):18273–18277. DOI: 10.1073/pnas.0608537103.
- Madan K, Batra Y, Gupta SD, et al. Non-alcoholic fatty liver disease may not be a severe liver disease at presentation among Asian-Indian. *World J Gastroenterol* 2006;12(21):3400–3405. DOI: 10.3748/wjg.v12.i21.3400.
- Singh SP, Kar SK, Panigrahi MK, et al. Profile of patients with incidentally detected non-alcoholic fatty liver disease (IDNAFLD) in coastal eastern India. *Trop Gastroenterol* 2013;34(3):144–152. DOI: 10.7869/tg.118.

14. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther* 2011;34(3):274–285. DOI: 10.1111/j.1365-2036.2011.04724.x.
15. World Health Organization, Western Pacific region. The Asia-Pacific perspective. Redefining obesity and its treatment. WHO/IASO/IOTF; 2000.
16. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363(9403):157–163. DOI: 10.1016/S0140-6736(03)15268-3.
17. Misra A, Vikram NK. Insulin resistance syndrome (metabolic syndrome) and obesity in Asian Indians: evidence and implications. *Nutrition* 2004;20(5):482–491. DOI: 10.1016/j.nut.2004.01.020.
18. Duseja A, Das A, Das R, et al. The clinicopathological profile of Indian patients with nonalcoholic fatty liver disease (NAFLD) is different from that in the West. *Dig Dis Sci* 2007;52(9):2368–2374. DOI: 10.1007/s10620-006-9136-y.
19. Misra A, Luthra K, Vikram NK. Dyslipidemia in Asian Indians: determinants and significance. *J Assoc Phys India* 2004;52:137–142. PMID: 15656049.