# Underestimation of metabolic unhealthiness and overestimation of non-alcoholic fatty liver disease

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We read with great interest the article by Mukherjee et al. and congratulate the authors on this mammoth effort.[1] However, we have a few concerns.

A previous study reports higher prevalence rates (10.7% in males and 20.3% in females) of metabolic syndrome in the population from Birbhum district.[2] In the study by Mukherjee et al. also, participants had a high (34,827, 43.6%) prevalence of metabolic risk factors [hypertension or random blood glucose (RBG) > 200 mg/dl/ diabetes mellitus (DM)].[1] In contrast, a markedly lower [1.1% (885/79,957)] prevalence of metabolic unhealthy (MU) status is reported. In step 2, the patients with fasting plasma glucose >100 mg/dl were ~4-fold higher than those with RBG >200 mg/dl. The biochemical screening for dysglycemia in step 1 included only RBG >200 mg/dl. This strategy might have missed a proportion of patients with impaired fasting glucose (IFG)/DM at step 1. Notably, nearly half (4536/9819) of the step 2 participants with normal glycemic status and normal alanine aminotransferase (ALT) were excluded from entering step 3. A proportion of these patients might have had hypertension and dyslipidemia and fulfilled the criteria for MU status. Most importantly, the majority of participants (~three-fourths), at comparable risk for MU as responders, did not respond in steps 2 and 3. These high rates of nonresponse underestimate the overall prevalence of MU status by ~15-fold. So, the prevalence of MU status has markedly been underestimated.[1]

Das et al. report serum ALT of 29.46 ± 26.4 U/L in controls and non-alcoholic fatty liver (NAFL) with elevated ALT (>40 U/L) in only 2.3% of the population from the Birbhum district.[3] A markedly higher prevalence of elevated ALT in step 2 of Mukherjee et al. may be the result of using more sensitive cut-offs, derived from the Italian population, to define elevated ALT.[4] Another concern is considering every elevated ALT as non-alcoholic fatty liver disease (NAFLD).[1] Surprisingly, the proportions of participants with elevated ALT were not remarkably different between subjects with IFG/ DM (42%) and normal glycemia (39%). More surprisingly, the proportions of persistently elevated ALT were higher in metabolically healthy non-obese and obese groups than the respective MU groups; also, the ALT levels were higher in the obese metabolically healthy group than in obese MU groups irrespective of the number of additional risk factors. These observations question elevated ALT as a marker of dysmetabolism in the study population. Although this might have partly resulted from graduating normal glycemic status participants with elevated ALT, not those with normal ALT, from step 2 to step 3, a potential role for other causes of transaminitis needs consideration. Notably, the contribution of alcohol consumption to transaminitis was underweighted by presuming its role as nil at the community level. So, there may be an overestimation of NAFLD.[1]

#### Contributors

Vijaya Sarathi drafted the initial manuscript, Dhananjaya MS and SL Sagar Reddy critically reviewed the draft. All authors approved the final manuscript.

#### Declaration of interests

The authors declare no conflict of interest.

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