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Is increased red cell distribution width an indicating marker of nonalcoholic steatohepatitis and fibrotic stage?

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Abstract

Red cell distribution width (RDW) may play an important role in predicting steatohepatitis and liver fibrosis. In the original study, it was aimed to determine whether RDW could be used for this purpose or not. There are studies indicating that higher RDW is correlated well with components of metabolic syndrome. Because nonalcoholic fatty liver disease is now recognized as the hepatic manifestation of metabolic syndrome, possible impact of the accompanying confounders on the study findings should have been detailed. There may be a patient selection bias due to use of improper cut-off values for alcohol consumption and inclusion of only subjects with normal aminotransferase levels and normal abdominal ultrasonography. Patients without hepatosteatosis on ultrasonography and with any restriction of aminotransferase levels should have been included in the control group, because isolated aminotransferase elevation is not decisive in the diagnosis of hepatosteatosis. Although iron, vitamin B_{12} and folic acid deficiencies were included in exclusion criteria, functional forms of these molecules like methylmalonic acid, homocysteine, ferritin levels and total iron binding capacity, which are more sensitive and specific parameters for vitamin B_{12} and folic acid deficiencies, were not mentioned. Consequently, RDW, an inexpensive, non-invasive, but powerful indicator overlooked on whole blood analysis, itself without other inflammatory markers may not accurately provide information about progression of nonalcoholic steatohepatitis and fibrosis.

Key words: Anemia; Fibrosis; Red cell distribution width; Steatohepatitis; Steatosis

Core tip: Red cell distribution width (RDW) may play an important role in predicting steatohepatitis and stage of liver fibrosis. Use of improper cut-off values for alcohol consumption and inclusion of only subjects with normal aminotransferase levels and normal abdominal ultrasonography may result in a patient selection bias. Instead of using the iron, vitamin B_{12} and folic acid, use of the functional forms of these molecules like methylmalonic acid, homocysteine, ferritin levels and total iron binding capacity is more sensitive and specific for vitamin B_{12} and folic acid deficiency. Consequently, RDW itself without other inflammatory markers may not accurately provide information about progression of nonalcoholic steatohepatitis and fibrosis.

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TO THE EDITOR

We read with great interest the recent published article

by Cengiz *et al*[1], "Is increased red cell distribution width an indicating marker of nonalcoholic steatohepatitis and fibrotic stage?". In this study, authors have evaluated red cell distribution width (RDW) as a marker indicating nonalcoholic steatohepatitis (NASH) and fibrotic stage, and as a conclusion, RDW was reported as a new non-invasive marker that can be used to demonstrate the presence of NASH and to indicate advanced fibrotic scores. There are some points that we would like to address from this study.

Firstly, in that study, it was stated that 30.6% of the patients with NASH had diabetes mellitus (DM) and 35.4% of those had hypertension (HT). As is well known, DM and HT are the two of five diagnostic criteria for metabolic syndrome (MetS) determined by the National Cholesterol Education Program Adult Treatment Panel Ⅲ[2]. There are studies indicating that higher RDW is correlated with hypertension[3]. Moreover, high level of RDW was also associated with the MetS, leading to postulation of a possible effect of an underlying inflammatory state which typically occurred in DM and MetS on increased destruction of erythrocytes[4]. Because *NAFLD* is now recognized as the hepatic manifestation of *MetS,* the possible impact of the accompanying confounders on the study findings should have been detailed.

Secondly, all the patients who had persistently elevated liver enzymes and hepatosteatosis on ultrasonography, in the absence of any cause of elevated aminotransferases, were evaluated in the original study. The control group was created among individuals who had normal aminotransferase levels and normal abdominal ultrasonography. However, patients without hepatosteatosis on ultrasonography and with any restriction of aminotransferase levels should have been included in the control group, because isolated aminotransferase elevation is not decisive in the diagnosis of hepatosteatosis. According to these selection criteria, it is obvious that there is a patient selection bias for aminotransferase levels. Another patient selection bias is derived from the selected cut-offs for the alcohol consumption value. In that study, alcohol consumption > 20 g/d for men and > 10 g/d for women was accepted as exclusion criteria. However, it is generally accepted as > 30 g/d for men and > 20 g/d for women[5]. Therefore, misuse of this cut-off value could have led more patients to be included into the original study.

Thirdly, although iron, vitamin B_{12} and folic acid deficiencies were included in exclusion criteria, functional forms of these molecules like methyl malonic acid, homocysteine, ferritin levels and total iron binding capacity were not mentioned; however, active forms of these vitamins, methyl malonic acid and homocysteine levels are more sensitive and specific parameters for vitamin B_{12} and folic acid deficiencies. Since RDW is directly related to these deficiencies, this situation makes an accuracy bias[6,7].

Consequently, RDW, an inexpensive, non-invasive, but powerful indicator overlooked on whole blood analysis, itself without other inflammatory markers may not accurately provide information about progression of NASH and fibrosis. So, we think that, when evaluating any marker associated with inflammation in patients with NASH, the effects of confounders like DM and HT should also be discussed in detail. In addition, factors affecting the RDW results like iron, vitamin B12 and folic acid deficiency should be considered to conclude that RDW is a useful diagnostic tool to discriminate patients with NASH from non-NASH, and advanced fibrosis from non-advanced fibrosis. In this way, further information can be obtained about the association between RDW and NASH.

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