Use of BARD scoring system in non-alcoholic fatty liver disease patients and its correlation with ultrasonographic grading in Giza, Saudi Arabia

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Abstract

Purpose: To assess the efficacy of the BARD scoring system in Saudi non-alcoholic fatty liver disease (NAFLD) patients attending Giza General Hospital and to identify the clinical variables associated with advanced fibrosis.

Methods: The cross-sectional study involved 120 patients aged ≥ 18 years who attended the Ultrasound Department of Giza General Hospital, Giza, Saudi Arabia, during January – June 2013. BARD scoring system comprised the following variables: body mass index (BMI) ≥ 28 = 1 point, aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio ≥ 0.8 = 2 points, and type 2 diabetes mellitus = 1 point.

Results: Patients with advanced fibrosis were older (55.0 years) than patients with no/mild fibrosis (48.6 years), albeit not significantly so. A higher BMI was associated with advanced fibrosis in males, females and all study participants (p = 0.013, 0.016 and 0.001, respectively). Advanced fibrosis was more common in older patients with a higher weight to height ratio. Logistic regression suggested that age ≥ 50 years was associated with a 2.52-fold increase in the risk of advanced fibrosis, but this did not have a significant clinical impact (p = 0.087). BMI > 28 was associated with a 26.73-fold increased risk of advanced fibrosis, while AST/ALT ≥ 0.8 was associated with an 18.46-fold increased risk of advanced liver fibrosis (p = 0.002 and 0.006, respectively).

Conclusion: The major risk factors for advanced fibrosis using BARD scoring system in patients with NAFLD were old age, BMI > 28, and AST/ALT ≥ 0.8. In addition, grade 3 ultrasonographic fatty liver significantly correlated with advanced fibrosis.

Keywords: BARD score, Non-alcoholic fatty liver disease, Body mass index, Fibrosis score, Ultrasonographic grading

INTRODUCTION

Fatty liver refers to a spectrum of diseases characterised by excessive fat accumulation in the liver. Fatty tissue gradually builds up in the liver when the amount of fat in the diet exceeds the body’s metabolic capacity [1,2]. Non-alcoholic fatty liver disease (NAFLD) was
first recognized in 1980 and its prevalence varies widely depending on the population studied and the definition used [1,2]. The prevalence of histologically defined NAFLD increases with age, ranging from less than 20 % in those under 20 years of age to more than 40 % in those over 60 years of age and reaching 60 – 85 % in risk groups such as those with diabetes and obesity [3-5]. The prevalence of NAFLD in Saudi Arabia has been reported to be 16.6 % [6].

Clinically NAFLD is recognized as a spectrum of closely related disorders that include non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). In NAFL, simple hepatic steatosis is present without evidence of significant inflammation, whereas in NASH, hepatic steatosis is associated with hepatic inflammation and hepatocyte ballooning that may be histologically indistinguishable from alcoholic steatohepatitis [7]. NASH may progress to liver cirrhosis within an average period of 8 to 10 years, while only 2 – 3 % sub-set of patients with NAFLD develop NASH, and 5–8 % of NASH patients develop liver cirrhosis [8,9].

According to recent studies, NAFLD is associated with “idiopathic” cases of hepatocellular carcinoma (HCC), and NASH cirrhosis has been demonstrated as the specific diagnosis for a considerable number of cases previously diagnosed as cryptogenic cirrhosis [10-12]. NAFLD is believed to be a hepatic manifestation of metabolic syndrome (MS) and thus is closely related to several cardiovascular disorders [13].

NAFLD is an emerging disease [4,5], even in developing countries, which can remain silent for years. The majority of patients suffering from NAFLD are asymptomatic, and invasive methods are not recommended routinely in such patients. The BARD and NAFLD scores were established specifically for assessing and predicting NAFLD. The main strength of the BARD score over the NAFLD fibrosis score is its simplicity. The components of the BARD score are body mass index (BMI), aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio, and diabetes. The BARD score is widely used to predict liver fibrosis in NAFLD patients and requires simple clinical data [14,15].

In this study, we assessed BARD scores among Saudi NAFLD patients attending Gizan General Hospital and identified clinical variables associated with advanced fibrosis. The study also attempted to correlate BARD scores with ultrasonographic NAFLD grades.

**EXPERIMENTAL**

This cross-sectional study involved 120 patients attending the Ultrasound Department in Gizan General Hospital, Gizan, Saudi Arabia, during January–June 2013. The main inclusion criteria were adult patients (18 years of age and older) with ultrasound-proven fatty liver. Patients with coexisting liver disease and those who consumed alcohol or used steatogenic drugs were excluded from the study.

A sample of 120 participants was estimated for the purpose of this study. The sample size was calculated using the formula for a single cross-sectional survey, n = [(z^2 * p * q)]/d^2. Sample size was calculated using the following parameters: p = prevalence of NAFLD 50 %, Z = 95 % confidence interval, d = error ≤ 10 %, and a 15 % non-response rate.

Clinical data collected from all participants, include: body mass index (BMI), history of alcohol consumption and the presence of systemic hypertension. Antecubital venous blood samples were taken from all subjects after a 12 h overnight fast. Using a multichannel autoanalyzer, we measured serum levels of complete blood counts, liver function tests alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), renal function tests, Fasting blood glucose (FBG), Low density cholesterol (LDL), high density cholesterol (HDL), triglycerides (TG), uric acid (UA) and serology for hepatitis B and C.

All subjects were screened for FLD by a single, expert radiologist using a sensitive Ultrasound machine (Toshiba. Apio XG, probe 305 hz). Fatty liver was diagnosed by the presence of increased hepatic echogenicity compared to the spleen or the kidneys. The diagnosis of NAFLD was based on the American Association for Study of Liver Disease (ASSLD) guidelines for the assessment and management of NAFLD [16].

Fatty liver was graded as follows first grade 1 (Mild) - minimal diffuse increase in hepatic echogenicity with normal visualization of diaphragm and intrahepatic vessel borders; second grade 2 (Moderate) - moderate diffuse increase in hepatic echogenicity with slightly impaired visualization of intrahepatic vessels and diaphragm. Grade 3 (Severe) - marked increase in echogenicity with poor penetration of posterior segment of right lobe of liver and poor or no
visualization of hepatic vessels and diaphragm [17].

BARD score was calculated by assigning points to following parameters: BMI ≥ 28 kg/m² = 1 point, BMI <28 kg/m² = 0 point; AST/ALT ratio ≥ 0.8 = 2 points, AST/ALT ratio < 0.8 = 0 points; freshly recognized or pre-existing DMt2 = 1 point. According to original methods, a total of 2 - 4 points indicate significant fibrosis [14,15].

Data were analyzed using SPSS version 20 (SPSS Inc, Chicago, IL, USA). Data analysis involved descriptive statistics as well as inferential statistics. Descriptive statistics included a simple tabulation, frequencies, proportion for categorical variability including cross-tabulations. Differences in proportions were compared for significance using Chi Square test, with a significance level set at p < 0.05. We also performed an independent t-test to assess differences in numerical variables between patients according to BARD score. Logistic regression model was also used to evaluate factors associated with BARD score.

Informed written consent was obtained from all enrolled patients, as per the ethics guidelines in Saudi Arabia. Purpose, potential risk and benefits of the study were communicated in the Arabic language, and consent was documented for all study participants. Ethical approval for the current study was obtained from the Ethics Committee of the Faculty of Medicine, Gizan University, (approval ref no. 15-FMRER). 

RESULTS

Table 1 shows the demographic and clinical characteristics of the enrolled patients. As shown in Table 1, the mean age of study participants was 49.5 ± 12.91 years, with no significant differences between males (49.0 ± 14.6 years) and females (50.2 ± 0.43 years). Patients had a BMI averaged at 30.21 kg/m², which is slightly higher for females 31.2k g/m² than for males who were 29.56 kg/m², but with no significant difference between the two groups. AST (aspartate aminotransferase) and ALT (alanine aminotransferase) levels were also higher in males than in females, but with no significant differences (p = 0.688 and 0.102 respectively). Regarding other indicators in the Table, only creatinine (CR) and PLT (platelet count) were significantly different between males and females (p = 0.003 and 0.046, respectively).

Patients with advanced fibrosis (F3-F4) had higher mean age (55.04 years) compared with 48.58 years for patients with no/mild fibrosis (F0-F2), but without significant difference (Table 2). The same applies for females (p value = 0.070), but for males there was significant difference between the two groups (p value = 0.029). Higher BMI for males, females and all study participants were associated with advanced fibrosis (p = 0.013, 0.016 and 0.001, respectively). Advanced fibrosis (F3-F4) was more common in older patients with higher W/H ratio and uric acid UA. TG, TC, CR, and serum AST were not significant risk factors for advanced fibrosis in this study. Serum CR level and FBG were lower in patients with F3 and F4 fibrosis stages, but this difference did not reach clinical significance (p = 0.103 and 0.920).

The factors associated with an increased risk of severe liver fibrosis are provided in Table 3.

Table 1: Demographic and clinical characteristics of the enrolled patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(Years)</td>
<td>49.5 ± 12.91</td>
<td>49.0 ±14.6</td>
<td>50.2 ±10.43</td>
<td>0.588</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.21 ± 5.35</td>
<td>29.56 ± 4.58</td>
<td>31.2 ± 6.22</td>
<td>0.168</td>
</tr>
<tr>
<td>W/H(kg/m)</td>
<td>0.48 ± 0.85</td>
<td>0.49 ±0.83</td>
<td>0.49 ±0.89</td>
<td>0.635</td>
</tr>
<tr>
<td>TG(mmol/L)</td>
<td>159.11 ± 45.51</td>
<td>161.00 ± 46.78</td>
<td>156.93 ± 44.44</td>
<td>0.670</td>
</tr>
<tr>
<td>TC(mmol/L)</td>
<td>203.20 ± 47.35</td>
<td>199.94 ± 50.27</td>
<td>206.95 ± 43.99</td>
<td>0.465</td>
</tr>
<tr>
<td>UA(μmol/L)</td>
<td>5.56 ± 2.13</td>
<td>5.62 ± 1.98</td>
<td>5.45 ± 2.43</td>
<td>0.758</td>
</tr>
<tr>
<td>CR(μmol/L)</td>
<td>0.80 ±0.15</td>
<td>0.84 ± 0.13</td>
<td>0.75 ± 0.16</td>
<td>0.003</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>33.32 ± 13.80</td>
<td>30.70 ± 14.60</td>
<td>28.55 ± 12.78</td>
<td>0.457</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>33.32 ± 16.37</td>
<td>33.96 ± 16.02</td>
<td>32.59 ± 16.92</td>
<td>0.688</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>85.43 ± 0.23</td>
<td>80.81 ± 29.39</td>
<td>91.02 ± 30.61</td>
<td>0.102</td>
</tr>
<tr>
<td>FBG(mmol/L)</td>
<td>193.5 ± 78.20</td>
<td>191.04 ± 81.70</td>
<td>196.71 ± 74.40</td>
<td>0.739</td>
</tr>
<tr>
<td>HbA1C (mmol/mol)</td>
<td>10.59 ± 2.69</td>
<td>10.16 ± 2.71</td>
<td>11.06 ± 2.61</td>
<td>0.136</td>
</tr>
<tr>
<td>PLT(mcL)</td>
<td>286.92 ± 71.19</td>
<td>267.96 ± 68.62</td>
<td>303.64 ± 71.19</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Values, mean±standard deviation (S.D.); BMI: body mass index; W/H: weight to height ratio; TG: Triglycerides; TC: total cholesterol; UA: Uric acid; FBG: Fasting plasma glucose; CR: Creatinine; ALT( alanine aminotransferase); AST (aspartate aminotransferase); ALP: alkaline phosphatase; HbA1C: glycated haemoglobin and PLT : platelet count
**DISCUSSION**

Liver biopsy remains the gold standard for differentiating NASH from NAFLD. However, it is not cost-effective and is associated with various morbidities [18]. Alternatives to liver biopsy include various non-invasive methods. Indeed, several non-invasive methods for early prediction of fibrosis in patients with NAFLD have been validated recently. The BARD score is easily calculated, and represents a simple method of excluding the presence of advanced fibrosis in NAFLD patients.

The BARD scoring system has been validated by liver biopsy. A recent study found that the BARD score has a negative predictive value (NPV) of 96% [14]. The BARD score was validated in 138 patients with biopsy-proven NAFLD and showed a sensitivity, specificity, positive predictive value (PPV) and NPV of 51, 77%, 45 and 81%, respectively [19]. The BARD score was also validated in a study involving 104 Polish patients.
with biopsy-proven NAFLD, which reported an NPV of 97% [20]. Furthermore, a study of 145 patients with biopsy-proven NAFLD reported a sensitivity, specificity, NPV, and PPV of 89, 44, 95 and 25%, respectively [21].

In the present study, BARD scoring system was applied in 120 ultrasonography- proven NAFLD patients in order to assess the risk factors of fibrosis and to correlate fibrosis with fatty liver grades. The study showed that participants with advanced fibrosis (F3-F4) as denoted by BARD score had higher age (55.04 years) compared with 48.58 years for patients with no or mild fibrosis (F0 - F2). Two studies reported a strong relationship between NAFLD-related fibrosis and advanced age [22,23].

In the present study advanced fibrosis (F3-F4) is more common in patients with high serum uric acid (UA) levels. Similar results were reported by Sertoglu et al, who concluded that serum UA levels in patients with biopsy-proven NASH were significantly higher than those of simple fatty liver [23]. In contrast to majority of the studies [20-22], our results concluded that, hypertriglyceridemia and hypercholesterolemia (according to TG and TC levels, respectively) were not significant risk factors for advanced fibrosis this may be attributed to the small size of our study.

Our study, revealed mean BARD score for grade 1 fatty liver was 2.21, compared with 1.86 and 2.60 for grades 2 and 3 fatty liver, respectively. ANOVA suggested that the three grades differed significantly; moreover, grade 3 was associated with advanced fibrosis. This is not in agreement with the findings of Kakrani et al, who reported that biochemical evidence of fibrosis or NAFLD in the form of BARD or NAFLD fibrosis scores did not correlate with Ultrasonography evidence of fatty liver [17]. These discrepancies between the two studies might be due to differences in the subject selection criteria. All participants in the study by Kakrani et al (106 patients) had a BMI > 25, whereas participants in our study were of different BMI categories.

Limitations of the study

The present study has three limitations. First, the study sample may not be representative of the population of Gizan, since it was conducted in only one hospital in the Gizan region. Second, the diagnosis of NAFLD was based on ultrasonography and was not confirmed by liver biopsy, which is important for assessing NAFLD [24]. Ultrasonography is by far the most common method of diagnosing NAFLD in clinical practice. Thirdly, a cross-sectional study design is not suitable for assessing risk factors for NAFLD, and no controls were included. Therefore, a case-control study of factors associated with advanced fibrosis is warranted.

CONCLUSION

The findings of the present study show that the major risk factors of advanced fibrosis using BARD scoring system in patients with NAFLD are old age, BMI > 28, and AST/ALT ratio ≥ 0.8. Furthermore, Grade 3 ultrasonographic fatty liver significantly correlates with advanced fibrosis, based on BARD score.

ACKNOWLEDGEMENT

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REFERENCES


