Cherry angioma has acceptable diagnostic value for non-alcoholic fatty liver disease: Diagnosis of fatty liver by cherry angioma

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is becoming a significant problem especially through substantial increase in the incidence of obesity worldwide. Currently it is the most common cause of abnormal serum aminotransferase levels both in low- and middle-income countries and in high-income countries and despite its high prevalence, well-defined screening recommendations are currently lacking. The purpose of this study was to calculate statistical values of cherry angioma in the diagnosis of NAFLD. We were looking for evidence to be able to recommend cherry angioma as a screening tool for NAFLD that needs further investigations including ultrasonography.

Methods: We studied individuals who visited the private clinic between July 2011 and December 2012 for health examinations. Physician evaluated each individual by different laboratory tests for systemic, viral and hereditary diseases and excluded those with any of these disease. After completion of physical examination, registration of the cherry angioma diagnosis and lab tests, 340 individuals referred to a radiologist for the diagnosis of NAFLD by abdominal ultrasonography.

Results: Among 340 study subjects, 150 (44%) were males and 190 (55%) were females. Mean of age and BMI were 47.9 years and 26.9 kg/m², respectively. Of referred individuals, we diagnosed 238 persons as fatty liver disease through abdominal ultrasonography. We assigned them as NAFLD group. The other 102 individuals were identified with normal livers and were assigned as non-NAFLD group. There was no difference in age and height but for weight and BMI between individuals of NAFLD and non-NAFLD groups. Individuals in NAFLD group were more obese than those in non-NAFLD group. There was no difference in age and height but for weight and BMI between individuals of NAFLD and non-NAFLD groups. Individuals in NAFLD group were more obese than those in non-NAFLD group. Overall, sensitivity, specificity, PPV, NPV and accuracy were, 76.9, 80.4, 95.8, 37.5, and 77.4, respectively. All values were higher among women than men. The highest sensitivity was observed in individuals with age >40 years, and the highest specificity was observed in individuals with age ≤40 years.

Conclusions: In conclusion, NAFLD can be sufficiently predicted by cherry angioma on physical examination.

Key words: Non-alcoholic Fatty Liver Disease (NAFLD), Cherry Angioma, Sensitivity, Specificity
Introduction

Nonalcoholic fatty liver disease (NAFLD) is becoming a significant issue following worldwide increase in the incidence of the obesity. NAFLD has become an urgent condition especially among obese patients as the most common cause of abnormal liver tests. In NAFLD more than 5% of weight of liver consists of hepatocytes that have accumulated with different fat molecules including triglycerides. Since the main mechanism for evolution of primary NAFLD is through insulin resistance it commonly coincides with metabolic syndrome parts including obesity, type II diabetes mellitus (DM) and dyslipidemia. Due to lack of prospective studies incidence and the real prevalence of NAFLD is not known. Prevalence of adult NAFLD in China and Japan reported to be 15% and 14%, respectively. European and Japanese populations showed a prevalence of 14 to 21% for NAFLD. Obesity, type II DM, and hyperlipidemia are diseases commonly found with NAFLD. Prevalence of obesity has been reported in a range of 30 and 100%, the prevalence for type II DM was between 10 and 75%, and for hyperlipidemia was between 20 and 92% among patients with NAFLD. The diagnosis of NAFLD is made by establishment of fatty liver in a non-alcoholic pattern of the disease. Even though sonography is the widely available cheapest imaging modality for the diagnosis of NAFLD but gold standard diagnosis procedure is liver biopsy that an invasive nature with its higher associated risk. NAFLD usually appears without clinical presentations and mainly diagnosed following an abnormal aminotransferase or incidental radiographic findings of fatty liver. To be cost-effective, clinicians desire to use sonography just after abnormal laboratory tests or physical examinations. In this case when physician suspect NAFLD through laboratory tests and physical examination then diagnosis will be made early and management and treatment would be appropriately and effective.

Liver diseases that are induced by alcohol (including fatty liver, hepatitis and cirrhosis) can cause many effects on the skin. These skin symptoms include: 1. Vascular changes (spider nevi, telangiectasia and palmar erythema); 2. Nail changes; 3. Glossy tongue and other mucosal membrane changes; and 4. Hormonal alterations (atrophy of testes, gynecomastia, female hair distribution) and 5. Skin color changes (icterus and melanosis cutis). As far as we know, there are no reports of skin symptoms due to non-alcoholic fatty liver disease. “Campbell De Morgan spot”, “Senile angioma”, or their famous name “Cherry angioma” contains abnormal proliferation of blood vessels that appears as cherry red papules of skin. Cherry angioma are commonly found in middle age people but can also occur in young individuals. Its aggressive eruptive form can occur in any age. Due to lack of study in the subject the main underlying cause of cherry angioma is not known. According to clinical observation Cherry angioma are seen in most patients with NAFLD.

Objectives

In this study we aimed at establishing a predictive role of cherry angioma, through calculation of its statistical diagnostic values, to choose people for abdominal ultrasonography and for early diagnosis of NAFLD.

Patients and Methods

We included individuals who visited the private clinic between July 2011 and December 2012 for health examinations. Physician evaluated each individual by different laboratory tests for systemic, viral and hereditary diseases and excluded those with any of these disease. We also made sure that the history of alcohol consumptions was negative. We measured heights and heights and calculated body mass index
Cherry angioma has acceptable diagnostic value for the screening of NAFLD. Considering almost high value for the specificity and sensitivity in all subgroups of the study, we can recommend using cherry angioma for the screening of NAFLD.

Results

Among 340 study subjects, 150 (44%) were males and 190 (55%) were females. Mean (± standard deviation) of age and BMI were 47.9 (± 13.5) years and 26.9 (±4.13) kg/m2, respectively. There was no difference in age and height but for weight and BMI between individuals of NAFLD and non-NAFLD groups (Table 1). Individuals in NAFLD group were more obese than those in non-NAFLD group.

Overall, sensitivity, specificity, PPV, NPV and accuracy were, 76.9, 80.4, 95.8, 37.5, and 77.4, respectively. As you can see in Table 2, all values were higher among women than men. The highest sensitivity was observed in individuals with age >40 years, and the highest specificity was observed in individuals with age ≤40 years.

Discussion

In this study we found cherry angioma has adequate diagnostic value for the screening of the NAFLD. Considering almost high value for the specificity and sensitivity in all subgroups of the study, we can recommend using cherry angioma for the screening of NAFLD.
of the NAFLED. This is more robust for the women. In one study, Lee and colleagues created a formula to screen NAFLD patients for sonography (hepatic steatosis index [HIS] = 8 × [ALT/AST ratio] + BMI [+2, if female; +2, if diabetes mellitus]). They could exclude NAFLD (93.1% sensitivity) with HIS value <30 and diagnose NAFLD (92.4% specificity) if HIS value was >36.0\(^{15}\). Young Jin Park and et al. proposed a simpler index system. In that study the index system was between 0 to 6 points and were assigned as follows: ALT/AST ratio > 1.5 =1 point; \(\gamma\)-GTP > 50 =1 point; triglyceride > 150 mg/dl =1 point; 23 kg/m\(^2\) ≤ BMI < 25 kg/m\(^2\) =2 points; and BMI \(\geq\) 25 kg/m\(^2\) = 3 points. They got 71.7% sensitivity and 75.9% specificity if 3 points was the cut-off value and if they used 4 points as a cut-off value they had 46.9% sensitivity and 92.3% specificity. Their PPV was 73.9%, and NPV was 78.8% in this case. They concluded that to strongly recommend abdominal ultrasonography scores from this index system should be \(\geq 4\) points\(^{12}\).

Forough Saki and et al. considered Plasma Retinol Binding Protein-4 (RBP4) as a useful, noninvasive predictive biomarker of intrahepatic lipid content in obese children before using radiological investigations\(^{16}\). Rui-Dan Zheng and et al. assume that waist-to-hip (WHR) is beneficial for the diagnosis of NAFLD. In that study WHR <0.9 for man and

| Table 1: Basic characteristics of NAFLED group and non-NAFLED group |
|-----------------------------|-----------------------------|-----------------------------|
|                             | NAFLED                     | Non-NAFLED                  | P_value     |
| Number                      | 238                        | 102                        |             |
| Age in year                 | 45.2 ± 11.7                | 46.5 ± 13.8                | 0.37        |
| Height in cm                | 166.7 ± 10.4               | 167.9 ± 9.7                | 0.32        |
| Weight in kg                | 76.4 ± 12.6                | 67.9 ± 12.7                | <0.0001     |
| BMI                         | 27.5 ± 4.2                 | 23.9 ± 3.5                 | <0.0001     |

| Table 2: Statistical diagnostic values of cherry angioma for NAFLD |
|----------------------------|-----------------------------|-----------------------------|-------------|-------------|
|                            | Sensitivity % | Specificity % | PPV % | NPV % | ACC % |
| Total                      | 76.9          | 80.4          | 95.8  | 37.5  | 77.4  |
| Age                        |               |               |      |       |       |
| \(\leq 40\)y               | 50.8          | 94.7          | 97.0  | 36.7  | 61.0  |
| >40y                       | 86.3          | 68.2          | 95.6  | 38.8  | 84.3  |
| BMI                        |               |               |      |       |       |
| <25                        | 75.0          | 78.3          | 91.0  | 51.4  | 75.8  |
| 25-30                      | 82.7          | 81.2          | 96.8  | 40.6  | 82.5  |
| Sex                        |               |               |      |       |       |
| Male                       | 67.0          | 76.5          | 93.0  | 33.3  | 68.8  |
| Female                     | 81.8          | 83.3          | 97.0  | 40.8  | 82.0  |
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<0.85 for women considered as 0 and WHR ≥0.9 for man ≥0.85 for woman as one. Cutoff value 0.89 had sensitivity 99% and specificity 66%17.

In another study researchers were able to confirm that BMI as a predictive factor for NAFLD onset in both men (with cutoff levels at 23) and women (with cutoff levels at 22.2 kg/m2)19. Kim CW and et al. proposed ferritin level in serum is an independent risk factor of fatty liver in normal weighted healthy Korean men diagnosed by sonography19.

Although all of the studies are beneficial for prediction of fatty liver, memorizing (recalling) of scores may be difficult, expensive tests are required and occasionally unavailability of tests causes these criteria impractical. Cherry angioma is a simple clinical symptom or sign with adequate sensitivity and specificity, low cost, ease of administration, is safe and available. The main limitation of our study was that we used abdominal ultrasonography as gold standard for diagnosis of NAFLD that is acceptable since validated ultrasonography have a sensitivity of 91.7% and a specificity of 100%20.

Contributions

Study concept and design: (JN, OB, BB), Acquisition of data: (JN, BB), Analysis and interpretation of data: (JN, OB, BB, MG, MA), Drafting of the manuscript: (JN, OB, BB), Critical revision of the manuscript for important intellectual content: (JN, OB, BB, MG, MA), Statistical analysis: (OB, BB), Administrative, technical, and material support: (JN, BB), Study supervision: (JN, OB).

References

