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Indian patients with nonalcoholic fatty liver disease presenting with raised transaminases are different at presentation

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TO THE EDITOR

We read with great interest the article, "Non-alcoholic fatty liver disease may not be a severe disease at presentation among Asian Indians" by Madan *et al*[1] in the recent issue of *WJG*. Twenty-eight (55%) out of 51 patients with non-alcoholic fatty liver disease (NAFLD) who presented with abnormal transaminases had histological evidence of nonalcoholic steatohepatitis (NASH). The majority of patients had grade 1 [32 (63%)] or grade 2 [16 (31%)] inflammation and either had no [23 (45%)] fibrosis or stage I [19 (37%)] fibrosis. None of the patients had cirrhosis[1]. We agree with Madan *et al*[1] that Asian Indians with NAFLD who present with unexplained increase in transaminases may have mild disease at presentation on the basis of similar observations made by us[2]. NAFLD has a spectrum which includes patients with only steatosis and NASH that can progress to cirrhotic and hepatocellular carcinoma[3]. Of the 127 NAFLD patients (July 2001-March 2006) who presented with raised transaminases for at least 6 mo with negative viral, autoimmune and metabolic workup analyzed in our study, 43 underwent liver biopsy (Table 1). Only half of them [22 (51%)] had histological evidence of NASH as defined by either class Ⅲ [8 (19%)] or class Ⅳ [14 (32%)] NAFLD according to Matteoni *et al*[4]. The other 21 (49%) patients either had class Ⅰ [2 (5%)] or class Ⅱ [19 (44%)] disease not amounting to histological NASH (Table 1). In the 22 patients with histological NASH evaluated as per Brunt *et al*[5], the majority had mild to moderate inflammation and either no fibrosis or stage Ⅰ to Ⅱ fibrosis. Only 18% patients had stage Ⅲ fibrosis and none of the patients had cirrhosis of the liver (Table 1).

The majority of patients studied by us were males with a mean age of 39.2 ± 10.7 years (Table 2), which is similar to data shown by Madan *et al*[1]. In addition to the mild histological disease at presentation, there are other differences in NAFLD patients from India and those from the West[2]. When we used the Asia Pacific criteria[6,7], even though most of our patients had central obesity [104 (82%)] and were either overweight [27 (21%)] or obese [86 (68%)] they did not have the kind of morbid obesity seen in patients from the West (Table 2). The mean body weight and body mass index (BMI) of our patients were 71 kg and 28.7 kg/m^2 respectively, much less than those reported from the West[8,9], but were similar to the data shown by Madan *et al*[1] who also found that the median BMI is 26.7 (range 21.3-32.5) kg/m^2 and the majority of them are obese (69%) according to the Asian Pacific criteria. When the ATP Ⅲ criteria with modified waist were used in 81 of our patients to define metabolic syndrome, around half of them [39 (48%)] had metabolic syndrome, also less than reported in patients from the West (Table 2)[10]. We attributed low prevalence of metabolic syndrome in our patients to the lower prevalence of diabetes mellitus [16 (13%)] and hypertension [13 (10%)] at presentation, which is similar to the data reported by Madan *et al*[1] (10% and 11.8% respectively) in their study. Furthermore, the low prevalence of metabolic syndrome (20.9%) in the study of Madan *et al*[1] could be due to their use of BMI as a surrogate marker for waist, which may not always be true. Indians may have a normal BMI with an abnormal waist which is related to more of central obesity rather than overall obesity. It is possible that diabetes mellitus occurs late in the course of this disease when the degree

Table 1 Liver histology in 43 patients with nonalcoholic fatty liver disease (NAFLD), *n* (%)

Class Ⅰ	2 (5)
Class Ⅱ	19 (44)
Class Ⅲ	8 (19)
Class Ⅳ	14 (32)
NASH (class Ⅲ + Ⅳ) on histology (*n* = 22)	
Grade 1	10 (45)
2	12 (55)
3	0
Stage 0	6 (27)
1	7 (32)
2	5 (23)
3	4 (18)
4	0
Perls' Prussian blue staining on liver biopsy (*n* = 30)	
0	20 (67)
1+	6 (20)
2+	4 (13)
3+	0
4+	0

Table 2 Clinical and laboratory parameters in 127 patients with nonalcoholic fatty liver disease (NAFLD)

mean age ± SD (yr)	39.2 ± 10.7
Males	84
Mean body weight (range) (kg)	71 (45-100)
Mean BMI (range) (kg/m^2)	28.7 (19-34)
Overweight	27 (21%)
Obesity	86 (68%)
Abnormal waist	104 (82%)
Insulin resistance	48/58 (83%)
Diabetes mellitus	16 (13%)
Hypertension	13 (10%)
Dyslipidemia	67 (53%)
Metabolic syndrome	39/81 (48%)

of insulin resistance increases and our patients could represent patients in the early spectrum of NAFLD with less severe disease and diabetes mellitus at presentation with raised transaminases. Diabetes mellitus is one of the risk factors for severe liver disease in NAFLD and absence of this risk factor in majority of our patients may explain the mild disease on liver biopsy.

Insulin resistance is very common in patients with NAFLD irrespective of the methodology used. Eighty percent of 51 patients in the study by Madan *et al*[1] had abnormal homeostasis model assessment for insulin resistance (HOMA-IR). We found insulin resistance in all of our 22 patients initially studied by insulin tolerance test (ITT) and later in 48 (83%) of 58 patients studied by HOMA-IR (Table 2)[2,11,12].

Though not studied by Madan *et al*[1], another difference in Indian patients and those from the West is the presence of serum and liver iron abnormalities and HFE gene mutations[2,13,14]. Only 4 (5%) of our 87 patients had abnormal serum ferritin or transferrin saturation and 4 (13%) of 30 patients studied were heterozygotes for H63D mutation. None of the patients had C282Y HFE gene mutation. The majority of our patients had negative Perls' staining for iron on liver biopsy (Table 1) and there was no correlation between the iron staining and degree of necro-inflammation and fibrosis, suggesting that serum and liver iron and HFE gene mutations play a very little role in Indian patients with NAFLD[2,13,14].

In conclusion, Indian patients with NAFLD who present with incidental detection of raised transaminases representing a part of spectrum of patients with NAFLD have a milder disease at presentation. Whether NAFLD in Indian patients is overall mild or overall different from other parts of the world requires analysis of full spectrum of NAFLD patients.

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